

## Weak Field-Induced Evolution of Spiral Wave in Small-World Networks of Hodgkin–Huxley Neurons \*

WANG Ya-Min(王亚民)<sup>1,2</sup>, LIU Yong(刘勇)<sup>3</sup>, WANG Jing(王晶)<sup>1</sup>, LIU Yu-Rong(刘玉荣)<sup>1\*\*</sup>

<sup>1</sup>School of Mathematical Science, Yangzhou University, Yangzhou 225002

<sup>2</sup>Basis Course of Lianyungang Technical College, Lianyungang 222006

<sup>3</sup>School of Mathematical Science, Yancheng Teachers University, Yancheng 224009

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An external weak electric field is introduced into the small-world networks of Hodgkin–Huxley neurons to study the control and breakup of a spiral wave. The effect of an external electric field on the neurons in the small-world network is described by an additive perturbation on the membrane potentials of neurons at the cellular level, in which an additive term  $V_E$  is imposed on the physiological membrane potential. A statistical factor of synchronization is used to measure the collective behaviour of spiral waves by changing the electric field; it is confirmed that a smaller factor of synchronization is associated with the survival of a spiral wave. In the case of no channel noise, the spiral wave could be removed under a certain intensity of constant electric field; it keeps robustly to the weak electric field when the electric field changes periodically. In the case of weak channel noise, a breakup of the spiral wave is observed when the intensity of the electric field exceeds certain thresholds, which could be measured from the curve for synchronization factors. No drift of the spiral wave is observed under the weak electric field.

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The spiral wave is one kind of characteristic spatiotemporal pattern,<sup>[1–6]</sup> and this problem has been extensively studied<sup>[7–12]</sup> to prevent the occurrence of ventricular fibrillation in the heart. Researchers began to investigate the pattern formation in the networks of neurons<sup>[13–16]</sup> since some experimental results<sup>[17,18]</sup> confirmed that spiral waves were observed in disinhibited mammalian cortex and that the appearance of a spiral wave could play a positive role in signal communication among neurons. For example, Ma *et al.* reported the formation and breakup of the spiral wave in the regular and small-world network of neurons<sup>[15,16]</sup>; the effect channel noise was also considered.<sup>[1]</sup>

A neuronal system consists of a large number of neurons, the normal function is dependent on the collective behaviour of the neurons; the electrical activities of the neurons could be measured by the biological network Hodgkin–Huxley equations<sup>[19]</sup> than the simplified network of Hindmarsh–Rose (HR) neurons.<sup>[3]</sup> Stable rotating spiral waves in rat neocortical slices visualized by voltage-sensitive dye imaging are found in experiments,<sup>[17,18]</sup> and it is confirmed that the spiral waves might serve as emergent population pacemakers to generate periodic activity in a nonoscillatory network without individual cellular pacemakers. As a result, it is reliable to study the development of spiral waves in neocortical slices with the scheme of complex networks. The electric activities of neurons are also greatly dependent on channel noise<sup>[20,21]</sup> and it is believed that the probabilistic gating of voltage-dependent ion channels is a source of electrical ‘channel noise’ in neurons.<sup>[20]</sup> For example, Schmid *et*

*al.*<sup>[21]</sup> reported that the capacitance fluctuations cause the channel noise reduction in stochastic HH systems. Fox *et al.*<sup>[22]</sup> presented the autocorrelation functions of channel noise to estimate the effect of channel noise. Therefore, it is also important to study the effect of channel noise on the formation and transition of a spiral wave in the networks of HH neurons. The external field often induces a transition of the spiral wave and other ordered waves in the media.<sup>[9]</sup> In the case of a reaction-diffusion system, a gradient force is often introduced into the reaction-diffusion equations to simulate the polarization effect of the external field.<sup>[23,24]</sup> It is critical to measure the polarization effect of the electric field on the networks of neurons. It is reported that a membrane potential perturbation at the cellular level<sup>[25]</sup> is suitable to measure the polarization effect when the external electric field is imposed on the neuron due to the medium characteristics of the cell membrane. Particularly, Wang *et al.*<sup>[26]</sup> suggested that a modified Hodgkin–Huxley neuron model subjected to a certain external electric field could be described by introducing an additive term  $V_E$  over the physiological membrane potential and the simulated circuit<sup>[26]</sup> was also presented to study the bifurcation and synchronization of Hodgkin–Huxley neuron exposed to an extremely low frequency electric field. Furthermore, Wang *et al.* investigated the effect of an external electric field on the spiral wave in the regular network of neurons.<sup>[28]</sup>

In this Letter, the removal and breakup of a spiral wave in the small-world networks of Hodgkin–Huxley neurons subjected to the external electric field is in-

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\*\*Corresponding author. Email: liuyurong@gmail.com

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vestigated and the channel noise is also considered. All the neurons in the two-dimensional array are connected with the small-world connection type, which is described by the local nearest-neighbour coupling and the long-range connection with a certain probability  $p$ . A factor of synchronization is used to study the phase transition and development of a spiral wave under different field conditions. A stable rotating spiral wave is regarded as the initial state to be changed by the external electric field. Our numerical results confirm that the death and breakup of the spiral wave in the networks can be detected under certain electric field actions, respectively.

The small-world networks of Hodgkin–Huxley neurons in the presence of channel noise<sup>[22]</sup> is described by

$$C_m \frac{dV_{ij}}{dt} = \tilde{g}_K n_{ij}^4 (V_K - V_{ij}) + \tilde{g}_{Na} m_{ij}^3 h_{ij} (V_{Na} - V_{ij}) + \tilde{g}_L (V_L - V_{ij}) + D \sum_{kl} \varepsilon_{ijkl} (V_{kl} - V_{ij}) \quad (1)$$

$$\frac{dy_{ij}}{dt} = a_y (1 - y_{ij}) - \beta_y y_{ij} + \xi_y(t), \quad (y = m, n, h) \quad (2)$$

$$a_m = \frac{0.1(V_{ij} + 40)}{1 - \exp(-(V_{ij} + 40)/10)}; \quad (3)$$

$$\beta_m = 4 \exp(-(V_{ij} + 65)/18);$$

$$a_h = 0.07 \exp(-(V_{ij} + 65)/20);$$

$$\beta_h = \frac{1}{1 + \exp(-(V_{ij} + 35)/10)}; \quad (4)$$

$$a_n = \frac{0.01(V_{ij} + 55)}{1 - \exp(-(V_{ij} + 55)/10)};$$

$$\beta_n = 0.125 \exp(-(V_{ij} + 65)/80); \quad (5)$$

where the variable  $V_{i,j}$  describes the membrane potential of the neuron in the node  $(i, j)$ . All the neurons are arranged in a two-dimensional array in space;  $m$ ,  $n$  and  $h$  are the parameters for gate channel, the capacitance of membrane is  $C_m = 1 \mu\text{F}/\text{cm}^2$ .  $D$  is the intensity of coupling,  $\varepsilon_{kl ij}$  describes the connection state between the node  $(k, l)$  and node  $(i, j)$ ,  $i$  and  $j$  are integers,  $\varepsilon_{kl ij} = 1$  if the node  $(k, l)$  is connected with node  $(i, j)$ , otherwise  $\varepsilon_{kl ij} = 0$ . Clearly, if the fraction of randomly introduced shortcuts, i.e. rewired links,  $p$  (probability) equals zero,  $\varepsilon_{kl ij} = 0$  only if the node  $(k, l)$  locates one of the four nearest neighbours of the node  $(i, j)$ . The maximal conductance of potassium is  $\tilde{g}_K = 36 \text{ mS}/\text{cm}^2$ , the maximal conductance of sodium is  $\tilde{g}_{Na} = 120 \text{ mS}/\text{cm}^2$ , the conductance of leakage current is  $\tilde{g}_L = 0.3 \text{ mS}/\text{cm}^2$ . The reversal potential  $V_K = -77 \text{ mV}$ ,  $V_{Na} = 50 \text{ mV}$  and  $V_L = -54.4 \text{ mV}$ ;  $\xi_m(t)$ ,  $\xi_h(t)$  and  $\xi_n(t)$  are independent Gaussian white noise, and the statistic properties<sup>[22]</sup> of the channel noise are represented by

$$\langle \xi_m(t) \rangle = 0,$$

$$\langle \xi_m(t) \xi_m(t') \rangle = \frac{2\alpha_m \beta_m}{N_{Na}(\alpha_m + \beta_m)} \delta(t - t') = D_m \delta(t - t'), \quad (6)$$

$$\langle \xi_n(t) \rangle = 0,$$

$$\langle \xi_n(t) \xi_n(t') \rangle = \frac{2\alpha_n \beta_n}{N_K(\alpha_n + \beta_n)} \delta(t - t') = D_n \delta(t - t'), \quad (7)$$

$$\langle \xi_h(t) \rangle = 0,$$

$$\langle \xi_h(t) \xi_h(t') \rangle = \frac{2\alpha_h \beta_h}{N_{Na}(\alpha_h + \beta_h)} \delta(t - t') = D_h \delta(t - t'), \quad (8)$$

where  $D_m$ ,  $D_n$  and  $D_h$  describe the intensity of noise, function  $\delta(t - t') = 1$  at  $t = t'$  and  $\delta(t - t') = 0$  at  $t \neq t'$ ,  $N_{Na}$  and  $N_K$  are the total numbers of sodium and potassium channels presenting in a given patch of the membrane, respectively. In the case of homogeneous ion channel density,  $\rho_{Na} = 60 \mu\text{m}^{-2}$  and  $\rho_K = 18 \mu\text{m}^{-2}$ , the total number of channels is decided by  $N_{Na} = \rho_{Na} s$  and  $N_K = \rho_K s$ , and  $s$  describes the membrane patch. As reported in previous works, optimized channel noise and multiplicative noise are helpful to support the survival of the spiral wave in the networks of neurons, which is helpful for the signal breaking through these quiescent areas. Based on the mean field theory, a statistic variable is defined to study the collective behaviour and statistic property,<sup>[15,16]</sup>

$$F = \frac{1}{N^2} \sum_{j=1}^N \sum_{i=1}^N V_{ij} = \langle V \rangle; \quad (9)$$

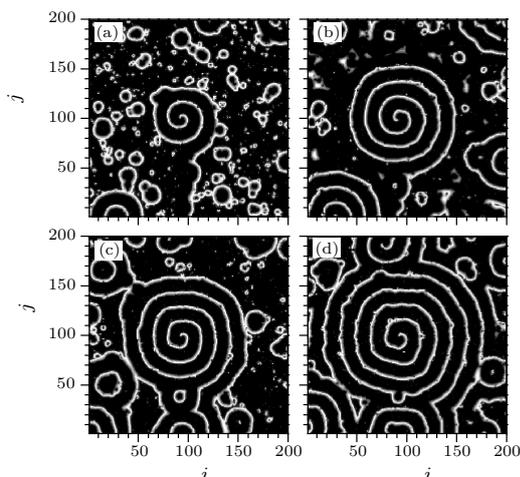
$$R = \frac{\langle F^2 \rangle - \langle F \rangle^2}{\frac{1}{N^2} \sum_{j=1}^N \sum_{i=1}^N (\langle V_{ij}^2 \rangle - \langle V_{ij} \rangle^2)}, \quad (10)$$

where  $R$  is a factor of synchronization, the number of neurons is  $N^2$  and the variable  $V_{ij}$  is the membrane potential of the neuron. As reported in Refs. [15,16], the smaller factor of synchronization is associated with no perfect synchronization and a spiral wave often occurs, while a higher factor about  $R \sim 1$  could make perfect synchronization. The curve for the factor of synchronization vs the bifurcation parameters measures the phase transition of the spiral wave by detecting sudden changing points in this curve. By using the modified Hodgkin–Huxley neuron model exposed to an external electric field,<sup>[26]</sup> the networks of the modified HH neuron model read

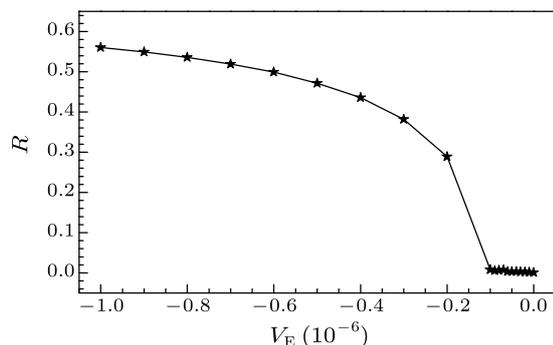
$$C_m \frac{dV_{ij}}{dt} = D \sum_{kl} \varepsilon_{ijkl} (V_{kl} - V_{ij}) - I_E + \tilde{g}_K n_{ij}^4 (V_K - V_{ij} - V_E) + \tilde{g}_{Na} m_{ij}^3 h_{ij} (V_{Na} - V_{ij} - V_E) + \tilde{g}_L (V_L - V_{ij} - V_E), \quad (11)$$

where the parameter  $V_E$  is the induced transmembrane potential from the external electric field<sup>[26,27]</sup> and  $I_E = C_m dV_E/dt$  is the mapped current flowing

through the capacitor due to the electric field stimulus.



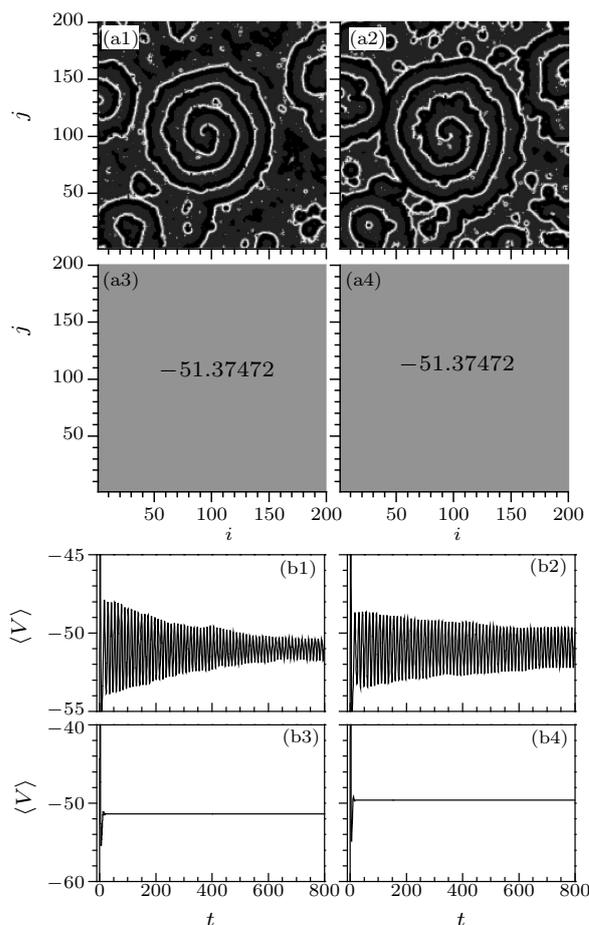
**Fig. 1.** The stable rotating spiral wave is developed as shown in (a) 200 time units, (b) 500 time units without channel noise at long-range probability  $p = 0.02$ . The stable rotating spiral wave is developed as shown in (c) 500 time units, (d) 2000 time units at long-range probability  $p = 0.02$  and channel noise (membrane patch  $s = 36$ ) is considered. The snapshots are plotted in gray from black (about  $-80$  mV) to white (about  $40$  mV) and the coupling coefficient  $D = 1$ .



**Fig. 2.** Factors of synchronization are calculated vs different intensities of constant external electric field within a transient period of about 800 time units.

In what follows, the external electric field-induced changes of the stable rotating spiral wave in the small-world network of the improved model of Hodgkin-Huxley neurons is investigated. A stable rotating spiral wave is used as the initial state in the numerical studies, the time step  $h = 0.001$ , coupling intensity  $D = 1.0$ , 40000 neurons are located in a two-dimensional array with  $200 \times 200$  nodes, and no-flux boundary condition is used. A spiral wave can cover the entire system with a smaller probability of long-range connection;<sup>[14]</sup> breakup of the spiral wave often occurs when the long range connection probability exceeds certain thresholds. The small-world connection network can be described by the local regular networks and the long-range connection with certain probability  $p$ . First, we investigate the case that no channel noise is considered, the long range connection proba-

bility  $p = 0.02$ , which is able to support the survival of the spiral wave when an external electric field is not imposed on the network. The developed spiral wave in the networks of HH neurons is plotted as shown in Figs. 1(a) and 1(b) with no channel noise considered, and snapshots in Figs. 1(c) and 1(d) show the developed spiral wave in the network in the presence of channel noise (membrane patch  $s = 36$ , noise is weak). Our aim is to investigate the effect of the external field on the spiral wave, so the long range connection probability  $p = 0.02$  is used without special statement.

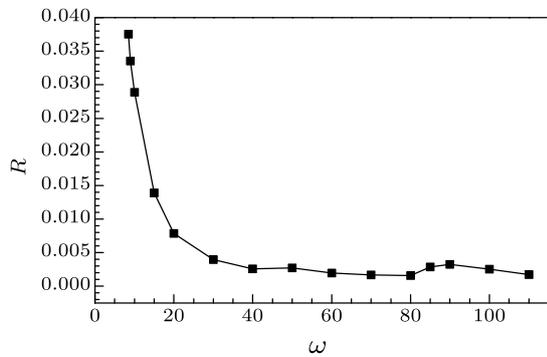


**Fig. 3.** Spatiotemporal patterns are developed within a transient period about 800 time units for  $t = 200$  (a1),  $t = 800$  time units (a2),  $V_E = -10^{-7}$ ;  $t = 200$  (a3),  $t = 800$  time units (a4),  $V_E = -2 \times 10^{-7}$ . The evolution of the average value for membrane potentials of all neurons in the networks under different  $V_E$  for  $V_E = -9 \times 10^{-8}$  (b1),  $V_E = -10^{-7}$  (b2),  $V_E = -2 \times 10^{-7}$  (b3),  $V_E = -3 \times 10^{-7}$  (b4). The snapshots are plotted in gray from black (about  $-80$  mV) to white (about  $40$  mV).

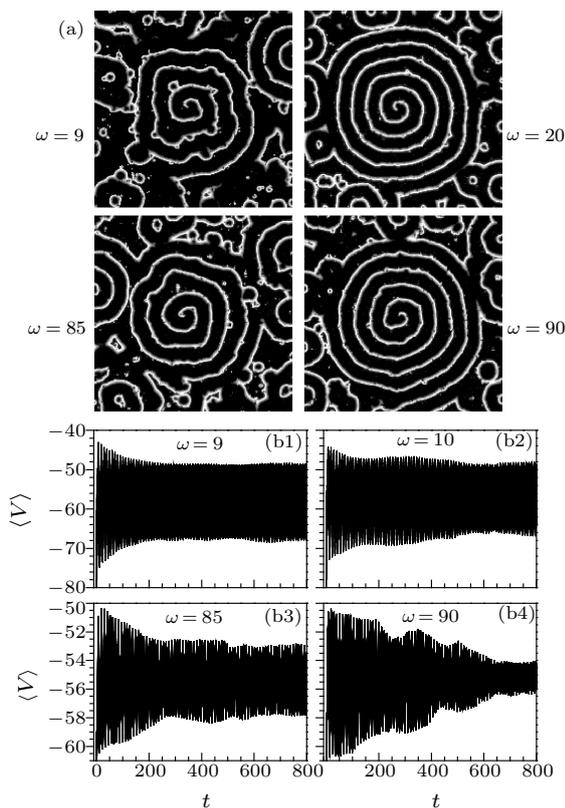
The numerical results in Fig. 1 show that a stable rotating spiral wave can be developed completely with an appropriate long-range probability; extensive numerical results confirm that no regular spiral wave can be generated when the long-range probability  $p$  exceeds a certain threshold (i.e.,  $p \sim 0.04$ ).

Next, an electric field with a very weak intensity is used and no channel noise is considered. The intensity

of the external electric field is selected with different constants and periodical signals with different angular frequencies, respectively. Statistical variable synchronization factors under different conditions are calculated to measure the sudden transition of the spiral wave.



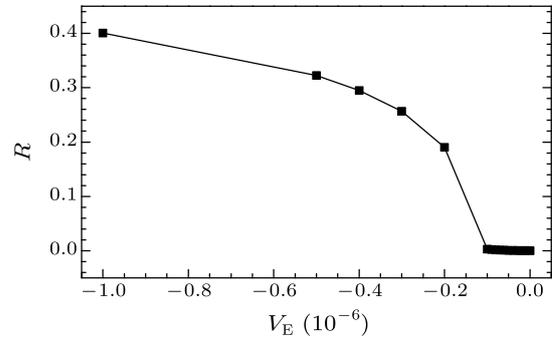
**Fig. 4.** Factors of synchronization are calculated vs angular frequencies of a periodical external electric field within a transient period of about 800 time units.



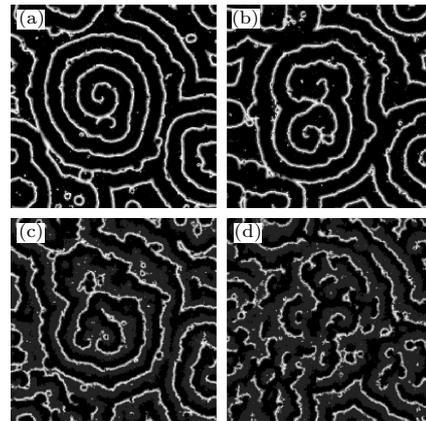
**Fig. 5.** Spatiotemporal patterns are developed within a transient period of about 800 time units under different angular frequencies (a) in  $V_E = -10^{-7} \sin(\omega t)$ . The evolution of the average value for the membrane potentials of all neurons in the networks under different angular frequencies (b1–b4). The snapshots are plotted in gray from black (about  $-80$  mV) to white (about  $40$  mV).

The curve in Fig. 2 confirms that the factors of synchronization change vs the external field intensity monotonously before the intensity of electric field reaching certain threshold, which is fixed to close the

sudden changing point in this curve. The corresponding snapshots are plotted to detect the transition of spiral wave when the electric field is selected with the value close to the sudden changing point, the results are shown in Fig. 3.



**Fig. 6.** Factors of synchronization are calculated vs the intensities of a constant external electric field within a transient period of about 800 time units, channel noise intensity is measured by membrane patch  $s = 36$ .



**Fig. 7.** Spatiotemporal patterns developed within a transient period of about 800 time units under different intensities of electric field, for  $V_E = -10^{-8}$  (a),  $V_E = -2 \times 10^{-8}$  (b),  $V_E = -9 \times 10^{-8}$  (c),  $V_E = -10^{-7}$  (d). The snapshots are plotted in gray from black (about  $-80$  mV) to white (about  $40$  mV).

The results in Fig. 3 confirm that a spiral wave can be removed (death of spiral wave) when the intensity of the external electric field exceeds the critical threshold, while the spiral wave keeps alive when the intensity is below the critical threshold, which can be measured from the sudden changing point in the curve for factors of synchronization. The time series of average values for the membrane potentials of neurons in the networks become stable when the spiral wave is removed, and the oscillating vs time just indicates that the spiral wave remains greatly robust. Furthermore, it is also interesting to investigate the case of the electric field vs time periodically. For simplicity,  $V_E = -10^{-7} \sin(\omega t)$  and the results are shown in Figs. 4 and 5.

The curve in Fig. 4 confirms that the factors of synchronization decrease monotonously vs the angular frequency of electric field, and a sudden drop is

observed in the curve when the angular frequency  $\omega$  is used in the intensity of the electric field. Snapshots are also illustrated to check the transition of the spiral wave when the angular frequency of the electric field is selected with the value close to the sudden point in the curve; the results are shown in Fig. 5.

The results in Fig. 5(a) show that the spiral waves stay alive when the electric field is adjusted with weak periodical signals. The time series of the average value of membrane potentials of neurons in the networks oscillate vs time because spiral waves often hold a certain rotating period. It just indicates that the spiral wave is removed when the time series of the average values of the membrane potentials of neurons in the networks decreases to a certain stable value. Compared with the results in Figs. 3 and 5, it is found that the spiral wave used to keep robust to the external electric field when the field is adjusted by weak periodical signals.

Optimized channel noise is helpful to support the survival of the spiral wave, while a channel noise with high intensity often causes the breakup of the spiral wave. In this subsection, weak channel noise intensity (i.e., membrane patch  $s = 36$ ) is considered to investigate the evolution of the spiral wave under different electric field conditions. The factors of synchronization are calculated under different kinds of electric field and the curve is plotted in Fig. 6.

The results in Fig. 6 also show that the factors of synchronization decrease vs the external field intensity of the monotonous electric field and that a sudden fall of the factors is observed at certain thresholds. It is found that the factors of synchronization change rapidly when the intensity of the constant external electric field is close to  $V_E = -10^{-8}$  when weak channel noise is considered. The breakup of the spiral wave is induced when the intensity of the electric field is close to this critical threshold; some snapshots are shown in Fig. 7.

The results in Fig. 7 confirm that the spiral wave stays alive before the intensity of the electric field is changed to a certain threshold about  $V_E = -10^{-8}$  when weak channel noise is considered. Compared to the case where without channel noise is considered, for example, the results in Figs. 2 and 6, it is found that the stable rotating spiral wave develops toward different targets, death (in the case of no channel noise) and breakup under weak channel noise. It is more interesting that the spiral wave stays robust to the external electric field at certain intensities of electric field, which could be estimated from the curve for factors of synchronization vs intensity of electric field. To our knowledge, some optimized channel noise intensity still can support the survival of the spiral wave when the electric field is imposed on the networks of neurons. Extensive numerical results confirm that the breakup of the spiral wave occurs easily in the pres-

ence of stronger channel noise and that the process is enhanced when the electric field effect on the neurons is considered.

In summary, a new additive term  $V_E$  is introduced on the membrane potentials to map the external electric field effect on the network of neurons. A statistical factor of synchronization is helpful to detect the phase transition of the spiral wave induced by the external electric field. The results are concluded as follows: (1) The factors of synchronization change monotonously with the intensity of the electric field, and sudden changing points in the curve for factors of synchronization mark the critical value of the electric field to induce the breakup or death of the spiral wave. (2) In the case of no channel noise, the spiral wave could be removed and the spiral wave also stays robust to the periodical electric field. (3) In the presence of weak channel noise, breakup of the spiral wave is observed at a certain intensity of the electric field. (4) Drift of the spiral wave is not observed in the networks of neurons, it is different from the results in the reaction-diffusion system. To our knowledge, the effect of an external electric field on the reaction-diffusion system is often described by an additive gradient force while it is simulated by introducing an additive perturbation on the membrane potentials of the neurons in the networks. It could provide a new way to understand the development of the collective behaviour of neurons.

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