A Neuronal Network Model with Plasticity for Tinnitus Management by Sound Therapy

H. Nagashino[1], Y. Kinouchi[2], A. A. Danesh[3] and A. S. Pandya[4]

[1] Department of Biomedical Information Science, The University of Tokushima, Tokushima, Japan
[2] Department of Biological Functions Engineering, The University of Tokushima, Tokushima, Japan
[3] Department of Communications and Disorders Florida Atlantic University, Boca Raton, USA
[4] Department of Computer Science and Engineering, Florida Atlantic University, Boca Raton, USA

Abstract—**A perception of hearing sounds in the ear or head without any external source is referred to as tinnitus. There are many therapeutic approaches for tinnitus and sound therapy techniques for its treatment has been proposed. In order to investigate mechanisms of tinnitus generation and the clinical effects of sound therapy from the viewpoint of neural engineering, we have proposed a computational model using a neural oscillator. In the present paper, we propose another model that is composed of model neurons described by simplified Hodgkin-Huxley equations. By computer simulation it was detected that this model also has a bistable state, i.e., a stable oscillatory state and a stable equilibrium (non-oscillatory) state coexist at a certain parameter region. It was also noticed that the oscillation can be inhibited by supplying constant or pulse train stimulus, which is hypothesized as an afferent signal that is employed as an acoustical stimulus for tinnitus treatment. By hypothesizing that the oscillation and the equilibrium correspond to generation and inhibition of tinnitus, respectively, these phenomena could explain the fact that the habituated human auditory system temporarily halts perception of tinnitus following sound therapy.**

Keywords— **tinnitus, sound therapy, neuronal network model, plasticity, oscillation**

I. Introduction

A perception of hearing sounds in the ear or head without any external source is referred to as tinnitus. Mechanism of tinnitus generation has been hypothesized from the viewpoint of neurophysiology [1, 2]. Contribution of neural plasticity to tinnitus has been discussed [3, 4]. Tinnitus has many subclasses and attempts has been made to categorize tinnitus based on its characteristics which in turn can facilitate the selection of treatment method [5]. Sound therapy techniques for tinnitus have been proposed. This kind of treatment has the clinical effect that tinnitus disappears or reduce in its loudness after the sound presentation [6]. The mechanisms of tinnitus and its management by sound therapy, however, are not clear. To account for those mechanisms from the viewpoint of neural engineering, we constructed a computational model using a neural oscillator [7-9]. It was attempted to reproduce conceptually tinnitus generation and its inhibition using sound stimuli. It was detected that by providing the model with sinusoidal or noise stimulus that is hypothesized as sound for treatment of tinnitus we can inhibit the oscillation changing the parameter value by introducing plasticity to the model. By hypothesizing that the oscillation and the equilibrium correspond to generation and inhibition of tinnitus, respectively, we reported that these phenomena could explain the fact that the habituated human auditory system temporarily halts perception of tinnitus following sound therapy [6]. Our model is built by a somewhat conservative simplification of the central auditory pathways and associated central nervous system areas that are relevant to tinnitus.

In the present paper, we propose a different model composed of model neurons described by simplified Hodgkin-Huxley equations [10, 11]. This model is still conceptual since it consists of only three neurons, but more realistic than the previous one because it shows time series of firings of neurons. We show here that inhibition of the oscillation can be observed in this model as well by constant or pulse train stimuli. Through numerical simulations we found out that adequate intensity of stimulus is required for inhibition of the oscillation.

II. Methods

We propose a neuronal network model shown in Fig. 1 in which firing sequences in the nervous system are simulated. This model of tinnitus generation network is conceptually simplified and composed of two excitatory neurons and one inhibitory neuron as shown in Fig. 1 (a). The two excitatory neurons, E_1 and E_2, are mutually coupled forming a positive feedback loop. The excitatory neuron E_1 and the inhibitory neuron I are also mutually coupled forming a negative feedback loop. The positive feedback loop brings sustained firings. The negative feedback loop controls the firing rate. The coupling strength between neurons is denoted by C_{ij} ($i, j \in \{1, 2, I\}$). The neuron E_1 receives external stimuli S that is afferent signal due to the acoustic stimuli that are

employed in sound therapy. We express the dynamics by a simplified version of Hodgkin-Huxley equations (HH) [10, 11]. We employed it instead of HH because of reduction of the number of state variables for each neuron from four to two.

External stimuli S by pulse train stimulus are given by multiple input neurons E_1,..., E_P as shown in Fig. 1 (b). Because cortical neurons receive input from a number of neurons, and the simulation with the stimulus of a wide range of firing rate is impossible from a single neuron model. The number of input neurons and the stimulus to input neuron E_{Sj} is denoted by P and S_j, respectively.

A. Formulation of the model without plasticity

We describe the basic dynamics of the model as

$$\frac{dv_1}{dt} = \frac{G(v_1, m^{\infty}(v_1), 0.8(1-h_1), h_1) + C_{12}z_2 + S}{C_m}, \tag{1}$$

$$\frac{dh_1}{dt} = \alpha_h(v_1)(1-h_1) + \beta_h(v_1)h_1, \tag{2}$$

$$\frac{dv_2}{dt} = \frac{G(v_2, m^{\infty}(v_2), 0.8(1-h_2), h_2) + C_{21}z_1 - C_{2I}z_I}{C_m}, \tag{3}$$

$$\frac{dh_2}{dt} = \alpha_h(v_2)(1-h_2) + \beta_h(v_2)h_2, \tag{4}$$

$$\frac{dv_I}{dt} = \frac{G(v_I, m^{\infty}(v_I), 0.8(1-h_I), h_I) + C_{I2}z_2}{C_m}, \tag{5}$$

$$\frac{dh_I}{dt} = \alpha_h(v_I)(1-h_I) + \beta_h(v_I)h_I, \tag{6}$$

where v is the membrane potential and h is the variable associated with activation of potassium ion channel in the neuron E_1, E_2 or I. The functions $G(v,m,n,h)$ and $m^{\infty}(v)$ are expressed as

$$G(v,m,n,h) = \bar{g}_{Na}m^3h(V_{Na}-v) + \bar{g}_K n^4(V_K - v) + \bar{g}_l(V_l - v) \tag{7}$$

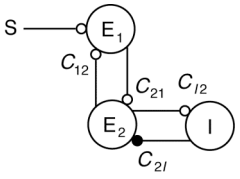
and

$$m^{\infty}(v) = \alpha_m(v)/\{\alpha_m(v) + \beta_m(v)\} \tag{8}$$

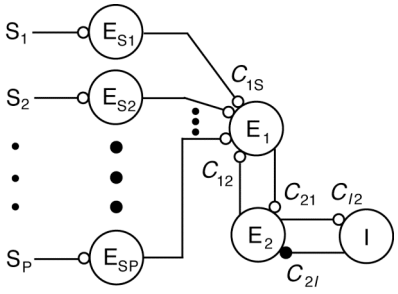
respectively. The functions $\alpha_m(v)$ and $\beta_m(v)$ in Eq. (8) are expressed respectively as

$$\alpha_m(v) = 0.1(25-v)/\{e^{(25-v)/10} - 1\} \tag{9}$$

and



(a) Basic structure of the present model



(b) Model structure with pulse train input

Fig. 1 Neuronal network model structure

$$\beta_m(v) = 4\,e^{-v/18} \tag{10}$$

Functions $\alpha_h(v)$ and $\beta_h(v)$ in Eq. (2), (4), (6) are expressed respectively as

$$\alpha_h(v) = 0.07\,e^{-v/20} \tag{11}$$

and

$$\beta_h(v) = 1/\{e^{(30-v)/10} + 1\}. \tag{12}$$

The parameters of the neuron model were fixed as C_m=1[μF/cm^2], $\bar{g}_{Na} = 120$[mS/cm^2], $\bar{g}_K = 36$[mS/cm^2], $\bar{g}_l = 0.3$[mS/cm^2], V_{Na}=115[mV], $V_K = -12$[mV], V_l=10.6 [mV], based on the values in Hodgkin-Huxley model. The output of the neuron is denoted by z_j and expressed as function of the membrane potential v_j as

$$z_j = \begin{cases} 1 & (v_j \geq 1) \\ 0 & (v_j < 1) \end{cases}. \tag{13}$$

B. Formulation of plasticity

To reproduce the effect of sound therapy, we assume that the coupling strength from the neuron E_1 to the neuron E_2, C_{12}, has plasticity in such a way that it increases when the neurons E_1 and E_2 fires simultaneously, and decreases when the firings of the neurons E_1 and E_2 are not synchronized. This assumption is based on Hebbian hypothesis regarding synaptic plasticity [12]. We describe the dynamics of C_{12} as follows. When both z_1 and z_2 are 0,

$$\frac{dC_{12}}{dt} = 0, \tag{14}$$

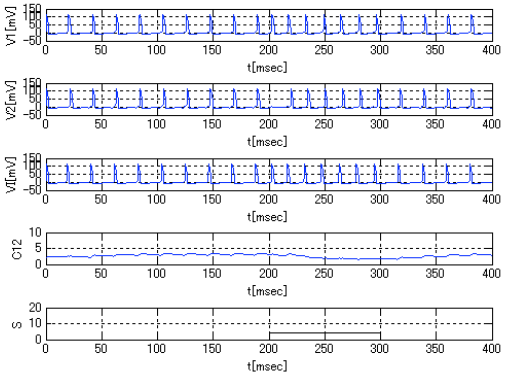
and otherwise

$$\frac{dC_{12}}{dt} = \frac{-C_{12} + b(z_1 - 0.5)(z_2 - 0.5) + C_0}{\tau}, \tag{15}$$

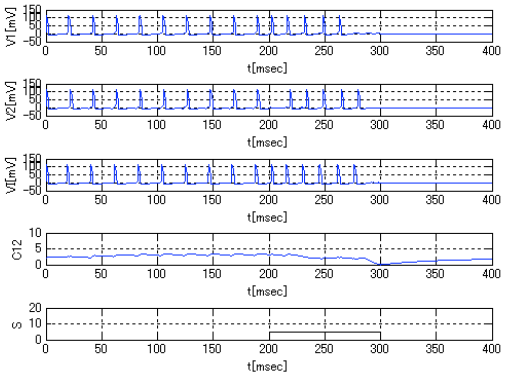
where C_0, b and τ are positive constants. The constant C_0 is associated with the equilibrium of C_{12}. The constants b and τ denote the efficacy of synaptic plasticity and the time constant of C_{12}, respectively.

III. Results

Throughout the simulation the parameter values except C_0 were given as $C_{21} = 10$, $C_{2I} = 10$, $C_{I2} = 20$, $b = 40$ and $\tau_C = 50\,[\mathrm{ms}]$.



(a) An unsuccessful result. $I = 4\,[\mu\mathrm{A/cm}^2]$.



(b) A successful result. $I = 5\,[\mu\mathrm{A/cm}^2]$.

Fig. 2 Inhibition of oscillation by constant input. $C_0 = 2$.

Without stimulation or plasticity, the model has two stable solutions, an oscillatory state by sustained firings and a non-firing state, which are bistable for a parameter region. The larger C_{12} brings the larger basin of the oscillatory solution in the state space of the model in the region.

A. Constant stimulus

First the inhibition of oscillation by constant stimulus to neuron E_1 was examined with plasticity. The amplitude I of the stimulus was increased one by one $[\mu\mathrm{A/cm}^2]$. Stimulation period is 100ms. Fig. 2 shows an unsuccessful result (a) and a successful result (b) when $C_0 = 2$. The amplitude I not less than $5\,[\mu\mathrm{A/cm}^2]$ was required for inhibition of oscillation.

B. Pulse train stimulus

Next the inhibition of oscillation by pulse train stimulus to neuron E_1 was examined. To simulate the input by neurons in the brain, the stimulus S to neuron E_1 was formulated as

$$S = \sum_{j=1}^{P} C_{1S} z_{Sj}, \tag{16}$$

where z_{Sj} is the output of neuron E_{Sj}. The membrane potential v_{Sj} and the variable h_{Sj} is given as

$$\frac{dv_{Sj}}{dt} = \frac{G(v_{Sj}, m^{\infty}(v_{Sj}), 0.8(1 - h_{Sj}), h_{Sj}) + S_j}{C_m} \tag{17}$$

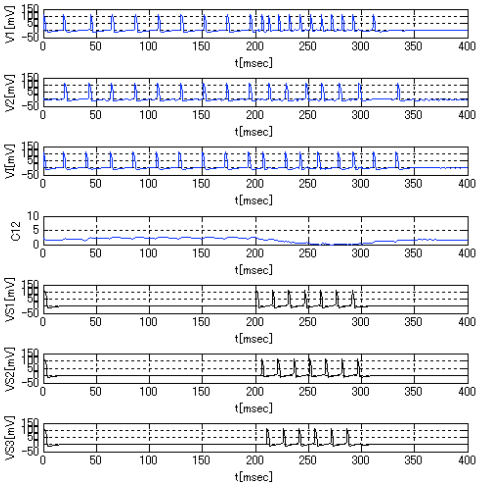


Fig. 3 Inhibition of oscillation by pulse train input. $C_0 = 2$, $I = 10\,[\mu\mathrm{A/cm}^2]$.

and

$$\frac{dh_{Sj}}{dt} = \alpha_h(v_{Sj})(1-h_{Sj}) + \beta_h(v_{Sj})h_{Sj}, \quad (18)$$

respectively. The stimulus S_j to input neuron E_{Sj} was expressed as

$$S_j = \begin{cases} I & (200+5(j-1) \le t \le 300 \quad [\text{ms}]) \\ 0 & (\textit{other time}) \end{cases}, \quad (19)$$

so that firing instances of each input neuron E_{Sj} are different from others. The amplitude I of stimulus to input neurons E_{Sj} is constant with time. The number of input neurons P is three in the present simulation. The amplitude I was increased one by one [μA/cm^2] as case for constant stimulus. Fig. 3 shows a successful result when $C_0 = 2$ and I=10[μA/cm^2]. The amplitude I not less than 10[μA/cm^2] was required for inhibition of oscillation.

IV. Discussion

The reason why inhibition of oscillation occurs is as follows. When no stimulus is provided, the firings of neurons E_1 and E_2 are synchronized. When constant or pulse train stimulus is provided, those firings are not synchronized. It makes the coupling strength C_{12} decrease according to Eq. (15). Once C_{12} is decreased to the value in which only non-oscillatory solution exists and the stimulus stops, the model neurons stop firing.

In order to investigate the characteristics of the model in more detail, simulation with different values of C_0 was performed. It was observed that there is a threshold of the amplitude I for each C_0. In order to inhibit the oscillation, larger I than the threshold is required. Moreover, the larger the value of C_0 is, the larger value of I is necessary to inhibit the oscillation. The reason is speculated as follows. The larger C_0 brings the larger stationary value of C_{12}. It additionally brings the larger basin of the oscillatory solution in the state space of the model equations. In order to reduce the value of C_{12} a stronger stimulation is required.

V. Conclusions

In this study a conceptual and computational neuronal network model with plasticity in the human auditory system was proposed to explain the mechanisms of tinnitus and its management by sound therapy. Through analysis of this model, it was shown that, similar to the previous neural oscillator model, oscillation can be inhibited due to the change of coupling strength between neurons in the model by supplying constant or pulse train stimulus to the model.

Our future work will expand this model so that it can more effectively relate to the underlying physiology of tinnitus, and explore better stimulation for its inhibition. This in turn will result in improvement in designing sound therapy techniques and stimuli.

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Address of the corresponding author:

Author: Dr. Hirofumi Nagashino
Institute: The University of Tokushima
Street: 3-18-15 Kuramoto
City: Tokushima
Country: Japan
Email: nagasino@medsci.tokushima-u.ac.jp