2022 International Symposium on Nonlinear Theory and Its Applications,
NOLTA2022, Virtual, December 12-15, 2022

Oscillatory behaviors of axon membrane potential using multi-compartment model of Bonhoeffer-Van der Pol oscillator

Naoki Matsumiya†, Kuniyasu Shimizu†, Naohiko Inaba‡

†Dept. of Information and Communication Systems Engineering, Chiba Institute of Technology,
2–17–1 Tsudanuma, Narashino, Chiba 275-0016, Japan
‡Graduate School of Electrical and Information Engineering, Shonan Institute of Technology,
1-1-25 Tsujidou-Nishikaigan, Fujisawa, Kanagawa 251-8501, Japan

Email: s18a5120kr@s.chibakoudai.jp, kuniyasu.shimizu@it-chiba.ac.jp

Abstract—This paper investigates multi-compartment model mimicing axon membrane potential by using simplified model of Hodgkin-Huxley model; Bonhoeffer-Van der Pol oscillator. In this study, we assume that a sinusoidal perturbation is injected to membrane potential at the single edge of the nerve fibre. We report that a traveling membrane potential consisting of mixed-mode oscillations is observed. Futhermore, the increment of small peaks of the mixed-mode oscillations originates from the coupling effect. In addition, the small peaks are also influenced by the angular frequency of the periodic perturbation.

1. Introduction

Hodgkin-Huxley (HH) model is known to mimic axon membrane potential, and show various nonlinear oscillations [1, 2]. Bonhoeffer-Van der Pol (BVP) oscillator is the simplified version of HH model where electrical activity of the membrane is represented by two variables [3]. Mixed-mode oscillations (MMOs) are phenomena found in chemical experiments. They have distinctive waveforms in the time series, and consist of L large amplitude excursions and s small peaks. We assign them symbol L^s. In our previous studies, we reported that BVP oscillator with periodic perturbation showed a complicated MMOs both in numerical and experimental results [3, 4].

This study investigates oscillatory behaviors in multi-compartment model of BVP oscillator, where the lumped BVP oscillators are coupled by the axoplasmic resistance. We assume that a sinusoidal perturbation is injected to the membrane potential at the single edge of the nerve fibre. We numerically show that a traveling membrane potential consisting of MMO-sequences exists. In particular, we report that the increment of small peaks of MMOs originates from the coupling effect via the axoplasmic resistance. In addition, the small peaks are also influenced by the angular frequency of the periodic perturbation.

ORCID iDs Naoki Matsumiya: 0000-0002-1385-5871, Kuniyasu Shimizu: 0000-0003-1983-2360, Naohiko Inaba: 0000-0003-1153-7025

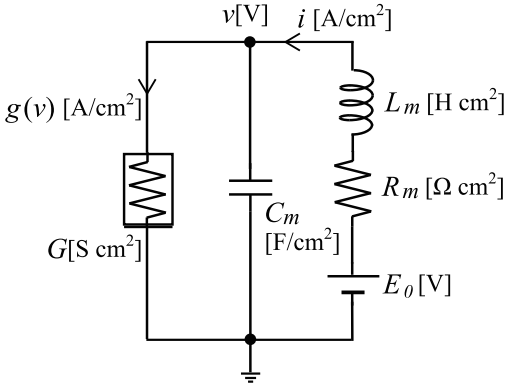


Figure 1: BVP oscillator.

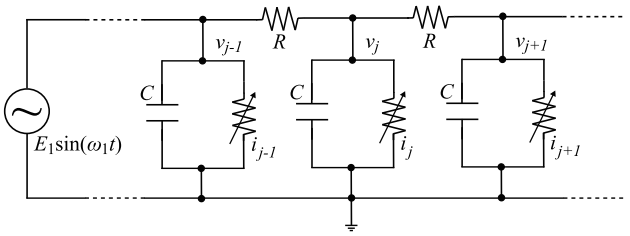


Figure 2: Multi-compartment model of BVP oscillator.

2. Circuit setup

Figure 1 shows a BVP oscillator which consists of an inductor(L_m[H·cm^2]), a capacitor(C_m[F/cm^2]), a resistor(R_m[Ω·cm^2]), a nonlinear conductance(G[S·cm^2]), and a DC voltage source(E_0[V]). In this study, we assume that the voltage-current characteristic of G is written by a third-order polynomial; $g(v) = -g_1 v + g_3 v^3$, where $g_1, g_3 > 0$. The BVP circuit is a simplified model mimicing axon membrane potential. The voltage between the capacitor C_m corresponds to a membrane potential. The membrane ionic current (i^{ion}[A/cm ^{2}]) is equivalently represented by

$$i^{ion} = i - g(v). \tag{1}$$

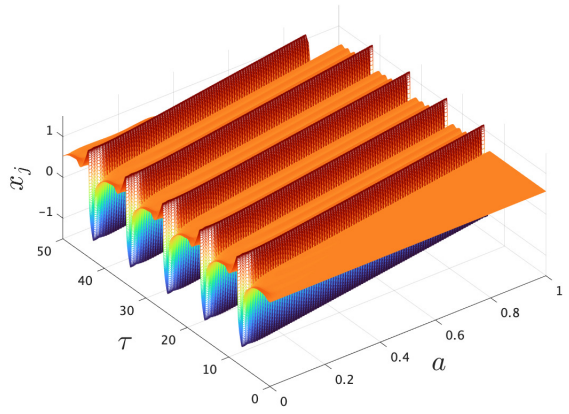


Figure 3: 3D plot of timeseries of membrane potential for $\omega = 0.7$.

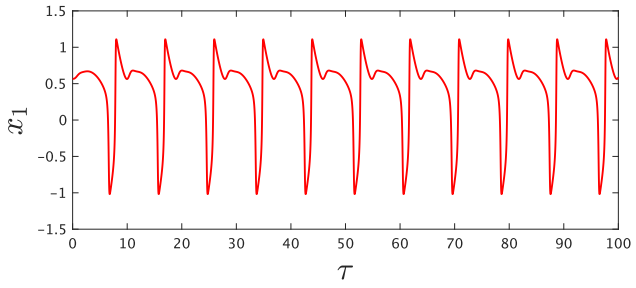
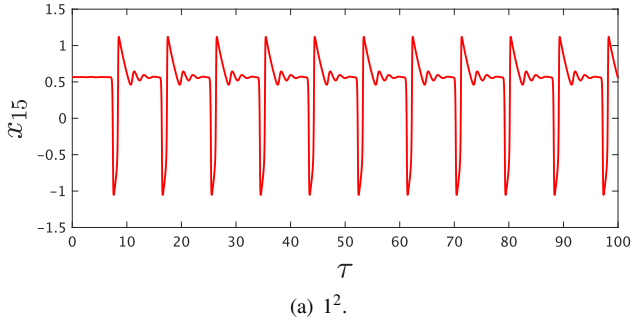
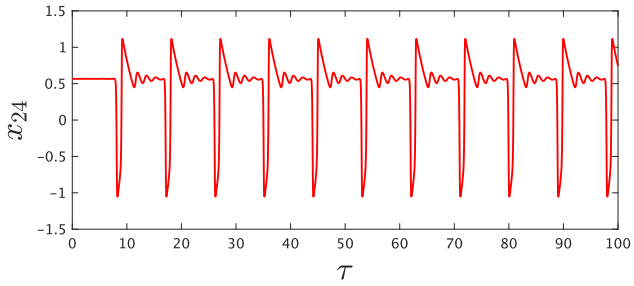


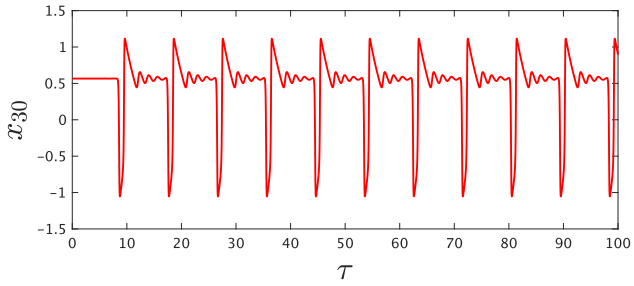
Figure 4: Timeseries of x_1 for $\omega = 0.7$.



(a) 1^2.



(b) 1^3.



(c) 1^4.

Figure 5: Timeseries of x_j, $j = 15, 24, 30$ for $\omega = 0.7$.

In this study, we consider a multi-compartment model based on BVP oscillator, where the model is a cylindrical axonal nerve membrane of radius r[cm] with length l[cm]. To realize the model, we discretize the nerve consisting of the BVP oscillator into a segment of length Δx[cm]. We assume that the axoplasmic resistance between the discretized two nodes($R[\Omega]$) depends on the Ohm's law; $R = \rho_j \Delta x/(\pi r^2)$, where $\rho_j[\Omega\cdot\text{cm}]$ represents the resistivity of the $j-$th node. In addition, the membrane capacitance(C[F]) and the membrane ionic current(i_j^o[A]) of the nerve segment are given by $C = 2\pi r \Delta x C_m$ and by $i_j^o = 2\pi r \Delta x i_j^{ion}$, respectively. Figure 2 shows the schematic diagram of the multi-compartment model. From the Kirchhoff's current law, the following differential equation for the $j-$th node can be written by

$$\frac{v_{j+1} - v_j}{\frac{\rho_j \Delta x}{\pi r^2}} + \frac{v_{j-1} - v_j}{\frac{\rho_j \Delta x}{\pi r^2}} = 2\pi r \Delta x C_m + 2\pi r \Delta x i_j^{ion}. \qquad (2)$$

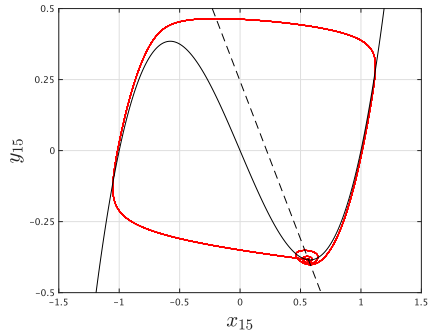
In the following, we consider that $l = 1$[cm] length nerve fibre with radius r is discretized using a spatial resolution of $\Delta x = 0.01$[cm]. That is, the number of nerve segments(M) is set to $M = \frac{l}{\Delta x} + 1 = 101$. We use the zero-flux boundary condition; $v_1 = v_2, v_M = v_{M-1}$. Futhermore, in this study, we assume that a sinusoidal perturbation $E_1 \sin(\omega_1 t)$ is injected to the membrane potential at the single edge of the nerve fibre; v_1 and v_2.

By introducing the following parameters and the variables as

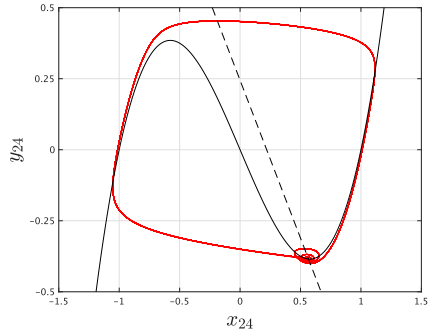
$$\varepsilon \equiv \frac{C_m}{g_1^2 L_m}, \quad k_1 \equiv g_1 R_m, \quad \sigma \equiv \frac{r}{2\rho_j g_1 (\Delta x)^2}, \quad a \equiv \frac{l}{10^{-2}},$$
$$B_0 \equiv \sqrt{\frac{g_3}{g_1}} E_0, \quad B_1 \equiv \sqrt{\frac{g_3}{g_1}} E_1, \quad \omega \equiv L_m g_1 \omega_1,$$
$$\tau \equiv \frac{t}{L_m g_1}, \quad x_j \equiv \sqrt{\frac{g_3}{g_1}} v_j, \quad y_j \equiv \sqrt{\frac{g_3}{g_1^3}} i_j,$$

the normalized version of Eq.(2) is derived as follows

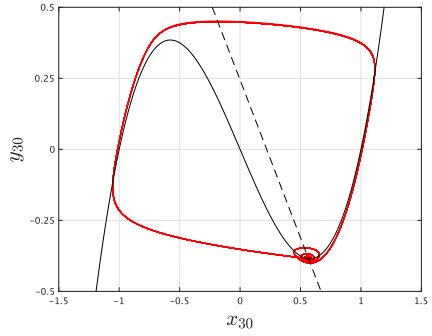
$$\varepsilon \frac{dx_j}{d\tau} = \begin{cases} \sigma_j (x_{j+1} - x_j) - y_j + x_j - x_j^3 & (j = 2) \\ \sigma_j (x_{j-1} - x_j) - y_j + x_j - x_j^3 & (j = M-1) \\ \sigma_j (x_{j+1} - 2x_j + x_{j-1}) - y_j + x_j - x_j^3 & \\ & (j = 3, \ldots, M-2) \end{cases}$$



(a) 1^2.



(b) 1^3.



(c) 1^4.

Figure 6: Trajectries of the timeseries in Figs. 5 (a)–(c) and the x_j-and y_j-nullclines on the phase plane.

(3)

,where the dynamics of the normalized current y_j is written by

$$\frac{dy_j}{d\tau} = \begin{cases} -x_j - k_1 y_j + B_0 + B_1 \sin(\omega\tau) & (j = 2) \\ -x_j - k_1 y_j + B_0 \quad (j = 3, \ldots, M-1). \end{cases} \tag{4}$$

3. Mixed-mode oscillations

In this study, we focus on MMOs in the multi-compartment model using BVP oscillator. In the following results, we fix the parameters as $\varepsilon = 0.1, k_1 = 0.9, B_0 = 0.22, B_1 = 0.16$ and $\sigma = 0.625$, and we employ the angular frequency of the forcing term ω as a control parameters. In addition, the initial condition of the dynamical system is set to $x_j(0) = 0.566218$ and $y_j(0) = -0.384687$ ($j = 1, 2, \ldots, M$). The initial condition is set to the equlibrium point of the isolated BVP oscillator with the fixed parameters and with no periodic perturbation.

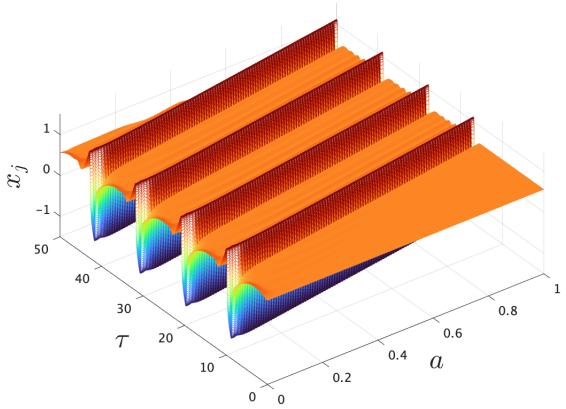


Figure 7: 3D plot of timeseries of membrane potential for $\omega = 0.57$.

Figure 3 shows 3D plot of timeseries of membrane potential x_j, $j = 1, 2, \ldots, M$, when we use $\omega = 0.7$. From the figure, the traveling membrane potential is observed. The timeseries of x_1 where the sinusoidal perturbation is injected represents MMOs of 1^1 as shown in Fig. 4. Figures 5 (a)–(c) show the timeseries of the membrane potential x_j, $j = 15, 24, 30$, respectively. From the timeseries, the number of small peaks of MMOs increases for larger j. That is, we are able to observe the three distinctive waveforms of MMOs; 1^2, 1^3 and 1^4. For $j > 30$, the waveform of the timeseries shows MMO-sequence 1^4 as shown in Fig. 5 (c). Figure 6 shows the trajectry on the phase plane of the timeseries in Fig.5. In this figure, the x_j-and y_j-nullclines with no periodic perturbation and with no coupling are depicted by the black solid curve and by the black dotted line, respectively. The small cycles around the equlibrium point correspond to the small peaks in the timeseries. The increment of the small peaks of MMOs was reported in our previous works [3, 4]. In the literatures, the number of small peaks for 1^s was determined by the angular frequency of the forcing term. Meanwhile, in this study, the increment of small peaks originates from the coupling effect via the axoplasmic resistance.

Futhermore, the number of small peaks for 1^s can be changed by the value of the angular frequency of forcing term ω. When we set the parameter $\omega = 0.57$, we are succeeded in observing the MMO sequences 1^s, $s = 1, 2, \ldots, 5$ as shown in Figs. 7 and 8, where the traveling membrane potential consisting of several distinctive MMO-sequences exist.

4. Conclusions

This paper investigated the oscillatory behaviors in the multi-compertment model where the periodic perturbation at the left edge of the model was injected. We reported that the traveling membrane potential consisting of several distinctive MMO-sequences was observed. In particular, we were succeeded in observing that the increment of small peaks originated from the coupling effect via the axoplasmic resistance.

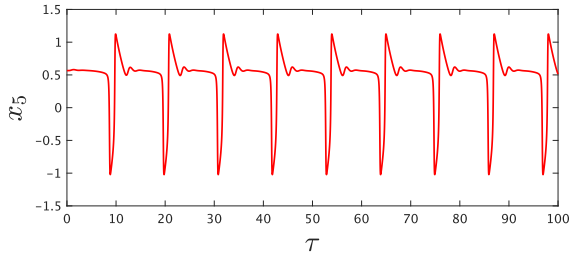
References

[1] F. Rattay and M. Aberham, "Modeling axon membranes for functional electrical stimulation," IEEE Trans. Biomed. Eng. vol.40, no.12, pp.1201–1209, 1993.

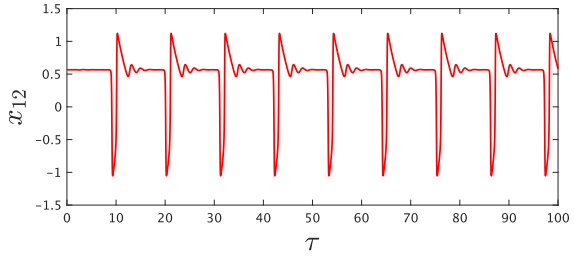
[2] F. Rattay and T. Tanzer, "A simple model considering spiking probability during extracellular axon stimulation," PLOS ONE, vol.17, no.4, 2022.

[3] K. Shimizu, M. Sekikawa, N. Inaba, "Mixed-mode oscillations and chaos from a simple second-order oscillator under weak periodic perturbation," Phys. Lett. A, vol.375, no.14, pp.1566-1569, 2011.

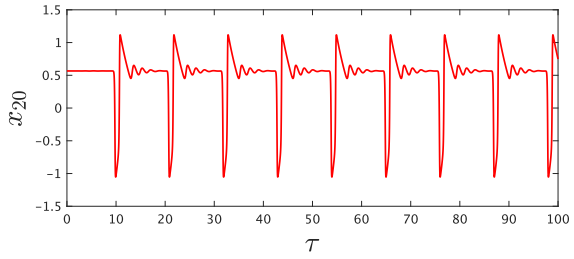
[4] K. Shimizu, M. Sekikawa, N. Inaba, "Experimental study of complex mixed-mode oscillations generated in a Bonhoeffer-van der Pol oscillator under weak periodic perturbation," Chaos, 25, 023105, 2015.



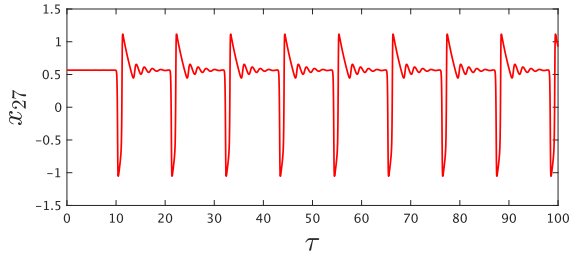
(a) 1^1.



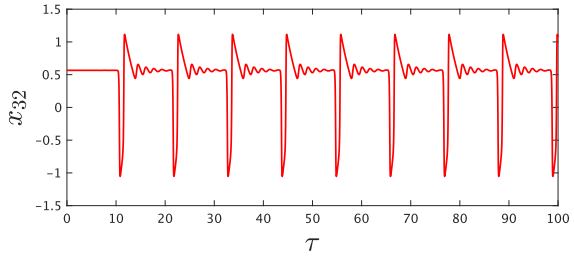
(b) 1^2.



(c) 1^3.



(d) 1^4.



(e) 1^5.

Figure 8: Timeseries of $x_j, j = 5, 12, 20, 27, 32$ for $\omega = 0.57$.