LOCAL LARGEST LYAPUNOV EXPONENT IS CRITICAL TO THRESHOLD VOLTAGE AND REFRACTORY PERIODS FOR HODGKIN-HUXLEY MODEL

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Abstract. It is not known whether the spike threshold voltage and refractory periods in neocortical neurons reflects the reliability of spike timing underlying mechanisms. The paper scrutinizes their relationship with local largest Lyapunov exponent ($lLLE$) in an excitatory Hodgkin-Huxley system under either sinusoidal drive or stochastic Poisson drive. The influence of the forcing on the response of the system is examined in the realm of suprathreshold amplitudes. Our results demonstrate that the average $lLLE$ in spike and non-spike regions is different under the physiological threshold voltage and refractory periods. These dynamics contains

(i) The average values of the $lLLE$ in spike region are almost negative, and almost positive in non-spike region under sinusoidal driving.

(ii) The values in spike region are nearly constant under sinusoidal drive with varying frequency; however, the values in non-spike region are different.

(iii) Under low Poisson spike rate and different Poisson inputs strength, the average values of $lLLE$ almost remain the same constant in spike and non-spike region.

Keywords: Hodgkin-Huxley, Lyapunov exponent, refractory periods, threshold voltage.

2010 Mathematics Subject Classification: 34H25, 92B99, 65L20, 65P20.

1. Introduction

Single neuron is the fundamental elements of every nervous system. Understanding the mechanism of these exquisitely structured elements is an important step to explore the mysteries of the brain. Besides, how do single-cell properties contribute to information processing and, ultimately, behavior? [8] is the core of neuroscience. The reliability of spike timing in the cerebral cortex [4] is a classical problem. Meanwhile, a spike produce in the external drive seems that the neurons are unable to adapt their response threshold to change. But it is well known that many sensory neurons do have adaptive capabilities [8], [5]. So, the threshold is very important to the neurons signal processing and system dynamics.

In addition, Berry et al. [3] investigated the relationship between the refractory period of a neuron and its firing precision. The refractoriness of the membrane in the wake of the action potential is another important quantity. The transitory changes make it harder for the axon to produce subsequent action potentials during an interval [15]. Thus, the refractory periods ensure the excitability of neurons more reasonable.

On the other hand, quantifying structures of attractors of dynamical systems has now become an important and common pursuit in scientific fields [20]. The spectrum of Lyapunov exponents (LEs) contains abundant physical information for dynamical system, and it is usually taken as one of the most important and precise dynamical diagnostics to provide characteristics of attractors [12]. Especially, the existence of positive largest Lyapunov exponent (LLE) is an indicator that determines whether the system is chaotic or not. Therefore, the computations of LLE is a very important part for analyze dynamical systems. For smooth dynamical systems [6], [11], the algorithms for computing the LEs have been well established, which often involve the Gram-Schmidt Reorthonormalization (GSR) procedure [2], [19], [13]. In this paper, we will use an accurate and stable numerical algorithm to compute Lyapunov exponents for the Hodgkin-Huxley system.

Scientists and other researchers focus their interests on the dynamics of systems, and hardly ever kick around the relationship between local largest Lyapunov exponent ($lLLE$) and voltage threshold, refractory periods. And we rarely find this point; thus, this is our motive for discuss these problems. Through some numerical results, we find the results of the average of $lLLE$ over samples are very different in spike and non-spike region under different sinusoidal stimuli, and an important observation is that the average values of $lLLE$ in spike region are nearly constant under different sinusoidal drive with varying frequency, even under low rate Poisson drive cases, at an appropriate choice of threshold voltage and refractory periods. Therefore, we can explain the wide application of the threshold voltage and refractory periods are reasonable from another perspective.

The paper is organized as follows. In Section 2, we briefly introduce the Hodgkin-Huxley model and different H-H structure in different stimuli. In Section 3, we discuss the numerical algorithm of calculating LEs for smooth dynamical systems. In Section 4, we apply the method to H-H model and investigate the relationship between the mean $lLLE$ and threshold, refractory periods for this model under different stimuli. Section 5 contains discussion and conclusion.

2. The Hodgkin-Huxley model

Hodgkin-Huxley model [9] is the well-known model of neural excitability. Some researchers show which combination of dynamical variables governs the threshold operation [18] and how adaptation [1] and spike-generation mechanisms [7] influence spike trains. Therefore, we hope to illustrate what $lLLE$ phenomena will emerge under appropriate threshold and refractory periods.

The dynamic equations for the Hodgkin-Huxley model to be considered in this paper are identical to those used by Sun and Zhou [17]:

$$c\frac{d}{dt}V = -G_{Na}m^3h(V-V_{Na})-G_Kn^4(V-V_K)-G_L(V-V_L)+I^{ext} \tag{2.1}$$

$$\frac{dm}{dt} = \alpha_m(V)(1-m)-\beta_m(V)m \tag{2.2}$$

$$\frac{dh}{dt} = \alpha_h(V)(1-h)-\beta_h(V)h \tag{2.3}$$

$$\frac{dn}{dt} = \alpha_n(V)(1-n)-\beta_n(V)n \tag{2.4}$$

where $C{=}1\mu F/cm^2$ is the cell membrane capacitance and V is its membrane potential, m and h are the activation and inactivation variables of the sodium current, respectively, and, n is the activation variable of the potassium current [5], [9]. The parameters $G_{Na}{=}120mS/cm^2$, $G_K{=}36mS/cm^2$, and $G_L{=}0.3mS/cm^2$ are the maximum conductances for the sodium, potassium and leak currents, respectively, $V_{na} = 50mV$, $V_K = -77mV$, and $V_L = -54.387mV$ are the corresponding reversal potentials.

$$\alpha_m(V) = 0.1(V+40)/(1-\exp(-V+40)/10)) \tag{2.5}$$

$$\beta_m(V) = 4\exp(-(V+65)/18) \tag{2.6}$$

$$\alpha_h(V) = 0.07\exp(-(V+65)/20) \tag{2.7}$$

$$\beta_h(V) = 1/(1+\exp(-(35+V)/10)) \tag{2.8}$$

$$\alpha_n(V) = 0.01(V+55)/(1-\exp(-V+55)/10)) \tag{2.9}$$

$$\beta_n(V) = 0.125\exp(-(V+65)/80) \tag{2.10}$$

There is also a current parameter I^{ext} which stands for an external periodic signal current or poisson current where

$$I^{ext} = I^{sine} = I^{shift} + \sin(2\pi\frac{f}{3}t) \tag{2.11}$$

or

$$I^{ext} = I^{poisson} = -G(t)(V(t)-V_G) \tag{2.12}$$

$I^{shift} = 10\mu A/cm^2$, being the amplitude of current shift, and f being the stimulus frequency, $G(t)$ are the conductances, and V_G is the reversal potential ($V_G^E = 0mV$,

$V_G^I = -80mV$). The dynamics of synaptic interactions by using a continuous function. Therefore, the dynamics of $G(t)$ is governed by

$$\frac{d}{dt}G(t) = -\frac{G(t)}{\sigma_r} + \tilde{G}(t) \tag{2.13}$$

$$\frac{d}{dt}\tilde{G}(t) = -\frac{\tilde{G}(t)}{\sigma_d} + \sum_k F\delta\left(t - T_k^F\right) \tag{2.14}$$

Each neuron is either excitatory or inhibitory, as indicated by its type E, I. In the whole work, we consider the coupled H-H systems with only excitatory neurons: a fast rise and a slow decay timescale ,$\sigma_r = 0.5ms$ and $\sigma_d = 3ms$, respectively.

The system is also driven by stochastic inputs: we use a spike train sampled from a Poisson process with rate r as the stimulus. We denote T_k^F as the kth spike from the poisson input to the neuron and its force strength is F.

Additionally, in order to analyze the $lLLE$ relationship with refractory periods, we will discuss the refractory periods of H-H neuronal model at first. Generally, the period from the initiation of the action potential to immediately after the peak is referred to as the absolute refractory period(ARP). During the ARP, a second stimulus (no matter how strong) will not excite the neuron. After the ARP, if strong enough stimuli are given to the neuron, it may respond again by generating action potentials. So, the period during which a stronger normal stimulus is needed in order to elicit an action potentials is referred to as the relative refractory period (RRP) [14].

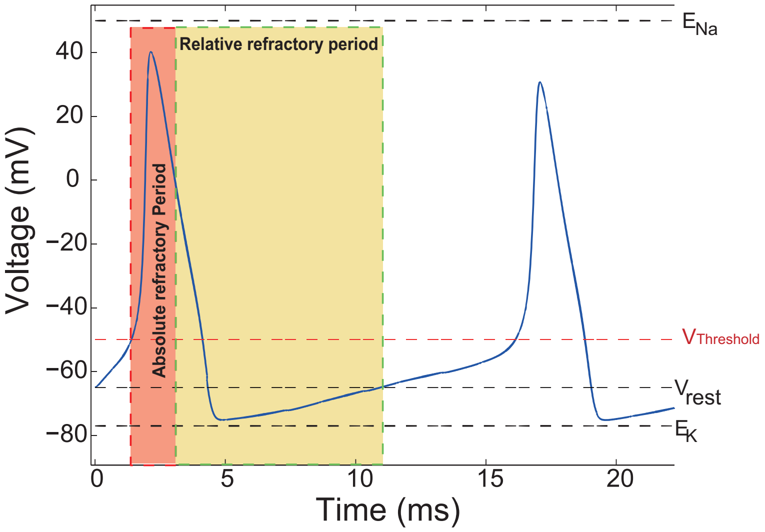


Figure 1: Absolute and relative refractory periods under sine driven at $I^{shift} = 10$, $f = 0$.

The ARP and RRP constitute the refractory periods in this paper. Different neurons have different scales of refractory period. Fig. 1 shows the refractory periods of H-H neuron. The refractory period time is about 10ms.

3. Lyapunov exponents in smooth dynamical systems

Lyapunov exponent is a useful tool for characterizing dynamics in a smooth dynamical system. Especially, the largest Lyapunov exponent (LLE) is very important quantity to measure whether the system is chaotic or not. Generally, the largest Lyapunov exponent λ_1 can be obtained by following two sufficiently close nearby trajectories $\mathbf{X}(t)$ and $\mathbf{X}'(t)$, and set $\mathbf{Z}(t) = \mathbf{X}'(t) - \mathbf{X}(t)$. Sometimes, $\|\mathbf{Z}(t)\|$ may grows unbounded as time interval ΔT is not sufficiently short in the log-ration: $\lambda_1[T_0 + \Delta T] = \frac{1}{\Delta T} \ln(\frac{\|\mathbf{Z}(T_0+\Delta T)\|}{\|\mathbf{Z}(T_0)\|})$. Therefore, a practical approach to avoid numerical overflows is to scale back one of the trajectories, say $\mathbf{X}'(t)$, to the vicinity of the other $\mathbf{X}(t)$ along the direction of separation whenever they become too far apart. We refer to this step as renormalization [13], [16].

To be more specific, the algorithm can be briefly described as Standard algorithm in [20].

In order to obtain that the $lLLE$ is stable, we have compared it with larger running time interval. Therefore, the total iterations of the computation proceeds set as Max_Num in Standard algorithm, the selection of the value of Max_Num is determined by convergence test of the Lyapunov exponent. Here we set the Max_Num is 10^6 when it produces convergent results. Besides, we also compute the LLE by the method described in the paper [10], and find that the result isn't a significant difference between them.

The $lLLE$ obtained by Standard algorithm is very important to analyze the threshold and refractory periods. The detailed analysis will be illustrated as follows.

4. Main results

In the following analysis we focus on the $lLLE$ for the different threshold and refractory periods in spike and non-spike region under either sinusoidal drive or stochastic Poisson drive.

4.1. Periods of external drive

First, we consider a single H-H neuron driven by a sinusoidal external input, which is the frequency f from 0 to 1 in equation (2.11). We perform simulations of this system for different threshold and refractory. A systematic scanning result of the LLE obtained by using the smooth method over a long time interval of $T = 10^5$ ms, as shown in Fig.2, and it demonstrates that there are essentially three dynamical regimes. If LLE is negative, the regime is a stable periodic pattern of spike. At most f, LLE jumps back and forth between zero and positive, it signifies that the dynamics of the system is either quasi-period or chaotic.

We will analyze the average $lLLE$ in these different dynamical regimes under a threshold and refractory which we obtained. Besides, we found that the refractory period time of H-H model is about 10ms (contain absolute refractory periods and relative refractory periods), as appears in Fig. 1.

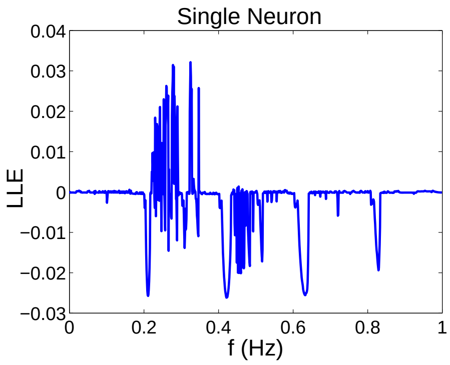
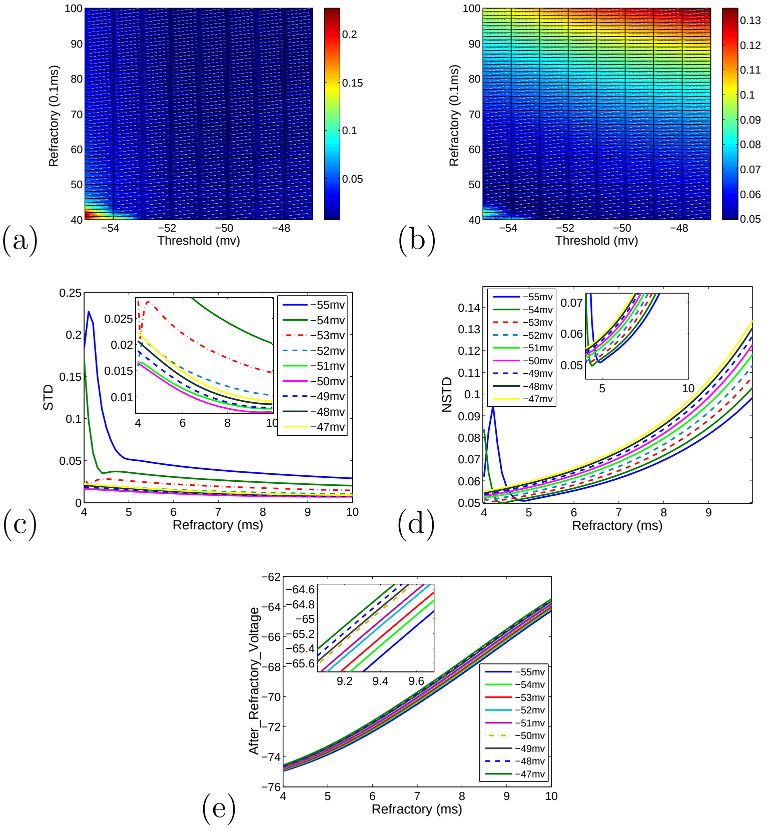


Figure 2: Largest Lyapunov exponent (by standard method) versus parameter f increased with step $0.01/3$ in one H-H neuron.



(a) (b)

(c) (d)

(e)

Figure 3: Pcolor plot of the standard deviation of average $lLLE$ in spike region (STD) (a) and non-spike region (NSTD) (b) as functions of refractory periods and spike threshold. The trend of STD and NSTD as functions of the refractory periods with different threshold is (c) and (d) respectively, (e) illustrate the voltage after the refractory periods with different threshold voltage. All the threshold voltage ranges from -55mV to -47mV, and refractory periods from 4ms to 10ms.

We now return to explore the relationship between $lLLE$ and voltage threshold and refractory periods in spike and non-spike region under different sinusoidal stimuli. The frequency f is changed from 0 to 1 regard as the different stimuli. Figs.3(a-d) display the graph of both refractory periods and threshold voltage with the standard deviation of the average $lLLE$ for various values of f (We set STD and $NSTD$ is the standard deviation of average $lLLE$ in spike and non-spike region respectively).

It is seen that the smallest STD in the area of threshold about -50mV, refractory periods from 7 ms to 10 ms, and the STD decreases along the axis from the bottom to the top as Fig.3(a) shows. The deeper the blue color is, the smaller the STD becomes. Fig.3(b) shows that the $NSTD$ is opposite STD except the lower-left corner. For more accurate description, Fig.3(c) shows that the STD decreases with the increase of refractory periods (RPT) under different spike threshold. From the vertical, when the threshold voltage is -50 mV, the smallest STD curve as showed in the enlarged portion of the above screenshot, and the STD reaches a minimum at RPT being 9.5 ms and threshold voltage is -50 mV. Fig.3(d) shows that the $NSTD$ increases with the increase of RPT with different spike threshold, and in most cases, the $NSTD$ is larger than STD, indicating that the average values of $lLLE$ in spike region are more stable than non-spike region. In order to verify whether or not the voltage is at resting state after RPT, we draw a picture as Fig.3(e) shows. In the enlarged portion of the Fig.3(e), the voltage is at resting state. Therefore, the RPT and threshold voltage have been chosen for analysis are reasonable that the RPT is 9.5 ms and threshold voltage is -50 mV respectively. Then, we compute the average values of the $lLLE$ in spike and non-spike region respectively, whose results are shown in Fig.4.

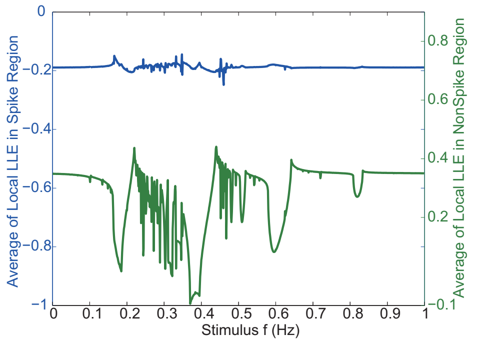


Figure 4: The average $lLLE$ as functions of stimulus f (Hz), the threshold voltage is -50 mV, refractory period is 9.5 ms.

In Fig.4, it reveals that the average values of $lLLE$ are stable about -0.19 in spike region (blue curve in Fig.4), with the STD is about 0.00704, indicating that the attractor of the system is contraction in spike region. However, the average values of $lLLE$ are unstable (dark green curve in Fig.4) and more vibrant in non-spike region, with the $NSTD$ is about 0.10973, and we find the curve is very similar to largest Lyapunov exponent as Fig.2. The average values of $lLLE$ are mostly greater than zero, indicating that attractor of the system is divergent in non-spike region. These phenomena can best demonstrate that the threshold and refractory periods express an especial neuron dynamics that the spike region is miraculous that the local Lyapunov exponent represents.

We will analyze the average local LLE in these three dynamical regimes in spike and non-spike region.

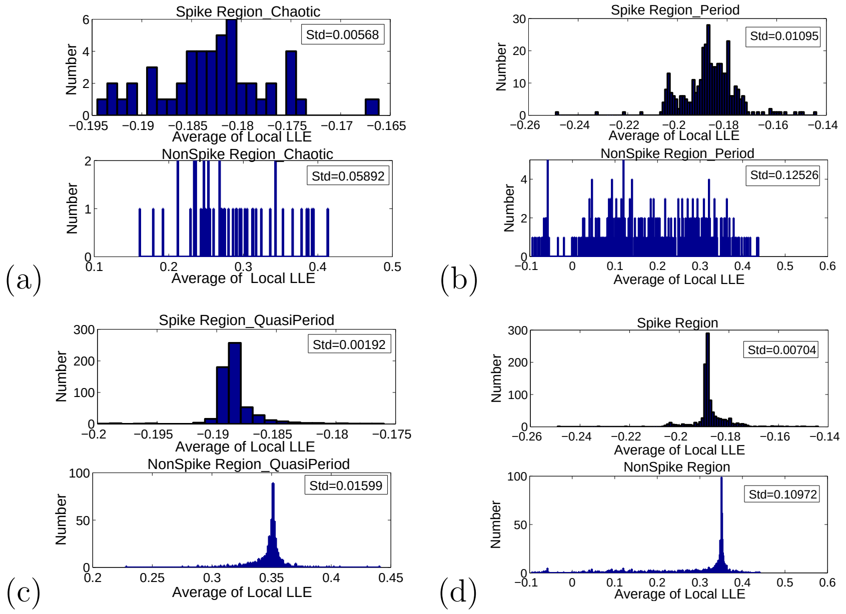


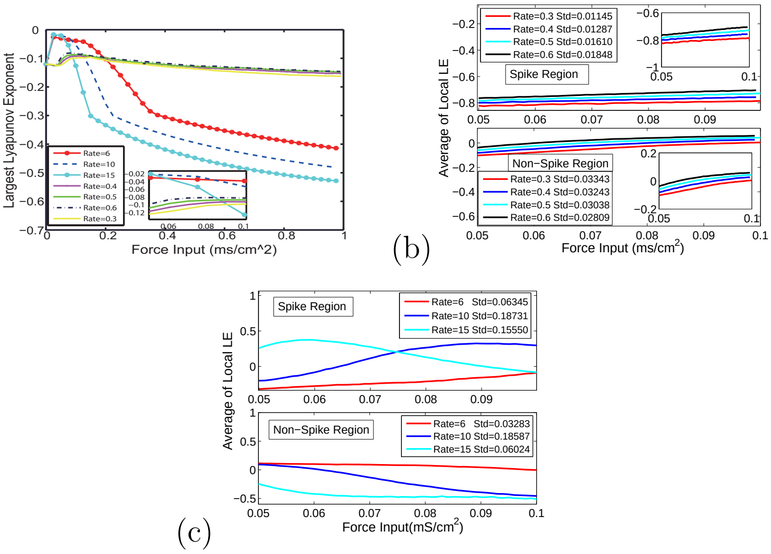
Figure 5: Histogram 1 to 3 graph is the average local LLE in Spike and Non-Spike region in three dynamical regimes (Chaotic, Period, Quasi-Period). The last graph is the average local LLE in Spike and Non-spike region. The standard deviation of spike are smaller than non-spike in chaotic, period and quasi-period. Threshold voltage is -50 mV and refractory period is 9.5 ms.

In Fig.5, we describe the average $lLLE$ in three dynamical regimes(Chaotic, Period, Quasi-Period)with spike and non-spike region. We find the average values of $lLLE$ are more directly concentrated in spike region than non-spike region. Besides, the mean $lLLE$ is smaller than zero in spike region, it is indicating that the attractor is contraction in these three dynamical regimes. Meanwhile, the reason that some value of the mean $lLLE$ in non-spike region is smaller than zero is that the attractor is divergent in period regime, as shown in Fig.5(b). What is the difference between the three dynamical regimes in no spike region? The most significant difference is the average value of $lLLE$ became more concentrated in quasi-period than other regimes.

4.2. Poisson of feedforward input

It has shown that chaos can arise in the dynamics of single H-H neuron, for example, under a periodic external drive as part 4.1. Therefore, there is a natural question: what about a single H-H neuron under a stochastic external Poisson input, and can it be chaotic?

So, the system is also considered as another drive by feedforward inputs. Here, we consider stochastic inputs: we use a spike train sampled from a Poisson process with rate r as the feedforward input. We also hope to find the different dynamical regimes, but only one dynamical regime is period in one neuron model. The results are shown in Fig.6(a). This case is consistent with Sun [17] results.



(a) (b)

(c)

Figure 6: (a) The Largest Lyapunov exponent of the HH neuron system with different rate of poisson input versus the force input strength parameter F is $[0, 1]$, the enlarged portion is the F ranging from 0.05 to 0.1, force strength F. (b) The average local LLE versus the different Poisson input strength in low frequency Poisson spike. (c) The average local LLE versus the different Poisson input strength in high frequency Poisson spike. Threshold is −50 mV and refractory periods is 9.5 ms.

Here, we vary the parameter of the strength of Poisson ranging from 0 to 1 mS/cm^2 to perform seven systematic scanning tests for seven different parameter values of the Poisson rate $r = 0.3, 0.4, 0.5, 0.6, 6, 10, 15$, respectively. We find the largest Lyapunov exponent is negative for any values of Poisson rate r and strength F, which indicates that the dynamics of a single neuron in this system is not chaotic. As shown in Fig.6(a), when the Poisson rate $r = 0.3, 0.4, 0.5, 0.6$, the value increases as the rate increases, but for the other case of large rate $r = 6, 10$ and 15, the value of LLE decreases as the rate increases in the strength F ranging from 0.15 to 1, and we also find the LLE in high frequency is smaller than low frequency when the strength F ranges from 0.25 to 1. In very low force strength of Poisson spike ranging from 0 to 0.05, the LLE increase with increasing Poisson rate in the high Poisson spike frequency region, however, in the low frequency region, the LLE decrease with increasing Poisson rate.

In Fig.6(b), we show that the average $lLLE$ in Spike and Non-Spike region are nearly constant under different stimuli of Poisson force strength input in each small rate of Poisson spike. We also show that the average values of $lLLE$ are negative about −0.8 in spike region; however, the average values of $lLLE$ are monotonically increasing as F increases in non-spike region. The Poisson force strength ranging from 0.05 to 0.1 mS/cm^2 followed as Sun and Zhou [17]. The standard deviation of the average $lLLE$ increases as the rate r increases and expands at large strength in spike region, but the value decreases as the r increases and tightens at large strength in non-spike region in the low frequency Poisson spike. Therefore, these results demonstrated that the average $lLLE$ is stable in different Poisson input strengths in each Poisson spike rate.

In Fig.6(c), we find that the average values of local lyapunov exponent are unstable in spike and non-spike region in high frequency Poisson spike stimuli. And the values sign of the mean $lLLE$ are different with the results of sinusoidal driven; therefore, in high frequency case, the conclusion as other case can not be reached.

5. Discussion and conclusion

We have presented a numerical study of the value of the average l$lLLE$ of HH neuron under Sinusoidal drive and conductance drive with a stochastic nature, such as feedforward Poisson spikes, which are more realistic as an approximation to cortical spike trains. We found three typical dynamical regimes in Sinusoidal drive as the sine frequency varies from weak to strong, and only one dynamical regime in Poisson input as the input strength varies from 0 to 1. We have also discovered the relationship between the $lLLE$ and spike threshold voltage and refractory periods. That is, the average $lLLE$ is stable in spike region and unstable in non-spike region, under different sinusoidal drive, and it has some similar results under Poisson force strength in each fix low Poisson spike rate in spike region. But the value is different with the case at sinusoidal external stimulus in non-spike region. Also, the analysis demonstrates that the reason of choosing the threshold voltage and refractory periods value in physiologically have an intrinsic dynamical structure. This phenomenon estranges us from the unfamiliarity with the threshold voltage and refractory periods from a new perspective, and carves out a specific way to uncover the physical interpretation of the spike encoding and reliability of spike timing.

Acknowledgment. We would like to thank Douglas Zhou and David Cai for originally suggesting this problem and stimulating discussions.

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Accepted: 29.10.2014