

# Mode locking, chaos and bifurcations in Hodgkin-Huxley neuron forced by sinusoidal current

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**Abstract.** The action potentials in a sinusoidally forced Hodgkin-Huxley neuron are known to possess mode locked or chaotic oscillations depending on the values of forcing parameters. We have numerically studied the spiking dynamics of the sinusoidally forced Hodgkin-Huxley neuron by making fine variations in the amplitude while keeping the frequency fixed. We find that the dynamics of the neuron is far richer than previously known. Increasing the resolution of forcing amplitude ( $I_0$ ) uncovers  $1/m$  mode locked oscillations with increasingly larger values of  $m$ . Moreover, a mode locked oscillation of type  $1/m$  can exist over multiple disconnected intervals of forcing amplitude. Chaotic oscillations are found interspersed with mode locked oscillations. By varying  $I_0$  we have further explored the transition between qualitatively different types of oscillations. On increasing  $I_0$ , every  $1/m$  mode locked oscillation is found to go through a sequence of period doubling bifurcations giving rise to  $1/2m, 1/4m, \dots$  mode locked oscillations and finally chaos. Chaotic oscillations further undergo a transition to a  $1/m'$  mode locked oscillation through a tangent bifurcation. The observed spiking patterns in mode-locked oscillations are unusual and encode the stimulus strength.

**Keywords:** Hodgkin-Huxley model, Neurons, Bifurcation.

## 1 Introduction

Hodgkin Huxley model serves as a paradigm for axonal membranes of spiking neurons. The model arose from the electrophysiological experiments of Hodgkin-Huxley with squid giant axons. Consequently, a lot of experimental work with squid axons and theoretical work with the Hodgkin-Huxley (HH) model has been carried out.

A nerve membrane is an excitable system. An appropriate stimulus evokes a strong response (action potential) resulting in a train of spikes in the membrane potential. For forcing by a steady current, a subcritical Hopf bifurcation causes the rest state of the neuron to become unstable giving rise to a periodic train of spikes (a limit cycle) (Xie *et. al.*[1]). Periodically varying stimuli evoke a



rich variety of response. Mode-locked (periodic), chaotic, and quasiperiodic oscillations of membrane voltage have been found in experiments with squid giant axons (Kaplan *et. al.* [2], Matsumoto *et. al.*[3], Aihara and Matsumoto[4], Guttman *et. al.*[5]) and in numerical simulations of the HH model (Lee[6], Borkowski[8], Borkowski[7], Parmananda *et. al.*[9]).

A periodically stimulated neuron does not fire action potentials unless the forcing amplitude is above a threshold value. The threshold amplitude depends on the forcing frequency. The firing threshold curve (in forcing parameter space) of a HH neuron under sinusoidal forcing has been explored extensively. Firing onset occurs through a variety of bifurcation mechanisms(Lee[6]). The firing region in parameter space is dominated by mode locked oscillations of the type 1/1, 1/2, and 1/3 while there is a smaller region that exhibits chaotic oscillations. Bifurcations mechanisms that bring about a change in the mode-locking ratio of the periodic oscillations have not been explored so far. Our work explores this question.

In their simulations Lee[6] carried out a characterization of the HH neuron's firing response in the forcing amplitude-frequency parameter space. However, there exists a strip in parameter space lying between the 1/1 and 1/2 mode locked regions that has not been explored adequately. In order to uncover the bifurcations between various mode-locked oscillations, it is imperative to carry out an exhaustive investigation of this strip. We have found that a complex structure of interwoven periodic and chaotic dynamics connected by period doubling and tangent bifurcations exist in this strip.

## 2 Hodgkin-Huxley Model

The Hodgkin-Huxley model of an axon describes the dynamics of its membrane voltage ( $V$ ), activation variable ( $m$ ) and the inactivation variable ( $h$ ) of its sodium channels, and the activation variable ( $n$ ) of its potassium channels. The model consists of the following set of four coupled differential equations

$$C \frac{dV}{dt} = -\bar{G}_{Na} m^3 h (V - V_{Na}) - \bar{G}_K n^4 (V - V_K) - \bar{G}_L (V - V_L) + I_{ext}, \quad (1)$$

$$\frac{dm}{dt} = \alpha_m (1 - m) - \beta_m m, \quad (2)$$

$$\frac{dh}{dt} = \alpha_h (1 - h) - \beta_h h, \quad (3)$$

$$\frac{dn}{dt} = \alpha_n (1 - n) - \beta_n n, \quad (4)$$

where,

$$\alpha_m = \frac{0.1(25 - V)}{\exp[(25 - V)/10] - 1}, \quad \beta_m = 4 \exp[-V/18], \quad (5)$$

$$\alpha_h = 0.07 \exp[-V/20], \quad \beta_h = \frac{1}{\exp[(30 - V)/10] + 1}, \quad (6)$$

$$\alpha_n = \frac{0.01(10 - V)}{\exp[(10 - V)/10] - 1}, \quad \beta_n = 0.125 \exp[-V/80]. \quad (7)$$

Capacitance of the axonal membrane  $C = 1 \mu F/cm^2$ . The reversal potentials of sodium, potassium, and leakage channels are  $V_{Na} = 115mV$ ,  $V_K = -12mV$ , and  $V_L = 10.5995mV$  respectively. The maximal conductances of the membrane for sodium, potassium, and leakage currents are  $\bar{G}_{Na} = 120mS/cm^2$ ,  $\bar{G}_K = 36mS/cm^2$ ,  $\bar{G}_L = 0.3mS/cm^2$  respectively. In our work we stimulate the neuron with a sinusoidal current  $I_{ext} = I_0 \sin(2\pi\nu_f t)$ , where  $I_0$  is the forcing amplitude and  $\nu_f$  is its frequency.

In our work we choose the frequency  $\nu_f = 50Hz$  and the amplitude  $I_0$  is varied in the range  $1.6\mu A/cm^2 - 2.0\mu A/cm^2$ . At the lower and upper end of this range, the neuron exhibits 1/1 and 1/2 mode locked spiking oscillations (Lee [6]). By carrying out fine variations in the amplitude over this range, we have uncovered a complex dynamical structure between these two periodic spiking oscillations.

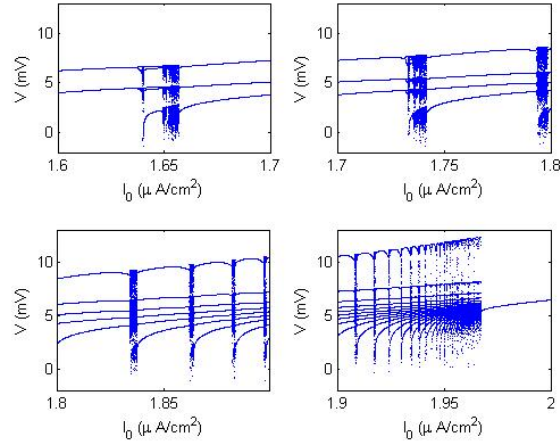
We carry out numerical simulations of the Hodgkin-Huxley equations (Eq. 1- 4) using the fourth order Rungke-Kutta method. We choose the time step  $dt$  in our simulations as  $dt = T_f/1000$ .

### 3 Results

Dynamics of forced nonlinear systems are often studied by sampling their phase space trajectory stroboscopically. Following this approach, we sample the phase space trajectory of the HH model once every time period of the sinusoidally varying external current. Doing so, yields a sequence of voltage values  $V_0, V_1, V_2, \dots, V_i, \dots$ . For periodic oscillations, a repetitive sequence will be present. Let  $T$  be the the time taken for the neuron's phase space trajectory to complete one full cycle. For periodic oscillations  $T_f/T = 1/m$ . We will characterize periodic oscillations by this ratio and refer to these as  $1/m$  mode locked oscillations. The repetitive sequence of voltage values for a  $1/m$  oscillation will contain  $m$  distinct values.

We have plotted the stroboscopically generated voltage sequences against the forcing amplitude as a bifurcation parameter. The resulting bifurcation plot is shown in Figure 1 over the amplitude range  $I_0 = (1.6 - 2.0)\mu A/cm^2$ . Two ends of the plot display the 1/2 and 1/1 mode locked oscillations, known from Lee's work (Lee [6]). This interval is believed to contain a rich dynamical structure (Lee [6], Parmananda *et. al.* [9]) but very few details are known.

Figure 1 shows that the amplitude interval between the known 1/1 and 1/2 oscillations contain many more periodic oscillations. Infact, the interval is dominated by periodic oscillations. On increasing the forcing amplitude from  $I_0 = 1.6\mu A/cm^2$  onwards we observe  $1/2, 1/3, 1/4, 1/5, \dots, 1/m, 1/(m + 1), \dots$  mode locked oscillations. A  $1/m$  oscillation contains  $m$  branches in the bifurcation diagram. A new branch gets added to the bifurcation diagram on crossing over from a  $1/m$  to a  $1/(m + 1)$  oscillation. Figure 1 suggests the presence of a  $1/m$  mode locked oscillation for every positive integer  $m$ .



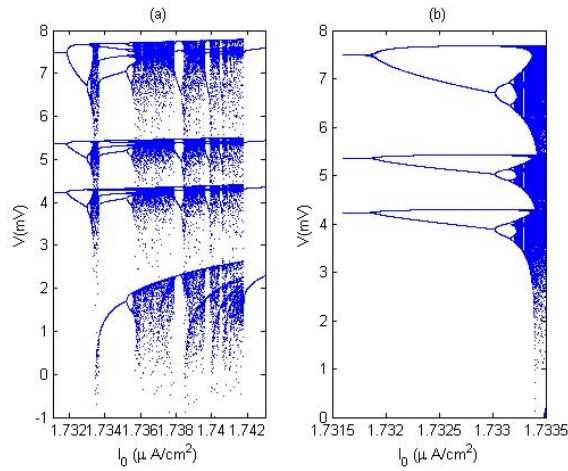
**Fig. 1.** Bifurcation diagram with variation in forcing amplitude  $I_0$  with forcing frequency fixed to  $\nu = 50Hz$ .

The amplitude interval lying between  $1/m$  and  $1/(m+1)$  oscillations described above contains a rich dynamical structure not discernible in Fig. 1. We see an instance of this richness on magnifying the amplitude interval lying between  $1/3$  and  $1/4$  mode locked oscillations (see Fig. 2(a)). This interval contains a myriad of periodic and chaotic oscillations. The region between every  $1/m$  and  $1/(m+1)$  oscillations of Fig. 1 contain such periodic and chaotic oscillations.

In Fig. 2(a)-(b) we observe that the  $1/3$  mode locked oscillations (on the extreme left of the figure) undergo a cascade of period doubling bifurcations giving rise to a sequence of  $1/6, 1/12, \dots$  oscillations finally converging to chaos. Similar period doubling bifurcations are present in other periodic windows in Fig. 2(a). In general, starting from a  $1/n$  periodic window, period doublings will result in  $1/(2n), 1/(4n), \dots$  oscillations. Each successive periodic oscillation obtained through period doubling takes double the time to go around its phase space trajectory once. Each cascade of period doublings finally converges to chaos.

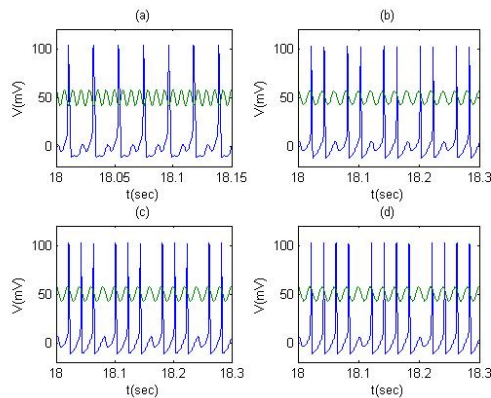
Periodic windows in Fig. 2(a) emerge from chaotic oscillations through a tangent bifurcation. The bifurcation is identified by plotting a return map between  $V_i$  and  $V_{i+n}$  if a  $1/n$  mode locked oscillation results from the bifurcation. Close to tangent bifurcation, the return map has  $n$  curve segments tangent to a  $45^\circ$  line. After the tangent bifurcation occurs the return map crosses the  $45^\circ$  line at  $2n$  points. Half of these points lie on a stable trajectory and the other half like on an unstable trajectory. All periodic windows arise in the same manner. Once a periodic oscillation is created through a tangent bifurcation, the subsequent changes in the qualitative dynamics of the membrane voltage arise from period doubling bifurcation.

Typical spike sequences generated due to sinusoidal forcing are depicted in Figs. 3 and 4. Figure 3(a) shows a  $1/3$  mode locked oscillation obtained



**Fig. 2.** (a) Bifurcation diagram for the amplitude interval lying between the 1/3 and 1/4 mode locked oscillation of Fig. 1. (b) Panel (a) figure is further magnified over its initial amplitude interval to depict period doubling.

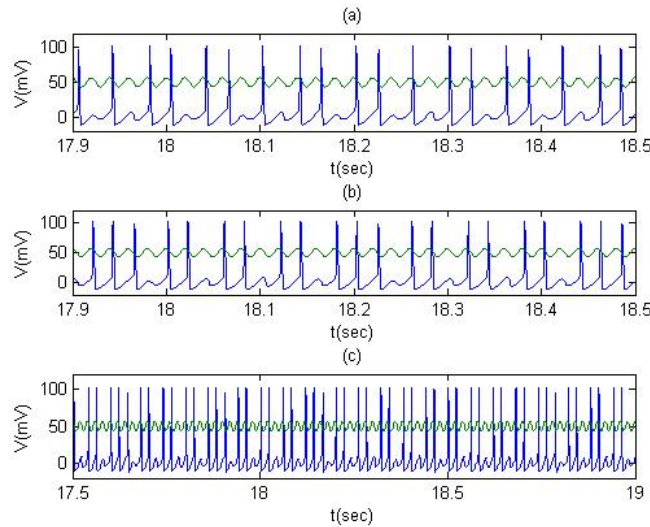
with forcing parameters chosen from the large region of 1/3 oscillations in Lee’s paper. Here a spike occurs once every three cycles of forcing. In our work we have found a novel set of spike patterns.



**Fig. 3.** Some typical spike sequences for periodic oscillations. Each figure gives the result for a different  $I_0$  (in units of  $\mu A/cm^2$ ) and  $\nu = 50Hz$ . The sinusoidal curve in each figure indicates the profile of this current (a)  $I_0 = 4$ , (b)  $I_0 = 1.7$ , (c)  $I_0 = 1.78$ , (d)  $I_0 = 1.82$ . Repeating units of spike sequences in (a)-(d) are of form  $\{1..\}$ ,  $\{2..\}$ ,  $\{3..\}$ , and  $\{4..\}$  respectively.

The spike sequences in Fig. 3(b)-(d) are representative of the  $1/m$  periodic oscillations that dominate the amplitude interval in Fig. 1. In each of these periodic oscillations, we find that a spike occurs consecutively over  $(m - 1)$

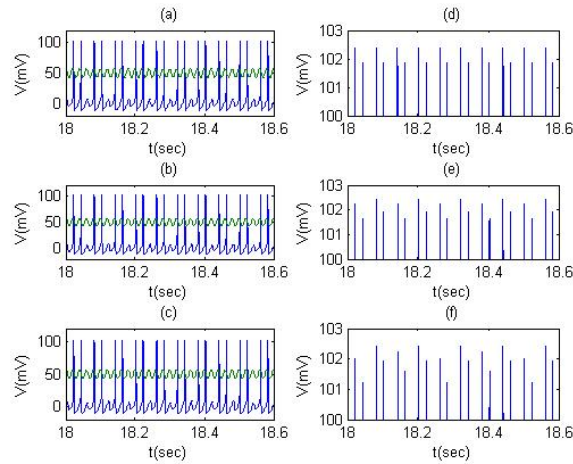
forcing cycles, following which there is no spike in the  $m^{\text{th}}$  forcing cycle. We will represent this spike pattern by  $\{(m-1).\}$ , with  $(m-1)$  representing the group of consecutive  $(m-1)$  spikes and the dot '.' representing the missing spike in the  $m^{\text{th}}$  forcing cycle. The  $\{(m-1).\}$  pattern repeats itself every  $m$  forcing cycles and thus we will regard it as a repeating unit. The  $1/3$  and  $1/4$  mode locked oscillations in Figs. 3(b) and (c) have  $\{2.\}$  and  $\{3.\}$  as their repeating units respectively. In contrast, the  $1/3$  oscillation [Fig. 3(a)] from Lee's work has a repeating unit of the form  $\{1..\}$ .



**Fig. 4.** Each figure gives the result for a different  $I_0$  (in units of  $\mu A/cm^2$ ) and  $\nu = 50Hz$ . (a) and (b) show some typical spike sequences of the fundamental oscillation of a periodic window. Here  $I_0 = 1.6518$  in (a) and  $I_0 = 1.7345$  in (b). In (c) we see an intermittent spike sequence for  $I_0 = 1.73365$ . A few sequences  $\{3.2.2.2.\}$  appear intermittently here.

Figure 4 shows spike patterns of oscillations in periodic windows. Here the repeating units have a form different from the ones in Fig. 3. A typical repeating unit is of the form  $\{m_1.m_2.m_3.\}$ , with multiple groups of spikes, whereas oscillations in Fig. 3 contain only one group of spikes. Here we have shown three groups of spikes containing  $m_1$ ,  $m_2$ , and  $m_3$  spikes each separated by a missing spike. However, the number of groups can be more or less (but not less than two) than represented by  $\{m_1.m_2.m_3.\}$ . Figure 4(a) and (b) shows a  $1/8$  and  $1/13$  oscillations with repeating units  $\{2.2.1.\}$ , and  $\{3.2.2.2.\}$  respectively.

Figure 5 shows the typical changes in  $V(t)$  that accompany period doubling bifurcations. As an illustrative example we choose the period doubling cascade starting from the  $1/3$  mode locked oscillation in Fig. 2. The repeating unit is  $\{2.\}$  here. We find that the number of spikes per group remain unchanged (equal to two) across all period doubling bifurcations starting from the  $1/3$



**Fig. 5.** Changes in the repeating unit of spike sequences across a period doubling bifurcation are shown here. All the figures are plotted for  $\nu = 50Hz$  and  $I_0$  is in units of  $\mu A/cm^2$  (a)  $I_0 = 1.731$  gives 1/3 mode locking (b)  $I_0 = 1.7324$  gives 1/6 mode locking, and (c)  $I_0 = 1.73315$  gives 1/12 mode locking, (d)-(e) show the variation in spike amplitude for (a)-(c) respectively by plotting  $V(t)$  on a smaller scale.

oscillation. However, the amplitudes of spikes undergoes a change. Hence, the repeating unit for 1/6, and 1/12 are  $\{2.2.\}$  and  $\{2.2.2.2.\}$  respectively. Likewise, in a period doubling of any other periodic oscillation with a repeating unit  $\{m_1.m_2.m_3.\}$ , every period doubling doubles the length of the repeating unit to  $\{m_1.m_2.m_3.m_1.m_2.m_3.\}$ .

A tangent bifurcation is known to be preceded by intermittency. We find that intermittency occurs through an interesting set of changes in spike patterns as we approach the bifurcation point on varying the forcing amplitude  $A$ . Far from the bifurcation point  $V(t)$  is chaotic. The spike sequence is of the same form as that for periodic oscillations. However, there exists no repetitive sequence for chaotic oscillations. As the amplitude is brought closer to the bifurcation point the frequency of a specific spike sequence  $\{m_1.m_2.m_3.\}$  within the chaotic sequence increases. Once the tangent bifurcation occurs  $\{m_1.m_2.m_3.\}$  becomes the repeating unit. Every periodic window arises through a similar increase in the frequency of some unit.

## 4 Discussion

In the paper we presented a few results of stimulating a HH neuron by a sinusoidal current in the regime where it evokes action potentials. We found a complex structure of  $1/m$  mode locked and chaotic oscillations between the 1/1 and 1/2 oscillations of Lee's work (Lee[6]). Chaotic oscillations arise through the period doubling route to chaos. Periodic windows emerge through a tangent bifurcation preceded by an intermittent spike sequence. Starting from 1/2 mode locked oscillations, period doubling cascade gives rise to 1/4, 1/8,.. mode

locked oscillations. Across a period doubling bifurcation, spike sequences do not undergo any change. However, the amplitudes of the spikes undergo an alteration. Intermittent spike sequences before a tangent bifurcation contain glimpses of the spike sequences that are finally realized in the periodic oscillation across the bifurcation. Infact, the neuron enters the 1/1 oscillation through a tangent bifurcation.

In our work the ratio  $1/m$  for a periodic oscillation is the ratio of time taken for one forcing cycle to the time taken for the neuron to go once around its closed orbit in phase space. In going around the limit cycle once the neuron may fire several spikes. However, in literature  $1/m$  usually implies that the neuron fires one spike in every  $m$  cycles of forcing.

The spike sequences presented in our paper are distinct from those obtained earlier. Spikes are organized in groups where each group may contain a different number of spikes. These sequences of spikes alone can carry information about the forcing amplitude. Implying that no knowledge of the rate of spiking or that of the interspike interval is necessary to extract information about the forcing parameters.

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