Influence of synaptic interaction on firing synchronization and spike death in excitatory neuronal networks

Sheng-Jun Wang,[1] Xin-Jian Xu,[2] Zhi-Xi Wu,[3] Zi-Gang Huang,[1] and Ying-Hai Wang*
[1]*Institute of Theoretical Physics, Lanzhou University, Lanzhou Gansu 730000, China*
[2]*Department of Mathematics, College of Science, Shanghai University, Shanghai 200444, China*
[3]*Department of Physics, Umeå University, 90187 Umeå, Sweden*

(Received 23 November 2007; revised manuscript received 26 September 2008; published 3 December 2008)

We investigate the influence of efficacy of synaptic interaction on firing synchronization in excitatory neuronal networks. We find spike death phenomena: namely, the state of neurons transits from the limit cycle to a fixed point or transient state. The phenomena occur under the perturbation of an excitatory synaptic interaction, which has a high efficacy. We show that the decrease of synaptic current results in spike death through depressing the feedback of the sodium ionic current. In the networks with the spike death property the degree of synchronization is lower and insensitive to the heterogeneity of neurons. The mechanism of the influence is that the transition of the neuron state disrupts the adjustment of the rhythm of the neurons oscillation and prevents a further increase of the firing synchronization.

DOI: 10.1103/PhysRevE.78.061906 PACS number(s): 87.18.Sn, 05.45.Xt, 87.18.Hf

I. INTRODUCTION

Synchronization of neural activity appears in different parts of the mammalian cerebral cortex [1] and underlies different neural processes in both normal and anomalous brain functions [2]. It has been suggested that synchronization plays a vital role in information processing in the brain: e.g., processing information from different sensory systems to form a coherent and unified perception of the external world [1–6]. On the other hand, synchronization has been detected in pathological conditions such as Parkinson's disease [7,8]. And epileptic seizures have long been considered to result from excessive synchronized brain activity [9], although some recent studies suggest that this picture may be an oversimplification [10,11]. Therefore understanding the mechanisms of synchronization may be a critical step in elucidating how neural systems work [11]. It has stimulated a great deal of theoretical and numerical works, such as studies on the effects of the topological properties of underlying networks [12–15] and the dynamical properties of synaptic coupling [16,17].

It was recently shown that the response time of synaptic couplings influences the stability of synchronized oscillations in the nonlocally coupled Hodgkin-Huxley (HH) equations [16]. If the response time of synaptic coupling is slower, synchronized activity of the systems is instable for excitatory coupling. However, the underlying dynamical mechanism of the influence is not clear. In experimental studies [18], it has been suggested that the generation of prolonged epileptiform neuronal synchronization is favored by the lower efficacy of synaptic transmission. Numerical studies [19] in a detailed computational model revealed that seizurelike activity occurs when the excitatory synapses are weakened, and the results were confirmed experimentally in mouse neocortical slices. According to the commonly accepted assumption that synchronization of neuronal activity underlies seizures, the dynamical mechanism of synchronization may be useful for understanding the way the biological neural system works.

In this work, we numerically investigate the dynamical mechanism underlying the influence of synaptic efficacy on firing synchronization in HH neuron networks. To do this, we first studied the dynamics of the response of HH neurons to excitatory synaptic current. When the efficacy of the synapse is low—namely, strength is weak and duration is short—the limit cycle is stable to the perturbation of the synaptic current. When synaptic efficacy is high, synaptic current can induce the transition of the neurons from the limit cycle to a fixed point or transient state. The transition is determined by dynamics of neuron's ionic channel. The decrease of synaptic current depresses the feedback of sodium ionic current which is responsible for the initiation of the spike. For simplicity we will refer to the transitions as spike death.

In neuronal networks, the synaptic input of a neuron is the accumulation of the currents received from all presynaptic neurons. When the coherence of the firing time of neurons is enhanced by an excitatory interaction, the synaptic input of neurons transforms from a fluctuant wave form into a pulse shape like the signal produced by one synapse. If synaptic efficacy is high, the input signal can induce a spike death of the neuron. Then the spike death disorders the adjustment of the rhythm of neurons and prevents neurons from firing spikes synchronously. In contrast, for synapses of lower efficacy, the duration of synaptic current is too short to induce the spike death of neurons. Additionally, the firing synchronization is different from the synchronous activity of oscillators for the existence of the transitions of the neuron's state.

The paper is organized as follows. The HH neuron model and the synaptic coupling are introduced in Sec. II. The response of a HH neuron to synaptic current is investigated in Sec. III. The influence of the dynamics of neurons on firing synchrony is shown in Sec. IV. A discussion and conclusion are given in Sec. V.

*yhwang@lzu.edu.cn

II. MODEL

To investigate the dynamics of a neuron under the perturbation of a synaptic stimulus, we adopted a system consisting of a HH neuron and a synapse. The HH neuron was originally proposed for the giant axon in a squid [20]. It serves as a paradigm for the spiking neuron models based on the nonlinear conductances of ion channels. The model describes the evolution of the membrane potential $V(t)$ and can be written as

$$C\frac{dV}{dt} = I_{ion} + I_{stim} + I_{syn}, \tag{1}$$

where I_{ion} is the ionic current, I_{stim} is the external current, and I_{syn} is the synaptic current. The ionic current describes the ion channel on the membrane and is defined as

$$I_{ion} = -g_{\mathrm{Na}}m^3h(V-E_{\mathrm{Na}}) - g_{\mathrm{K}}n^4(V-E_{\mathrm{K}}) - g_l(V-E_l), \tag{2}$$

where g_{Na}, g_K, and g_l are the maximum conductances for the sodium, potassium, and leak currents, and E_{Na}, E_K, and E_l are the corresponding reversal potentials. m and h are the activation and inactivation variables of the sodium current, and n is the activation variable of the potassium current. The gating variables $y=m,h,n$ satisfy the differential equation

$$\frac{dy(t)}{dt} = \alpha_y[1-y(t)] - \beta_y y(t), \tag{3}$$

with the nonlinear functions α_y and β_y given by

$$\alpha_m = 0.1(V+40)/\{1-\exp[-(V+40)/10]\}, \tag{4}$$

$$\beta_m = 4\exp[-(V+65)/18], \tag{5}$$

$$\alpha_h = 0.07\exp[-(V+65)/20], \tag{6}$$

$$\beta_h = 1/\{1+\exp[-(V+35)/10]\}, \tag{7}$$

$$\alpha_n = 0.01(V+55)/\{1-\exp[-(V+55)/10]\}, \tag{8}$$

$$\beta_n = 0.125\exp[-(V+65)/80]. \tag{9}$$

The parameter values are $E_{Na}=50$ mV, $E_K=-77$ mV, $E_l=-54.4$ mV, $g_{Na}=120$ mS/cm^2, $g_K=36$ mS/cm^2, $g_l=0.3$ mS/cm^2, and $C=1$ μF/cm^2 [21,22].

The external current I_{stim} determines the firing rate of the neuron. In the absence of synaptic coupling I_{syn}, the HH neuron has the following bifurcation diagram as a function of I_{stim}: In the parameter regions $I_{stim}<I_0$ and $I_{stim}>I_2$ the fixed point is the global attractor. For $I_0<I_{stim}<I_1$ the neuron possesses coexisting stable attractors, the fixed point and the limit cycle, which are separated by an unstable limit cycle. For $I_1<I_{stim}<I_2$ the fixed point becomes unstable. The values of the bifurcation points are $I_0\approx 6.2$ μA/cm^2, $I_1\approx 9.8$ μA/cm^2, and $I_2\approx 154$ μA/cm^2 [23].

We adopted the synaptic current I_{syn} described by an α function [22]. The α-function synapse is a phenomenological model based on an approximate correspondence of the time course of the wave form to physiological recordings of the postsynaptic response [24]. The equation of the synapse is like

$$I_{syn}(t) = -g_{syn}\alpha(t-t_{in})[V(t)-E_{syn}], \tag{10}$$

with

$$\alpha(t) = (t/\tau)\exp(-t/\tau)\Theta(t), \tag{11}$$

where τ is the characteristic time of the interaction, $\Theta(t)$ is the Heaviside step function, and t_{in} is the beginning time of the synaptic interaction—i.e., the firing time of the presynaptic neuron (all delays are neglected). The synaptic effect is traditionally classified as excitatory or inhibitory depending on the value of E_{syn}. Here, we took $E_{syn}=30$ mV for excitatory synapses and -80 mV for inhibitory ones. Equation (11) yields pulses with the maximum value of e^{-1} at $t=t_{in}+\tau$ and with a half width of 2.45τ [25]. So τ characterizes the duration of the synaptic interaction. For the α-function synapse, we equated the synaptic efficacy to the maximum synaptic conductances g_{syn} and the characteristic time τ. The high efficacy means that synaptic current possesses a strong strength and long duration.

III. SPIKE DEATH OF NEURONS

We focused on the dynamics of the system in the parameter region near the bifurcation point I_1. First, we studied the response of bistable neurons ($I_0<I_{stim}<I_1$) to the excitatory synaptic current. In simulations, firing was identified as the membrane potential V is over 20 mV. When the neuron fired a spike, we triggered a pulse of synaptic current into it. We observed two types of dynamics of the response, which depended on the efficacy of synapse. For a slow response time and strong synaptic strength, the neuron transited from the limit cycle to the fixed point. The transition of the neuron state is shown in Fig. 1. In Fig. 1(a) the response of the neuron to the synaptic current is represented by the membrane potential V. In the figure, the synaptic current is illustrated by the pulse added on the external current. One can see that the periodic firing was eliminated after the synaptic current was injected. The value of the membrane potential tended to -61.15 mV through subthreshold oscillations. In Fig. 1(b) the transition of the neuron state is shown in a three-dimensional space (V,h,m), which is a projection of the phase space (V,h,m,n). The trajectory left the limit cycle and was attracted to the basin of the fixed point. At last, through a transient process, the trajectory stopped at the fixed point, which is indicated by the dashed lines in the figure. The fixed point was $(V,h,m,n)=(-60.15,0.423,0.092,0.394)$ as the parameter $I_{stim}=8.5$ μA/cm^2. On the other hand, for systems with a quick response time and weak synaptic strength, the transition did not occur and the trajectory was attracted back to the limit cycle from a weak perturbation.

When the external signal I_{stim} is larger than but near I_1, the neuron possesses a stable limit cycle and an unstable fixed point. In this case there were also two types of dynamics of response. For high synaptic efficacy, the neuron exhibited a transient behavior when it received the synaptic current. Figure 2(a) shows that the membrane potential responded to the

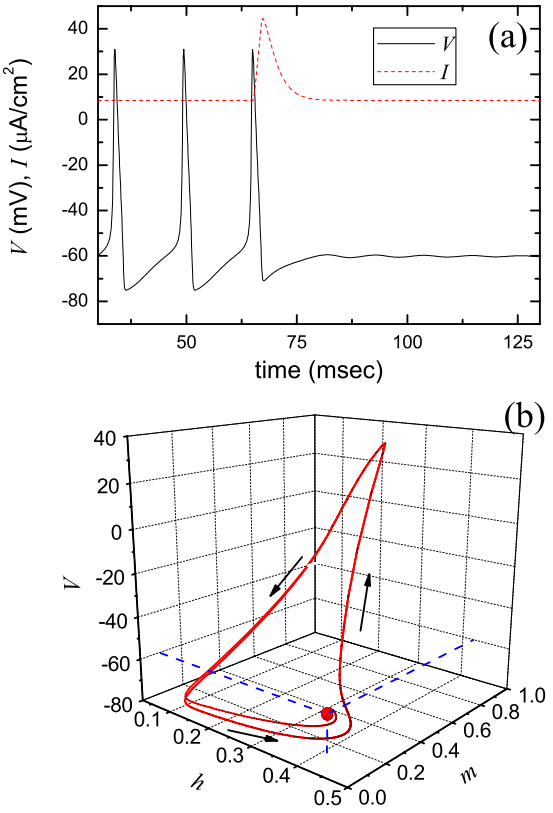

FIG. 1. (Color online) (a) The response of bistable HH neuron to excitatory synaptic current. The symbol I denotes the sum of the external current I_{stim} and the synaptic current I_{syn}. (b) The corresponding phase portrait. The values of the parameters are τ=2 ms, g_{syn}=1 mS/cm^2, and I_{stim}=8.5 μA/cm^2.

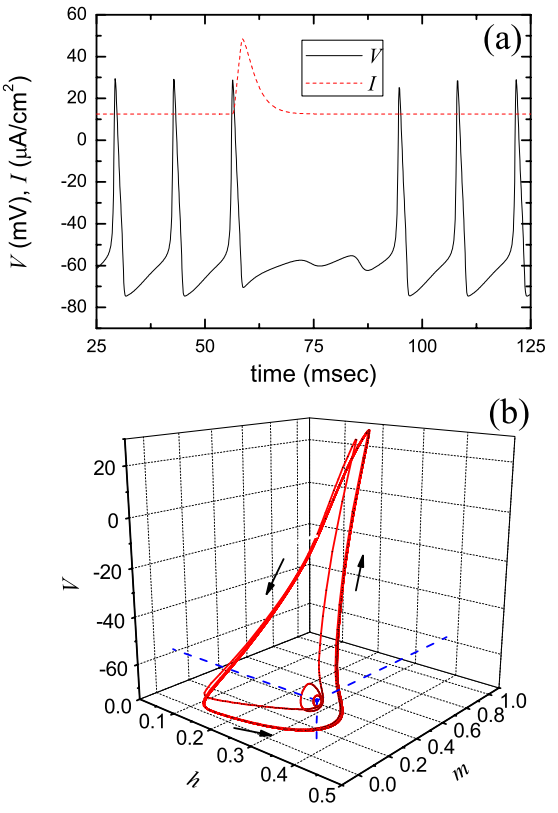

FIG. 2. (Color online) (a) The response of the neuron with I_{stim}=12.5 μA/cm^2 to excitatory synaptic current. (b) The corresponding phase portrait. The synaptic parameters are the same as Fig. 1.

synaptic current with a transient subthreshold oscillation. The subthreshold oscillation interrupted the periodic firing of the neuron. In phase space the transient behavior was a motion around the unstable fixed point. This is explicitly shown in the corresponding three-dimensional phase space (V,h,m). In Fig. 2(b) one can see that the trajectory of the neuron left the limit cycle and transiently moved around the unstable fixed point, which is indicated by the dashed lines. The unstable fixed point was (V,h,m,n) $=(-58.704,0.374,0.108,0.417)$ as the parameter I_{stim} $=12.5$ μA/cm^2. On the other hand, for low synaptic efficacy, the coupling cannot induce transient motion around the unstable fixed point. Like bistable neurons, the trajectory returned to the limit cycle from a weak perturbation.

Figure 3 shows the boundary between the two types of dynamics on the parameter plane g_{syn} vs τ. For the bistable neuron of the external current I_{stim}=8.5 μA/cm^2, the boundary between the two types of dynamics is represented by squares. Above the curve, neurons responded to synaptic currents with transitions between attractors. Inversely, the limit cycle of neurons was stable to the perturbation. For the neuron of the external current I_{stime}=12.5 μA/cm^2, the boundary is shown by circles. It is notable that a stronger strength and longer duration of synaptic current were needed by transitions of the neuron state. Based on numerical simulations, we obtained that the transitions of the neuron state can be induced by synaptic current in the parameter region 6.2 μA/cm^2 $<I_{stim}<$ 28.8 μA/cm^2. Above the upper boundary of the region, the transient motion around the unstable fixed point cannot be induced by the synaptic current.

In the following, we referred to the phenomena shown in both Figs. 1 and 2 as spike death. Different from oscillator death which is the quenching of oscillation of coupled systems, spike death is the behavior of a single neuron. And spike death includes both the transition between stable attractors and the transient behavior.

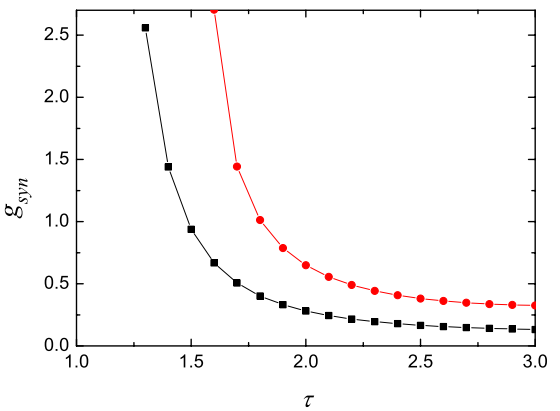

FIG. 3. (Color online) The dynamics diagram of minimal synaptic intensity g_{syn} vs the characteristic time τ for the neurons with the external current I_{stim}=8.5 μA/cm^2 (squares) or I_{stim} =12.5 μA/cm^2 (circles).

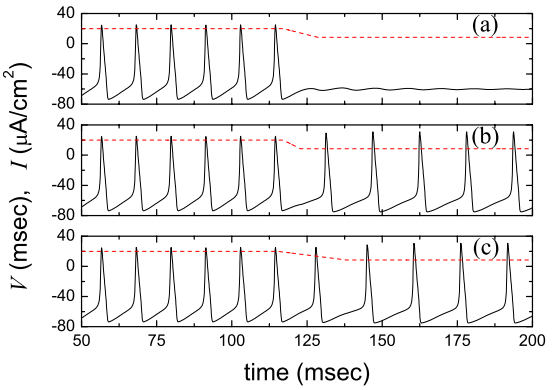

FIG. 4. (Color online) The change of the activity of the HH neuron as external current decreases. The external current is reduced from 20 μA/cm^2 to 8.5 μA/cm^2 with the slop (a) -1 μA/(cm^2 ms), (b) -2 μA/(cm^2 ms), or (c) -0.5 μA/(cm^2 ms).

Next we gave a qualitative interpretation of the spike death phenomenon. Although the synaptic current consists of a rise and a decay stage, we want to show that the decrease of the synaptic current induces the transition of neuronal activity. We illustrate the role of the decreased current in Fig. 4. In the simulations, external currents linearly decreased from 20 μA/cm^2 to 8.5 μA/cm^2, and synaptic current was absent. The time of beginning to decrease and the different slopes of the decrease current were chosen to represent the distinct duration and rate of decay of the current. In Fig. 4(a), the activity of the neuron transited from the periodic firing to the silent state through transient subthreshold oscillations. The decrease of current induced the spike death of the neuron. In Fig. 4(b), the decay of the current occurred in the refractory period of the neuron. The decreased current did not depress the next spike. This is similar to the scenario of a synaptic current of short duration. So spike death requires that the decrease of current occur at the end of the refractory period and the stage of the initiation of the next spike. In Fig. 4(c), the external current decreased with the slope -0.5 μA/(cm^2 ms). Comparing with Fig. 4(a), the rate of decrease was small. Although the current decreased at the stage of initiating a spike, it did not depress the firing of the neuron. Thus spike death requires that the rate of decrease of current be large at the stage of initiating spikes.

To interpret the effect of the decrease of current on the oscillation of neurons, we reviewed the generation of spikes. For a fixed value of the membrane potential V, the variable y $(=m,h,n)$ approaches the value $y_0(V)=\alpha_y(V)/[\alpha_y(V)+\beta_y(V)]$ with the time constant $\tau_y(V)=[\alpha_y(V)+\beta_y(V)]^{-1}$. The variable $m_0(V)$ increases with V, and the corresponding time scale τ_m is smaller than τ_h and τ_n. If external current injects into the cell and raises the membrane potential V, the conductance of sodium channels, $g_{Na}m^3h$, increases due to increasing m. Then sodium ions flow into the cell and raise the membrane potential even further. If this positive feedback is large enough, a spike is initiated [21]. When external current decreases at the onset of the generation of a spike, the rise of the membrane potential slows down. Then the increase of m is slowed down. So positive feedback is weakened. If the current decreases quickly, the spike of the neuron can be depressed. Therefore, for depressing the positive feedback of sodium ionic current, the decrease of current must occur at the onset of the generation of spikes, and the current must decrease at a large rate. This interpretation is consistent with the above simulated results, that a strong strength and long duration of synaptic current are necessary for spike death.

IV. INFLUENCE ON FIRING SYNCHRONIZATION

Next, we investigated the influence of spike death on the firing synchronization in neuronal networks. We considered a directed random network consisting of N nonidentical HH neurons. The network was generated as follows: With a probability p, we connected each of the probable directed couplings (such as the one from the jth neuron to the ith neuron). The network is described by an adjacency matrix $\{a^{ij}\}$, the entry a^{ij} of which is equal to 1 when the coupling from j to i exists and zero otherwise. In the directed network, a^{ij} cannot be equal to a^{ji}, and the signal travels in only the direction from j to i if $a^{ij}=1$ and $a^{ji}=0$. The signal received by the neuron i is the accumulation of all input synaptic currents, which is defined as

$$I_{syn}^{i}(t) = -\frac{1}{q^i}\sum_{j=1}^{N} a^{ij} g_{syn}\alpha(t-t_{in}^{j})[V^i(t)-E_{syn}^{ij}], \qquad (12)$$

where q^i is the rescaled factor which equals the number of inputting synapses of neuron i $(i=1,\ldots,N)$. t_{in}^{j} is the latest firing time of the presynaptic neuron j. E_{syn}^{ij} is the reverse potential of the synapse connecting j to i.

To study the global behavior of neuronal networks we computed the average activity $\bar{V}(t)=(1/N)\Sigma_{i=1}^{N}V^i(t)$ of the network. The amplitude of average activity can intuitionally reveal the coherence of the activity of neurons, which is defined as [12]

$$\sigma^2 = \frac{1}{T_2-T_1}\int_{T_1}^{T_2}[\langle\bar{V}(t)\rangle_t - \bar{V}(t)]^2 dt, \qquad (13)$$

where the angular brackets denote temporal average over the integration interval. In this work we studied the firing synchrony for the reason that neuronal states may transit away from the limit cycle and the synchronization of oscillators will be disrupted. Here we focused on the coherence of the firing time of neurons. We adopted the average cross correlation of the firing time of neurons [26,27] to quantify the degree of firing synchronization. The average cross correlation is obtained by averaging the pair coherence $K_{ij}(\gamma)$ between neurons i and j—i.e.,

$$K = \frac{1}{N(N-1)}\sum_{i=1}^{N}\sum_{j=1,j\neq i}^{N} K_{ij}(\gamma). \qquad (14)$$

The pair coherence $K_{ij}(\gamma)$ is defined as

$$K_{ij}(\gamma) = \frac{\Sigma_{l=1}^{k}X(l)Y(l)}{[\Sigma_{l=1}^{k}X(l)\Sigma_{l=1}^{k}Y(l)]^{1/2}}, \qquad (15)$$

which is measured by the cross correlation of spike trains at zero time lag within a time bin γ. To transform the neuronal

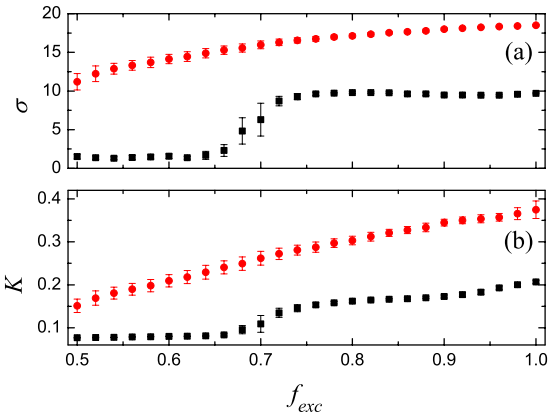

FIG. 5. (Color online) (a) The amplitude of average activity σ versus the fraction of excitatory neurons, f_{exc}. Squares (cycles) represent the relations in networks with $\tau=2$ ms (1 ms). The error bars were the standard deviation across 20 realizations. (b) The relation between the average cross correlation K and the fraction of excitatory neurons, f_{exc}.

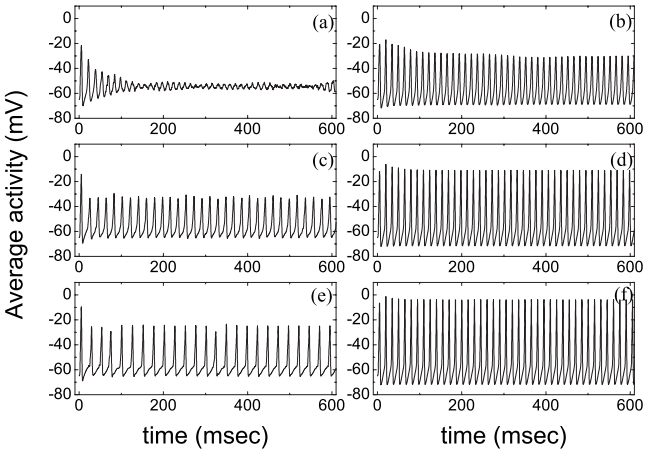

FIG. 6. Average membrane potential of the networks with $\tau=2$ ms (left) and $\tau=1$ ms (right). The fraction of excitatory neurons is $f_{exc}=0.5, 0.8, 1.0$ from top to bottom.

activity into a spike train, the interval T_2-T_1 is divided into k bins of $\gamma=1$ ms. Then spike trains of neurons i and j are given by $X(l)=0$ or 1 and $Y(l)=0$ or 1 $(l=1,\ldots,k)$, where 1 represents a spike generated in the bin and 0 otherwise.

We numerically investigated the collective activity of networks versus the fraction of excitatory neurons, f_{exc}, in the networks. In general, excitatory synapses tend to synchronize the activity of neurons in networks. However, it was shown that in neural systems different types of dynamics of response of neurons to couplings produce different synchrony properties [29]. Here we studied the influence of the new type of response, spike death, on the formation of synchrony as the excitatory interactions increase. In simulations, the networks consisted of 1000 neurons and the connecting probability was $p=0.01$. The synaptic conductance took the value $g_{syn}=1$ mS/cm^2. As an example, we used synapses with the characteristic time $\tau=2$ or 1 ms to generate neuronal networks with or without spike death, respectively. To ensure that the neurons had nonidentical properties, the external currents I^i_{stim} were of $(8.0, 12.0)$ μA/cm^2 and were generated at random.

In Fig. 5(a) we plotted the amplitude of average activity σ versus the fraction f_{exc} of excitatory neurons. Squares represent the results obtained in networks with $\tau=2$ ms, and circles represent the results with $\tau=1$ ms. In Fig. 5(b) we did the same for the average cross correlation K. The relations showed that the coherence of activity increases with the fraction of excitatory neurons. It is notable that the networks with $\tau=2$ ms—i.e., with the spike death property—had obviously lower values of σ and K than networks with $\tau=1$ ms. So the degree of synchrony in networks with the spike death property was obviously lower than in networks without the property.

The difference of the degree of synchrony between two types of networks is shown more intuitionally by the average activity in Fig. 6. We made neurons in the networks beginning to oscillate with a high degree of coherence. In simulations the first firing time of neurons was randomly distributed in $(0,5)$ ms. When $f_{exc}=0.5$, the average activity of the network with $\tau=2$ ms decreased obviously and the network changed quickly to oscillating randomly, as shown in Fig. 6(a). In the network without the spike death property, coherent oscillation [12] appeared, as shown in Fig. 6(b). When the fraction of excitatory neurons increased, the excitatory interaction enhanced the average activity in the networks both with and without the spike death property, while the average activity in the latter was obviously larger. Furthermore, the frequency of the average activity $\bar{V}$ in networks with $\tau=1$ ms was higher than the frequency in networks with $\tau=2$ ms.

The synchrony properties can be qualitatively explained by spike death. In networks, if the fraction of excitatory neurons is increased, the coherence of the firing time of neurons is enhanced. Then the input synaptic current of a neuron may transform from a fluctuating wave form into a smooth pulse. If the pulse of the accumulated synaptic current has long enough duration to depress the next spike, the synaptic current may lead to spike death. Therefore the synaptic current disorders the adjustment of the rhythm of the neuron firing and prevents synchronization. To demonstrate this, we show the synaptic currents and spike death events in Fig. 7. In Figs. 7(a) and 7(b) we plot the input synaptic currents of a neuron, which was randomly chosen in networks with $f_{exc}=0.5$ and $f_{exc}=0.8$, respectively. A transformation from a fluctuate wave form to a smooth pulse was observed. In simulations we took the peak of subthreshold oscillations of a neuron as a spike death event. Figure 7(c) shows the histogram of the frequency of spike death events—i.e., the number of spike death events in 1 ms. The spike death events periodically appeared with the same rhythm as the average activity of the network. In contrast, spike death events cannot be obtained in networks of low synaptic efficacy. Thus the spike death can explain the above synchrony property.

If network consists of identical neurons, the influence of spike death also exists and is more remarkable. Figure 8(a) shows the relation of K to f_{exc} of the networks in which the external current of all neurons was $I_{stim}=10.0$ μA/cm^2. One

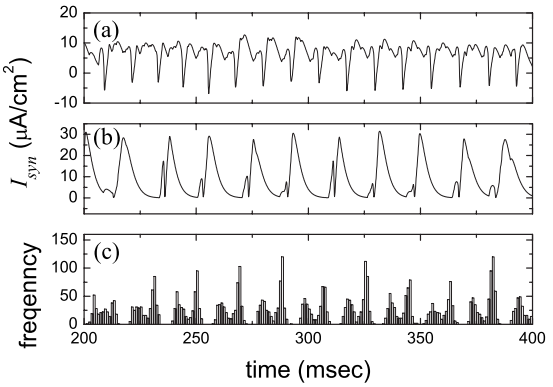

FIG. 7. (a) The input synaptic current of a randomly chosen neuron from the network with $\tau=2$ ms, $f_{exc}=0.5$. (b) The input synapse current when f_{exc} increased to 0.8. (c) The histogram of spike death events in the network with $\tau=2$ ms, $f_{exc}=0.8$.

can see that the values of K of the networks with $\tau=2$ ms (squares) were similar to Fig. 5. For networks with $\tau=1$ ms (circles), however, the value of K tended to 1 as f_{exc} increases. We calculated the degree of synchrony as a function of the heterogeneity of neurons in purely excitatory networks. In simulations the value of external currents I_{stim} was distributed in the region $(10.0-0.5w, 10.0+0.5w)$ μA/cm^2. Figure 8(b) shows the relation between K and the width w of the parameter region of I_{stim}. For networks with $\tau=2$ ms (squares), the degree of synchrony was insensitive to the heterogeneity of neurons. In contrast, the degree of synchrony in networks with $\tau=1$ ms (circles) remarkably increased and tended to 1 as the heterogeneity of neurons decreased. For networks with $\tau=1$ ms, the relation between K and the width w of the parameter region was fitted to the first-order exponential decay curve. The fitted curve (dashed line) is $K=A\exp(-w/B)+K_0$ with $K_0=0.362\pm0.005$, $A=0.595\pm0.007$, and $B=1.017\pm0.030$. The remarkable difference between the two kinds of networks shows that spike

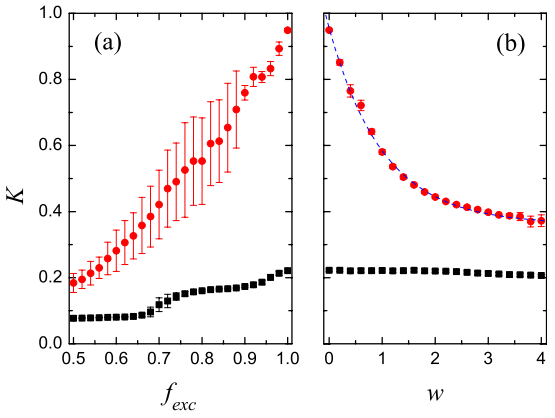

FIG. 8. (Color online) (a) The average cross correlation K versus the fraction of excitatory neurons for the networks consisting of identical neurons. Squares (circles) represent the relation in networks with $\tau=2$ ms (1 ms). The error bars were the standard deviation across 20 realizations. (b) The average cross correlation K changes with the width w of parameter region of I_{stim}. The dashed line is the fitted exponential curve.

death can effectively prevent the firing synchronization in neuronal networks.

V. DISCUSSION AND CONCLUSION

We have used HH neuron networks to investigate the dynamical origin of the influence of synaptic efficacy on the firing synchronization. A new dynamics of response of neurons to coupling, spike death, was suggested as a possible mechanism underlying the influence. When the firing time of neurons is so coherent that synaptic currents have a pulse wave form in excitatory networks, synaptic current induces the transition of the neuron state from the limit cycle to a fixed point or transient state. The transitions disrupt the adjustment of rhythm of the neuron oscillations and prevent further increase of the firing synchronization.

We studied the dynamics of the HH neuron responding to the excitatory synaptic perturbation. We numerically demonstrated that the synapse of high efficacy—i.e., large characteristic time and strong strength—induces the spike death of the neuron. For bistable neurons, spike death means the transition from the limit cycle to a fixed point. For the neuron with an unstable fixed point, spike death means the transition from the limit cycle to a transient state. The transient state is the motion around the unstable fixed point in phase space. Spike death of neurons results from the decrease of synaptic current, which depresses the feedback of the sodium ionic current at the stage of initiating a spike.

We demonstrated the influence of spike death on the degree of firing synchronization. In simulations we considered the networks with or without the spike death property, which were generated using synapses of characteristic time $\tau=2$ and 1 ms, respectively. The degree of synchrony of the former was lower. This is consistent with results of [16], that synchronous state is not stable for the excitation coupling of a slow response time. However, we also showed that for a slow response time, the degree of synchrony increased with the fraction of excitatory and the oscillation rate of whole network slowed down. Our main results are that in a network with $\tau=2$ ms, spike death events were observed. And spike death can explain the mechanism of preventing the rise of the degree of synchrony. Related synchrony properties were found also in weakly coupled HH neurons [22,29]. In the case of weak coupling, the phase of the neuron was perturbed by couplings, but the oscillation of the neuron was not destroyed. In contrast, the dynamical mechanism we suggested is proper for strong coupling and underlies the synchrony of the interrupted oscillations. Additionally, it is notable that, for the existence of spike death, the firing synchronization of neuronal networks is different from the usual oscillator synchronization in which each oscillator is stable to perturbations [28].

Our work relates to that of Drover *et al.* [30]. In this elegant work, using a simplified neuron model of two variables, they proposed a mechanism for slowing firing down. They found that a slow decay synaptic variable induces a situation where trajectory is attracted toward the unstable fixed point of the simplified model. This is similar with the transient behavior of the HH neuron we proposed here. How-

ever, with their mechanism, synaptic excitation is strongly synchronizing in networks in contrast with the fact that spike death prevents synchrony. In neural networks, collective behaviors sensitively depend on the intrinsic dynamics of neurons [30], and many types of response of neurons to synaptic coupling may exist [29]. It is interesting to make further studies on the relations among different responses and their effects on the collective behaviors of networks.

The variability of the strength of synapses was not involved in the present investigation. The synaptic strength is often affected by the activity of neurons through synaptic plasticity [31] and synaptic adaptation [32]. The effect of changes of synaptic strength will be studied elsewhere.

As mentioned above, the phenomenon that a low efficacy of synapses favors the generation of neuronal synchronization underlying seizure was obtained in experiments and numerical simulations [18,19]. Here we equated the strength and especially the characteristic time of synapses to the synaptic efficacy and studied the mechanism by which synapses influence firing synchronization. The mechanism of the influence may have potential values for understanding the way the realistic neural system works.

ACKNOWLEDGMENTS

We thank L. Wang for many helpful discussions and C.-F. Feng for comments on the manuscript. This work was supported by the NSF of China, Grant Nos. 10775060 and 10805033 . X.-J.X. acknowledges financial support from FCT (Portugal), Grant No. SFRH/BPD/30425/2006.

[1] W. Singer and C. M. Gray, Annu. Rev. Neurosci. **18**, 555 (1995).
[2] A. K. Engel, P. Fries, and W. Singer, Nat. Rev. Neurosci. **2**, 704 (2001).
[3] C. von der Malsburg, Neuron **24**, 95 (1999).
[4] A. Roskies, Neuron **24**, 7 (1999).
[5] W. Singer, Neuron **24**, 49 (1999).
[6] M. I. Rabinovich, P. Varona, A. I. Selverston, and H. D. I. Abarbanel, Rev. Mod. Phys. **78**, 1213 (2006).
[7] A. Nini, A. Feingold, H. Slovin, and H. Bergman, J. Neurophysiol. **74**, 1800 (1995).
[8] C. Hammond, H. Bergman, and P. Brown, Trends Neurosci. **30**, 357 (2007).
[9] R. K. Wong, R. D. Traub, and R. Miles, Adv. Neurol. **44**, 583 (1986).
[10] T. I. Netoff and S. J. Schiff, J. Neurosci. **22**, 7297 (2002).
[11] D. Takeshita, Y. D. Sato, and S. Bahar, Phys. Rev. E **75**, 051925 (2007).
[12] L. F. Lago-Fernández, R. Huerta, F. Corbacho, and J. A. Sigüenza, Phys. Rev. Lett. **84**, 2758 (2000).
[13] B. Percha, R. Dzakpasu, M. Zochowski, and J. Parent, Phys. Rev. E **72**, 031909 (2005).
[14] S. Feldt, H. Osterhage, F. Mormann, K. Lehnertz, and M. Żochowski, Phys. Rev. E **76**, 021920 (2007).
[15] D. H. Zanette and A. S. Mikhailov, Phys. Rev. E **58**, 872 (1998); Q. Li, Y. Chen, and Y. H. Wang, *ibid.* **65**, 041916 (2002); S. J. Wang, X. J. Xu, Z. X. Wu, and Y. H. Wang, *ibid.* **74**, 041915 (2006).
[16] H. Sakaguchi, Phys. Rev. E **73**, 031907 (2006).
[17] R. Zillmer, R. Livi, A. Politi, and A. Torcini, Phys. Rev. E **74**, 036203 (2006).
[18] U. Sayin and P. A. Rutecki, Epilepsy Res. **53**, 186 (2003).
[19] W. van Drongelen, H. C. Lee, M. Hereld, Z. Chen, F. P. Elsen, and R. L. Stevens, IEEE Trans. Neural Syst. Rehabil. Eng. **13**, 236 (2005).
[20] A. L. Hodgkin and A. F. Huxley, J. Gen. Physiol. **117**, 500 (1952).
[21] W. Gerstner and W. M. Kistler, *Spiking Neuron Models: Single Neurons, Populations, Plasticity* (Cambridge University Press, Cambridge, England, 2002).
[22] D. Hansel, G. Mato, and C. Meunier, Europhys. Lett. **23**, 367 (1993).
[23] B. Hassard, J. Theor. Biol. **71**, 401 (1978).
[24] A. Destexhe, Z. F. Mainen, and T. J. Sejnowski, Neural Comput. **6**, 14 (1994).
[25] H. Hasegawa, Phys. Rev. E **61**, 718 (2000).
[26] X. J. Wang and G. Buzsaki, J. Neurosci. **16**, 6402 (1996).
[27] S. Wang, W. Wang, and F. Liu, Phys. Rev. Lett. **96**, 018103 (2006).
[28] A. Pikovsky, M. Rosenblum, and J. Kurths, *Synchronization: A universal concept in nonlinear sciences* (Cambridge University Press, Cambridge, England, 2001).
[29] D. Hansel, G. Mato, and C. Meunier, Neural Comput. **7**, 307 (1995).
[30] J. Drover, J. Rubin, J. Su, and B. Ermentrout, SIAM J. Appl. Math. **65**, 69 (2004).
[31] J. J. Hopfield, Rev. Mod. Phys. **71**, 431 (1999).
[32] A. Levina, J. M. Herman, and T. Geisl, Nat. Phys. **3**, 857 (2007).