Comparison of Neuronal Network Models for Tinnitus Management by Sound Therapy

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***Abstract*—Tinnitus is a condition in which sounds heard in the ear or head without any external sound. There are many therapeutic approaches for tinnitus and sound therapy is one of the techniques for its treatment that have 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 computational models with plasticity and inhibitory feedback using a neural oscillator or model neurons described by simplified Hodgkin-Huxley equations. By hypothesizing that the oscillation and the non-oscillatory state in the models correspond to generation and inhibition of tinnitus, respectively, we found out that the models could explain the fact that the habituated human auditory system temporarily halts perception of tinnitus following sound therapy. However, a simpler model without inhibitory feedback can exhibit the solutions that exist in the former models. In the present paper, outcomes of the neuronal network model, which is incorporated with inhibitory feedback, are compared with the model without inhibitory feedback. It was revealed that the former is superior since it has a larger parameter region in which the effects of sound therapy can be restored due to synaptic plasticity.**

I. Introduction

Tinnitus is a condition in which sounds heard in the ear or head without any external sound [1, 2]. Contribution of neural plasticity to tinnitus has been discussed [3, 4]. Tinnitus has many subclasses and attempts have been made to categorize tinnitus based on its characteristics which in turn can facilitate the selection of treatment method [5]. Among a number of therapies sound therapy techniques for its treatment have the clinical effect that tinnitus disappears or reduces 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, previously we had proposed a computational model using a neural oscillator [7]. We demonstrated that the model conceptually reproduces 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 oscillations. This was accomplished by incorporating neural plasticity through parameters such that their values can be updated. 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. However, that model relied on a somewhat conservative simplification of the central auditory pathways and associated central nervous system areas that are relevant to tinnitus.

Later we proposed a different model composed of model neurons described by simplified Hodgkin-Huxley equations [8]. This model is still conceptual since it consists of only three neurons with positive and negative feedbacks, but more realistic than the previous one because it shows time series corresponding to the firings of neurons. We showed that inhibition of the oscillation can be observed in this model as well by constant or pulse train stimuli.

The model that consists of only two excitatory neurons that are coupled to each other also has a bistable state, a stable oscillatory state and a stable non-oscillatory state. It was discovered that in this model oscillation can be inhibited by external stimulus.

In order to verify whether two excitatory neurons with only positive feedback are sufficient or inhibitory feedback is required for the conceptual model, a comparison of the models by simulation study with different parameter values was conducted.

In the present paper, the results of comparison of the models are described. The results show that the model with both positive and negative feedbacks is better since it has a larger parameter region in which the effect of sound therapy can be reproduced by synaptic plasticity.

II. Neuronal Network Models with Simplified Hodgkin-Huxley Equations

We propose neuronal network models shown in Fig. 1 in which firing sequences in the nervous system are simulated. These models are conceptually simplified systems of tinnitus generation network. The first one is composed of only two excitatory neurons as shown in Fig. 1 (a). The two excitatory

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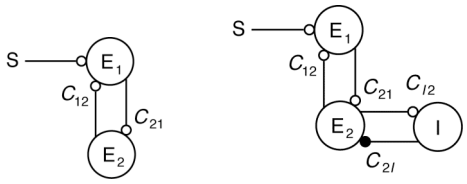
neurons, E_1 and E_2, are mutually coupled forming a positive feedback loop. The positive feedback loop brings sustained firings. This model is referred to as model 1.

The second model is composed of two excitatory neurons and one inhibitory neuron as shown in Fig. 1 (b). In addition to the positive feedback loop of the excitatory neurons E_1 and E_2 as in model 1, this model includes a negative feedback loop with the excitatory neuron E_2 and the inhibitory neuron I that are also mutually coupled. The negative feedback loop controls the firing rate. This model is referred to as model 2. Both the models can be bistable with a sustained firing state and a non-firing state.

In both the models, 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 of the model by a simplified version of Hodgkin-Huxley equations (HH) [9-11]. We employed it instead of HH to save the time of simulation by reduction of the number of state variables for each neuron from four to two.



(a) Model 1 (b) Model 2

Fig. 1. Basic structure of the present models

A. Formulation of model 1 without plasticity

We describe the basic dynamics of the model 1 as

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

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

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

and

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

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

$$G(v,m,n,h) = \bar{g}_{Na}m^3h(V_{Na} - v) + \bar{g}_K n^4(V_K - v) + \bar{g}_l(V_l - v) \tag{5}$$

and

$$m^{\infty}(v) = \alpha_m(v) \big/ \{\alpha_m(v) + \beta_m(v)\} \tag{6}$$

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

$$\alpha_m(v) = 0.1(25 - v) \big/ \{e^{(25-v)/10} - 1\} \tag{7}$$

and

$$\beta_m(v) = 4\, e^{-v/18} \tag{8}$$

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

$$\alpha_h(v) = 0.07\, e^{-v/20} \tag{9}$$

and

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

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

$$z_j = \begin{cases} 1 & (v_j \geq 1) \\ 0 & (v_j < 1) \end{cases}. \tag{11}$$

B. Formulation of model 2 without plasticity

We describe the dynamics of the membrane potential v_2 instead of Eq. (3) as

$$\frac{dv_2}{dt} = \frac{G(v_2, m^{\infty}(v_2), 0.8(1-h_2), h_2) + C_{21}z_1 - C_{2I}z_I}{C_m}. \tag{12}$$

We describe the dynamics of the variables associated with neuron I, v_I and h_I as

$$\frac{dv_I}{dt} = \frac{G(v_I, m^{\infty}(v_I), 0.8(1-h_I), h_I) + C_{I2}z_2}{C_m}, \tag{13}$$

and

$$\frac{dh_I}{dt} = \alpha_h(v_I)(1-h_I) + \beta_h(v_I)h_I. \tag{14}$$

C. 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,

$$\frac{dC_{12}}{dt} = 0, \tag{15}$$

and otherwise

$$\frac{dC_{12}}{dt} = \frac{-C_{12} + b(z_1 - 0.5)(z_2 - 0.5) + C_0}{\tau}, \quad (16)$$

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 $\tau = 50\,[\mathrm{ms}]$.

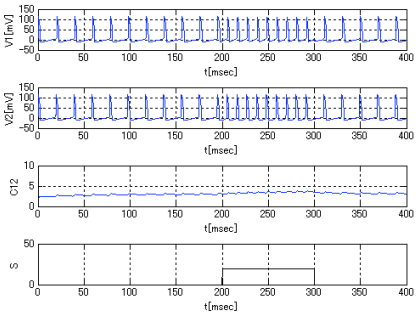
Without stimulation or plasticity, the models have two stable solutions, a firing state and a non-firing state, which are bistable for a certain parameter region. We obtained the regions of the two solutions with respect to the value of the coupling coefficient C_{12} by simulation with different values of C_{12} which were increased in steps of 0.1 in the range of $0 < C_{12} \le 30$. The results are shown in Table I. The non-oscillatory state exists stably for any value of C_{12} in the above range in both the models. The region of the oscillatory state is included within that of the non-oscillatory state. Which state appears depends upon the initial states of the models, that is, the initial values of the potentials v_i and the variables h_i associated with activation of potassium ion channel in the neurons ($i \in \{1, 2, I\}$). The larger C_{12} brings the larger basin of the oscillatory solution in the state space of the model.

TABLE I
Regions of Two Stable States With Respect To The Coupling Coefficient C_{12} In Two Models

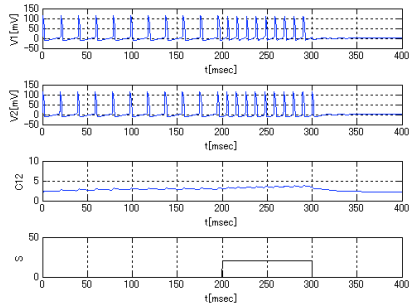
Model	Non-oscillatory State	Oscillatory State
model 1	$0 < C_{12}$	$0.4 \le C_{12}$
model 2	$0 < C_{12}$	$1.5 \le C_{12} \le 8.9$

Next the inhibition of oscillation by constant input to neuron E_1 was examined with plasticity of the coupling coefficient C_{12}. The amplitude I of input was increased in steps of 1 [μA/cm^2]. Stimulation period is 100ms. Fig. 2 shows an unsuccessful result (a) and a successful result (b) in model 1 when $C_0 = 2$. The amplitude I not less than 20 [μA/cm^2] was required for inhibition of oscillation. Fig. 3 shows an unsuccessful result (a) and a successful result (b) in model 2 when $C_0 = 3$. The amplitude I not less than 5 [μA/cm^2] was required for inhibition of oscillation.

In order to investigate the characteristics of the models in more detail, simulation with different values of C_0 was performed. The amplitude I was given in the rage of $0 < I \le 30$ [μA/cm^2]. The results are shown in Table II. For model 1, an input in that range did not inhibit the oscillation when $C_0 = 2.5, 3, 3.5$ and 4. For model 2, the region in which the inhibition of oscillation occurred was investigated for those values of C_0.



(a) An unsuccessful result. $I = 19$[μA/cm^2].



(b) A successful result. $I = 20$[μA/cm^2].

Fig. 2 Inhibition of oscillation by constant input in model 1. $C_0 = 2$.

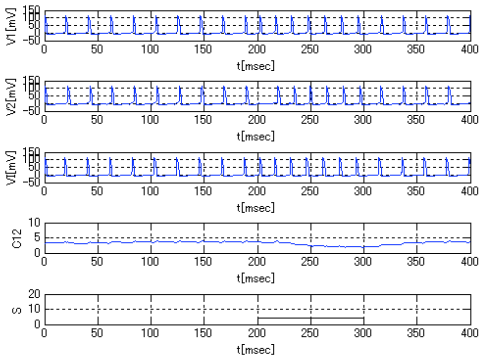
It was observed that there is a threshold of the amplitude I for each C_0. In order to inhibit the oscillation, an I value larger than the threshold is required. Moreover, for larger values of C_0, larger values of I are necessary to inhibit the oscillation in model 2.

IV. Discussion

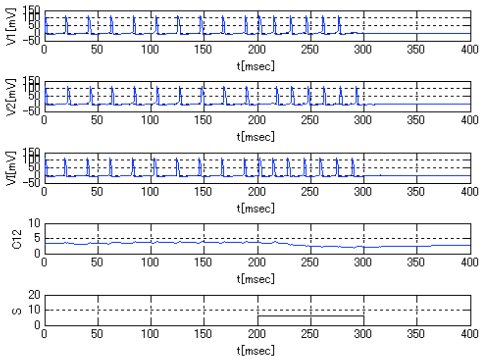
For model 2, the reason why inhibition of oscillation occurs is speculated as follows. When no stimulus is provided, the firings of neurons E_1 and E_2 are synchronized. When constant stimulus is provided, those firings are not synchronized. It causes the coupling strength C_{12} to decrease according to Eq. (16). Once C_{12} decreases to a value in the region where only non-oscillatory solution exists and the stimulus stops, the model neurons stop firing. Even if it does not decrease to such a value, the smaller C_{12} results in a smaller basin of the state space for oscillation. Therefore, the model stops firing after the external stimulus ends.

For model 1, it is observed in Fig. 2 that the stimulus to neuron E_1 does not make the coupling strength C_{12} decrease. It seems that the inhibition of oscillation occurred due to the states of the model just fell into the basin of non-oscillatory solution when C_0 is equal to 2. It seems that that did not happen for the range of the amplitude of input employed in the simulation when the value of C_0 was larger. The inhibition might be realized with larger amplitude or longer addition of input. It can be stated, however, that it is more

difficult to inhibit the oscillations in model 1 than in model 2.



(a) An unsuccessful result. $I = 5[\mu\text{A/cm}^2]$.



(b) A successful result. $I = 6[\mu\text{A/cm}^2]$.

Fig. 3 Inhibition of oscillation by constant input in model 2. $C_0 = 3$.

TABLE II
MINIMAL CONSTANT INPUT VALUES WITH WHICH THE OSCILLATION CAN BE INHIBITED IN TWO MODELS IN THE SIMULATIONS $[\mu\text{A/cm}^2]$

Model	$C_0 = 2$	$C_0 = 2.5$	$C_0 = 3$	$C_0 = 3.5$	$C_0 = 4$
model 1	20	-	-	-	-
model 2	5	5	6	7	7

Therefore, it is concluded that model 2 is better as the model for tinnitus management.

The reason why a larger value of I is necessary to inhibit the oscillation in cases where C_0 values is larger is speculated as follows. A larger C_0 results in a larger stationary value of C_{12}. Moreover, it causes a 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.

The plasticity is introduced only to C_{12} in the present models for simplification of the models. For those models with more plastic couplings further investigation is required.

V. CONCLUSION

In the present study two models with plasticity for tinnitus generation and its management by sound therapy are compared regarding the characteristics of inhibition of oscillations by a constant input. The models are composed of neurons described by simplified Hodgkin-Huxley equations. Model 1 consists of two excitatory neurons which are mutually coupled. Model 2 is configured by addition of an inhibitory neuron to model 1. Through simulation of the models, it was detected that the negative feedback in model 2 plays an important role in giving the model the effect of plasticity that leads to inhibition of oscillations.

The present models are composed of neurons as conceptual blocks. 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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