Dynamics of period-doubling bifurcation to chaos in the spontaneous neural firing patterns

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Received: 10 May 2011 / Revised: 6 November 2011 / Accepted: 28 November 2011 / Published online: 7 December 2011
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Abstract Period-doubling bifurcation to chaos were discovered in spontaneous firings of Onchidium pacemaker neurons. In this paper, we provide three cases of bifurcation processes related to period-doubling bifurcation cascades to chaos observed in the spontaneous firing patterns recorded from an injured site of rat sciatic nerve as a pacemaker. Period-doubling bifurcation cascades to period-4 ($\pi(2,2)$) firstly, and then to chaos, at last to a periodicity, which can be period-5, period-4 ($\pi(4)$) and period-3, respectively, in different pacemakers. The three bifurcation processes are labeled as case I, II and III, respectively, manifesting procedures different to those of period-adding bifurcation. Higher-dimensional unstable periodic orbits (UPOs) can be detected in the chaos, built close relationships to the periodic firing patterns. Case III bifurcation process is similar to that discovered in the Onchidium pacemaker neurons and simulated in theoretical model-Chay model. The extra-large Feigenbaum constant manifesting in the period-doubling bifurcation process, induced by quasi-discontinuous characteristics exhibited in the first return maps of both ISI series and slow variable of Chay model, shows that higher-dimensional periodic behaviors appeared difficult within

the period-doubling bifurcation cascades. The results not only provide examples of period-doubling bifurcation to chaos and chaos with higher-dimensional UPOs, but also reveal the dynamical features of the period-doubling bifurcation cascades to chaos.

Keywords Neural firing pattern · Period-doubling bifurcation · Chaos · Unstable periodic orbits · Feigenbaum constant · Non-smooth characteristic · Quasi-discontinuous characteristic · Period-adding bifurcation

Introduction

In recent years, nonlinear behaviors in biological rhythm have attracted much attention (Glass and Mackey 1987; Chay et al. 1995; Izhikevich 2000, 2007; Li et al. 2004; Yang et al. 2009). The dynamics of neural firing patterns and the bifurcations of firing patterns were of fundamental importance to the elucidation of neural coding mechanism (Braun et al. 1994; Yang et al. 2006). Various firing patterns, such as periodic firing, chaotic firing and stochastic resonance induced stochastic firing, were inspected in different nervous system (Chay 1985; Braun et al. 1994; Ren et al. 1997; Gu et al. 2001, 2003, 2011a, b; Jia et al. 2011; Du et al. 2010; Guo 2011). The bifurcation process of firing patterns, such as period-adding bifurcation process with chaotic firing patterns or with stochastic firing patterns, were simulated in the theoretical models (Fan and Holden 1993; Fan and Chay 1994; Chay et al. 1995) and observed in the experiments (Gu et al. 2004; Li et al. 2004; Lu et al. 2009). Recently, different cases of bifurcation process of neural firing patterns in one-dimensional (Li et al. 2004) or two-dimensional parameter space have been studied (Wu et al. 2008; Zheng et al. 2009). These

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bifurcation structures provide a basic framework to understand the relationships between the neural firing patterns in parameter space.

Among these diverse studies, the bifurcations to chaos in neural firing pattern have been put much attention (Hayashi et al. 1982, 1983; Aihara et al. 1984; Aihara and Matsumoto 1987; Abarbanel et al. 1993; Ren et al. 1997; Gu et al. 2004; Wang et al. 2010). Three routes to chaos, period-doubling bifurcation, intermittency, and collapse of tori, were discovered in the pioneering studies on the neurons and axons, both stimulated by the external periodic stimulus (Hayashi et al. 1982, 1983; Aihara et al. 1984; Aihara and Matsumoto 1987). In spontaneous neural firing patterns, the intermittency to chaos (Wang et al. 2010) were observed in site of rat sciatic nerve as a pacemaker (called as an experimental neural pacemaker in a series of studies (Gu et al. 2001, 2003, 2004, 2011a; Wu et al. 2008; Zheng et al. 2009; Li et al. 2004; Lu et al. 2009). The intermittent chaos locates near a period-3 firing pattern, exhibiting non-smooth characteristics (Wang et al. 2010). Period-doubling bifurcation to chaos was firstly discovered in the experiment on the *Onchidium* pacemaker neurons (Hayashi et al. 1992), whose procedure from period-1 firing, to period-2 firing, to period-4 firing, to chaotic firing, and to period-3 firing. The bifurcation process was simulated in a theoretical model and is consistent with many other simulation results of theoretical models. In the experimental neural pacemaker, period-doubling bifurcation cascades (period-1 to period-2 firstly and then to period-4) to chaos was also observed (Li et al. 2003). Unfortunately, the chaotic firing could not further change into a periodic firing such as period-3 firing. Except these findings, period-doubling bifurcation to chaos in the experiment has been seldom reported, despite many simulations in theoretical models such as Chay model and Hindmarsh-Rose model, composed of slow and fast variables (Chay 1985; Canavier et al. 1990; Fan and Holden 1992a, 1993). In such systems, the first return map of the ISI series or the slow variable of the model exhibit quasi-discontinuous characteristics or nearly non-smooth characteristics (Wu and He 2000, 2001; Wang et al. 2010; Mo et al. 2010). If the behavior of model is period-adding bifurcation process, the map manifests nearly non-smooth characteristic (Mo et al. 2010). If the behavior is period-doubling bifurcation cascades, the map manifests quasi-discontinuous characteristic with a local high negative slope, which can induce extra-large Feigenbaum constants in the period-doubling bifurcation cascades (Wu and He 2000, 2001). It leads to that the parameter range of higher-dimensional periodic behaviors in the period-doubling bifurcation cascades is extra-narrow or some periodic behaviors disappear (Wu and He 2000, 2001). The researchers speculate that the higher-dimensional periodic

behaviors, such as period-16 and even if the period-8, disappear in the period-doubling bifurcation cascades in the experiment. Except the extraordinary Feigenbaum constants, the quasi-discontinuous characteristics can induce intermittent chaos with properties between those of type I and type V (Wang et al. 2010).

Nonlinear time series analyses such as the largest Lyapunov exponent, the correlation dimension, the first return map, nonlinear prediction and detection of unstable periodic orbits (UPOs) played very important roles in the identification of the spontaneous chaotic neural firing patterns discovered in various real nervous system (Abarbanel et al. 1993; Elbert et al. 1994; Hayashi et al. 1992, 1995, 1996; So et al. 1998; Di Mascio et al. 1999a, b; Lovejoy et al. 2001), for example, in the brain (Hayashi et al. 1995, 1996). UPOs are the skeleton of the chaos and can determine basic properties of chaos (Auerbach et al. 1987; So et al. 1996, 1997, 1998). In the last 20 years, detection of UPOs has been a central issue to analyze chaotic firing patterns from the experiments (Auerbach et al. 1987; Schiff et al. 1994; Pierson and Moss 1995; Pei and Moss 1996; So et al. 1998; Braun et al. 1999a; Wan et al. 2004; Gu et al. 2004; Yang et al. 2009). UPOs were suggested to play important roles in sensory perception (Braun et al. 1997, 1999a, b), and even thought to be a language for neuronal dynamics (So et al. 1998). In addition, the evolution of UPOs can also be employed to understand the bifurcation processes the chaos lying in (Ren et al. 2001; Gu et al. 2004, 2007; Yang et al. 2009). The UPOs detected in the chaos are always related to the neighbouring stable periodic behaviors (Ren et al. 2001; Gu et al. 2004). The chaos lying between higher-dimensional periodic behaviors has seldom reported, led to that higher-dimensional UPOs such as period-4 orbit and period-5 orbit have rarely been detected in the chaos.

In this paper, three cases of bifurcation process of the spontaneous firing patterns, each composed of period-doubling bifurcation to chaos and bifurcation from the chaos to periodicity, were observed in the different experimental neural pacemakers. The procedure of period-doubling bifurcation to chaos is from period-1 firing firstly, and then to period-2 firing, to period-4 ($\pi(2,2)$) firing, at last to chaotic firing, for all three cases of bifurcation process. The chaotic firing can change to period-5 firing for case I bifurcation process, to period-4 ($\pi(4)$) firing for case II and period-3 firing for case III, respectively. The three cases of bifurcation procedures are different to those of period-adding bifurcation process. Higher-dimensional UPOs such as two kinds of unstable period-4 orbit, or unstable period-5 orbit can be detected in the chaotic firing patterns. In case II, the coexistence of two kinds of unstable period-4 orbits is detected. In addition, the case III bifurcation process is simulated with Chay model. The extra-

large Feigenbaum constants and the quasi-discontinuous characteristics in the first return maps of ISI series and the slow variable are provided. The rest of the paper is divided into 5 parts, the experimental model, theoretical model and the methods to analyze the chaotic firing, the experimental results of bifurcation processes, the UPOs of the chaotic firing patterns, the simulation of case III bifurcation process, and the discussion and conclusion.

Experimental model, theoretical model and methods to analyze the chaotic firing

Experimental model

An animal model of chronic constriction nerve injury (CCI) developed by Bennet and Xie (1988) appears to reproduce many features of neuropathic pain disorder. Electrophysiological recordings from myelinated primary afferent axons revealed that spontaneous impulsive activity which originated at the site of nerve construction (Tal and Eliav 1996; Xie and Xiao 1990). The CCI model has been widely employed in the studies about neuropathic pain.

In a series of studies (Ren et al. 1997; Gu et al. 2001, 2003, 2004, 2011a, c; Wu et al. 2008; Zheng et al. 2009; Yang et al. 2009; Wang et al. 2010; Zhao et al. 2010), the CCI model are used to be an experimental pacemaker to study the nonlinear dynamics of neural firing patterns, for instance, bifurcation and chaos. Experimental pacemakers were formed at the injured site of adult male Sprague-Dawley rat (200–300 g) sciatic nerve subjected to chronic ligation. Rats were anesthetized with pentobarbital sodium (40 mg/kg, ip). Three or four loose ligatures were made at the level of the middle thigh of the right sciatic nerve. After a survival time of 8–12 days, the animals were anesthetized and prepared with tracheal cannula. The previously injured site in which the pacemaker was formed was exposed and was perfused continuously with warm (34°C) Krebs's solution. The injured site was disconnected from the receptive field by acutely crushing the nerve just peripheral to the injury. About 20–30 mm proximal to the injured site, the sciatic nerve was exposed separately and covered with warm (34°C) paraffin oil. The spike trains of individual fibers ending at the pacemakers were recorded in this oil pool. A fine bundle of fiber which was disconnected from the central nervous system but whose connection to the injured site was left intact, and was placed on a single platinum electrode referred to a nearby indifferent. If the observed bundle contained only one active fiber, the spontaneous spike trains were recorded with a PowerLab system (Australia) at sampling frequency being 10.0 kHz. Meanwhile the spike trains were monitored with the PowerLab system during the whole experiment to make sure that the recording was of a single unit.

The extra-cellular calcium concentration ($[Ca^{2+}]_o$) was changed as bifurcation parameter. The time intervals between the maximum values of the successive spikes were recorded seriatim as interspike interval (ISI) series. The value of an ISI is shown as ordinate and the number of the ISI as abscissa in the bifurcation figures of the ISI series.

Theoretical model-Chay model

Bifurcation process and chaos can be simulated in autonomous Chay model, verified to be closely relevant to those discovered in the experimental neural pacemaker (Gu et al. 2001; Yang et al. 2009). The deterministic Chay model (1985) is as follows:

$$\frac{dV}{dt} = g_i m_\infty^3 h_\infty (v_i - V) + g_{kv} (v_k - V) n^4 + g_{kc} \frac{C}{1+C} (v_k - V) + g_l (v_l - V) \quad (1)$$

$$\frac{dn}{dt} = \frac{n_\infty - n}{\tau_n} \quad (2)$$

$$\frac{dC}{dt} = \frac{\rho(m_\infty^3 h_\infty (v_c - V) - k_c C)}{\tau_c} \quad (3)$$

where t is the time, V is the membrane potential, n is the probability of potassium channel activation, and C is the dimensionless intracellular concentration of calcium ion. m_∞ and h_∞ are the probabilities of activation and inactivation of the mixed inward current channel. n_∞ is the steady state value of n . $\tau_n = \frac{1}{\lambda_n(\alpha_n + \beta_n)}$ is the relaxation time. k_c is the rate constant for efflux of the intracellular Ca^{2+} ions, τ_c is a proportionality constant. The explicit expressions for m_∞ , h_∞ , and n_∞ obey the equation $y_\infty = \frac{\alpha(y)}{\alpha(y) + \beta(y)}$, where y stands for m , h , and n . In the model, $\alpha_m = 0.1(25 + V)/(1 - e^{-0.1V-2.5})$, $\beta_m = 4e^{-(V+50)/18}$, $\alpha_h = 0.07e^{-0.05V-2.5}$, $\beta_h = 1/(1 + e^{-0.1V-2})$, $\alpha_n = 0.01(20 + V)/(1 - e^{-0.1V-2})$ and $\beta_n = 0.125e^{-(V+30)/80}$.

The explicit interpretation of Chay model was given in previous studies (Chay 1985; Gu et al. 2001, 2011a). v_c is the reversal potential of Ca^{2+} ion. The parameter values are $v_i = 100$ mV, $v_k = -75$ mV, $v_l = -40$ mV, $g_{kc} = 10$ mS/cm², $g_{kv} = 1,700$ mS/cm², $g_i = 1,800$ mS/cm², $g_l = 7$ mS/cm², $\lambda_n = 221.6$, $k_c = 3.3/18$ and $\tau_c = 1/0.27$, respectively.

Chay model is an ordinary system with fast variables and slow variable, similar to many theoretical neuronal model such as Hindmarsh-Rose model (Izhikevich 2000, 2007). The fast variables are V and n , and the slow variable is C . The system composed of fast and slow variables can manifest some special characteristics, such as extraordinary Feigenbaum constants within period doubling bifurcation cascades (Wu and He 2000, 2001) or intermittent chaos between those of type I and type V (Wang et al. 2010).

The model is solved by 4-th Runge-Kutta integration method with integration step being 10^{-3} s. An action potential is said to occur when the voltage crossed a value of -20.0 mV from below.

Methods to analyze the chaotic firing

Nonlinear prediction

The deterministic property of chaotic rhythm is estimated by computing the normalized prediction error (NPE) of the ISI series, using the simple nearest-neighbor method (Farmer and Sidorowich 1987; Sauer 1994; Gu et al. 2004; Yang et al. 2009) whose algorithm is as follows:

With a reconstruction dimension m , an time series, $t_i (i = 1, 2, \dots, L)$, is transformed to $L - m + 1$ state points in space R^m . For a point $V_n = (t_n, t_{n+1}, \dots, t_{n+m-1})$ ($n = 1, 2, \dots, L - m + 1$) in space R^m , $M = \beta(L - m + 1)$ points nearest to V_n are chosen and written as $U_k = (t_{j_k}, \dots, t_{j_k+m-1}) (1 \leq k \leq M)$. The average $p_{n,h} = \frac{1}{M} \sum_{k=1}^M t_{j_k+h}$ is then used to approximate the future value t_{n+h} . The difference $p_{n,h} - t_{n+h}$ is the h -th step prediction error for point V_n . For all state points, the normalized prediction error (NPE) is defined as

$$NPE = \frac{(\frac{1}{L-m+1} \sum_{n=1}^{L-m+1} (p_{n,h} - t_{n+h})^2)^{\frac{1}{2}}}{(\frac{1}{L-m+1} \sum_{n=1}^{L-m+1} (\bar{t} - t_{n+h})^2)^{\frac{1}{2}}} \quad (4)$$

where $\bar{t}$ is the average of time series t_i . From the definition, a value of NPE much less than 1.0 means that there is linear or nonlinear predictability in the time series beyond the baseline prediction of the series mean.

NPE of raw data and surrogate data (Theiler et al. 1992; Ren et al. 2001; Gu et al. 2004, 2007; Yang et al. 2009) are calculated. The surrogate data generated by random shuffle method, shuffling the original sequence randomly, has the same probability distribution as the original data, but the deterministic temporal structures within ISI series are broken. NPE value of the original chaotic ISI series is much less than 1 in a short term of prediction and approaches 1 in a long term, while which of the surrogate data (10 realizations) always nearly equals to 1, showing the deterministic property of the original series.

In this paper, NPE is calculated with $m = 4$ and $\beta = 2\%$.

Detection of unstable periodic orbit

A method to detect unstable periodic orbits (UPOs), based on an algorithm of enhancing density (So et al. 1996, 1997, 1998) and tested in a series of studies (Ren et al. 2001; Gu et al. 2004, 2007; Lu et al. 2008; Yang et al. 2009), is employed in this paper.

The basic strategy of the method is to transform the time series by using information of local linear dynamics along a trajectory, such that the transformed series is concentrated on the periodic orbits. Histograms of the transformed data thus have sharp peaks at the locations of the periodic orbits where can then be read off. This reduces the identification of UPOs to simply looking for peaks in the distribution of the transformed data. The statistical significance of these peaks (i.e. UPOs) can be assessed by the probability of these peaks with help of the multiple realizations of surrogate data and the statistics of extremes. The significance of UPOs is interpreted in terms of the probability of the density of transformed data fall outside of the distribution of maximal peaks extracted from the density of all the transformed surrogates. The locations whose probability are more than certain value are thought to be significant UPOs. In this paper, 100 surrogates are done for each original chaotic ISI series. The probability more than 95% is thought to be significant. With help of the first return map, the sequence of the k discrete pieces can be identified for a period- k orbit. In a delay embedded state space, a period- k orbit comprises k discrete pieces that are cyclically symmetrical.

Experimental results of bifurcation process

Bifurcation processes

Period-adding bifurcation process, including period adding bifurcation with chaos (Ren et al. 1997; Gu et al. 2004, 2007; Xu et al. 2007) and with stochastic firing patterns (Gu et al. 2003, 2004, 2007; Yang et al. 2009), are the most popular bifurcation process in the experimental neural pacemaker. The procedure of the period-adding bifurcation with chaos is from period-1 firing firstly, and then to period-2 firing, to chaotic firing, to period-3 firing, to chaotic firing, at last to period-4 firing, as shown in Fig. 1a. The period-adding bifurcation scenario with stochastic firing is another popular bifurcation process, changed from period-1 firing, to stochastic firing, to period-2 firing, to stochastic firing, to period-3 firing, to stochastic firing, to period-4 firing, to stochastic firing, and to period-5 firing, as shown in Fig. 1b.

In addition, when $[Ca^{2+}]_o$ was decreased from 1.2 mmol/L to zero, a bifurcation process from bursting to spiking pattern, including the period-doubling bifurcation to chaos, can be manifested in a few pacemakers, reported in previous study (Li et al. 2003) and shown in Fig. 2. Unfortunately, the chaotic firing can not change into a periodic firing before the “shrink” phenomenon (Chay et al. 1995).

Fig. 1 Period-adding bifurcation process of the neural firing pattern recorded in the experimental neural pacemaker when $[Ca^{2+}]_o$ was decreased. **a** Period-adding bifurcation scenario with chaotic firing; **b** Period-adding bifurcation scenario with stochastic firing

In this paper, we change the experimental scheme, $[Ca^{2+}]_o$ decreased to from 1.2 to 0.6 mmol/L instead, to study period-doubling bifurcation to chaos. Based on the new scheme, three cases of bifurcation processes related period-doubling bifurcation to chaos firstly and then to periodic firings were observed in different neural pacemakers. Case I, II and III bifurcation processes were discovered in 3, 4 and 24 pacemakers, respectively.

Case I bifurcation process

Bifurcation procedure

An example of case I bifurcation process is as follows. Period-1 firing is changed to period-2 firing firstly, and then to period-4 firing, to chaotic firing and at last to period-5 firing. The spike trains of the period-1, 2, 4, 5 and the chaotic firing patterns are shown in Fig. 3a–e, respectively.

The bifurcation process of the ISIs is shown in Fig. 4a. The ISI numbers in the ISI series of period-1, period-2, period-4, chaotic and period-5 firings are 0–550, 551–2260, 2261–2500, 2500–4250 and 4251–4600, respectively. Another example of case I bifurcation process is illustrated in Fig. 4b.

Fig. 2 Bifurcation process from bursting to spiking observed in the experimental neural pacemaker when $[Ca^{2+}]_o$ was decreased from 1.2 mmol/L to zero. **a** Period-1 bursting is changed into period-2 firstly and then to period-2 bursting, to period-4 ($\pi(2,2)$) bursting, to chaotic bursting, via “shrink” to spiking pattern (chaotic spiking, to period-2 spiking, at last to period-1 spiking). **b** A bifurcation process similar to (a)

Differences between firing patterns

According to Fan’s proposal (Fan and Holden 1992a, b, 1993; Fan and Chay 1994), the period-1, period-2, period-4 and period-8 firing patterns lying in a period-doubling bifurcation cascades were called $\pi(1)$, $\pi(2)$, $\pi(2,2)$ and $\pi(2,2^2)$, respectively. The firing patterns such as period-3, period-4 and period-5 lying in the period-adding bifurcation scenario should be called $\pi(3)$, $\pi(4)$ and $\pi(5)$, respectively. $\pi(3)$, $\pi(4)$ and $\pi(5)$ firing patterns were also named as type I bursting according to the classification proposed by Rinzel (1987) or saddle-homoclinic bursting according to the definition by Izhikevich (2000), respectively. The ISIs within a period of $\pi(3)$, $\pi(4)$ and $\pi(5)$ firing pattern should be increased monotonously.

The four ISIs within a period of the period-4 firing, beginning from the shortest ISI, are labeled as ISI_1 , ISI_2 , ISI_3 and ISI_4 , respectively. For the $\pi(2,2)$ firing, $ISI_1 < ISI_3 < ISI_2 < ISI_4$, as shown in Figs. 3d and 5a. For $\pi(4)$ firing, $ISI_1 < ISI_2 < ISI_3 < ISI_4$. The differences within

Fig. 3 Spike trains of the different firing patterns lying in the period-doubling bifurcation to chaos. **a** Period 1 firing; **b** Period 2 firing; **c** Period 4 ($\pi(2,2)$) firing; **d** Period 5 firing; **e** Chaotic firing

ISI sequence between the $\pi(2,2)$ and $\pi(4)$ firings lead to different locations of the four points in the first return map of ISI series. The four points are (ISI_1, ISI_2) , (ISI_2, ISI_3) , (ISI_3, ISI_4) and (ISI_4, ISI_1) , respectively, labeled as P12, P23, P34 and P41, respectively, as shown in Fig. 4b, d. For $\pi(2,2)$ firing, the point P34 is between the point P12 and point P23 in space. While for $\pi(4)$ firing, the point P23 is between the point P12 and point P34. The $\pi(4)$ firing shown in Fig. 5 is that lies in the period-adding bifurcation scenario with stochastic firing shown in Fig. 1b.

The spike train of the $\pi(4)$ firing is shown in Fig. 5e, different to that of $\pi(2,2)$ firing shown in Fig. 3c.

For the period-5 firing lying in case I bifurcation scenario, the 5 ISIs did not increase monotonously, as shown in Figs. 3d and 6a, showing that the period-5 firing is non- $\pi(5)$ firing. The 5 ISIs of period-5 ($\pi(5)$) firing, lying in the period-adding bifurcation scenario with stochastic firing (Fig. 1b), increase monotonously, as shown in Fig. 6c. The

five ISIs beginning from the shortest ISI within a period are labeled as ISI_1 , ISI_2 , ISI_3 , ISI_4 and ISI_5 , respectively. The 5 points in the first return map of ISI series are (ISI_1, ISI_2) , (ISI_2, ISI_3) , (ISI_3, ISI_4) , (ISI_4, ISI_5) and (ISI_5, ISI_1) , labeled as P12, P23, P34, P45 and P51, respectively. The differences within the ISI sequence between two kinds of period-5 firing also lead to the different locations of five points in the first return map, as shown in Fig. 6b and d, respectively.

The spike train of $\pi(5)$ firing is shown in Fig. 6e, different to that of non- $\pi(5)$ firing shown in Fig. 3d.

Deterministic mechanism of the chaotic firing

The spike trains and ISI series of the chaotic firing (ISI number is 2501–4250) exhibit irregular characteristics, as shown in Figs. 3e and 4, respectively. Compared to the surrogate data (Fig. 7b), the first return map of the original

Fig. 4 The bifurcation scenario of ISI series from period-1 firing (ISI number is 0–550), to period-2 (551–2260) firing, period-4 ($\pi(2,2)$) firing (2261–2500), to chaotic firing (2501–4250), and to period-5 firing (4251–4600) when $[Ca^{2+}]_o$ was decreased

chaotic ISI series exhibits a deterministic structure, as shown in Fig. 7a, similar to those of the chaotic firings lying in the period-adding bifurcation scenario with chaos (Fig. 1a), as shown in Fig. 7d and e, respectively. The chaotic ISI series can be predicated in a short term but can not be predicated for a long term, as shown in Fig. 7c, showing that the chaotic firing contains deterministic mechanism.

Case II bifurcation process

Bifurcation process

The case II bifurcation process is from period-1 firing (ISI number is 1–1280), changed to period-2 firing (1281–3280), to period-4 ($\pi(2,2)$) firing (3281–3548), to chaotic firing (3549–4700), and to period-4 ($\pi(4)$) firing (4700–5100), as shown in Fig. 8a. In this paper, it is labeled as case II bifurcation scenario, related to period-doubling bifurcation to chaos. The procedure is different to those of the period-adding bifurcation scenarios.

The period-4 ($\pi(2,2)$) firing exhibits characteristic similar to that of cases I (not shown here). The ISI series and the first return map of the period-4 ($\pi(4)$) firing are shown in Fig. 8b and c, respectively, exhibiting characteristics similar to type I bursting.

Deterministic mechanism of the chaos

The first return map of ISI series of the chaotic firing exhibits a deterministic structure, as shown in Fig. 8d. The chaotic ISI series can be predicated in a short prediction step but can not be predicated for a long step, as shown in Fig. 8e, implying that there exists deterministic mechanism within the firing.

Case III bifurcation process

Bifurcation process

The case III bifurcation process is as follows. Period-1 firing (ISI number is 0–550) is changed to period-2 firing (551–3500) firstly, and then to period-4 ($\pi(2,2)$) firing (3501–4200), to chaotic firing (4201–6200), and at last to period-3 ($\pi(3)$) firing (6201–6410), as shown in Fig. 9a.

The period-4 ($\pi(2,2)$) firing is similar to those of case I and II, not shown here. The three ISIs within a period of the period-3 ($\pi(3)$) firing is gradually increased, as shown in Fig. 9b, same as type I bursting. The first return map of ISI series of the $\pi(3)$ firing is shown in Fig. 9c. The bifurcation between the chaotic firing and period-3 ($\pi(3)$) firing is intermittency or tangent bifurcation, studied in the previous study (Wang et al. 2010).

Deterministic mechanism of the chaos

The first return map of ISI series of the chaotic firing exhibit a deterministic structure, as shown in Fig. 9d. The chaotic ISI series can be predicated in a short term but can not be predicated for a long term, as shown in Fig. 9e. It shows that the chaotic firing contains deterministic mechanism.

Non-smooth characteristics

The first return map (Fig. 8d) is composed of four parts, from left to right, an upstroke branch, a branch with a small positive slope, a down-stroke branch with very high negative slope, and a branch with a small negative slope, demonstrates non-smooth like characteristics. The first part, connection between the first and second part, the connection between the second and third part and the third

Fig. 5 **a** ISI series of period-4 ($\pi(2,2)$) firing; **b** The first return map of ISI series corresponding to **(a)**; **c** ISI series of period-4 ($\pi(4)$) firing; **d** The first return map of ISI series corresponding to **(c)**; **e** Spike trains of the period-4 ($\pi(4)$) corresponding to **(c)**

part are sharply non-smooth. In previous study, the intermittent chaos also manifested non-smooth characteristics (Wang et al. 2010).

UPOs detected in the chaotic firings

Case I

Significant unstable period-4 and 5 orbits can be detected in the ISI series of the chaotic firing.

Unstable period-4 orbit

Significant unstable period-4 orbit whose probability is 98% can be detected in the chaotic ISI series when ISI number is between 2501 and 3056.

The results of the chaotic ISI series when ISI number is between 2501 and 2756 are as follows. The first return map of the chaotic ISI series is shown in Fig. 10a. The transformed density of raw ISI series is much higher than the mean density of surrogate data, as shown in Fig. 10b. The significant probabilities are higher than 95% at multiple ISI values, as illustrated in Fig. 10c. The unstable period-4 orbit can be identified by the first return map, wherein 4 point groups labeled as P12, P23, P34 and P41, are corresponded to (ISI_1, ISI_2) , (ISI_2, ISI_3) , (ISI_3, ISI_4) and (ISI_4, ISI_1) , respectively, as shown in Fig. 10d. ISI_1 is about 0.0052 s. ISI_2 is between 0.02 and 0.035 s. ISI_3 is between 0.01 and 0.02 s. ISI_4 is about 0.058 s. The locations and ISI sequence of the unstable period-4 orbit are similar to those of the neighbouring period-4 ($\pi(2,2)$) firing shown in Fig. 3b. This unstable period-4 orbit is called as unstable period-4 ($\pi(2,2)$) orbit in this paper.

Fig. 6 **a** The ISI series of period-5 firing corresponding to Fig. 1d; **b** The first return map of ISI series corresponding to (a); **c** The ISI series of period-5 ($\pi(5)$) firing; **d** The first return map of ISI series corresponding to (c); **e** Spike train of the period-5 ($\pi(5)$) firing

Unstable period-5 orbit

Significant unstable period-5 orbit whose probability is 100% can be detected in the chaotic ISI series when ISI number is between 3051 and 4250. The results of the chaotic ISI series when ISI number is 3901–4156 are illustrated in Fig. 12.

The first return map of the chaotic ISI series, transformed density and significant probability of unstable period-5 orbit are shown in Fig. 11a–c, respectively. The first return map of the unstable period-5 orbit exhibits 5 point groups, labeled as P12, P23, P34, P45 and P51, as shown in Fig. 12d. The five ISIs of unstable period-5 orbit should be ISI_1 (0.0046 s), ISI_2 (0.0052–0.0112 s), ISI_3 (0.022–0.0356 s), ISI_4 (0.0052–0.008 s) and ISI_5 (0.0592–0.066 s). The locations and ISI sequence of the unstable period-5 orbit are similar to those of the neighbouring period-5 firing shown in Fig. 5b.

Case II

A single unstable period-4 ($\pi(2,2)$) orbit

A single significant unstable period-4 ($\pi(2,2)$) orbit whose probability is 100% can be detected in the chaotic ISI series near period-4($\pi(2,2)$) firing, when ISI number is between 3549 and 3676.

The results of unstable period-4 orbit detected in the chaotic ISI series when ISI number is between 3549 and 3804 are shown in Fig. 12. The significant probability is shown in Fig. 12a. The first return map of the unstable period-4 ($\pi(2,2)$) orbit is shown in Fig. 14b, whose locations and ISI sequence are similar to those of the $\pi(2,2)$ bursting. The period-4 ($\pi(2,2)$) orbit should be ISI_1 (0.002–0.004 s), ISI_2 (0.008–0.012 s), ISI_3 (0.005–0.01 s) and ISI_4 (0.044–0.048 s) in sequence.

Fig. 7 **a** The first return map of the chaotic ISI series (ISI number is 2500–4250); **b** The first return map of the surrogate data of the chaotic ISI series corresponding to **(a)**; **c** Nonlinear prediction of the chaotic ISI series; *lower line*, original data; *upper line*, surrogate data. **d** The first return map of the chaotic ISI series lying between period-2 firing and period-3 firing corresponding to Fig. 1a; **e** The first return map of the chaotic ISI series lying between period-3 firing and period-4 firing corresponding to Fig. 1a

A single unstable period-4 ($\pi(4)$) orbit

A single significant unstable period-4 ($\pi(4)$) orbit whose probability is 100% can be detected in the chaotic ISI series near period-4 ($\pi(2,2)$) firing, when ISI number is between 4027 and 4700. The results of the chaotic ISI series when ISI number is between 4149 and 4404 are shown in Fig. 13.

The significant probability of unstable period-4 ($\pi(4)$) orbit is shown in Fig. 13a. The first return map of the unstable period-4 ($\pi(4)$) orbit exhibits 4 point groups with circle symmetry, as shown in Fig. 13b. The unstable period-4 ($\pi(4)$) orbit should be $ISI_1(0.0015\text{--}0.0040\text{ s})$, $ISI_2(0.0057\text{--}0.0070\text{ s})$, $ISI_3(0.0070\text{--}0.0090\text{ s})$ and $ISI_4(0.0460\text{--}0.0490\text{ s})$ in sequence. The locations and ISI series of the unstable period-4 orbit are not similar to those of the ($\pi(2,2)$) orbit, but similar to those of $\pi(4)$ bursting.

Coexistence of unstable period-4 ($\pi(2,2)$) orbit and unstable period-4 ($\pi(4)$) orbit

Both of significant unstable period-4 ($\pi(2,2)$) orbit and unstable period-4 ($\pi(4)$) orbit whose probability are both 100% can be detected in the chaotic ISI series when ISI number is between 3805 and 4026.

The results of the chaotic ISI series when ISI number is between 3849 and 3976 are shown in Fig. 14. The significant probability of unstable period-4 orbit is shown in Fig. 14a. The corresponding first return map of the unstable period-4 orbit exhibits double 4 point groups with circle symmetry, as shown in Fig. 14b. One is the point groups composed of $P_{2,2}12$, $P_{2,2}23$, $P_{2,2}34$ and $P_{2,2}41$, whose locations and ISI sequence are similar to those of $\pi(2,2)$ firing. The other is composed of $P_{4}12$, $P_{4}23$, $P_{4}34$ and $P_{4}41$,

Fig. 8 **a** Case II bifurcation scenario from period-1 firing, to period-2 firing, to period-4 ($\pi(2,2)$) firing, to chaotic firing, to period-4 ($\pi(4)$) firing. **b** ISI series of period-4 ($\pi(4)$) firing. **c** The first return map of ISI series of the period-4 ($\pi(4)$) firing. **d** First return map of the chaotic ISI series. **e** Nonlinear prediction of the chaotic ISI series. *Lower line*, raw chaotic ISI series; *upper line*, the surrogate data

whose location and ISI sequence are similar to those of $\pi(4)$ firing. The results provide an interesting phenomenon that two different unstable period-4 orbits, $\pi(2,2)$ orbit and $\pi(4)$ orbit, coexist.

Case III

Unstable period-4 ($\pi(2,2)$) orbit

Significant unstable period-4 ($\pi(2,2)$) orbit whose probability is 98% is detected in the chaotic ISI series when ISI number is between 4201 and 5225.

The significant probability of unstable period-4 orbit when ISI number is between 4201 and 4256 is shown in Fig. 15a. The first return map of the unstable period-4 orbit exhibits 4 point groups whose locations and ISI sequence are similar to those of the period-4 ($\pi(2,2)$) firing, as

shown in Fig. 15b. The period-4 ($\pi(2,2)$) orbit should be $ISI_1(0.0043\text{--}0.0047\text{ s})$, $ISI_2(0.015\text{--}0.02\text{ s})$, $ISI_3(0.005\text{--}0.008\text{ s})$ and $ISI_4(0.041\text{--}0.044\text{ s})$ in sequence.

Unstable period-3 orbit

Significant unstable period-3 ($\pi(3)$) orbit whose probability is 100% is detected in the chaotic ISI series when ISI number is between 4701 and 6200.

The significant probability of unstable period-3 orbit is shown in Fig. 16a. The first return map of the unstable period-3 orbit exhibits 3 point groups with triangular symmetry, whose locations and ISI sequence are similar to those of the period-3 ($\pi(3)$) firing, as shown in Fig. 16b. The period-3 orbit should be $ISI_1(0.004\text{--}0.005\text{ s})$, $ISI_2(0.008\text{--}0.01\text{ s})$ and $ISI_3(0.041\text{--}0.047\text{ s})$ in sequence, as shown in Fig. 18b.

Fig. 9 **a** Case III bifurcation process from period-1 firing, to period-2 firing, to period-4 ($\pi(2,2)$) firing, to chaotic firing, to period-3 ($\pi(3)$) firing. **b** ISI series of period-3 ($\pi(3)$) firing. **c** First return map of the ISI series of period-3 firing. **d** First return map of the chaotic ISI series. **e** Nonlinear prediction of the chaotic ISI series. *Lower line*, raw chaotic ISI series; *upper line*, the surrogate data

Simulation results of case III bifurcation process

Case III bifurcation processes

When v_c is decreased, a period-doubling bifurcation cascades whose process is from period-1, to period-2 ($v_c = 265.9$), to period-4 ($\pi(2,2)$) ($v_c = 186.11$), to period-8 ($\pi(2,2^2)$) ($v_c = 183.12$), to period-16 ($v_c = 182.75$), and so on, then to chaos, at last to period 3 ($\pi(3)$) is simulated in Chay model, as shown in Fig. 17a. In this condition, the ranges of v_c of period-2, period-4 and period-8 ($\pi(2,2^2)$) are 79.69, 2.99 and 0.37, respectively. The period-4 exists in a narrow range and period-8 exists in a very narrow range. The results show that period-8 seldom appear while the period-4 appear occasionally before chaos in the period-doubling bifurcation cascades to chaos.

Extra-large Feigenbaum constant

The Feigenbaum constants are about $79.69/2.99 \approx 26.65$ and $2.99/0.37 \approx 8.08$, much higher than 4.669 in Logistic map which is a smooth system, similar to those in a non-smooth map or Hindmarsh-Rose model to simulate the quasi-discontinuous characteristic in previous studies (Wu and He 2000, 2001). It is the extra-large Feigenbaum constants that induce the narrow ranges of the higher-dimensional periodic behaviors, such as period-8, within the period-doubling bifurcation cascades.

Quasi-discontinuous characteristics in the map

The first return map of ISI series of the chaos corresponding to $v_c = 181$ mV is shown in Fig. 18a, similar to that of the experiment shown in Fig. 9d. The first return

Fig. 10 **a** The first return map of chaotic ISI series (ISI series number is 2501–2756). **b** Transformed density of unstable period-4 orbit of original data (*thin line*) and mean transformed density of 100 realizations of surrogate data (*solid line*). **c** Significant probability of unstable period-4 orbit. **d** The first return map of the unstable period-4 ($\pi(2,2)$) orbit, exhibiting 4 point groups with cycle symmetry

Fig. 11 **a** The first return map of chaotic ISI series (ISI series number is 3901–4156). **b** Transformed density of the unstable period-5 orbit of original data (*thin line*) and mean transformed density of 100 realizations of surrogate data (*solid line*). **c** Significant probability of the unstable period-5 orbit. **d** The first return map of the unstable period-5 orbit, exhibiting 5 point groups with cycle symmetry

map of slow variable C when V reaches maximal values is illustrated in Fig. 18b. The map contains a part manifesting a high negative slope (as shown with the arrow), being as the quasi-discontinuous characteristic, according to the definition in previous studies (Wu and He 2000, 2001).

It show that Chay model also manifests quasi-discontinuous characteristic that can induce many features apparently different from those of everywhere-differentiable system, such as the extra-large Feigenbaum constants in this paper and the intermittent chaos similar to those between type I

Fig. 12 UPOs of the chaotic firing near period-4 ($\pi(2,2)$) firing lying in case II bifurcation scenario. **a** Significant probability of the unstable period-4 ($\pi(2,2)$) orbit. **b** The first return map of the unstable period-4 ($\pi(2,2)$) orbit, exhibiting 4 point groups with cycle symmetry

and type V (Wang et al. 2010). The quasi-discontinuous map should be build to further study the dynamics of the period-doubling bifurcation cascades in neuronal firing.

Discussion and conclusion

In this paper, three cases of bifurcation scenarios containing a period-doubling bifurcation to chaos, whose procedure are different to those of period-adding bifurcation scenarios (Ren et al. 1997; Gu et al. 2003, 2004, 2007; Yang et al. 2009), are reported. The period-4($\pi(2,2)$) firing lying in the period-doubling bifurcation cascades have been observed in the spontaneous firing patterns in a few studies on Onchidium pacemaker neuron and the experimental pacemakers (Hayashi et al. 1992; Li et al. 2003). In theory, an ideal period-doubling bifurcation cascades in every-where differentiable system such as Logistic map should include period-1, period-2, period-4($\pi(2,2)$), period-8($\pi(2,2^2)$), and so on. But in the experiment on neural firing, the higher-dimensional periodic behaviors, for

Fig. 13 UPOs of the chaotic firing near period-4 ($\pi(4)$) firing lying in case II bifurcation scenario. **a** Significant probability of the unstable period-4 ($\pi(4)$) orbit. **b** The first return map of the unstable period-4 ($\pi(4)$) orbit, exhibiting 4 point groups with cycle symmetry

instance, period-8, are difficult to be observed because the neuronal system manifest quasi-discontinuous characteristics (Wu and He 2000, 2001) induced by the interaction between the fast and slow variables (Rinzel and Lee 1987). In such systems, extra-large Feigenbaum constant is exhibited, led to that higher-dimensional periodic behaviors appear within an extra-narrow parameter range or disappear (Wu and He 2000, 2001). Up to now, the period-4($\pi(2,2)$) appears in a few experimental neural pacemakers while the period-8($\pi(2,2^2)$) seldom appear. In general, chaos generated after a cascade of a period-doubling bifurcations from period-1 bifurcates into period-3, such as the experimental discovery on Onchidium pacemaker (Hayashi et al. 1992) and case III bifurcation process in this paper, and the theoretical simulations. The period-3 firing whose ISIs increase gradually, is classified as type I bursting related to intermittency, or tangent bifurcation. The intermittent chaos near period-3 firing was studied in Ref. Wang et al. (2010). But the mechanism that generated

Fig. 14 Coexistence of unstable period-4 ($\pi(2,2)$) orbit and unstable period-4 ($\pi(4)$) orbit of the chaotic firing lying in case II bifurcation scenario when ISI number is between 3849 and 3976. **a** Significant probability of the unstable period-4 orbit. **b** The first return map of the unstable period-4 ($\pi(2,2)$) orbit and period-4 ($\pi(4)$) orbit, exhibiting double 4 point groups with circle symmetry

after a cascade of a period-doubling bifurcations from period-1 bifurcate into period-5 (non- $\pi(5)$) firing in case I bifurcation process and into period-4 ($\pi(4)$) firing in case II bifurcation process remain unclear, awaited further studies.

With help of the first return map, nonlinear prediction and detection of UPOs, the deterministic mechanism within the chaotic firings lying between period-4 ($\pi(2,2)$) firing and period- k firing ($k = 5, 4$ and 3 , respectively) are analyzed. The first return map of ISI series exhibit deterministic structures and non-smooth characteristic. Unstable period-4 ($\pi(2,2)$) orbit and unstable period- k ($k = 5, 4$, and 3 , respectively) orbit can be detected in the chaotic firing. The classifications and evolutions of UPOs in the chaotic firing build a close relationship between the chaotic firing and neighboring stable periodic firing (Ren et al. 2001; Gu et al. 2004, 2007). For all three bifurcation scenarios, unstable period-4 ($\pi(2,2)$) orbit could be detected in the chaotic firing near the stable period-4 ($\pi(2,2)$) firing. The locations and ISI sequence of the unstable period-4 ($\pi(2,2)$) orbit are similar to those of the stable period-4 ($\pi(2,2)$) firing. The unstable period- k orbits can be detected in the chaotic firings near corresponding periodic k firings lying

Fig. 15 UPOs of the chaotic firing near period-4 ($\pi(2,2)$) firing lying in case III bifurcation scenario. **a** Significant probability of the unstable period-4 ($\pi(2,2)$) orbit. **b** The first return map of the unstable period-4 ($\pi(2,2)$) orbit, exhibiting 4 point groups with cycle symmetry

in case I ($k = 5$), II ($k = 4$) and III ($k = 3$) bifurcation processes, respectively. The result implies that the unstable periodic orbit is stem from the loss of the stability of the neighboring stable periodic firing. For the chaotic firing lying in case II bifurcation process, both of different unstable period-4 orbits, one is $\pi(2,2)$ orbit and the other is $\pi(4)$ orbit, are detected within an identical ISI series. It show that the co-existence of unstable period-4 orbits with different structures. In addition, unstable period-2 and 3 orbit can also be detected in the different windows of ISI series of chaotic firing lying in case I bifurcation process. But a stable period-3 was not observed in the bifurcation process. The detected unstable period-3 orbit is lack of convincing evidence. Therefore, the unstable period-3 orbit is not given in the results. The results provide examples of chaos with interesting phenomenon of UPOs, such as higher-dimensional UPOs(period-4 and period-5 orbits) and coexistence of two different period-4 orbits (case II). In previous studies, only lower-dimensional UPOs such as

Fig. 16 UPOs of the chaotic firing near period-3 ($\pi(3)$) firing lying in case III bifurcation scenario. **a** Significant probability of the unstable period-3 ($\pi(3)$) orbit. **b** The first return map of the unstable period-3 ($\pi(3)$) orbit, exhibiting 3 point groups with triangular symmetry

period-1, period-2 and period-3 orbit were detected (Pei and Moss 1996, Braun et al. 1997, 1999a, b; So et al. 1998), because chaos lying between two kinds of lower-dimensional periodic firings.

In addition, UPOs were suggested to play important roles in different nervous system (Braun et al. 1997, 1999a, b; So et al. 1998), might be a language for neuronal dynamics. The unstable periodic orbits were detected in the firing recorded in the catfish electroreceptors, which can sense weak external electric fields and respond to the ambient temperature and to the ionic composition of the water, and in the rat facial cold receptors that are unique in response to temperature changes. The lower-dimensional dynamical behavior whose characteristics depend on the ambient temperature range, impulse pattern, and temperature transients were demonstrated. It was speculated that the appearance of unstable orbits in sensory biology may be indicative of a state of heightened sensory awareness by the animal (Braun et al. 1997, 1999a, b). UPOs were

Fig. 17 Period-doubling bifurcation to chaos with respect to decrease of v_c simulated in Chay model

Fig. 18 The first return map in Chay model when $v_c=181\text{mV}$. **a** ISI; **b** The C value when V is maximal

detected in the discharges from a patient with an epileptic focal seizure. The approaches of trajectories toward the unstable periodic patterns were observed in the sequences following the perceptual tasks. It implies that the act of perception contributes to pulling the epileptic activities towards particular unstable periodic orbits (LeVan Quyen et al. 1997). UPOs were detected in the synaptic noise recorded from teleost Mauthner cells. The non-random

component of the noise reproducibly and persistently reduced when the level of background sound, a natural stimulus for networks afferent to the Mauthner cell. The presence of chaos in synaptic noise that can regulate the excitability of the Mauthner cell and its sensitivity to external stimuli suggests that it modulates this neuron's function (Faure and Korn 1987). The potential roles of the evolution of UPOs embedded in the chaotic firing patterns generated in the experimental neural pacemaker, related to neuropathic pain in some studies (Tal and Eliav 1996; Xie and Xiao 1990), should be studied in future.

Acknowledgments Supported by National Natural Science Foundation of China under Grant Nos 11072135, 10772101 and 30300107, as well as by the Fundamental Research Funds for the Central Universities under Grant No. GK200902025.

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