# Synchronization of bursting neurons with delayed chemical synapses

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The synchronization of bursting Hindmarsh-Rose neurons coupled by a time-delayed fast threshold modulation synapse was studied. It is shown that there is a domain of the coupling parameter and nonzero time-lag values such that the bursting neurons are exactly synchronized. Furthermore, and contrary to the case of electrical synapses, such synchronous bursting is stochastically stable.

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## I. INTRODUCTION

Synchronized neuronal activity has been observed at all levels of the nervous system and has been suggested as particularly important in information processing [1–3]. The most common type of neuronal dynamics and synaptic connections is that of bursting and relatively complicated chemically mediated synapses. It is well known that the properties of synchronization between electrically and chemically coupled bursting neurons are quite different [4]. In this paper we shall analyze the synchronization of bursting neurons coupled by chemical synapses under realistic conditions that include synaptic time delays and noise. In particular, we shall stress the important differences that occur between the effects of time delay in the synaptic connections on the synchronization of electrically versus chemically coupled bursting neurons.

There are two different broad types of single-neuron oscillatory dynamics [5]: (a) Bursting is a neuronal activity such that a neuron fires two or more spikes followed by a period of quiescence, which is again followed by similar periods of spiking and quiescence; (b) spiking is the dynamical regime when a sequence of spikes continues, more or less regularly, for a relatively large period of time uninterrupted by periods of quiescence. It is believed that a burst of spikes is more reliable than a single spike in producing responses in postsynaptic neurons. However, synchronization between bursting neurons has been much less studied than the synchronization between simple or chaotic oscillators.

Two general types of synaptic connection between neurons called electrical (or gap junction) and chemical are clearly distinguished. The chemical synapses are much more common, and the synaptic transmission time is especially significant for synapses of the chemical type, as opposed to electrical synapses. It is well known that the explicit time lag in modeling of a synaptic connection of physically reasonable duration can have profound effects on the dynamics of coupled neurons [6–8] (see also [9] and the references therein). For example, an important effect that has been recently demonstrated [10,11] is that the time delay facilitates exact synchronization among bursting electrically coupled neurons. On the other hand, mathematical models of oscillatory neurons coupled by instantaneous chemical synapses are much more difficult to synchronize than those with instantaneous electrical synapses. We shall see that sufficient time delay in a specific model of the chemical synapse leads to synchronization of bursting dynamics that is stochastically stable under perturbation by small noise, in contrast to the case of the same bursting neurons synchronized by delayed electrical coupling [12].

The paper is organized as follows. In the next section we present the model of two bursting neurons coupled by a chemical synapse with an explicit time lag that we shall analyze. Each of the neurons is modeled by the Hindmarsh-Rose equations, and for the chemical synapse we use the so-called fast threshold modulation (FTM) model with explicit time lag. In Sec. III we derive delay-differential equations for small deviations from the manifold of the exact synchronization that we used to study the stability of the synchronization. The equations are analogous to those derived in [10] for Hindmarsh-Rose neurons coupled by delayed electrical synapses. The results of our analysis of the effects of the synaptic time delay on the bursting dynamics and synchronization are presented in Sec. IV. There we also discuss the effects of small white noise on the stability of the time-delay-induced synchronous dynamics. The paper is summarized in Sec. V.

## II. THE MODEL

An elementary current-based model of bursting behavior in real neurons requires three variables and is of the form of the Hindmarsh-Rose (HR) equations [13,6], given by

$$\dot{x} = y + bx^2 - ax^3 - z + I,$$

$$\dot{y} = c - dx^2 - y,$$

$$\dot{z} = -rz + rS(x - x_0), \tag{1}$$

where $x$ is the membrane potential, $y$ represents the fast current, like that of $Na^+$ or $K^+$, and $z$ corresponds to the slow current, for example, a current of $Ca^+$. Slow oscillations of the $z$ variable drive the fast subsystem $(x, y)$ through periods of oscillatory and quiescent behavior. The constant parameter $I$ in the model (1) represents the external current and is the

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bifurcation parameter, determining its qualitative behavior. When $I=0$ there can be only one stable stationary solution of (1) and it corresponds to the stable quiescence behavior of the neuron. However, for constant $I$ in the domain $I \in (2.92, 3.40)$, and for commonly used values of the other parameters $S=4.0$, $r=0.006$, $x_0=-1.6$, $a=1$, $b=3$, $c=1$, and $d=5$, the model (1) describes chaotic bursting, i.e., a series of spikes that are chaotically interspersed with refractory periods and quiescence behavior [14]. In our analysis, the parameter values for each neuron are fixed precisely to such values $I=3.2$ that imply chaotic bursting of the isolated units.

In order to model the coupling among neurons by a chemical synapse, we shall use the so-called fast threshold modulation scheme proposed by Somers and Kopell in 1993 [15] and often used by others, e.g., [4]. The form of the FTM coupling that we shall use, which explicitly incorporates the synaptic time lag, is given by the following function:

$$f(x_1,x_2^\tau) = -g(x_1 - V_s)\frac{1}{1+\exp[-k(x_2^\tau - \theta_s)]}. \tag{2}$$

The variable parameter $g$ is the coupling strength between the first neuron at time $t$ and its neighbor at some previous time $t-\tau$. Thus, $x_2^\tau \equiv x_2(t-\tau)$. The coupling model (2) when $\tau=0$ is called fast, because it does not incorporate any real synaptic dynamics. The model exhibits either a hard or a more gradual thresholdlike behavior, depending on the size of the parameter $k$, with $k\to\infty$ corresponding to the hard threshold. The type of coupling is characterized by the sign of the difference between the synaptic reversal potential, denoted $V_s$, and the synaptic potential $x$. A positive or negative sign of the difference corresponds to an excitatory or inhibitory effect of the synapse. In this paper the values of the parameters $\theta_s$, $V_s$, and $k$ will be held fixed as $\theta_s=-0.25$, $V_s=2$, and $k=10$.

Our aim in this paper is to analyze the possibility and stability of the synchronized dynamics of a pair of delayed coupled chaotically bursting HR neurons, given by the following delay-differential equations (DDE's):

$$\begin{aligned}
\dot{x}_1 &= y_1 + 3x_1^2 - x_1^3 - z_1 + I + f(x_1,x_2^\tau),\\
\dot{y}_1 &= 1 - 5x_1^2 - y_1,\\
\dot{z}_1 &= -rz_1 + rS(x_1+1.6),\\
\dot{x}_2 &= y_2 + 3x_2^2 - x_2^3 - z_2 + I + f(x_2,x_1^\tau),\\
\dot{y}_2 &= 1 - 5x_2^2 - y_2,\\
\dot{z}_2 &= -rz_2 + rS(x_2+1.6).
\end{aligned} \tag{3}$$

The time delay plays a crucial role in the dynamics of the coupled system (3). For example, similarly to the case of electrically time-delayed coupled bursters [7] or relaxation oscillators [3,9], the time lag in a certain domain leads to stabilization of the quiescent behavior, i.e., to the phenomenon of oscillation death. Furthermore, it has been shown that the time delay facilitates exact synchronization among bursting electrically coupled neurons [10]. However, such time-delay-induced synchronization with electrical coupling is unstable under arbitrary small white noise [12].

The main result of our analysis of synchronization in the standard HR model of bursting is that, similarly to the electrical coupling, the time delay in FTM coupling facilitates exact synchronization, and, in contrast to the electrical coupling, such synchronous bursting is stochastically stable. In fact, we have found several combinations of the parameter values in model (3) such that the bursting dynamics of a pair of instantaneously FTM-coupled HR neurons in the form (3) with $\tau=0$ cannot be bursting and exactly synchronous for any value of the coupling strength, but an appropriate time delay in the FTM coupling, and the same values of the parameters, lead to exactly synchronous bursting. This is not in contradiction with the results presented in [4]. There, the authors used a model of bursting dynamics similar to but different from (1), and proved, using the standard Lyapunov function, that sufficiently strong instantaneous FTM coupling can lead to stability of exact synchronization. However, nothing can be claimed about the nature of the exactly synchronous solution established using the Lyapunov function. It could be stationary or oscillatory or bursting, depending on the parameter values. Nevertheless, the authors give an example of parameter values for their model such that sufficiently strong instantaneous coupling implies exactly synchronous bursting. However, we were not able to find a single combination of the parameter values such that the standard form of the HR bursters (1), instantaneously FTM coupled [as in Eq. (3)], leads to exactly synchronous bursting dynamics. As we pointed out, for all combinations of the parameters in the model (3) with $\tau=0$ that we have analyzed numerically for parameter values corresponding to chaotically bursting HR neurons, the stable synchronous solution achieved with sufficiently strong instantaneous coupling is in fact a stationary point. As we shall see, the time delay changes the situation.

## III. LINEAR STABILITY ANALYSIS OF SYNCHRONIZATION

In the system of coupled bursting neurons (3), one can think of different degrees of synchronization. For example, a type of weak synchronization is achieved when the bursts in the two units occur roughly at the same time without synchronization of spikes within the bursts. The strongest type of synchronous dynamics is exact synchronization. The two neurons in Eqs. (3) are exactly synchronous if the following conditions are satisfied for all $t$:

$$\delta x = x_1 - x_2 = 0, \quad \delta y = y_1 - y_2 = 0, \quad \delta z = z_1 - z_2 = 0. \tag{4}$$

In order to study the stability of the exact synchronization of the system (3) we have employed the method of numerical calculation of the Lyapunov exponent near the stationary solution of the equations that describe the dynamics of small deviations from the manifold of exact synchronization [10].

On the synchronization manifold (4) the dynamical equation are

$$\dot{x} = -x^3 + 3x^2 + y - z + I + f(x,x^\tau),$$

$$\dot{y} = 1 - 5x^2 - y,$$

$$\dot{z} = -rz + rS(x + 1.6),$$

$$x = x_1 = x_2, \quad y = y_1 = y_2, \quad z = z_1 = z_2. \tag{5}$$

The motion transverse to the synchronization manifold can be described in terms of infinitesimally small variations $\delta x \sim o(x)$, $\delta y \sim o(y)$, $\delta z \sim o(z)$ by the equations

$$\dot{\delta x} = -3x^2\delta x + 6x\delta x + \delta y - \delta z + g\left((x - V_s)\frac{k\exp[-k(x^\tau - \theta_s)]}{(1+\exp[-k(x^\tau - \theta_s])^2}\delta x^\tau - \frac{\delta x}{1+\exp[-k(x^\tau - \theta_s)]}\right),$$

$$\dot{\delta y} = -10x\delta x - \delta y,$$

$$\dot{\delta z} = rs\delta x - r\delta z, \tag{6}$$

where we have used $x_1^2 - x_2^2 \sim 2x\delta x$, $x_1^3 - x_2^3 = 3x^2\delta x$, and

$$f(x_1,x_2^\tau) - f(x_2,x_1^\tau) \sim -g\left(\frac{1}{1+\exp[-kx^\tau + k\theta_s]}\delta x - (x - V_s)\frac{k\exp[-kx^\tau + k\theta_s]}{[1+\exp(-kx^\tau + k\theta_s)]^2}\delta x^\tau\right).$$

Equations (6) can be treated as a nonautonomous system of DDE's for the dynamics of small variations $\delta x, \delta y, \delta z$ where the time dependences of $x, y, z$ are determined by Eq. (4). Stability of the stationary solution $(\delta x, \delta y, \delta z) = (0,0,0)$ corresponds to the stability of the synchronous dynamics of (3). The synchronization manifold is stable or unstable depending on whether the solutions of (6) $[\delta x(t), \delta y(t), \delta z(t)]$ shrink to zero or grow asymptotically as $t \to \infty$. A sufficient condition for the stability is that the largest Lyapunov exponent associated with (6) is negative. The largest Lyapunov exponent of (6), which can be obtained by numerical solutions of the joint equations (6) and (5), thus provides information about the local stability of the synchronization manifold.

## IV. DOMAINS AND STABILITY OF SYNCHRONIZED BURSTING

We have studied the conditions for synchronization on parameters $g$ and $\tau$ by numerical solutions of Eqs. (3), (5), and (6). The results of these calculations are presented in this section, and enable us to form a clear picture of possible qualitatively different dynamical regimes of the system of bursters coupled by delayed FTM coupling. We have restricted our attention to the domain of initial states near the stationary solution of the system (3), and the main questions that we wanted to answer are (a) what are the values of $g$ and $\tau$ for which the stationary solution is unstable and the initial states close to the stationary solution lead to bursting dynamics; (b) for which values of $g$ and $\tau$ is such bursting dynamics exactly synchronous; and (c) is such exactly synchronous dynamics qualitatively perturbed by small noise.

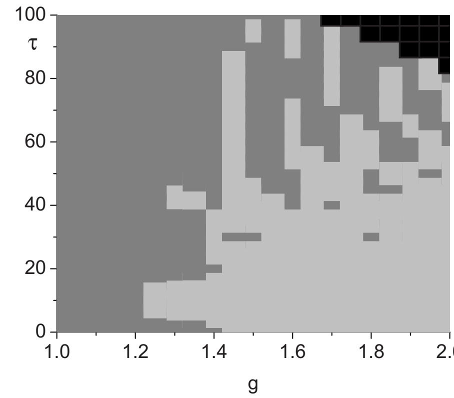


FIG. 1. Domains in $(g,\tau)$ parameter plane that imply stability of stationary state (light gray), instability of the stationary state with asynchronous bursting (gray), and instability of the stationary state with synchronous bursting (black).

The computations of the largest Lyapunov exponent near the stationary solution for the DDE system (3) and for the motion transverse to the synchronization manifold (5) are used to determine the domain of $(g,\tau)$ parameters that imply stability or instability of the stationary solution and of the synchronization manifold, respectively. These computations are also compared with direct observations of numerical solutions of Eq. (3). The computations show that there is a domain (black in Fig. 1) such that the stationary solution is unstable but the synchronization manifold is stable. The stable dynamics of the neurons for $(g,\tau)$ in that domain is exactly synchronized bursting.

Qualitatively different types of dynamics are illustrated in Figs. 2 and 3. The values of the fixed parameters are such that the stationary solution of the uncoupled units is unstable and the units display bursting behavior. For $\tau=0$ or small and for the values of the positive parameter $g$ up to $g \approx 1.4$, the bursting of the two units shows a weak type of synchrony. The bursts occur at the same time in each of the two units but the spikes within the bursts are not synchronized. This is illustrated in Figs. 2(a) and 2(b). Larger time delay, for $g$ in the same interval, desynchronizes the occurrence of the bursts. There are also domains of nonzero time lag such that the stationary state is stabilized by the time delay. In this case, the system is bistable, with a small stability domain of initial conditions near the stationary solution, and the other initial conditions leading to nonsynchronous bursting. So the bursting dynamics for $g < 1.4$ cannot be synchronized by any time lag. Instantaneous ($\tau=0$) coupling stronger then $g \approx 1.4$ stabilizes the stationary solution, so that after an initial period of bursting the system collapses onto the stationary state. This is illustrated in Figs. 2(c) and 2(e). However, such a stable stationary solution bifurcates for some nonzero time lag and becomes unstable, as is illustrated in Figs. 2(d) and 2(f). A different stable solution supporting the bursting dynamics appears. This time-delay-induced bursting can be

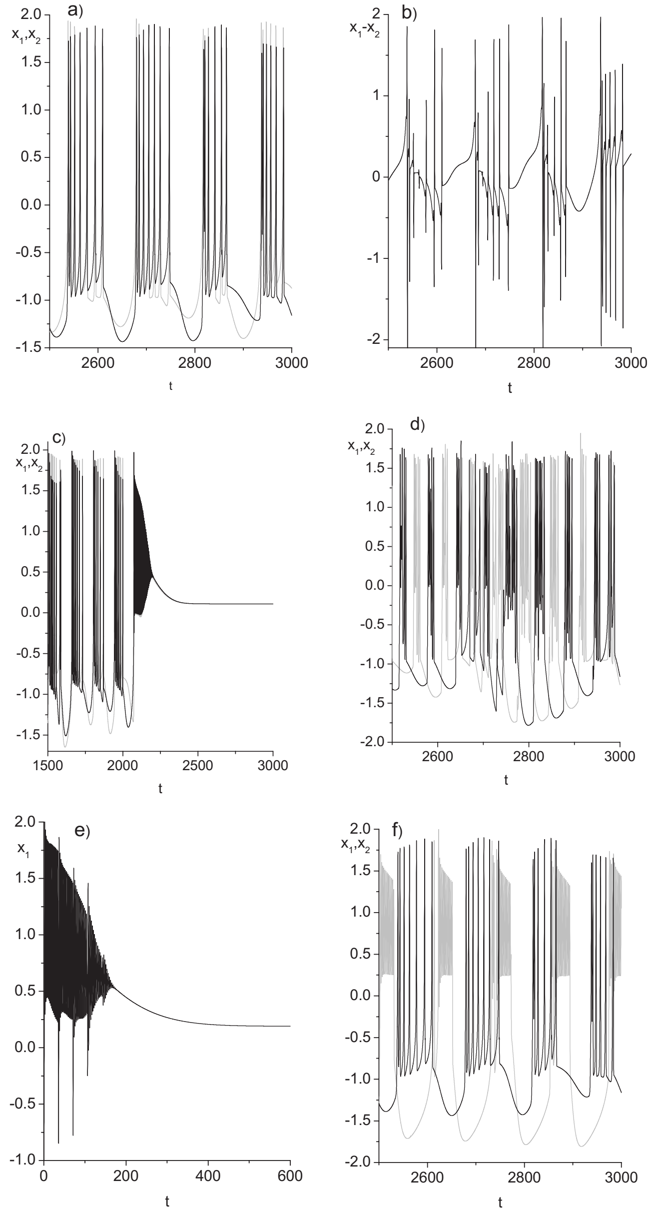


FIG. 2. Dynamics for $(g,\tau)$ parameters in Fig. 1, corresponding to stable stationary state (c), (e) and asynchronous bursting (a), (b), (d), (f). Values of $(g,\tau)$, and the plotted curves are (a) (1,0) $x_1$ (black), $x_2$ (light gray); (b) (1,0), $x_1 - x_2$; (c) (1.45,0) $x_1$ (black), $x_2$ (light gray); (d) (1.45,30) $x_1$ (black), $x_2$ (light gray); (e) (1.7,35), $x_1$ (black), $x_2$ (light gray); (e) (1.7,60), $x_1$ (black), $x_2$ (light gray).

completely asynchronous, but there is also a domain of sufficiently large values of $g$ and the corresponding $\tau$ such that the bursting is exactly synchronized. The asynchronous time-delay-induced bursting is illustrated in Figs. 2(d) and 2(f). The exact synchronization that occurs with increasing time lag and for fixed $g$ is illustrated in Fig. 3.

As pointed out, the $(g,\tau)$ parameter domain that implies stability of the synchronization is also the parameter domain where the trivial stationary solution of Eqs. (6) is stable. In this sense, the stabilization of synchronization by increasing the time lag (for fixed sufficiently large $g$) corresponds to a bifurcation of the trivial stationary solution of (6). Numerical evidence indicates that there is (a very small) interval of the values of the bifurcation parameter $\tau$ just below the critical value where the long-term dynamics generated by (6) is that of periodic oscillations with a very small amplitude around the unstable stationary state $(\delta x, \delta y, \delta z) = (0,0,0)$. Increase of $\tau$ leads to the death of oscillations in Eqs. (6), i.e., to the stability of synchronous dynamics. On the other hand, decrease of $\tau$ implies large oscillations in the system (6), and strongly asynchronous dynamics of (3). The existence of a small stable limit cycle for parameter values near the bifurcation is typical of the Hopf bifurcation of a stationary solution.

It is important to investigate if the exactly synchronous dynamics achieved with sufficiently large $g$ and $\tau$ is stable under perturbations by random noise. To this end we have studied numerically the system (3) with an additional random term in the form of an independent white noise with increment $dW$ added to the membrane equations for each of the neurons. Thus the equations for the $x$ variable in (3) are perturbed into

$$dx_1 = [y_1 + 3x_1^2 - x_1^3 - z_1 + f(x_1, x_2^{\tau})]dt + D\, dW, \qquad (7)$$

and analogously for $x_2$. The resulting stochastic delay-differential equations are solved numerically for different small values of the noise parameter $D$, and for many different realizations of the process. The conclusion suggested by such computations, illustrated in Figs. 4(a) and 4(b), is that the small noise induces only a proportionally small perturbation of the synchronization manifold. Such stability to noisy perturbations of the synchronous bursting, achieved by an appropriate time lag, is a special property of the FTM coupling and is not present in the system of bursting neurons coupled by electrical synapses [12]. In the case of electrical synapses, arbitrary small noise destroys the exact synchrony, but it should be pointed out that the weaker form of synchrony, in which the bursting periods almost coincide, survives small noise. The effects of the same noise on the synchronization in the cases of electrical and FTM coupling are compared in Figs. 4.

## V. SUMMARY AND DISCUSSION

We have studied the exact synchronization of bursting dynamics in a pair of realistic neurons with the FTM model of the chemical synapse. The Hindmarsh-Rose neuron was used as a model of each of the bursting units, and we have included explicitly the time delay in the synapses. Numerical calculations are used to solve the DDE's of the model and calculate the largest Lyapunov exponent for the equations of perturbations transverse to the synchronization manifold. These calculations served to determine the domains of the values of the coupling strength and time delay that imply asynchronous or exactly synchronous bursting dynamics for initial states in some domain near the (unstable) stationary state. We have concentrated on the effects of the synaptic time delay on the stability of synchronous bursting dynamics, and other effects of the time delay, like delay-induced oscillation death, were observed but have not been studied in any detail.

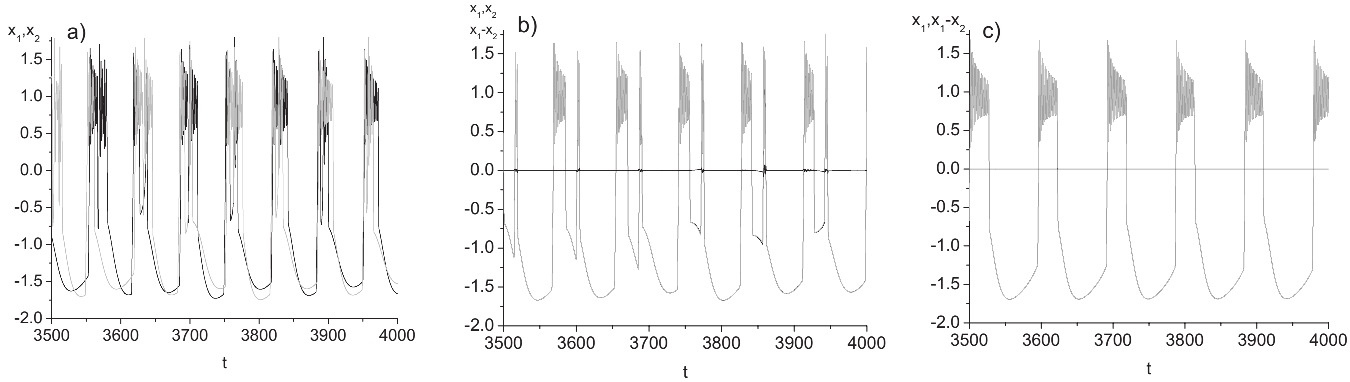


FIG. 3. Synchronization by increase of the values of the time lag $\tau$. Values of $(g,\tau)$, and the plotted curves are (a) (2,65) $x_1$ (black), $x_2$ (light gray); (b) (2,85) $x_1$ (light gray), $x_1-x_2$ (black); (c) (2,95) $x_1$ (light gray), $x_1-x_2$ (black).

The following picture emerges from our calculations. Weak coupling and small time-delays lead to bursting of the coupled neurons, which is not exactly synchronous but can be weakly synchronous in the sense that the times of bursts of the two neurons roughly coincide. Increase in the time delay cannot synchronize the bursting dynamics for the coupling strength below $g\approx 1.4$ For $g>1.4$ and small time lag the stationary state becomes stable. However, increase of the time lag leads to a bifurcation in which the stationary state loses stability. The resulting bursting dynamics is asynchronous for smaller time lags, but can become synchronized with the time lag in a certain domain. Thus, we have dem-

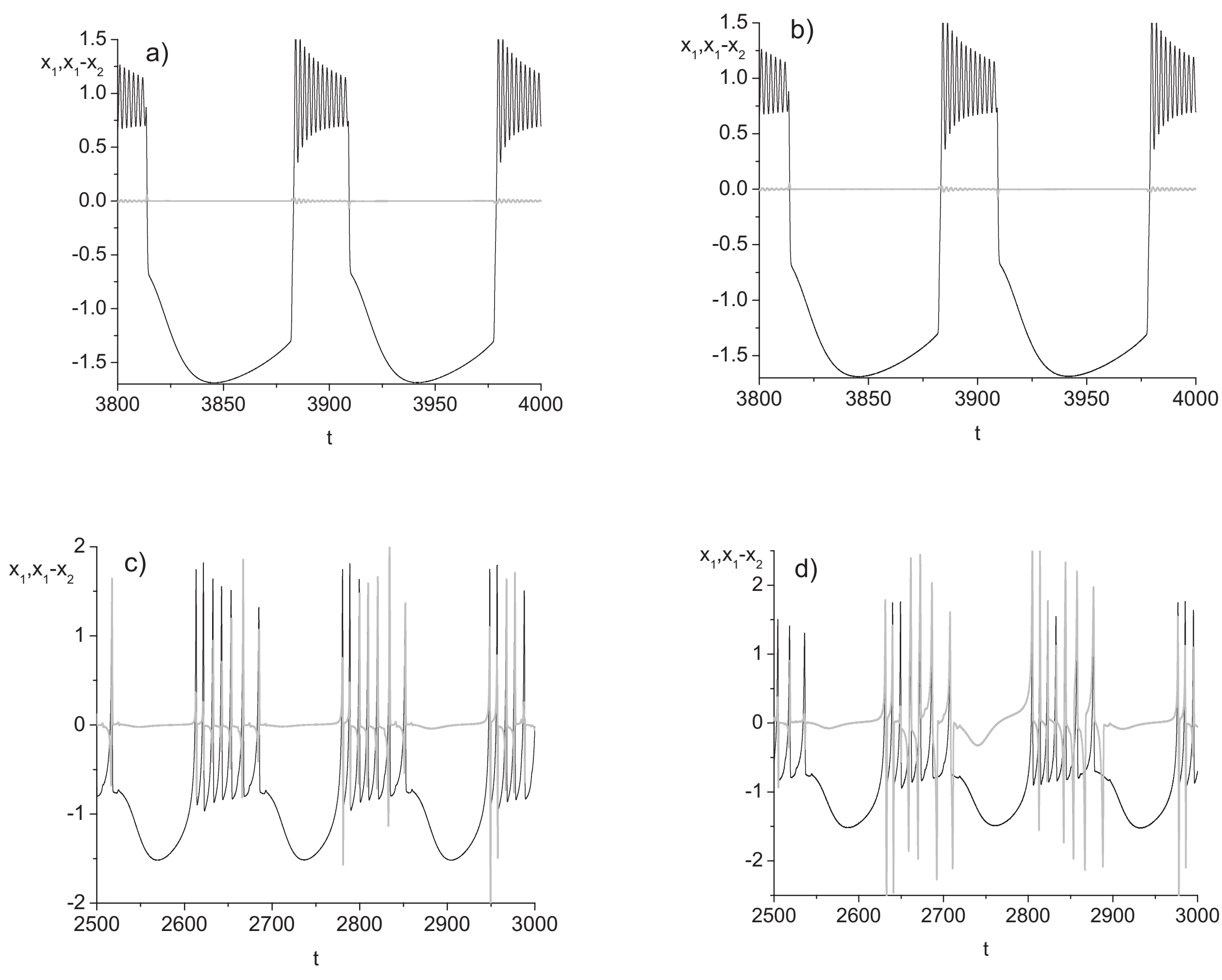


FIG. 4. Effect of small noise on the time-delay-induced synchronization of bursting for chemical FTM coupling (a), (b) and for electrical $[g(x_1-x_2)$; see [10,12]] coupling (c), (d). Presented are $x_1$ (black) and $x_1-x_2$ (light gray). Values of the parameters are (a) $D=0.001$, $g=2$, $\tau=95$; (b) $D=0.01$, $g=2$, $\tau=95$; (c) $D=0.001$, $g=0.1$, $\tau=8$; (d) $D=0.01$, $g=0.1$, $\tau=8$.

onstrated that the time delay in the model of the chemical synapse leads to exact synchronization of bursting. Furthermore, such exactly synchronous bursting, achieved with the coupling and time lag in a specific domain, is stable under small stochastic perturbations. The existence of stochastically stable exact synchronization of bursting by delayed chemical coupling is the main phenomenon described in this paper

It would be interesting to study the relative importance of time-delayed and instantaneous FTM coupling in the synchronization in more complicated networks [4] of noisy bursting neurons.

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