AIP | Chaos
An Interdisciplinary Journal of Nonlinear Science

Key role of time-delay and connection topology in shaping the dynamics of noisy genetic regulatory networks

X. L. Yang, D. V. Senthilkumar, Z. K. Sun, and J. Kurths

Citation: Chaos **21**, 047522 (2011); doi: 10.1063/1.3629984

View online: http://dx.doi.org/10.1063/1.3629984

View Table of Contents: http://chaos.aip.org/resource/1/CHAOEH/v21/i4

Published by the American Institute of Physics.

CHAOS **21**, 047522 (2011)

Key role of time-delay and connection topology in shaping the dynamics of noisy genetic regulatory networks

X. L. Yang,[1,2] D. V. Senthilkumar,[2] Z. K. Sun,[3] and J. Kurths[2,4]
[1]*College of Mathematics and Information Science, Shaanxi Normal University, Xián 710062, People's Republic of China*
[2]*Potsdam Institute for Climate Impact Research, 14473 Potsdam, Germany*
[3]*Department of Applied Mathematics, Northwestern Polytechnical University, Xián 710072, People's Republic of China*
[4]*Institute of Physics, Humboldt University, 12489 Berlin, Germany*

(Received 16 June 2011; accepted 1 August 2011; published online 29 December 2011)

This paper focuses on a paced genetic regulatory small-world network with time-delayed coupling. How the dynamical behaviors including temporal resonance and spatial synchronization evolve under the influence of time-delay and connection topology is explored through numerical simulations. We reveal the phenomenon of delay-induced resonance when the network topology is fixed. For a fixed time-delay, temporal resonance is shown to be degraded by increasing the rewiring probability of the network. On the other hand, for small rewiring probability, temporal resonance can be enhanced by an appropriately tuned small delay but degraded by a large delay, while conversely, temporal resonance is always reduced by time-delay for large rewiring probability. Finally, an optimal spatial synchrony is detected by a proper combination of time-delay and connection topology. © *2011 American Institute of Physics*. [doi:10.1063/1.3629984]

Complex networks have been used to model many self-organizing systems such as food webs, genetic control networks, neural networks, or social networks. Much work has been devoted to understanding the collective response emerged in complex networks. In the case that the elements constituting the network are subject to random forcing and periodic modulation, the most widely studied phenomena are stochastic/coherence resonance and spatial synchronization. Interactions among the individual oscillators are generally assumed to be instantaneous. However, the information from one unit reaches the others after a certain time-delay if taking into account the finite velocity of propagation of the interactions. Thus, some researchers have gradually shifted their attentions to the dynamics of a time-delayed network. Some interesting results such as delay-induced multiple resonance and delay-enhanced resonance have been discussed in delayed neural networks. There is an ongoing debate about the functional role played by time-delay. Here, we further participate in this issue by elaborating the profound effects of delayed-coupling on the temporal resonance and spatial synchrony in a paced genetic regulatory network with different small-world connection topologies. When the delay in the coupling is fixed, we find that temporal resonance is degraded by adding the randomness of network connectivity and we also detect an optimal spatial synchrony at certain connection topology. On the other hand, the phenomenon of delay-induced temporal resonance is uncovered when varying the time-delay. Moreover, for small rewiring probability, temporal resonance is enhanced by an appropriately tuned small time-delay, but it is depressed by a large time-delay, while conversely, temporal resonance is always reduced by the time-delay for large rewiring probability. Since noise and time-delay are important for the proper functioning of genetic network, our results may have implications, in particular, in understanding the complexity in genetic regulation.

I. INTRODUCTION

It is well known that noisy fluctuations can interact with the system nonlinearities to render counter-intuitive effects such as stochastic resonance or coherence resonance.[1,2] Thus, the properties of nonlinear systems under the influence of random noise have become a subject with relevance in diverse fields including biology, physics, and chemistry.[3,4] Stochastic resonance is one of the aspects which has received substantial attention after it emerged in the early 1980s.[5,6] Frank Moss was the first to demonstrate it in biological systems and human perception.[7–10] Seminal papers on stochastic resonance are related with analyzing the output of a stochastic overdamped particle in the presence of an external driving force and noise, revealing that an optimal amount of noise can enhance the response of the system to a weak periodic modulation in a resonant manner.[5,11–13] Following initial advances in understanding the mechanism of stochastic resonance in an individual dynamical oscillator, variations and extensions of the classical definition of stochastic resonance have also appeared in the literature, e. g., in connection with an array of regularly coupled elements and low-dimensional systems involving time-delay.[14–24]

In 1998, Watts and Strogatz proposed a small-world network of coupled oscillators.[25] This is a kind of complex network with small-world connection topology and it lies between two extremes of a completely regular lattice and a completely random graph. Since that time the collective dynamics over small-world network has been widely investigated and it has been found that such network is excellent for modeling many self-organizing systems ranging from biological oscillators, excitable media to social network.[26–29] Meanwhile, the scope of stochastic resonance in a regular diffusively coupled network has also been shifted towards complex networks with small-world properties. For instance, the striking effects induced by random shortcut links in an ensemble of bistable units are discussed,[30,31] from which one can find that temporal stochastic resonance and spatial synchronization are remarkably improved by increasing the random long-range connectivity. Later on, the profound effect of the randomness or disorder of the underlying network on the width of the stochastic resonance peak is revealed in an Ising-like system with small-world connection topology.[32] Recently, the emergence of stochastic resonance has been expanded to complex networks under the influence of subthreshold pacemaker activity.[32–37] Precisely, the external periodic driving, acting as a pacemaker to impose its rhythm on the whole network, is introduced only to a single unit of the network rather than to all oscillators of the network as usual. Pacemaker activity has showed its important role in real life systems.[33]

Time-delay is ubiquitous in nature and it often fundamentally changes the dynamical behavior of the systems. Thus, it is naturally to stimulate researchers to explore resonance properties of complex networks with time-delay. At present, some novel phenomena have been observed by numerically simulating networks. In particular, delay-induced multiple stochastic resonance was reported in paced scale free neural networks,[36,37] effects caused by random delay and topology structure on diversity-induced stochastic resonance were discussed in an array of bistable systems with Newman-Watts small-world connectivity,[38] and delay-enhanced temporal coherence and spatial synchrony were uncovered in a small-world network of noisy neuron oscillators.[39] Though some advance on delay-induced effects has already reported, the combined influence of noise, time-delay, and complex topology on the dynamics of the networks as well as the underlying mechanism is not yet fully understood.

In this work, we aim to investigate this issue by exploring the cooperative influences of time-delay and connection topology on temporal resonance and spatial synchronization in a delay-coupled genetic regulatory small-world network. For vanishing time-delay between interacting units, Perc has discussed resonance behaviors not only in the case that the potential of the constitute gene oscillator is symmetric, but also in the case of an asymmetric potential.[35] In fact, time-delay has considered to be one of the fundamental operating constraints in ideal genetic networks.[40] Recent work has already demonstrated the important role played by time-delay in gene networks, e.g., time-delay in gene networks could strongly affect stimulus responses, and it can generate oscillations and complex transients.[41,42] Thus, it has become increasingly evident that time-delay needs to be included to fully understand the dynamics of genetic network. In the following, the key role of time-delay and topology connection on the behavior of the gene network will be analyzed.

This paper is structured as follows. In Sec. II, the delayed genetic regulatory small-world network together with two measures is introduced. The main results are presented in Sec. III, followed by the conclusion in Sec. IV.

II. DYNAMICAL MODEL AND SETUP

In this paper, we consider a genetic regulatory model by Smolen *et al.*[41] which incorporates a signal activated transcription and positive feedback on the rate of the transcriptional activator x. Perc[35] studied the effects of asymmetric potential on stochastic resonance in this model in a network with small-world topology but without any delay. In particular, in this work, we consider time-delay coupling in a small-word network of noisy genetic regulatory oscillators and investigate the effects of this delay in the coupling on stochastic resonance and the synchronization properties of the network. The individual transcriptional activator, denoted by x_i, in the network is described by the following differential equation:

$$\frac{dx_i}{dt} = \frac{k_f x_i^2}{x_i^2 + K_d} - k_d x_i + R_{bas} + \sum_j \varepsilon_{ij}(x_j(t-\tau) - x_i) + \sqrt{2D}\xi_i(t), \tag{1}$$

where $i = 1, 2, \ldots, N$. Here, k_f is the saturation rate of x_i, K_d is the dissociation constant, and k_d and R_{bas} denote the degradation reaction rate and the synthesis reaction rate, respectively. ε_{ij} describes the coupling strength between the units. If the units i and j are connected, we set the coupling strength to a constant value of $\varepsilon_{ij} = \varepsilon_{ji} = \varepsilon$, otherwise $\varepsilon_{ij} = \varepsilon_{ji} = 0$. τ is the time-delay in the coupling, so that the state of each element influences that of the other elements only after a certain time. $2D$ is the variance of the Gaussian noise with zero mean and autocorrelation $\langle \xi_i(t)\xi_j(t')\rangle = \delta_{ij}\delta(t-t')$. We set $k_f = 5.6352$, $K_d = 10.0$, $k_d = 1.0$, $R_{bas} = 0.4$, and $\varepsilon = 0.4$ throughout this work unless otherwise stated. A subthreshold periodic pacemaker of the form $f\cos(\Omega t)$ with $f = 0.08$ and $\Omega = \pi/300$ is introduced to the arbitrary ith unit of the network.

We study such coupled genetic regulatory elements on a network with small-world topology. According to the procedure proposed by Watts and Strogatz,[25] the network is constructed as follows: starting from a one-dimensional regular lattice with $N = 300$ genetic regulatory units with periodic boundary condition and $k = 4$ nearest neighbors, and then rewiring each edge at random with a probability p. The final degree of randomness or disorder of the network is determined by the rewiring probability p. Two extreme cases are the completely regular and completely random network corresponding to $p = 0$ and $p = 1$, respectively. A complex network with small-world properties, i.e., a relative high clustering coefficient and small characteristic path length, corresponds to $0 < p < 1$.

We are here mainly interested in the impacts of time-delay, random noise, and the rewiring probability on the collective response of temporal resonance and spatial synchronization of system (Eq. (1)). To study these influences

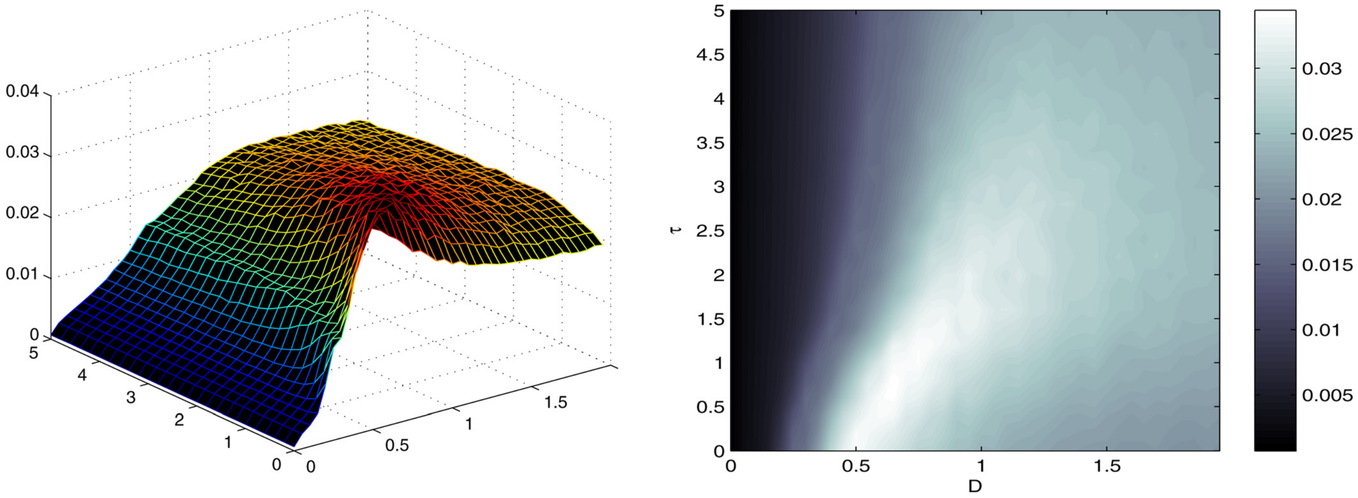

FIG. 1. (Color online) The whole network response S as a function of the time-delay τ and noise strength D (left panel) and its resulting contour (right panel).

vividly, we introduce two indexes. One is the response of the whole network obtained by averaging the Fourier coefficients over all units,[43] i.e.,

$$S = \frac{1}{N}\sum_{i=1}^{N} Q_i, \tag{2}$$

where $Q_i = \sqrt{R_i^2 + S_i^2}$, $R_i = \frac{2}{t_{max}}\int_0^{t_{max}} x_i \sin(\Omega t)dt$, $S_i = \frac{2}{t_{max}}\int_0^{t_{max}} x_i \cos(\Omega t)dt$. Note that the Fourier coefficients are proportional to the square of the spectral power amplification,[44] S is frequently used as a measure for stochastic resonance. If there is a maximum in the evolution of S, one can pronounce that this is a characteristic signature of stochastic resonance.

The other index is the mean square deviation,

$$\sigma = \frac{1}{t_{max}}\int_0^{t_{max}} \bar{\sigma} dt, \tag{3}$$

in which $\bar{\sigma} = \frac{1}{N}\sum_{i=1}^{N} x_i^2(t) - \left(\frac{1}{N}\sum_{i=1}^{N} x_i(t)\right)^2$. Clearly, σ can be used to quantitatively measure the synchronous property of the interacting elements and a smaller one means better spatial synchronization.

III. RESULTS

In this section, we discuss the combined effect of the time-delay, rewiring probability p, and the noise intensity on temporal resonance and synchronization properties of the network of bistable genetic regulatory units, Eq. (1).

A. The role of time-delay in temporal resonance

First, we describe how temporal resonance manifests itself in the small-world paced gene network under the combined influence of time-delay and random noise. Note that the final results presented in the following figures are obtained by averaging over 80 independent realizations for each set of parameter values to guarantee appropriate statistical accuracy with respect to small-world configurations and numerical calculations. To globally reveal the collective response of the whole network dependent on delay and noise, a three-dimensional plot of the whole network response S over noise intensity $0 \le D \le 2$ and time-delay $0 \le \tau \le 5$ is illustrated in Fig. 1(a), when the rewiring probability is fixed as $p = 0.04$, and its resulting contour plot is depicted in Fig. 1(b). We find that there is a peak in S, i.e., a maximum in S, for an appropriate noise value. Once upon increasing the delay, the peak first decreases, then increases, and reaches a maximum, after which it gradually lowers and broadens on the whole. At the same time, the peak shifts to slightly higher values of noise as the time-delay increases. This can be further confirmed by the characteristic curves shown in Fig. 2.

Figure 2(a) demonstrates the evolution of S as a function of time-delay for various noise intensities. We can easily note that for small D, S decreases rapidly at the first increase of delay, then reaches almost a horizontal level with a further increase of the delay, implying that in this case a large time-delay has no profound influence on S. For intermediate D, S first increases and later decreases with delay, showing a peak at a proper amount of time-delay, which we call *delay-induced stochastic resonance*. While for large D, the peak broadens and lowers during the course of time-delay.

Figure 2(b) features the resonance curves in the dependence on D in case of different time-delay. The results presented in this figure evidence that S first increases with the addition of noise level, reaches a maximum, and then decreases again. This is a characteristic signature of classical stochastic resonance. Moreover, the maximum of S first decreases a bit and then increases for small time-delay, after a critical value of τ, it decreases again with increasing delay. Meanwhile, upon increasing delay, the position of the peak moves to a larger value of D. To give a better quantitative view of the above findings, variations of the peak of S (denoted by S_{max}) and the optimal value of noise intensity (denoted by D_{opt}) are plotted in Figs. 3(a) and 3(b), respectively. Clearly, S_{max} first decreases at the beginning of time-delay, then increases, and reaches a maximum value, after which it decreases instead with a further increase in time-delay, and simultaneously, D_{opt} increases basically as τ

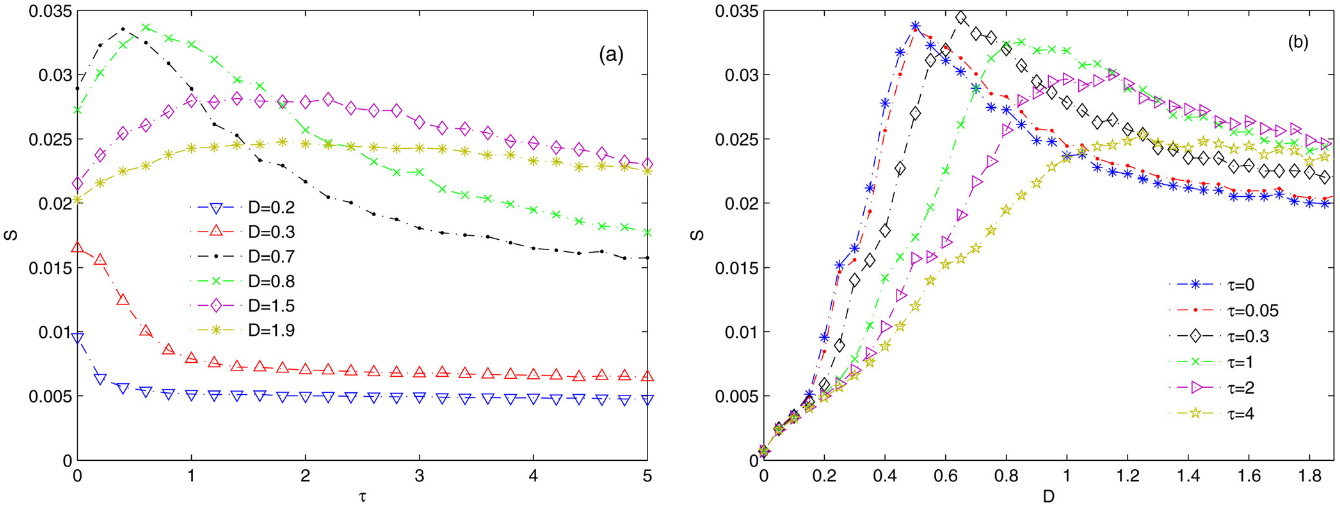

FIG. 2. (Color online) S as a function of time-delay for various noise intensities (left panel); S as a function of the noise intensity for different time-delays (right panel).

increases. The variations of S_{max} indicate that either weak or strong time-delay can remarkably suppress temporal resonance with respect to that without time-delay, while an intermediate delay can significantly enhance stochastic resonance. Thus, we can conclude that the introduction of a delay in the coupling can be used as a method to control temporal resonance in the paced gene network.

The underlying mechanism for the significant effects induced by the time-delay can be interpreted from an intuitive picture of stochastic resonance. Imaging that a classical particle subject to an external periodic signal and noise moves in a symmetric double-well potential, as implied in the seminal works,[45,46] it manifests stochastic resonance by a synchronization of noise-activated hopping events between the potential minima under a weak periodic driving. In fact, this stochastic synchronization takes place when the timescale associated with the transition rate of the particle equals approximately half of the external signal period. On the other hand, Tsimring and Pikovsky[20] have reported that the transition rate can be dependent on earlier states of oscillators when introducing a time-delay in the involved oscillator. Hence, we can infer that time-delay plays a crucial role in noise-induced inter-well transitions. Thus, for a given period of the external forcing, the time-matching condition for the occurrence of stochastic resonance can be fulfilled not only by tuning the noise level, but also by the value of the time-delay or other system parameters. So, it is reasonable for our above findings that under certain conditions time-delay can induce stochastic resonance, as well as enhance and depress stochastic resonance.

B. The role of connection topology in temporal resonance

The connection topology of the underlying network may also has drastic effects on the network's response. Thus, it is natural to explore whether the above delay-enhanced or depressed resonance would appear when the rewiring probability of the network is changed. Now, we elaborate it by analyzing the correlation of the peak of the whole network

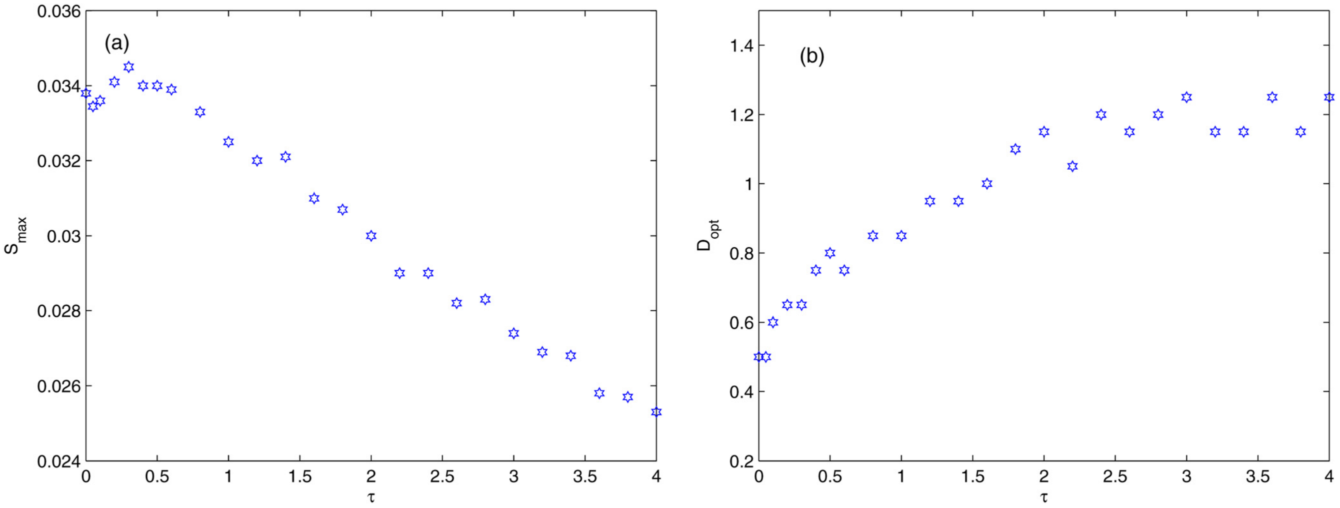

FIG. 3. (Color online) The peak of $S(S_{max})$ and the optimal noise intensity (D_{opt}) versus time-delay.

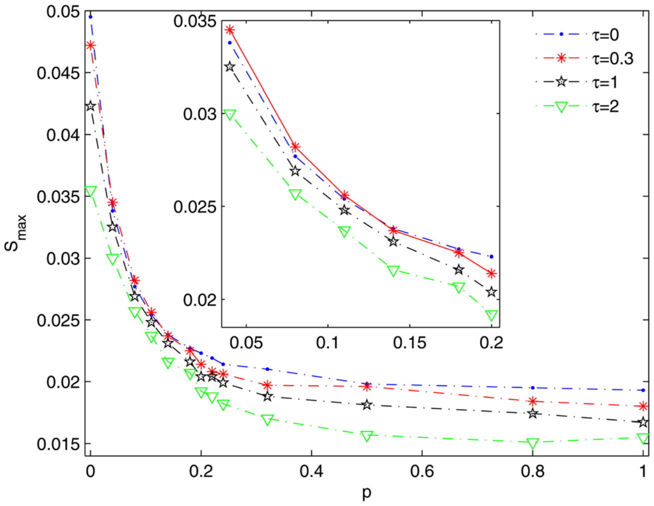

FIG. 4. (Color online) S_{max} in dependence on the rewiring probability p for different time-delays.

response S with the network connectivity. Figure 4 gives the evolution of the peak of S in dependence on the rewiring probability p for different time-delays. From this figure, one can detect two distinctive aspects as p increases: For small p, especially when p lies in the interval $p \in (0.04, 0.11)$, an appropriate amount of small time-delay, for example, $\tau = 0.3$, raises the value of S_{max}, while a proper amount of large time-delay, for example, $\tau = 2.0$, lowers the value of S_{max}. The vivid variation of S_{max} imposed by p and τ is further described in the inset of Fig. 4. This result implies that time-delay not only can enhance but also can depress temporal resonance when the gene network has a suitable small-world connection topology. However, for large p, S_{max} is reduced by the presence of time-delay, moreover, the larger the delay, the smaller S_{max}. That is to say, a large rewiring probability together with a large delay has an unfavorable role on the resonance dynamics.

On the other hand, we note that S_{max} decreases on the whole with the increase of p. Upon increasing the rewiring probability, more edges are rewired and thus additional short-cut links are introduced, which in return makes the pacemaker impact spread to more distant units of the network. Then the Fourier coefficients Q_i for the units that are within an immediate proximity to the pacemaker are decreased, and the values of Q_i for some oscillators relatively far from the location of the pacemaker are increased. If the increase in Q_i cannot compensate for the simultaneous decrease in Q_i, the maximum of S is decreased. So, the decrease in the peak of S is reasonable. In particular, through a clear inspection of the inset in Fig. 4, in the absence of time-delay, we can detect a local maximum around $p = 0.22$ in the evolution of S_{max}. As expounded in Ref. 35, the ratio $R = C/L$ between the normalized clustering coefficient C and the normalized characteristic path length L is selected as a suitable quantity to assess the optimal property of a small-world network to facilitate the spreading of a localized pacemaker-emitted subthreshold rhythm. The higher the value of this ratio, the better the network structure is adapted to transmit the pacemaker's activity to units far from the pacemaker. For our gene network, the maximal value of R is roughly obtained at $p = 0.209$,[47,48] Thus, there is a local maximum in S_{max} around $p = 0.22$. The network with this detected small-world network topology can warrant the best outreach of the pacemaker to units that are not in its immediate proximity. When a delay is present in the coupling of interacting elements, S_{max} shows a decreasing tendency during the course of p, and a small peak of S_{max} disappears.

C. Spatial synchronous dynamics in the gene network

Finally, we focus on the joint influences of noise, time-delay, and topology on the synchronization dynamics of the network. The degree of spatial synchronization is measured by the mean square deviation σ, Eq. (3). First, the dependence of σ on τ is plotted in Fig. 5(a), when the topology of the network is generated for $p = 0.04$. From this figure, it is seen that for a fixed noise level, σ decreases monotonically as τ increases; at the same time, the $\sigma \sim \tau$ curve gets higher and higher as the noise level D increases. That is to say, the larger the time-delay, the better the spatial synchronization,

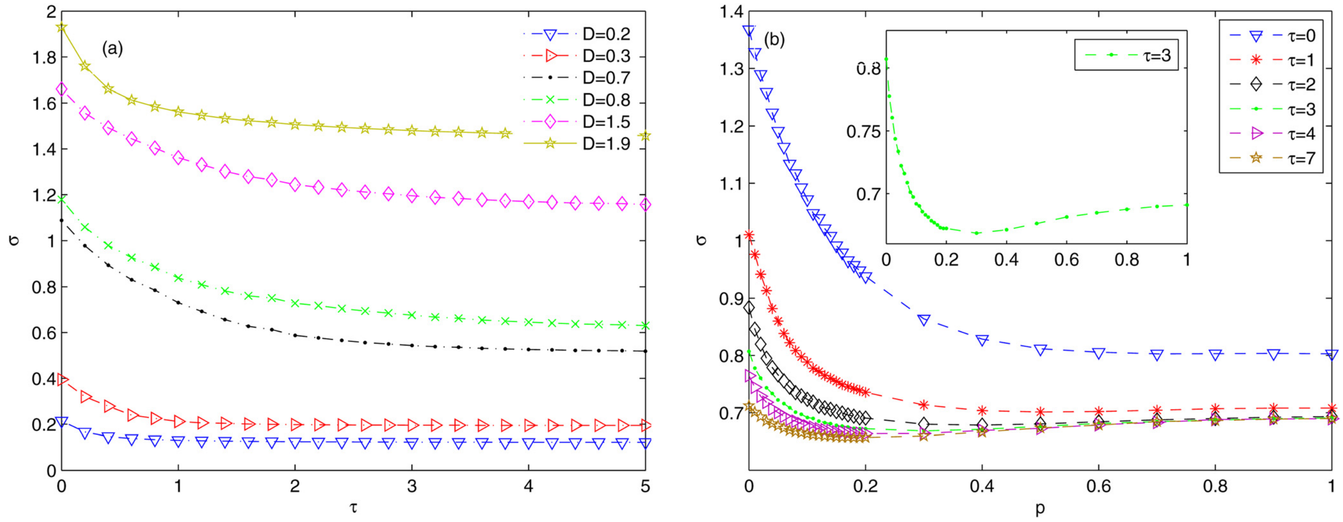

FIG. 5. (Color online) σ in dependence on τ for various D (left panel); σ in dependence on p for various τ (right panel).

and the larger the noise intensity, the less the spatial synchronization. In the following, we will explore how the combination of connection topology and time-delay affects the synchronous property when the noise level is fixed. Figure 5(b) depicts σ in dependence on p for various time-delay in the case of $D = 0.85$, from which we can see that σ decreases rapidly at the first increase of p. Nevertheless, because the elements in the gene network are not identical, σ cannot get zero during the course of p. We also note that the $\sigma \sim p$ curve gets lower and lower as the delay increases. More interestingly, at a closer inspection of Fig. 5 (especially in the inset of Fig. 5(b)), we observe an asymmetric valley in each $\sigma \sim p$ curve. That is to say, with the assistance of time-delay there exits an optimal topology connectivity warranting the units in the network to achieve the best spatial synchrony. Moreover, the optimal p moves to larger values as the delay increases.

IV. CONCLUSION

This paper generalizes the paced small-world network of coupled genetic regulatory oscillators[35] to allow time-delayed interactions. We focus on the collective dynamics of temporal resonance and spatial synchrony over this network. The most important parameters in our analysis are noise intensity, time-delay, and rewiring probability. By introducing two suitable measures in Sec. II, the crucial influences of these parameters on the spatial dynamics can be described as follows: First, for fixed network topology, the whole network response S passes through a maximum with varying noise intensity irrespective of time-delay, which shows a characteristic signature of classical stochastic resonance in the network. Similarly, at certain noise strength, there also exhibits a peak in the evolution of S as the time-delay increases; we call this phenomenon *delay-induced temporal resonance*. Second, for fixed time-delay, the peak of S shows a decreased tendency as the rewiring probability increases, which implies that temporal resonance is degraded by the randomness of the network. On the other hand, temporal resonance is enhanced by an appropriately tuned small delay but depressed by a large time-delay for small rewiring probability, while temporal resonance is always reduced by time-delay for large rewiring probability. Third, we find that time-delay as well as the randomness of the network can dramatically enhance the spatial synchrony of the noisy network. Moreover, with the assistance of time-delay there exits an optimal connection topology warranting the units in the network to achieve the best spatial synchrony.

Since noise and time-delays are important factors in the genetic network function, our results may have implications, in particular, in understanding the complexity in genetic regulation.

ACKNOWLEDGMENTS

This work is partially supported by the National Natural Science Foundation of China (Grant Nos. 10902062, 10871123, 10902085, and 11026131), the NSF of Shaanxi Province (Grant Nos. 2009JQ1002 and 2009JQ1007). D.V.S. and J.K. acknowledge the support from EU under Project No. 240763 PHOCUS(FP7-ICT-2009-C).

[1] F. Sagus, J. M. Sancho, and J. Garca-Ojalvo, Rev. Mod. Phys. **79**, 829 (2007).
[2] A. S. Pikovsky and J. Kurths, Phys. Rev. Lett. **78**, 775 (1997).
[3] X. L. Yang and Z. K. Sun, Int. J. Non-Linear Mech. **45**, 621 (2010).
[4] J. Dunkel, W. Ebeling, L. Schimansky-Geier, and P. Hanggi, Phys. Rev. E **67**, 061118 (2003).
[5] L. Gammaitoni, P. Hanggi, P. Jung, and F. Marchesoni, Rev. Mod. Phys. **70**, 223 (1998).
[6] T. Wellens, V. Shatokhin, and A. Buchleitner, Rep. Prog. Phys. **67**, 45 (2004).
[7] J. K. Douglass, L. A. Wilkens, E. Pantazelou, and F. Moss, Nature **365**, 337 (1993).
[8] K. Wiesenfeld and F. Moss, Nature **373**, 33 (1995).
[9] D. F. Russell, L. A. Wilkens, and F. Moss, Nature **402**, 291 (1999).
[10] E. Simonotto1, M. Riani, C. Seife, M. Roberts, J. Twitty, and F. Moss, Phys. Rev. Lett. **78**, 1186 (1997).
[11] R. Benzi, A. Sutera, and A. Vulpiani, J. Phys. A **14**, L453 (1981).
[12] P. Jung and P. Hanggi, Phys. Rev. A **44**, 8032 (1991).
[13] V. S. Anishchenko, A. B. Neiman, F. Moss, and L. Schimansky-Geier, Phys. Usp. **42**, 7 (1999).
[14] P. Jung, U. Behn, E. Pantazelou, and F. Moss, Phys. Rev. A **46**, R1709 (1992).
[15] A. R. Bulsara and G. Schmera, Phys. Rev. E **47**, 3734 (1993).
[16] H. S. Wio, Phys. Rev. E **54**, R3075 (1995).
[17] H. Gang, H. Haken, and X. Fagen, Phys. Rev. Lett. **77**, 1925 (1996).
[18] T. Ohira and Y. Sato, Phys. Rev. Lett. **82**, 2811(1999).
[19] C. H. Zeng and C. W. Xie, Chin. Phys. Lett. **25**, 1587 (2008).
[20] L. S. Tsimring and A. Pikovsky, Phys. Rev. Lett. **87**, 250602 (2001).
[21] J. Houlihan, D. Goulding, T. Busch, C. Masoller, and G. Huyet, Phys. Rev. Lett. **92**, 050601 (2004).
[22] N. B. Janson, A. G. Balanov, and E. Scholl, Phys. Rev. Lett. **93**, 010601 (2004).
[23] S. Kim, S. H. Park, and H. B. Pyo, Phys. Rev. Lett. **82**, 1620 (1999).
[24] T. Ohira, Physica A **314**, 146 (2002).
[25] D. J. Watts and S. H. Strogatz, Nature **393**, 440 (1998).
[26] K. McCann, A. Hastings, and G. R. Huxel, Nature **395**, 794 (1998).
[27] B. A. Huberman and L. A. Adamic, Nature **401**, 131 (1999).
[28] S. Wasserman and K. Faust, *Social Network Analysis* (Cambridge University Press, Cambridge, 1994).
[29] P. K. Swain and A. Longtin, Chaos **16**, 026101 (2006).
[30] Z. Gao, B. Hu, and G. Hu, Phys. Rev. E **65**, 016209 (2001).
[31] X. J. Sun, M. Perc, Q. S. Lu, and J. Kurths, Chaos **18**, 023102 (2008).
[32] M. Kuperman and D. Zanette, Eur. Phys. J. B **26**, 387 (2002).
[33] M. Perc, Phys. Rev. E **76**, 066203 (2007).
[34] M. Perc and M. Gosak, New J. Phys. **10**, 053008 (2008).
[35] M. Perc, Eur. Phys. J. B **69**, 147 (2009).
[36] Q. Y. Wang, M. Perc, Z. S. Duan, and G. R. Chen, Chaos **19**, 023112 (2009).
[37] C. B. Gan, M. Perc, and Q. Y. Wang, Chin. Phys. B **19**, 040508 (2010).
[38] D. Wu, S. Q. Zhu, and X. Q. Luo, Europhys. Lett. **86**, 50002 (2009).
[39] H. Wu, Z. H. Hou, and H. W. Xin, Chaos **20**, 043140 (2010).
[40] M. Kerszberg, Curr. Opin. Genet. Dev. **14**, 440 (2004).
[41] P. Smolen, D. A. Baxter, and J. H. Byrne, Am. J. Physiol.: Cell Physiol. **274**, 531 (1998), http://ajpcell.physiology.org/content/274/2/C531.full.pdf+html.
[42] S. Paul, D. A. Baxter, and J. H. Byrne, Neuron **26**, 567 (2000).
[43] W. H. Press, S. A. Teukolsky, W. T. Vetterling, and B. P. Flannery, *Numerical Recipes in C* (Cambridge University Press, Cambridge, 1995).
[44] L. Holden and T. Erneux, SIAM J. Appl. Math. **53**, 1045 (1993).
[45] L. Gammaitoni, E. Menichella-Saetta, S. Santucci, and F. Marchesoni, Phys. Lett. A **142**, 59 (1989).
[46] L. Gammaitoni, E. Menichella-Saetta, S. Santucci, F. Marchesoni, and C. Presilla, Phys. Rev. A **40**, 2114 (1989).
[47] M. E. J. Newman and D. J. Watts, Phys. Lett. A **263**, 341 (1999).
[48] A. Barrat and M. Weight, Eur. Phys. J. B **13**, 547 (2000).