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An alternating periodic–chaotic ISI sequence of HH neuron under external sinusoidal stimulus*

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A study of Hodgkin–Huxley (HH) neuron under external sinusoidal excited stimulus is presented in this paper. As is well known, the stimulus frequency is to be considered as a bifurcate parameter, and numerous phenomena, such as synchronization, period, and chaos appear alternatively with the changing of the stimulus frequency. For the stimulus frequency less than $2f_{\rm B}$ ($f_{\rm B}$ being the base frequency in this paper), the simulation results demonstrate that the single HH neuron could completely convey the sinusoidal signal in anti-phase into interspike interval (ISI) sequences. We also report, perhaps for the first time, another kind of phenomenon, the beat phenomenon, which exists in the phase dynamics of the ISI sequences of the HH neuron stimulated by a sinusoidal current. It is shown furthermore that intermittent transition results in the general route to chaos.

Keywords: Hodgkin–Huxley neuron, period, chaos, bifurcation, stimulus
PACC: 0547, 8730E

1. Introduction

A neuron, fundamental element of the brain, can generate various temporal patterns of spike pulses, and a great deal of researches have been focused on it. As is well known, the neuronal oscillation responds to the periodical stimulus not only periodically, but also chaotically.[1] Based on the Poincaré sections, in the papers of Aihara *et al*[2–4] the oscillation of membrane potential of a squid giant axon has been experimentally analysed. The chaos appears in the subthreshold dynamics when the squid giant axon is stimulated periodically,[5] and one can use the external periodic stimulus to control the degree of chaos by means of computing the quantitative characteristics of the chaotic outputs, such as spectrum, correlation dimension, and the largest Lyapunov exponent, as in Ref.[6]. The responses of a squid giant axon could be categorized into three kinds: phase-periodic, quasi-periodic and chaotic.[2,7] Synchrony firing of coupled neurons has been studied in Ref.[8].

The main function of the nervous system is to collect, process, and store information from both the internal and external environments, and then respond with appropriate reactions. Neural information is conveyed along nerve fibres in the form of series of propagating action potentials and encoded in the ISI sequence. In this work, the numerical simulation is conducted to study the neuron of the Hodgkin–Huxley (HH) model. The transitions of chaos and alternating periodic–chaotic sequence have been observed in the oscillation of neuron, which is stimulated periodically. In other words, the chaotic oscillation, periodical synchronized oscillation, and beat oscillation takes place successively in the ISI sequence during the variation of the stimulus frequency; and for a few of fixed stimulus frequency, this alternation actually occurred.

2. HH model neuron

As is well known, the HH model equations have been derived from a squid giant axon. These equations can describe the spiking behaviour and refractoriness of a real neuron very well (see Refs.[9–11]), thus this kind of model is employed in this work. The HH equations include four first-order ordinary differ-

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ential equations as follows:

$$C\frac{\mathrm{d}V}{\mathrm{d}t} = -g_{Na}m^3h(V-V_{Na}) - g_Kn^4h(V-V_K) - g_L(V-V_L) + I_{\text{ext}},$$
$$\frac{\mathrm{d}m}{\mathrm{d}t} = \frac{m_\infty - m}{\tau_m}, \quad \frac{\mathrm{d}n}{\mathrm{d}t} = \frac{n_\infty - n}{\tau_n}, \quad \frac{\mathrm{d}h}{\mathrm{d}t} = \frac{h_\infty - h}{\tau_h}, \tag{1}$$

where

$$m_\infty = \frac{\alpha_m}{\alpha_m+\beta_m}, \quad n_\infty = \frac{\alpha_n}{\alpha_n+\beta_n}, \quad h_\infty = \frac{\alpha_h}{\alpha_h+\beta_h},$$
$$\tau_m = \frac{1}{\alpha_m+\beta_m}, \quad \tau_n = \frac{1}{\alpha_n+\beta_n}, \quad \tau_h = \frac{1}{\alpha_h+\beta_h},$$

with

$$\alpha_m = \frac{0.1(V+40)}{1-\exp\left(-\frac{V+40}{10}\right)},$$
$$\beta_m = 4\exp\left(-\frac{V+65}{18}\right),$$
$$\alpha_n = \frac{0.01(V+55)}{1-\exp\left(-\frac{V+55}{10}\right)},$$
$$\beta_n = 0.125\exp\left(-\frac{V+65}{80}\right),$$
$$\alpha_h = 0.07\exp\left(-\frac{V+65}{20}\right),$$
$$\beta_h = \frac{1}{1+\exp\left(-\frac{V+35}{10}\right)}.$$

The first equation describes the functional relation of the following variables: the time evolution of membrane voltage (V), membrane current, ionic current, and external stimulus current (including synaptic current). The ionic current is the summed current of sodium, potassium, and leakage, i.e.

$$I_{\text{ion}} = -g_{\text{Na}}m^3h(V-V_{\text{Na}}) - g_{\text{K}}n^4h(V-V_{\text{K}}) - g_{\text{L}}(V-V_{\text{L}}), \tag{2}$$

where I_{ion} is coupled with the gating dynamics of three different ionic currents m, n and h; g_{Na}, g_{K}, and g_{L} are maximum conductance; V_{Na}, V_{K}, and V_{L} are reversal potential; m_∞, n_∞, and h_∞ are saturation values; τ_m, τ_n, and τ_h represent relation time of gating variable.[8] Due to the coupling of these nonlinear equations, a sort of complex behaviour with the neuron appears.

The parameters are set at C=1μF/cm^2, g_{Na}=120mS/cm^2, g_{K}=36mS/cm^2, g_{L}=0.3mS/cm^2, V_{Na}=50mV, V_{K} = $-$77mV, V_{L} = $-$54.4mV; α_m, α_n, α_h, β_m, β_n, and β_h are defined as dimensionless factors.[10,11] The initial values of m, n, h, membrane potential, and integral step are 0.1, 0.4, 0.45, $-$65 and 0.05, respectively. The excitation current of the external stimulus I_{ext} is sinusoidal.

3. Simulation results and discussion

3.1. Periodical stimulation and interspike interval (ISI) sequence

The investigation is focused on the single HH neuron stimulated periodically by a sinusoidal current $I_{\text{ext}} = A + \sin(2\pi f_{\text{B}}t)\mu\text{A/cm}^2$, where A is the amplitude of shift and $f_{\text{B}} = \frac{1}{3000}\text{ms}^{-1}$ is the base frequency in this paper. Figure 1 shows the oscillation of a typical dynamical response of the membrane potential, and the oscillation of the ISI sequence of single HH neuron under a sinusoidal current I_{ext} with A=10μA/cm^2, $f_{\text{B}} = \frac{1}{3000}\text{ms}^{-1}$. It is clear that neuronal ISI (as shown in Fig.1(c)) oscillates in the manner of anti-phase synchrony as contrasted with that for external stimulus current (as shown in Fig.1(a)).

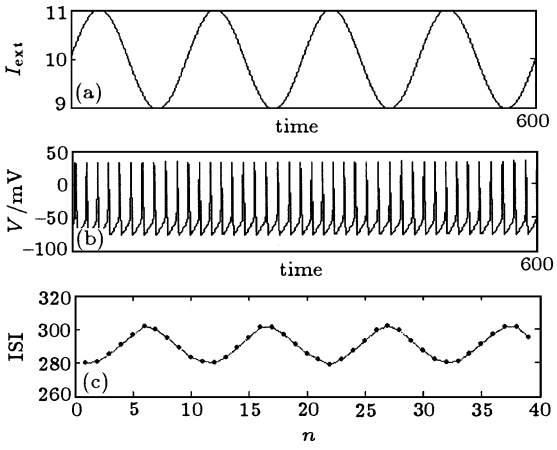


Fig.1. Evolution of membrane potential V (b) and ISI ($\times$0.05ms, marked by dots) (c) of HH neuron under external sinusoidal stimulus I_{ext} (μA/cm^2) (a), the duration of stimulus time being 600ms.

3.2. Bifurcation and response pattern classification

While the amplitude of the shift of the stimulating current A is fixed at 10μA/cm^2, and the bifurcation parameter,[12,13] i.e. the stimulation frequency, is changed from $0.1f_{\text{B}}$ to $50f_{\text{B}}$, the chaotic oscillation, periodical synchronized oscillation and beat oscillation will take place alternately as an ISI sequence.

3.2.1. Synchronous oscillation

In the range of frequency from $0.1f_{\text{B}}$ to $2f_{\text{B}}$, the

neuron exhibits synchronous behaviour followed along with the external stimulus current. Namely, the neuron's ISI varies in the manner of anti-phase synchronization, as shown in Fig.1 and explained in detail in the foregoing paragraph. And there is a gradually increasing delay time along with the stimulus frequency changes from $0.1f_{\mathrm{B}}$ to $2f_{\mathrm{B}}$.

3.2.2. Beat oscillation

When stimulation frequency changes from $2.1f_{\mathrm{B}}$ to $50f_{\mathrm{B}}$, a great deal of phase dynamics will alternate in the ISI sequence successively. It is observed that the HH neuron driven by sinusoidal current is sensitive to certain stimulus frequencies, which means that the beat phenomenon (shown in Figs.2(a) and (b)) exists at several locations; this phenomenon implies that if two harmonic functions with equal amplitude and nearly equal frequency are added, then the resulting function will be an amplitude-modulated harmonic function with a frequency equal to their average frequency, where the frequency of modulation is called the beat frequency (BF). For example, when the stimulus frequency increases from $4.5f_{\mathrm{B}}$ to $5.6f_{\mathrm{B}}$ with a step $0.1f_{\mathrm{B}}$, the BF decreases monotonically, and then increases monotonically, the smallest value is approximately 0.6Hz, located at $5.1f_{\mathrm{B}}$. The similar state occurs at several locations, such as in the range of 36–$37f_{\mathrm{B}}$.

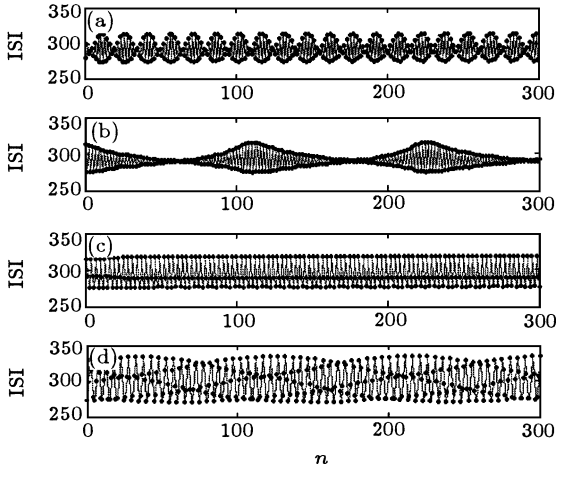


Fig.2. Evolution of ISI ($\times$0.05 ms, marked by dots) of HH neuron under external sinusoidal stimulus with frequency of $4.8f_{\mathrm{B}}$(a), $5.2f_{\mathrm{B}}$(b), $6.8f_{\mathrm{B}}$(c), and $8.0f_{\mathrm{B}}$(d), the duration of stimulus time being 5000ms.

Figures 2(a) and (b) show remarkably the typical phase dynamics of beat phenomenon. As seen from these figures, the BF of Fig.2(b) becomes one seventh of that in Fig.2(a). There are some phenomena, similar to the beat phenomenon, to be found at several locations. They are called quasi-beat phenomena in this paper for the time being. As an example, the ISI sequence is modulated by the five sinusoidal functions as shown in Fig.2(d). Certainly, the ISI sequence could also be modulated by three or four sinusoidal functions in other cases. In Fig.2(c), the period of neuronal spiking is period-three, where the stimulus frequency is $6.8f_{\mathrm{B}}$.

3.2.3. Chaos and period

As shown in Fig.3, an alternating periodic–chaotic sequence appears as the stimulus frequency changes from 11.5–$45f_{\mathrm{B}}$, meanwhile, the beat oscillation occurs in this range of frequency. And two kinds

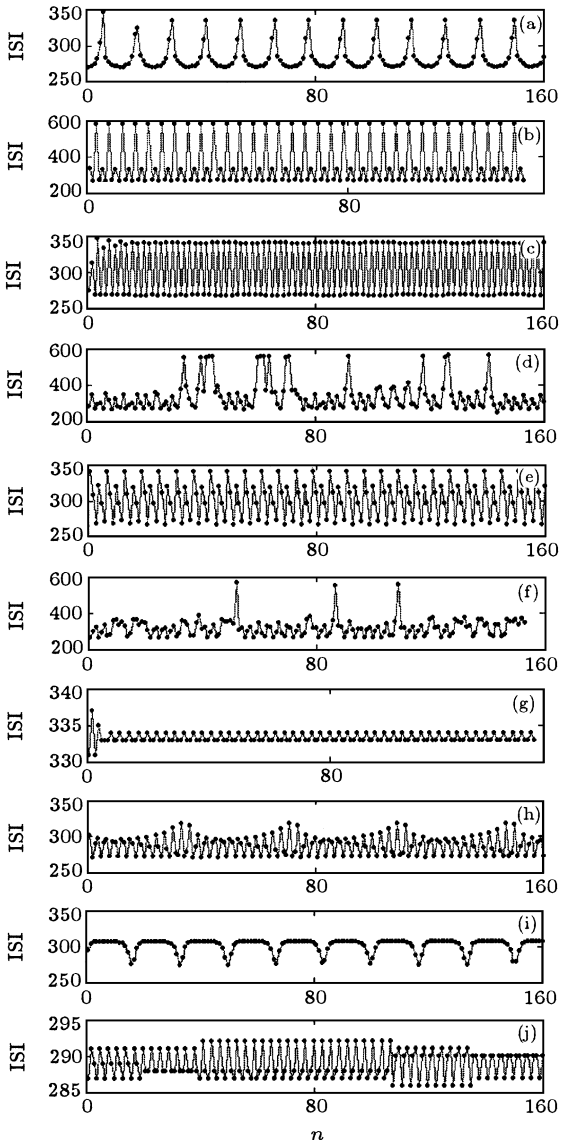


Fig.3. Evolution of ISI ($\times$0.05ms, marked by dots) of HH neuron under external sinusoidal stimulus with frequency of $11.5f_{\mathrm{B}}$(a), $14.5f_{\mathrm{B}}$(b), $14.8f_{\mathrm{B}}$(c), $16.3f_{\mathrm{B}}$(d), $16.6f_{\mathrm{B}}$(e), $16.9f_{\mathrm{B}}$(f), $18f_{\mathrm{B}}$(g), $24.5f_{\mathrm{B}}$(h), $29.3f_{\mathrm{B}}$(i), and $45f_{\mathrm{B}}$(j), the duration of stimulus time being 2500ms.

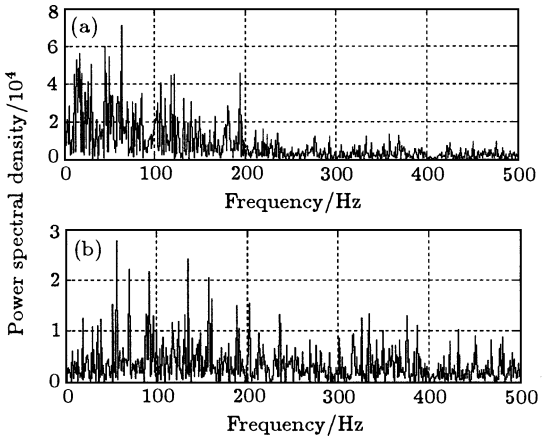


Fig.4. Distribution of power spectral densities of two chaotic ISI sequences. (a) for ISI shown in Fig.3(d); (b) for ISI shown in Fig.3(f).

of burst spiking are found in the HH neuron, the one of slow-bursting is shown in Fig.3(a) and the other is fast-bursting as shown in Fig.3(i). The neuronal periodic spiking are shown in Figs.3(b), (c), (e), and (g), i.e. period-four, period-two, period-six, and period-one, respectively. The two chaotic ISI sequence are shown in Figs.3(d) and (f), and their power spectral densities are shown in Fig.4. In the ISI sequence shown in Fig.3(d) there is a continuous part of power spectral density (see also Fig.4(a)) apart from its continuous wide flat (see Fig.4(b)) in the ISI sequence shown in Fig.3(f). This phenomenon suggests that the degree of chaos of the first is greater than that of the second. Also, a similar beat oscillation is observed in Fig.3(h). The duration of the ISI sequence varies alternately when the stimulus frequency is fixed at $45f_{\mathrm{B}}$, as shown in Fig.3(j), but the evolution of the ISI keeps the pattern with sub-period-three.

3.2.4. Phase space classification

Some typical attractors [1,14,15] reconstructed from a few of ISI sequences are shown in Fig.5. From these figures, the alternating periodic–chaotic ISI sequence is also obtained when the bifurcation parameter is changed. The attractor shown in Fig.5(b) corresponds to the anti-phase synchronous state, and it is similar to the attractor of sinusoidal signal shown in Fig.5(a), in contrast to the attractors in Fig.5(c) for beat and Fig.5 (d) for chaos state. A similar attractor could be obtained as that in Fig.5(b) when the stimulus frequency is less than $2.0f_{\mathrm{B}}$. The above phenomena show that the HH neuron can transfer the sinusoidal signal within this frequency range. In contrast, the single neuron cannot transfer the pre-neuron's signal to the post-neuron completely.

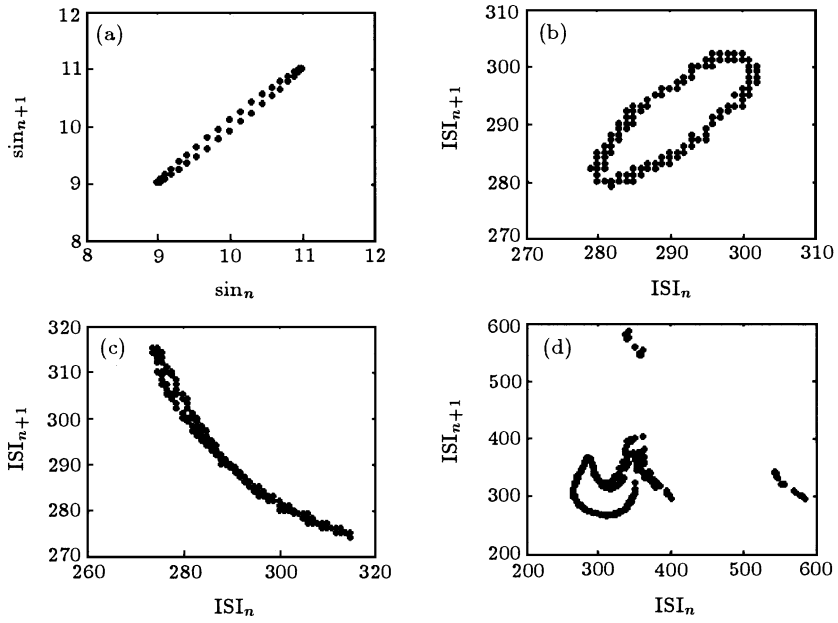


Fig.5. Attractor reconstructed from sinusoidal signal with frequency $45f_{\mathrm{B}}$ (a), from ISI sequences for stimulus frequencies $1.0f_{\mathrm{B}}$ (b), $5.2f_{\mathrm{B}}$ (c), and $16.9f_{\mathrm{B}}$ (d).

3.3. Discussion

Up to now, several types of the neuronal ISI sequence stated in the previous paragraph take place alternately at different stimulus frequencies, and the pattern of transition is different, too, such as period-one into the slow-bursting, chaos into beat, and the fast-bursting into period-one. While the stimulus frequency changes from 17.6–22f_B, the neuronal spike interval remains as period-one with monotonic decay. At several locations, the backward period-adding bifurcation [16] will appear during the changing of stimulus frequency, such as period-three bifurcates into period-two and period-two into period-one while the stimulus frequency is continuously increased from 14.7–14.8f_B and from 17.5–17.6f_B, respectively. These behaviours of transition were partly observed in the experiment given by Long's dissertation,[17] and the author suggested that these seem to result from the effect of the elements of biophysical chemistry on ionic channels, e.g. on potassium channel.

4. Route to chaos

After studying the chaotic transition near the frequency range mentioned above, it is found that the intermittent transition is the general route to chaos due to the variation of stimulus frequency: i.e., with gradual increase of the stimulus frequency, the behaviour of the ISI's periodic orbit is intermittently interrupted by a finite duration of the 'burst', in which the orbit behaves in a decidedly different manner;[16] and as the stimulus frequency increases substantially above the critical transition threshold, the bursts occur so frequently that the regular oscillation can no longer be distinguished, and the periodic orbit is finally replaced by chaos. The above phenomenon is well illustrated in Fig.6(a) by presentation of four groups in ISI sequences of the route to chaos at the frequency 16.9f_B. From 16.8–16.9f_B with a step 0.005f_B, the position on the top ISI plot of Fig.6(a) at 16.86f_B corresponds to a stable periodic motion, the middle two groups are intermittent tent 'burst' ISI, and the burst becomes more frequent as the stimulus frequency is increased until the motion becomes truly chaotic. In this case, the critical transition threshold is approximately equal to 18.86f_B. Figure 6(b) shows the Poincaré map of ISI(n+10) versus ISI(n) constructed from ISI with 16.865f_B and its schematic traverse tunnel, which displays intermittency of Type-III.[18]

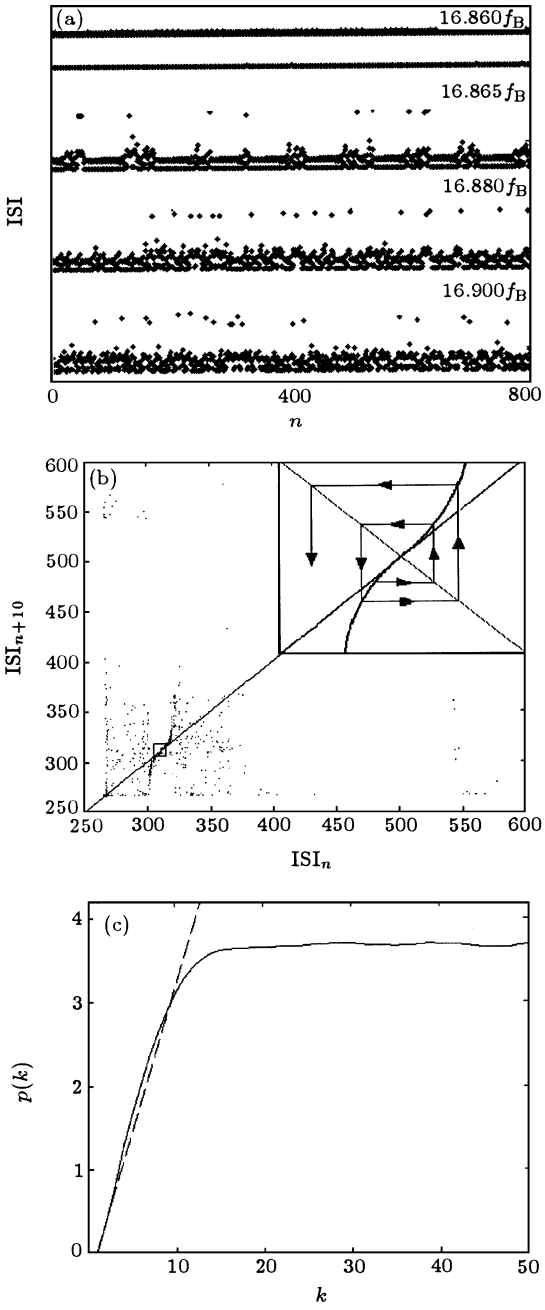


Fig.6. Representative intermittent ISI transition to chaotic oscillation with frequency 16.86f_B, 16.865f_B, 16.88f_B and 16.9f_B (a). Poincaré map ISI(n+10) versus ISI(n) constructed from the data in (a) for 16.865f_B and schematic traverse tunnel (inserted plot) (b). The curve $p(k)$ for estimating the largest Lyapunov exponent at frequency 16.9f_B and its linear part (broken line) (c).

Finally, the largest Lyapunov exponent is estimated by using the nonlinear statistical tests based on the nearest neighbours' dynamics (see details in Ref.[19]). The slope of linear part of the curve dependent variable $p(k)$ with variable number of time step k approaches the largest Lyapunov exponent. Figure 6(c) shows the curve $p(k)$ with the stimulus frequency of 16.9f_B ISI, with embedding dimension m=10, de-

lay time τ=1; and the largest Lyapunov exponent estimated is 0.3186±0.0936.

5. Conclusion

After studying the HH neuron subjected to the excitation of external sinusoidal stimulus, the simulation results show that several kinds of oscillation such as synchronization, period, and chaos appear alternately as the stimulus frequency is changed. It can be reported first that beat oscillation and quasi-beat oscillation exist in the phase dynamics of ISI sequence. Furthermore, the intermittent transition is the general route to chaos, and the single HH neuron cannot completely transfer the pre-neuron's signal to post-neuron by ISI. The results from this work may be helpful for understanding of the complex dynamic behaviour of the neuron.

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