Electronic version of an article published as International Journal of Bifurcation and Chaos Vol. 14, No. 7, 2004, 2241-2252,
DOI: 10.1142/S0218127404010564 © World Scientific Publishing Company, https://www.worldscientific.com/worldscinet/ijbc

A DESIGN METHOD OF BURSTING USING TWO-PARAMETER BIFURCATION DIAGRAMS IN FITZHUGH-NAGUMO MODEL

Shigeki Tsuji [*], Tetsushi Ueta [†], Hiroshi Kawakami [‡] and Kazuyuki Aihara [§]

June 22, 2004

Spiking and bursting observed in nerve membranes seem to be important when we investigate information representation model in the brain. Many topologically different bursting responses are observed in the mathematical models and their related bifurcation mechanisms have been clarified. In this paper, we propose a design method to generate bursting responses in FitzHugh-Nagumo model with a simple periodic external force based on bifurcation analysis. Some effective parameter perturbations for the amplitude of the external input are given from the 2-parameter bifurcation diagram.

1. Introduction

To understand the mechanism of the information processing in the brain or the problem of information representation of a neuron, construction of mathematical models is inevitable. For now, many mathematical models to simulate the neuronal dynamics are proposed, and they have been carefully analyzed in the bifurcational point of view. Some models can describe dynamical responses faithfully under certain conditions.

We recognize a bursting response in a signal when the wave form of the potential in a nerve membrane changes periodically between the resting interval and repetitive firing states. For classification of statistical properties of bursting, a number of spikes and interspike intervals seem to be essential for considering information representation problems in the brain. Due to physical experiment results, many mathematical models of neuronal activities have been classified. Various bursting responses observed in several neuronal models have so far been reported [Bertram *et al.*, 1995; de Vries, 1998; Izhikevich, 2000a; Rinzel, 1987]. Hoppensteadt and Izhikevich [Hoppensteadt & Izhikevich, 1997; Izhikevich, 2000a] investigated a complete survey of all bifurcation phenomena and proposed a scenario; the slow change between quiescent state and oscillating state forms a bursting motion. They have classified typical bursting phenomena in the corresponding neuronal oscillators, e.g., Hodgkin-Huxley [Hodgkin & Huxley, 1952], FitzHugh-Nagumo [FitzHugh, 1961; Nagumo *et al.*, 1962] (abbr. FHN), Morris-Lecar [Morris & Lecar, 1981] and Wilson-Cowan [Wilson & Cowan, 1996] models. However, although such a neural oscillator is given, there exist neither concrete criterion nor design method to generate a bursting signal.

In this paper, we choose the forced FHN model as a neural oscillator. By using Bonhöffer-van der Pol oscillator as an analogy of FHN model, based on the information acquired by the analysis of FHN model, the bursting generator may be realizable by an electric circuit. Thereby we show a concrete design method to demonstrate bursting motion in the state space. As an autonomous system, some models are proposed by which the bursting response is observed. However, these models do not have a parameter to generate

[*] Dept. Information Science and Intelligent Systems, Tokushima University, Japan
[†] Center for Advanced Information Technology, Tokushima University, Japan
[‡] Dept. Electrical and Electronics Engineering, Tokushima University, Japan
[§] Mathematical Engineering and Information Physics, Tokyo University, Japan

desired bursting patterns. In contrast with this, by using external force, a model with various bursting modes can be built by introducing the external force which can change frequency and amplitude freely. Firstly, we analyze the FHN model without external force. The bifurcation diagram of equilibria and limit cycles is obtained, then we specify how to set a parameter perturbation to this system. Secondly, we show bifurcation diagrams in the forced FHN model with numerical calculation. Typical bifurcation sets in the 2-parameter plane. It is clarified that a parameter region in which the periodic solution has the same number of spikes is segmented by the tangent bifurcation curve as the frequency of the external force is gradually changed. Additionally, we propose a simple design method of bursting responses with specified ratio between spiking state and quiescent state in bursting response, and show example bursting responses with specified ratio.

2. Design Method of Bursting Model

Firstly, as one of the models by which bursting response is observed, we consider the Hindmarsh-Rose [Hindmarsh & Rose, 1984] type model which is 3-dimensional fast-slow system of the form

$$\begin{cases} \dfrac{dx_1}{dt} &= f_1(x_1,\, x_2,\, u) + I \\ \dfrac{dx_2}{dt} &= f_2(x_1,\, x_2) \\ \dfrac{du}{dt} &= \varepsilon g(x_1,\, u) \end{cases} \tag{1}$$

where $\boldsymbol{x} = (x_1, x_2)$ is fast processes associated with generation of action potentials. In particular, we hypothesize that x_1 corresponds to membrane potentials and I is constant stimulus. u is x_1-dependent variables, and relatively slow processes that modulate $\boldsymbol{x}$ by slow time constant $0 < \varepsilon \ll 1$.

This system can separate dynamics of $\boldsymbol{x}$ and u . In other words, if the quiescent state(i.e. stable equilibrium) changes to the repetitive spiking state(i.e. stable limit cycle) by changing parameter I, moreover, we hypothesize that dynamical system $\boldsymbol{x}$ has a bistable state like Hindmarsh-Rose model. It is called the hard oscillation. Bursting responses is generated by slow modification of u. However, when fast subsystem does not have bistability, bursting response do not be generated in this model since u is dependent on behavior to $\boldsymbol{x}$. In fact, behavior of u has to be oscillating independently when fast subsystem does not have bistability. To overcome this problem, either slow subsystem has to consist of 2 or more -dimensional system or two additional current which consists of another motion has to add for the fast-slow system(1) [Rinzel *et al.*, 1987; Smolen *et al.*, 1993; Izhikevich, 2000a]. This results that the model should become a higher dimensional system. Moreover, it is difficult to adjust for specific bursting behavior (e.g. bursting with the specified number of spikes and firing rate) using these autonomous systems.

Consequently, we consider simple and low dimensional fast system with a forced external term independent to $\boldsymbol{x}$ as follows:

$$\begin{cases} \dfrac{dx_1}{dt} &= f_1(x_1, x_2) + I(t) \\ \dfrac{dx_2}{dt} &= f_2(x_1, x_2) \end{cases} \tag{2}$$

In the case of equation(2), intended system changes to non-autonomous system from autonomous system. Additionally, if the external term is designed as $I(t) = I + B \sin \omega t\, (0 < \omega < 1)$, the initial condition of the fast system is determined by the constant parameter $I(t) = I$ $(B = 0)$. In this case, we call this parameter value *operating point* as shown in the bifurcation diagram Fig. 1. Variation and its velocity of parameter I is changed by $B \sin \omega t$ in Fig. 1.

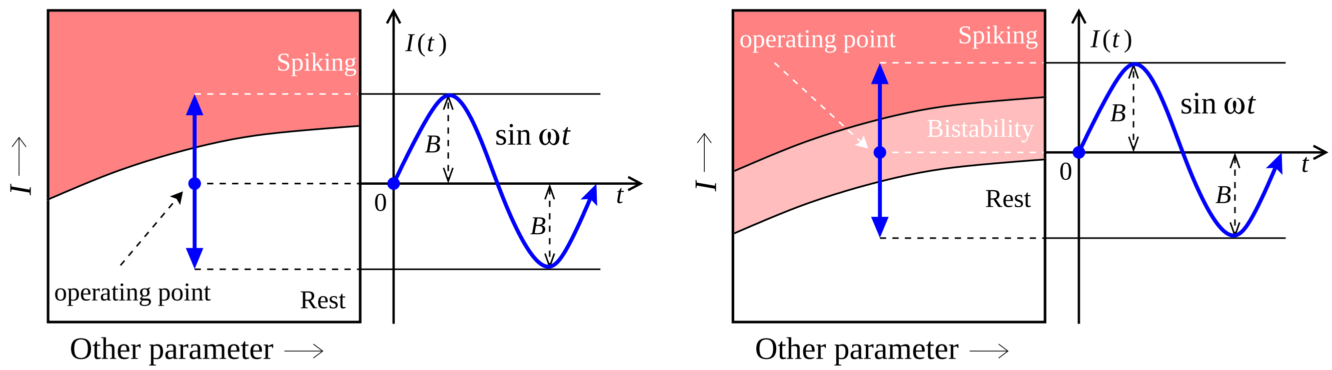


Figure 1: Schematic bifurcation diagram for fast system with external perturbation.

As shown in Fig. 1, regardless of the process which shifts to quiescent(repetitive spiking) state from repetitive spiking(quiescent) state via bifurcation curves, and even if fast system is n-dimensional system, this system can become some bursting [Izhikevich, 2000a] generator.

3. FHN Model

Let us consider the FHN model which is one of the simple models in the following form:

$$\begin{cases} \dfrac{dx}{dt} &= c\left(x - \dfrac{x^3}{3} + y + z\right) \\ \dfrac{dy}{dt} &= -\dfrac{x + by - a}{c} \end{cases} \tag{3}$$

where, x corresponds to an inverted value of cell membrane potential, y is refractory value, and z is the external stimulus intensity to a nerve cell. Moreover, parameter a, b, and c are often limited into the following ranges from physiological point of view:

$$1 - 2b/3 < a < 1, \quad 0 < b < 1, \quad b < c^2. \tag{4}$$

Equation(3) describes a two-dimensional autonomous system and corresponds to the fast system in the fast-slow system.

4. Bifurcations

The system (3) contains three parameters, and it is known that limit sets of the system are equilibrium and limit cycle by changing some parameter values. However, there only exists an equilibrium in Eq. (3) under the condition Eq.(4). We keep this condition and focus on the dynamical properties when the free parameters z and c are changed. For other parameters, we fix $a = 0.7$, $b = 0.8$ holding the condition Eq. (4).

Figure 2 shows a bifurcation diagram for Eq. (3). In this bifurcation diagram, h and G indicate Andronov-Hopf bifurcation of equilibrium and tangent bifurcation of a limit cycle, respectively.

Figure 1 can be divided into three regions as follows:

- In region **I**, there only exists a stable equilibrium.
- In region **II**, there exist a stable equilibrium, a stable limit cycle and an unstable limit cycle.
- In region **III**, there exist an unstable equilibrium and a stable limit cycle.

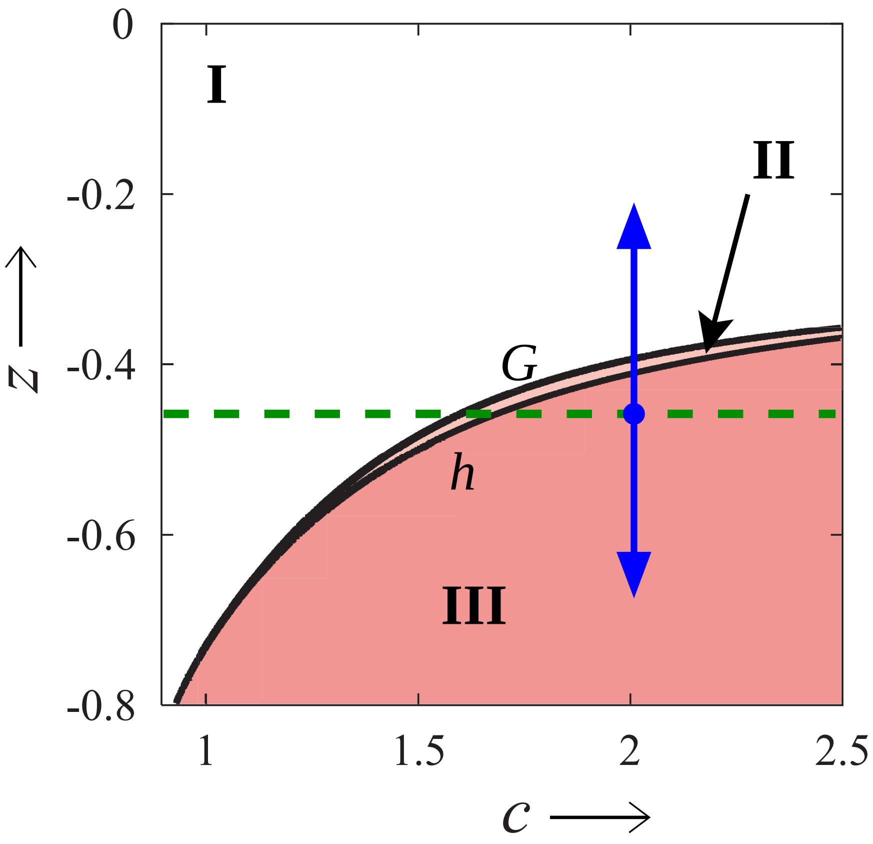


Figure 2: Bifurcation diagram of equilibria and periodic solution for Eq. (3).

According to each region, typical solution orbits and nullclines in the phase plane are shown in Fig. 3.

Consequently, Fig. 1 can be divided into two regions. In the region **I**, there only exists a stable equilibrium (i.e. the quiescent state). On the other hand, there exists a big and stable limit cycle (i.e. spiking) in the shaded regions **II** and **III**. However, in region **II**, two stable states (an equilibrium and a limit cycle) coexist.

5. Designing of Bursting Generator

We simply propose an external force formulated as $z(t) = z + B \sin \omega t$ into the autonomous system(3). The equation is described by the 2-dimensional non-autonomous system such as Eq. (2), investigation about existence of bursting is transfered solving bifurcation problem of the non-autonomous system. Sinusoidal wave $B > 0$ forms a vertical half line including the *operating point*, and it is designed to go across regions among **I** and **III**, and the parameter z traces along this half line. Thus, the state would change its topological property periodically between a quiescent and repetitive spiking states. (Even if the amplitude of $z(t)$ does not reach exactly the bifurcation curves, the bursting state can be expected.)

In the following, we fix the *operating point* as ($c = 2.0$, $z = -0.45$) in Fig. 2. In these parameter, a state of the system changes to repetitive spiking state from quiescent state via Subcritical Andronov-Hopf bifurcation and to quiescent state from repetitive spiking state via Tangent (Fold Limit Cycle) bifurcation. In fact, we show example busting in Fig. 4.

A combination of such two bifurcations generates the bursting that is frequently called *elliptic*. It is classified as subHopf/fold cycle burster [Izhikevich, 2000a, 2000b]. Such a bursting occurs in neonatal

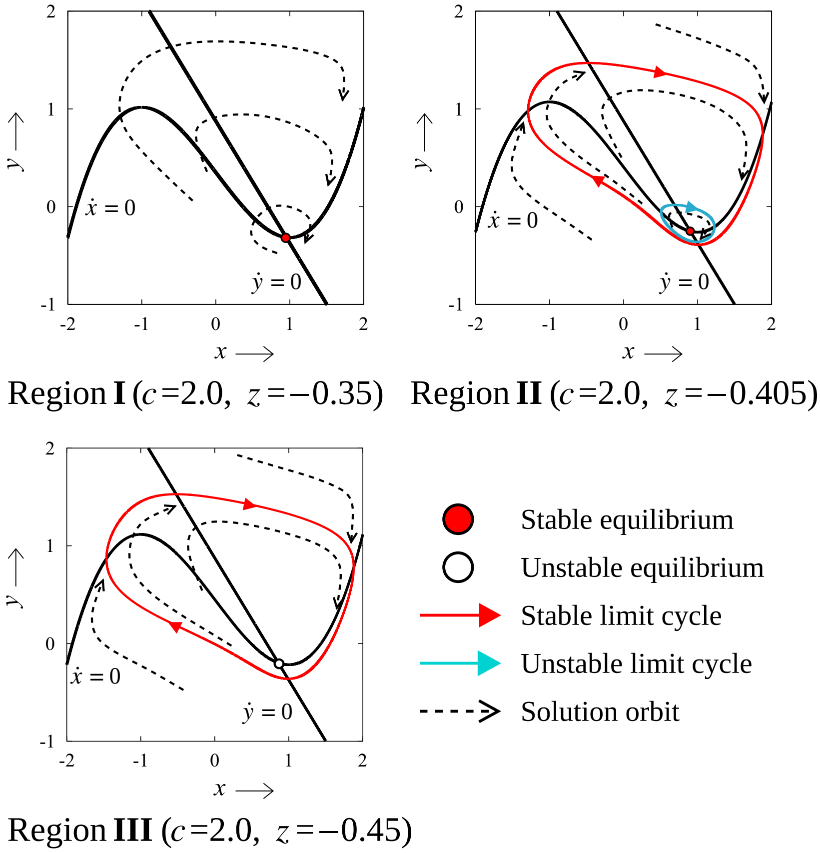


Figure 3: Typical solution orbits for each region in Fig. 3.

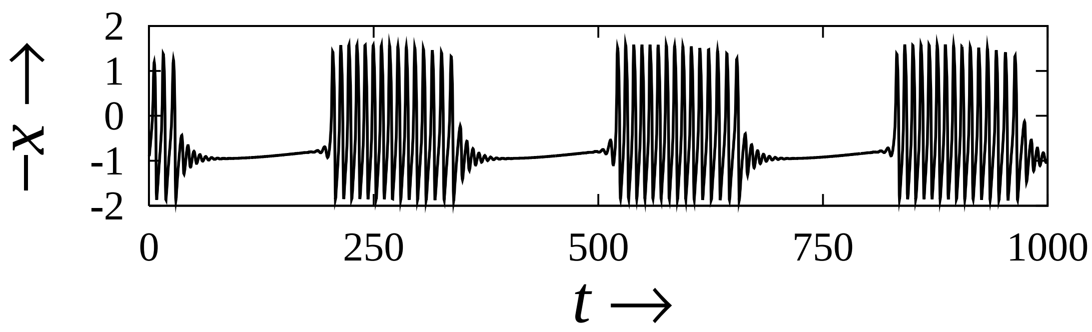


Figure 4: Example bursting with small value of ω ($\omega = 0.02$, $B = 0.1$).

rat trigeminal interneurons [Del Negro *et al.*, 1998], and it is exhibited by the FitzHugh-Rinzel model [Rinzel, 1987] consists of FHN model (2-dimensional fast system) and 1-dimensional slow system such as Eq. (1). In the following, we investigate various bursting responses by choosing appropriate B and ω. B and ω are principal parameters which determine a bursting mode, and it is important to investigate how change of behavior appeared by changing parameter B and ω.

6. Bifurcations of Bursting

We investigate bifurcation phenomena of periodic solution in ω-B parameter plane. Basically we easily observe quasi-periodic solutions with a comparatively small value of B since the system at the *operating point* ($c = 2.0$, $z = -0.45$) has a limit cycle. Two frequencies of the FHN model(ω_0) and external force (ω) makes the quasi-periodic motion. We are interested in periodic solution (possible bursting) emerged by period-locking phenomena. Parameter regions having such periodic solutions usually forms Arnold's tongue. Since $\omega_0 = 0.639$ at fixed system parameters, fundamental harmonic resonance emerges the vicinity area of $\omega = \omega_0 = 0.639 < 1.0$. Moreover, $p = 2 \cdots n$ -higher harmonic resonances and some q/p -subharmonic resonances exist uncounted period-locking area as ω shrinks to 0. where we set a relational expression between frequency of FHN model and external force such as $\omega/\omega_0 = q/p$. Accordingly, we pursue these regions for bursting mode classifications in the followings.

Firstly, we show the results of the range $0.4 \le \omega \le 1.0$, the bifurcation diagram is shown in Fig. 5. The phase portraits and wave forms corresponding to the points (1)–(6) marked in Fig. 6. A solid line is wave form of forced FHN model, and dashed line is sinusoidal force. In this bifurcation diagram, G^i_j and I^i_j represent respectively tangent and period-doubling bifurcation. i indicates a number of period, and j is a nominal number.

In Fig. 5, the period-locking region of fundamental harmonic resonance is formed of tangent bifurcation G^1_1, period-1 solution is observed the point (1) in this region, and the wave form as a repetitive spiking response. Moreover, at point (2), it becomes period-2 solution by period doubling bifurcation I^1_2. The repetitive spiking chaos is obtained via a period doubling cascade at the point (3). However, quasi-periodic solution is observed in the point (4) which exists outside period-locking region, and this solution becomes a chaotic response by increasing the parameter B. In this area, the bursting response is not observed, since the frequency of external force is comparatively higher than the frequency of a system.

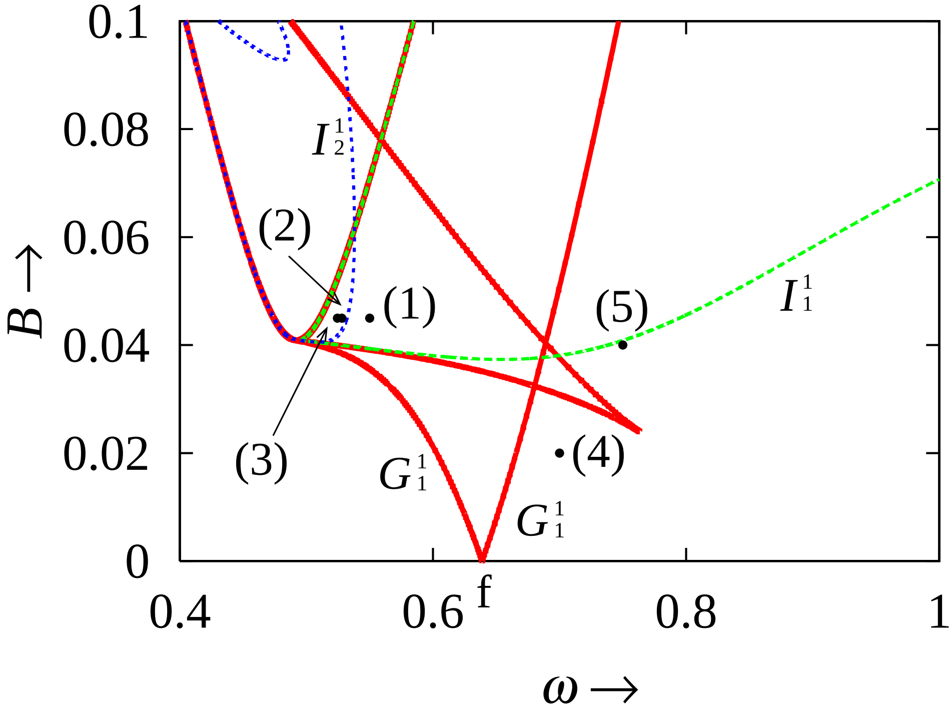
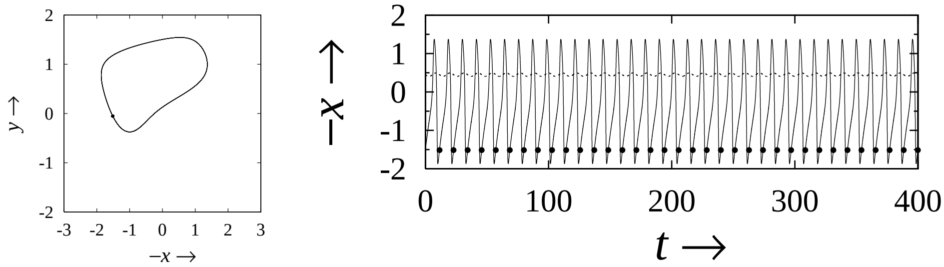
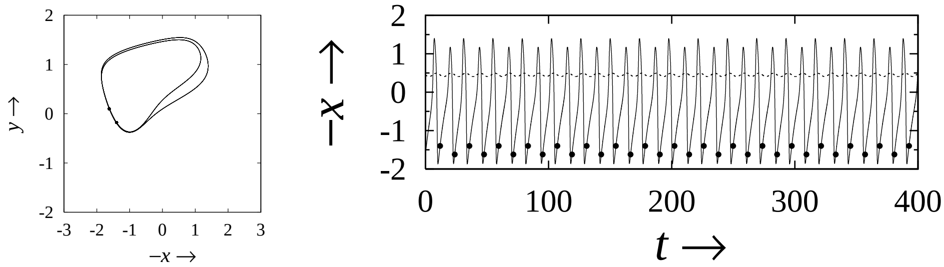


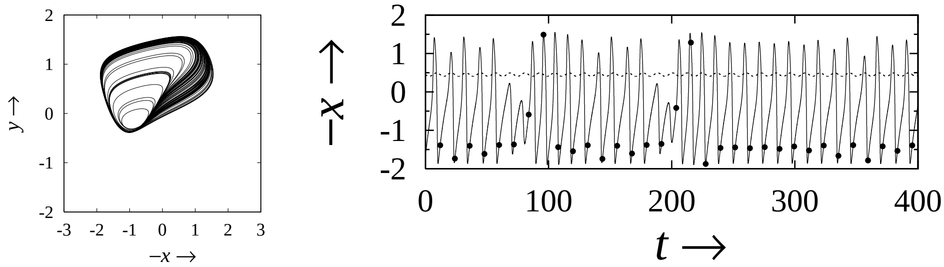
Figure 5: Bifurcation diagram of periodic solutions (1)



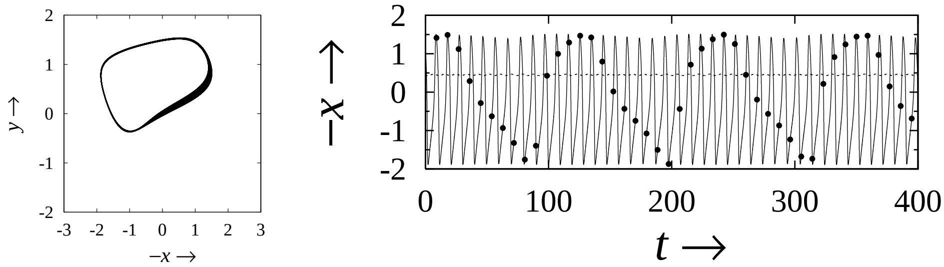
(1) period-1 repetitive spiking : $\omega = 0.55$, $B = 0.045$



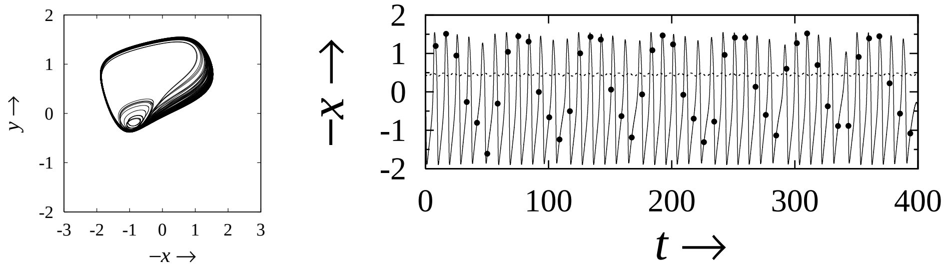
(2) period-2 repetitive spiking : $\omega = 0.528$, $B = 0.045$



(3) chaotic spiking : $\omega = 0.5245$, $B = 0.045$



(4) quasi-periodic spiking : $\omega = 0.75$, $B = 0.04$



(5) chaotic spiking : $\omega = 0.70$, $B = 0.02$

Figure 6: Phase portraits and wave forms of the point (1)–(5) in Fig. 5.

The period-locking region of 2-higher harmonic resonance ($\omega/\omega_0 = 1/2$) consists of G_2^1 in Fig. 7. In this region, period-1 repetitive spiking and single spiking response exist as shown Fig. 8, and each response become a chaotic response via a period doubling cascade along the line (a) and (b). Moreover, the period-locking region of 3-higher harmonic resonance consists of tangent bifurcation curves G_3^1 and G_4^1 in Fig. 9 as well as previous results. period-1 repetitive spiking, single spiking and double spiking response exist as shown Fig. 10, and each response become a chaotic response via a period doubling cascade along the line (c),(d) and (e).

The region of fundamental harmonic resonance and $p = 2 \cdots n$ -higher harmonic resonances exist uncounted period-locking area as ω shrinks to 0 in the ω-B plane. We solve some period-locking area consist of the bifurcation sets and spiking responses. In the following, we show that what response is observed in each region.

- period-locking region of fundamental harmonic resonance
  - repetitive spiking response
- period-locking region of 2-higher harmonic resonance
  - repetitive spiking response
  - single spiking response
- period-locking region of 3-higher harmonic resonance
  - repetitive spiking response
  - single spiking response
  - double spiking response

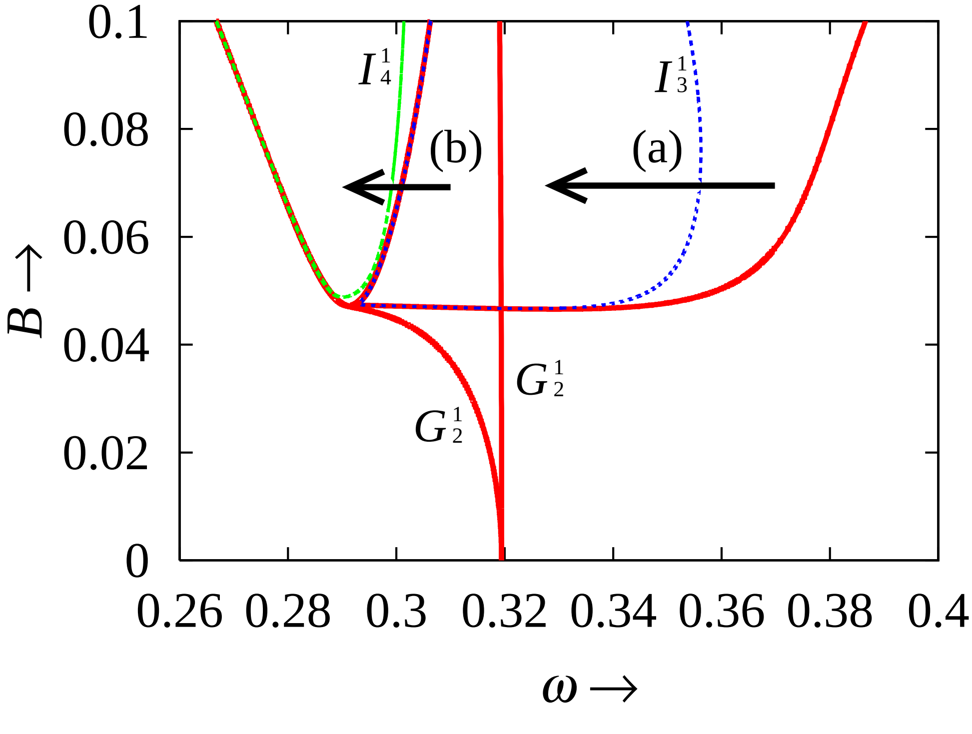
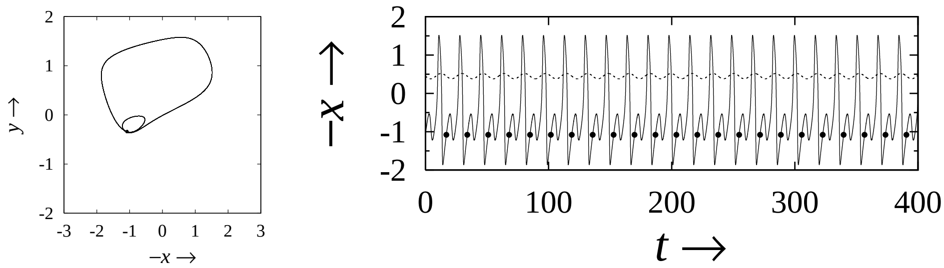
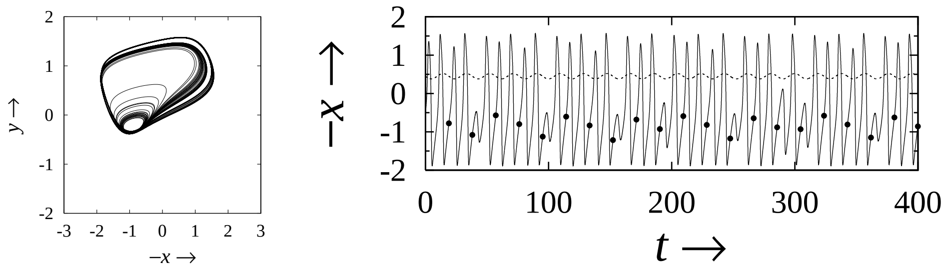


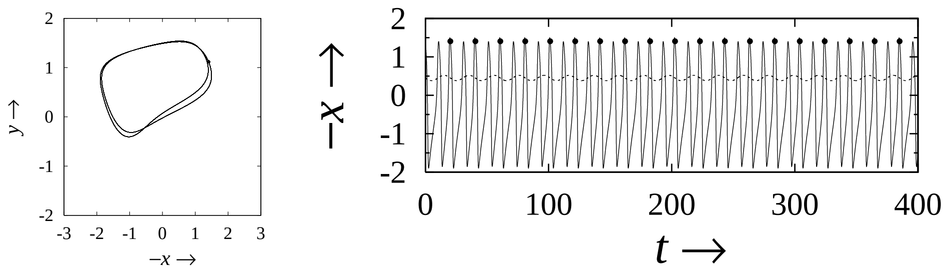
Figure 7: Bifurcation diagram of periodic solutions (2)



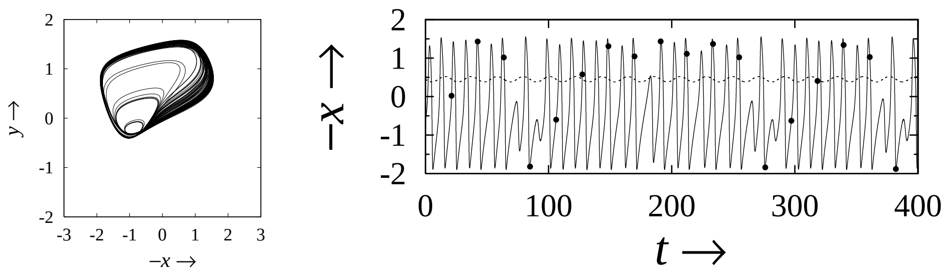
period-1 single spiking : $\omega = 0.37$, $B = 0.07$



chaotic spiking : $\omega = 0.33$, $B = 0.07$



period-1 repetitive spiking : $\omega = 0.31$, $B = 0.07$



chaotic spiking : $\omega = 0.296$, $B = 0.07$

Figure 8: Phase portraits and wave forms of the line (a) and (b) in Fig. 7.

From these results, we show that only period-1 repetitive spiking response exists in the period-locking region of fundamental harmonic resonance, and period-1 repetitive spiking response and period-1 bursting responses with $r = \{1, 2, \cdots, p-1\}$ spikes exist in the period-locking region of p-higher harmonic resonance. Moreover, we explained that each response becomes chaotic response via period-doubling cascade. It is possible that this phenomenon is shown in the areas where ω is very small value. For example, bursting response of 7-higher harmonic resonance is observed in the vicinity period-locking region of 7-higher harmonic resonance where ω is equal to $\omega_0/7 = 0.0913$ as shown in Fig. 5. Additionally if any choice of the region of some p/q-subharmonic resonance, more bursting response is observed.

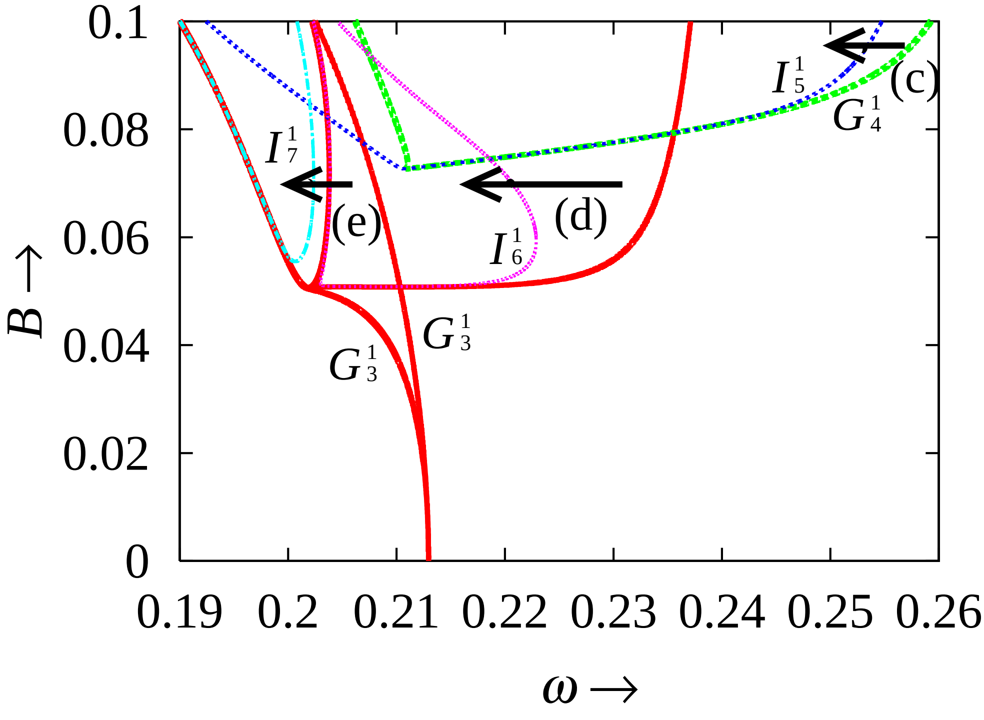
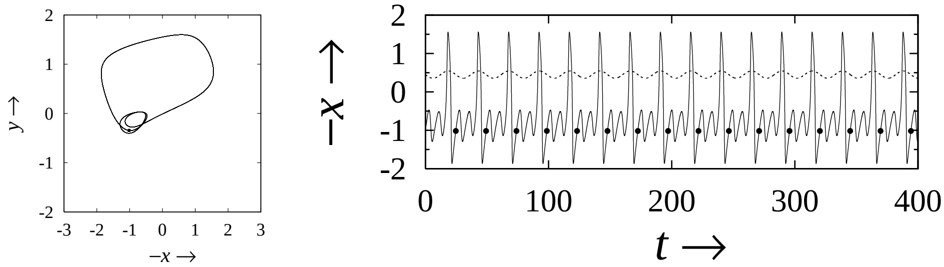
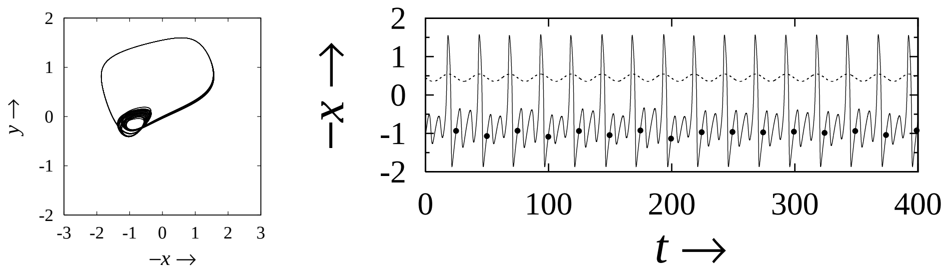


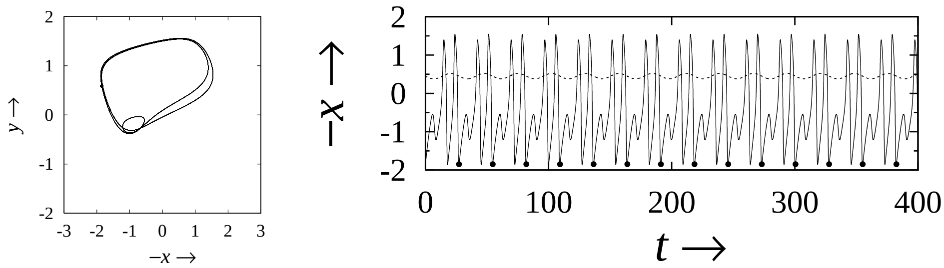
Figure 9: Bifurcation diagram of periodic solutions (3)



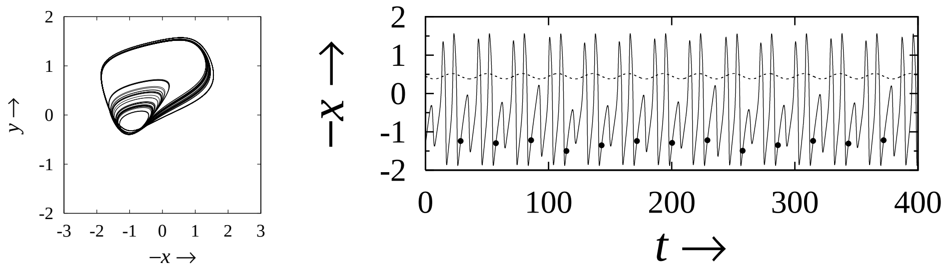
period-1 single spiking : $\omega = 0.255,\ B = 0.095$



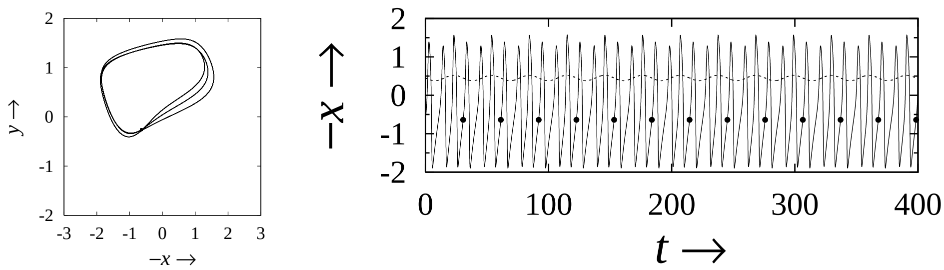
chaotic spiking : $\omega = 0.252,\ B = 0.095$



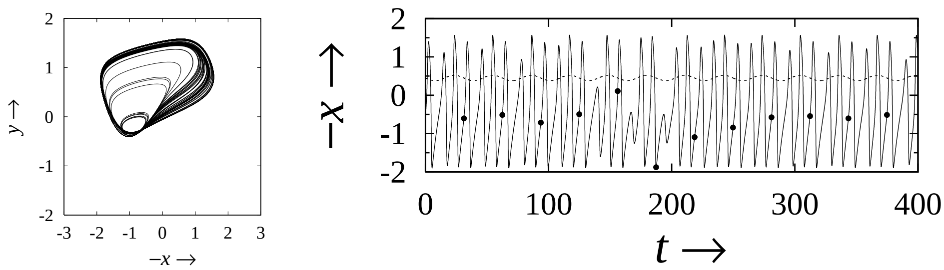
period-1 double spiking : $\omega = 0.23$, $B = 0.07$



chaotic spiking : $\omega = 0.2195$, $B = 0.07$



period-1 repetitive spiking : $\omega = 0.205$, $B = 0.07$



chaotic spiking : $\omega = 0.2012$, $B = 0.07$

Figure 10: Phase portraits and wave forms of the line (c), (d) and (e) in Fig. 9.

7. Design of Bursting

In previous section, we investigate that shifting of bursting mode by changing parameter ω and B. Therefore, we explained that number of spikes in bursting response changes by changing parameter ω and B, and its responses are separated by the period-locking regions consist of some tangent bifurcations. However, since the ratio between spiking state and quiescent state in bursting response have no concern with bifurcations, we can not set hoped ratio between both state.

Hence, we consider the problem; how to obtain B, ω and B_0 for desired wave form of bursting

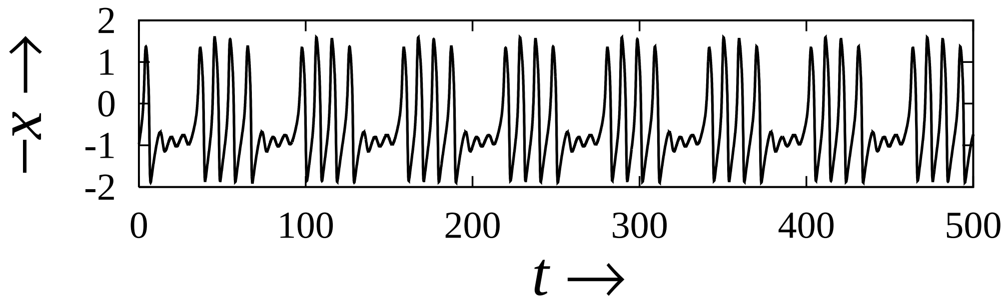


Figure 11: Example bursting with small value of ω ($\omega = 0.103$, $B = 0.1$).

[Tsuji *et al.*, 2002]. Figure 12 shows the relationship between the wave of sine function and bifurcation parameter values. Let $\theta = \omega t$. In the interval $[0, \pi]$, there exist two bifurcation parameter value G (tangent bifurcation of a limit cycle) and h (Hopf bifurcation of the equilibrium) when B_0 is added to this system until the state of the system changes spiking sate. For this reason, quantities of θ_1 and θ_3 are spiking state, and quantity of θ_2 is quiescent state in Fig. 12. where we show each interval of time as follows:

$$\begin{cases} t_1 = \theta_1/\omega = \dfrac{\sin^{-1}((G - B_0)/B)}{\omega} \\ t_2 = \theta_2/\omega = \dfrac{\pi - \sin^{-1}((G - B_0)/B) - \sin^{-1}((h - B_0)/B)}{\omega} \\ t_3 = \theta_3/\omega = \dfrac{\pi + \sin^{-1}((h - B_0)/B)}{\omega} \end{cases} \tag{5}$$

So if we want to control the specified ratio $X : Y = t_1 + t_3 : t_2$ between resting interval Y and bursting intervals X, one of B_0, B and ω is solved from following equations by fixing other two parameters:

$$\sin^{-1}\left(\frac{G - B_0}{B}\right) + \sin^{-1}\left(\frac{h - B_0}{B}\right) = \frac{\pi(X - Y)}{X + Y} \tag{6}$$

Figure 13 show burstings with specified ratio under $a = 0.7$, $b = 0.8$, $c = 2.0$, $\omega = 0.05$, $B = 0.5$. Then B_0 is solved by Newton's method. In this case, by solved parameter B_0, we obtained some responses which have specified ratio, but changing both state does not change rapidly for Hopf and tangent bifurcation points. Hence, exact interval does not be solved by this way, but we can know parameter sets which have kind of interval between spiking state and rest state. By using information of solved bifurcation structures and a design method of bursting response which has specified ratio, we may be able to design the bursting modes with arbitrary numbers of spikes and specified ratios between bursting state and quiescent state.

8. Concluding Remarks

We proposed a simple design method in the FHN model by using external sinusoidal force, and we investigated some spiking or bursting responses via bifurcation phenomena in the bursting generator. Usually, if the external force is added to the autonomous system which is oscillating, many period-locking regions which shows form of Arnold's tongue exist in the frequency and amplitude plane. In fact, the responses to which the ratio of the autonomous system and external force is rational number are divided by period-locking regions. In the FHN model with external force, spiking or bursting responses with various rational number ratios are divided by period-locking regions, and decrease of frequency of

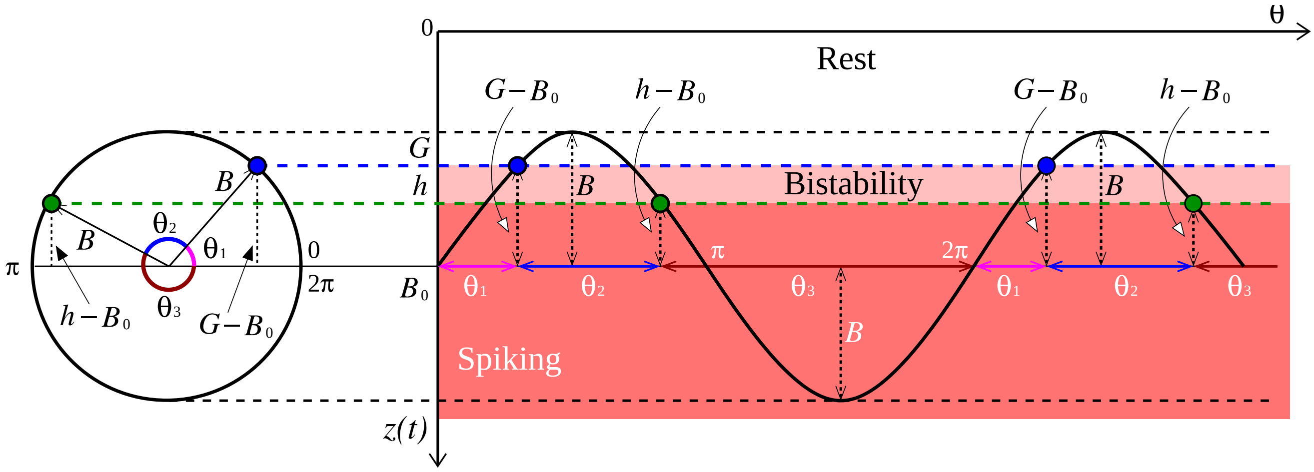
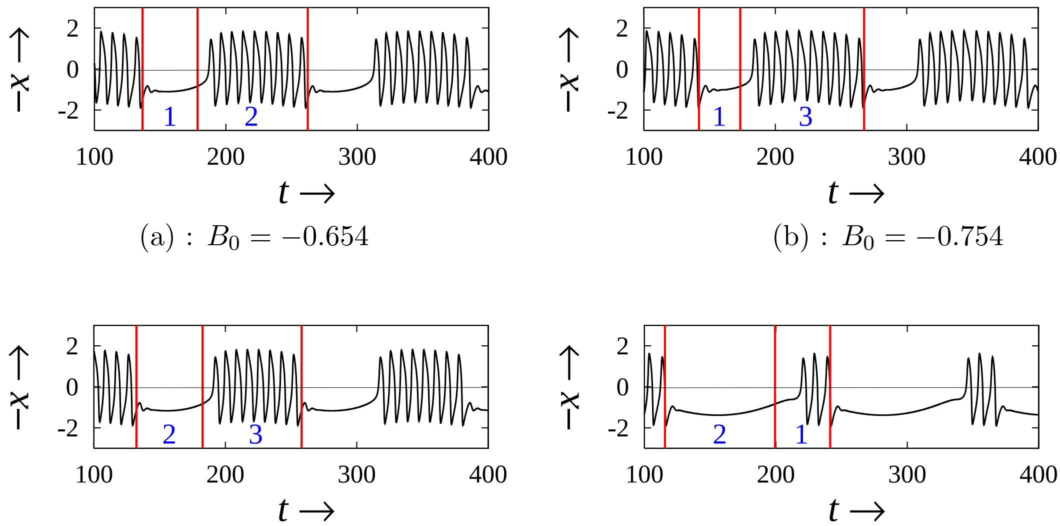


Figure 12: Relationship between the external force and the bifurcation parameter values.



(a) : $B_0 = -0.654$ (b) : $B_0 = -0.754$

(c) : $B_0 = -0.558$ (d) : $B_0 = -0.154$

Figure 13: Example burstings with the specified ratio $X : Y$

external force increases a number of spikes in bursting response. Actually, we solved some period-locking regions consist of tangent bifurcation sets and the responses which exist in each region. Some results obtained form the bifurcation analysis are summarized as follows:

1. only period-1 repetitive spiking response exists in the period-locking region of fundamental harmonic resonance, and period-1 repetitive spiking response and period-1 bursting responses with $r = \{1, 2, \cdots, p-1\}$ spikes exist in the period-locking region of p-higher harmonic resonance.

2. number of spikes(comprehend the sub-threshold oscillation) in bursting response increase one-by-one with increase of p.

3. observed responses change to chaotic response via period doubling cascade in all regions.

We are interested in realizing a bursting generator in an electric circuit, therefore, we will be demonstrated above results to Bonhöffer-van der Pol oscillator [Bautin, 1975] with sinusoidal wave generator as an analogy of FHN model indicates an expected type of bursting. Moreover, we will be analyzed the coupled system using a proposed bursting generator in future.

References

[1] Bautin, A. N. [1975] "Qualitative Investigation of a Particular Nonlinear System," *Journal of Applied Mathematics and Mechanics* **39**, 606–615.

[2] Bertram, R., Butte, M. J., Kiemel, T. & Sherman, A. [1995] "Topological and phenomenological classification of bursting oscillations," *Bull. Math. Biol.* **57**, 413–439.

[3] Del Negro, C. A., Hsiao, C.-F., Chandler, S. H. & Garfinkel Alan [1998] "Evidence for a Novel Bursting Mechanism in Rodent Trigeminal Neuros," *Biophys. J.* **75**, 174–182.

[4] de Vries, G. [1998] "Multiple bifurcations in a polynomial model of bursting oscillations," *J. Nonlin. Sci.* **8**, 281–316.

[5] FitzHugh, R. [1961] "Impulses and physiological state in theoretical models of nerve membrane," *Biophy. J.* **1**, 445–467.

[6] Hindmarsh, J. L. & Rose, R. M. [1984] "A model of neuronal bursting using three coupled first order differential equations," *Philos. Trans. R. Soc. London*, *Ser.* **B221**, 87–102.

[7] Hodgkin, A. L. & Huxley, A. F. [1952] "A qualitative description of membrane current and its application to conduction and excitation in nerve," *J. Physiol.* **117**, 500–544.

[8] Hoppensteadt, F. C. and Izhikevich, E. M. [1997] *Weakly Connected Neural Networks*, Springer, ASM 126.

[9] Izhikevich, E. M. [2000a] "Neural Excitability, Spiking and Bursting," *International Journal of Bifurcation and Chaos* **10**, 1171–1266.

[10] Izhikevich, E. M. [2000b] "Subcritical Elliptic Bursting of Bautin Type," *SIAM J. Appl. Math.* **60**, 503–535.

[11] Morris, C. & Lecar, H. [1981] "Voltage oscillations in the Barnacle giant muscle fiber," *Biophys.* **35**, 193-213.

[12] Nagumo,J., Arimoto, S. & Yoshizawa S. [1962] "An active pulse transmission line simulating nerve axon," In *Pro. of IRE* **50**, 2061–2070.

[13] Rinzel, J. & Lee, Y. S. [1987] "Dissection of a model for neural parabolic bursting," *J. Math. Biol.* **25**, pp. 653–675.

[14] Rinzel, J. [1987] "A formal classification of bursting mechanisms in excitable systems," *Mathematical Topics in Population Biology*, *Morphogenesis and Neurosciences*, *Lecture Note in Biomathematics* **71**, E. Teramoto and M. Yamaguti, eds., (Springer-Verlag, Berlin).

[15] Smolen, P., Terman, D. & Rinzel, J. [1993] "Properties of a bursting model with two slow inhibitory variables," *SIAM J. Appl. Math.* **53**, 861–892.

[16] Tsuji, S., Ueta, T., Kawakami, H. & Aihara, K. [2002] "An Advanced Design Method of Bursting in FitzHugh-Nagumo Model," *Proc. ISCAS 2003* **I**, 389–392.