A neuronal network model with STDP for tinnitus and its management by sound therapy

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***Abstract*—Tinnitus is a phantom sound that one hears in the ears or in the head without any external source. Sound therapy is one of the most effective techniques for tinnitus treatment that have been proposed. In order to investigate mechanisms of tinnitus generation and the clinical effects of sound therapy, we have proposed computational models with plasticity using a neural oscillator or a neuronal network model described by simplified Hodgkin-Huxley equations. In the present paper, another neuronal network model with a different structure based on a recent physiological consideration is proposed and the simulation results of the model are described. The model is able to replicate the clinical results that human auditory system temporarily halts perception of tinnitus following sound therapy.**

I. Introduction

TINNITUS is a phantom sound that one hears in the ears or in the head without any external sound [1]. A variety of environmental and pathological conditions can result in the tinnitus generation. Tinnitus and hearing loss may coexist or be present independently from each other. In other words, many of individuals with tinnitus have clinically normal hearing sensitivity and not all of those with hearing loss report tinnitus.

Neurophysiological models have been proposed to understand the mechanism of the tinnitus [2], [3]. Many researchers have discussed the contribution of neural plasticity to tinnitus in order to understand the neural correlates of tinnitus [4]-[9]. Auditory electrophysiological studies have demonstrated an evidence for thalamic plasticity via top-down modulation [8]. It has been suggested that the damage of the peripheral system decreases auditory nerve activity and this change leads to plastic adjustments, a shift in the balance of excitation and inhibition, and increase of spontaneous firings in the central auditory system [6], [7]. Structural brain changes in tinnitus have been discovered using MRI [10].

Computational modeling is another promising approach to understanding of tinnitus [11]-[14]. It has been addressed that a lot of portions in the brain are related with the tinnitus. However, it has been pointed out that the thalamo-cortical network could be essentially important for tinnitus generation [10], [15]. The model structure in the present paper is based on these considerations. A computational model of thalamocortical correlates with plasticity from the perspective toward understanding of the tinnitus has been reported [11].

A number of approaches have been proposed by clinicians and scientists for management and treatment of tinnitus [16] such as medications, supplemental vitamins and micronutrients, surgical procedures, psychotherapy and biofeedback, electrical stimulation, magnetic stimulation, laser therapy, and sound therapy or acoustic therapy.

Sound therapy is one of the most effective methods in tinnitus management among the therapies. Sound therapy techniques for tinnitus treatment have the clinical effect that tinnitus disappears or reduces in its loudness after the sound presentation [17]. Sound therapy employs a variety of stimuli such as music, white noise, narrow band noise and environmental sounds to facilitate the habituation process to tinnitus. The mechanisms of tinnitus management by sound therapy, however, are not clear.

Previously we proposed computational models using a neural oscillator [11], [18] or a neuronal network [19], [20] to replicate tinnitus generation and its management by sound therapy. We demonstrated that the model conceptually reproduces activity of tinnitus and its inhibition using sound stimuli by providing the model with constant, sinusoidal or noise stimulus that is hypothesized as sound for treatment of tinnitus. This was accomplished by incorporating neural plasticity through parameters such that their values can be modified.

We employed Hebbian hypothesis [21] for the synaptic plasticity in one of the couplings between the components in the previous models. Hebbian hypothesis has been adopted in a number of neural network models for many years.

As a newer and biologically plausible hypothesis for synaptic plasticity in the nervous system, "spike-timing-dependent plasticity (STDP)", was proposed [22]. It does not replace the idea of Hebbian hypothesis, but describes Hebbian synaptic plasticity more specifically. This

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hypothesis has been adopted in a number of computational models of neuronal networks [23]. We proposed a neuronal network model with a plastic coupling of neurons expressed by STDP equations and demonstrated the inhibition of oscillation as in the former models [24].

In the present paper, we propose a neuronal network model with a different structure based on the recent physiological consideration [9], [15]. The equations for the membrane potentials of the neurons are the same as those in the former neuronal network models. We demonstrate the results of computer simulation of this model. The results show that the inhibition of oscillation can be replicated with appropriate input and model parameters, similarly to the previous models, which explains the effect of sound therapy. What is different from the models with Hebbian hypothesis is that the inhibition of oscillation takes place with the increase of the plastic synaptic strength.

II. A Neuronal Network Model

The neuronal network model we propose in this paper is shown in Fig. 1. In the model the firing sequences in the nervous system are simulated. The present model only replicates the inhibition of tinnitus by external sound stimulation. Modeling the habituation would much larger network configuration. The present model is a conceptually simplified system of a tinnitus generation network. However, we believe that the neural mechanism proposed here could form components of models involving large-scale neural correlates for providing a neurophysiological framework [2].

The model is composed of two excitatory neurons and one inhibitory neuron as shown in Fig. 1. The excitatory neurons E_1 and E_2 are mutually coupled forming a positive feedback loop. The inhibitory neuron I receives input from both E_1 and E_2. It inhibits E_1 making a negative feedback loop. The negative feedback loop controls the firing rate. The neurons represent those in thalamus, cortex and thalamic reticular nucleus, respectively. The model can be bistable with a sustained firing state and a non-firing state.

The coupling strength between neurons is denoted by C_{ij} ($i, j \in \{1, 2, I\}$). The output of each neuron is denoted by z_j and expressed as a threshold function of the membrane potential of the neuron [25]. 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) as in the previous models [19], [20], [25]. 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.

To replicate 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 the present model the plasticity based on STDP hypothesis [22] is introduced. The key idea of this hypothesis is that when the presynaptic neuron fires before the postsynaptic neuron, the synaptic strength becomes stronger (long term potentiation), and when the postsynaptic

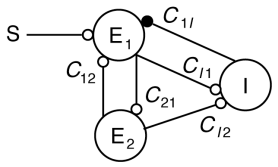


Fig. 1. Basic structure of the present model.

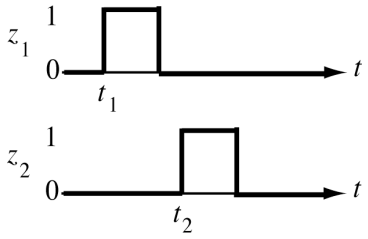


Fig. 2. Definition of firing time.

neuron fires before the presynaptic neuron fires, the synaptic strength becomes weaker (long term depression). The hypothesis has been adopted in a number of computational models of neuronal networks [13]. This mechanism is simply modeled in the present study as follows.

The time difference between firings of neuron E_2 and neuron E_1, t_{12}, is defined as

$$t_{12} = t_2 - t_1, \tag{1}$$

where t_1 and t_2 are the latest firing times of E_1 and E_2, respectively as shown in Fig. 2. The value of coupling strength with plasticity C_{12} at time $t + \Delta t$, $C_{12}(t + \Delta t)$, is given by addition of the value at time t, $C_{12}(t)$, and the change of C_{12}, ΔC_{12},

$$C_{12}(t + \Delta t) = C_{12}(t) + \Delta C_{12}\ , \tag{2}$$

where Δt is the time step of calculation, and ΔC_{12} is given as

$$\Delta C_{12} = \frac{dC_{12MIN}}{T_1} t_{12} - dC_{12MIN}, \tag{3}$$

when $0 < t_{12} < T_1$,

$$\Delta C_{12} = \frac{dC_{12MAX}}{T_2} t_{12} + dC_{12MAX}, \tag{4}$$

when $-T_2 < t_{12} \le 0$, and

$$\Delta C_{12} = 0, \tag{5}$$

when $t_{12} \le -T_2$ or $t_{12} \ge T_1$, where T_1 and T_2 are parameters that give the time span in which the plastic change of the synaptic coefficient occurs.

III. Results

We demonstrate the results of computer simulation of the model. Throughout the simulation the parameter values $C_{21} = 10$, $C_{2I} = 10$, $C_{I1} = 10$, $C_{I2} = 20$ are employed. A

bias current $D = 18\,[\mu\mathrm{A/cm}^2]$ in neuron E_1 was used for sustaining oscillation.

A. Analysis of the model without input or plasticity

Without stimulation or plasticity, the model has two stable solutions, an oscillatory state by sustained firings and a non-firing state. They are bistable for a parameter region. We performed the simulation changing the value of the coupling coefficient C_{12} by 0.1 in the range $0 < C_{12} \le 30$.

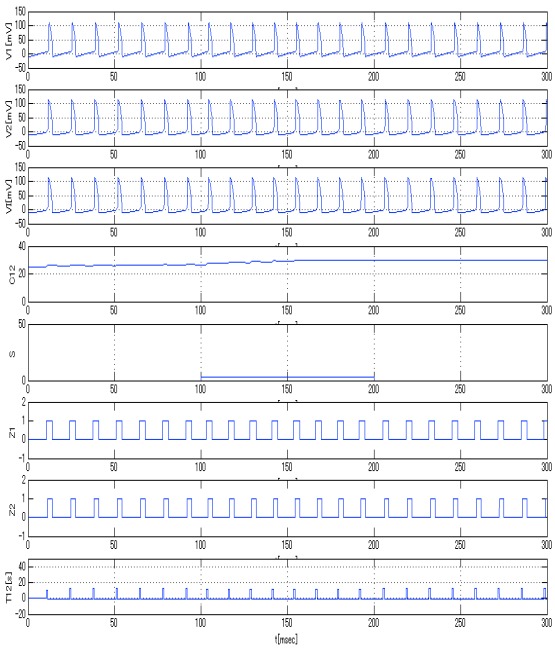
The non-firing state exists for any value of C_{12} in the range. On the other hand, the oscillatory state exists when $C_{12} \ge 23$. That is, the two states coexist when $C_{12} \ge 23$. The larger C_{12} brings the larger basin of the oscillatory solution in the state space of the model. It corresponds to the clinical fact that a number of patients of tinnitus claim that they do not always hear sound when there is no external sound. Some triggering stimulus invokes tinnitus and it lasts until some other stimulus make the tinnitus perception stop.

B. Analysis of the model with input and plasticity

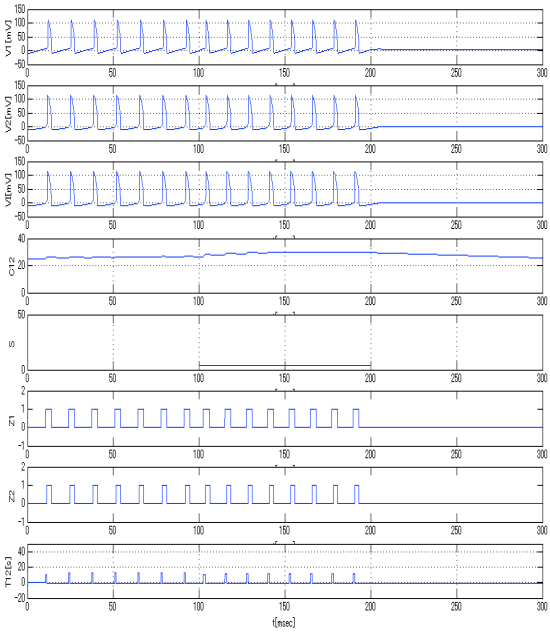
The inhibition of oscillation by constant input with amplitude I as stimulus S to neuron E_1 was examined with plasticity. The constant input I was applied for 100ms from 100ms to 200ms to the network that is oscillating in the simulation. The parameter values $dC_{12MAX} = 0.048$, $dC_{12MIN} = 0.0005$, $T_1 = 15\,[\mathrm{ms}]$, $T_2 = 5\,[\mathrm{ms}]$ and $\Delta t = 0.01\,[\mathrm{ms}]$ were employed for plasticity. The time scale of the change of the synaptic strength is much smaller than the clinical process. It was arranged so that the simulation is completed in a reasonable time. The initial value of the coupling strength C_{12} is denoted by C_0. Simulations were performed where the parameter C_0=23, 24 and 25. The amplitude I of the input was changed by 1 μA/cm^2 in the range of $0 < I \le 10\,[\mu\mathrm{A/cm}^2]$.

Fig. 3 shows the examples of simulation results when $C_0 = 25$. In the figure, the rows illustrate the membrane potentials v_1, v_2, v_I, the coupling strength C_{12}, input S, output of the neurons z_1 and z_2, and time difference between firings of neuron E_2 and neuron E_1, t_{12}, respectively from the top. As shown in Fig. 3, when $C_0 = 25$, the input with I=4 $[\mu\mathrm{A/cm}^2]$ for 100ms makes the network stop the oscillation after the input is removed, while the input with I=3 $[\mu\mathrm{A/cm}^2]$ fails to stop the oscillation. For $C_0 = 25$, the amplitude I=4, 5 or 6 $[\mu\mathrm{A/cm}^2]$ was required for inhibition of oscillation. When $C_0 = 23$, the input with I=5, 6, 7 $[\mu\mathrm{A/cm}^2]$ for 100ms was required to make the network stop the oscillation after the input is removed. For $C_0 = 24$, the amplitude I=5, 6 $[\mu\mathrm{A/cm}^2]$ brought the inhibition of oscillation.

In summary, it was observed that the model succeeds in demonstrating the effect of the introduction of the external stimulus S. This leads to termination of firing of the neurons.



(a)



(b)

Fig. 3. Simulation results with $C_0 = 25$, (a) an unsuccessful result, $I = 3\,[\mu\mathrm{A/cm}^2]$, (b) a successful result, $I = 4\,[\mu\mathrm{A/cm}^2]$.

The coupling coefficient does not decrease during the stimulation, which occurred in previous models. The oscillation stops in the present model due to the change of the state of the model as well as the change of the coupling

coefficient C_{12} by the input. Hence, further investigation of modeling is necessary in order to reproduce the inhibition of oscillation by synaptic plasticity only.

IV. Conclusion

In this study a conceptual and computational neuronal network model as a dynamical system with plasticity in the human auditory system is proposed to explain the mechanisms of tinnitus and its management by sound therapy. The model structure was constructed based on physiological considerations. Neurons are modeled with simplified Hodgkin and Huxley equations. STDP hypothesis is employed for plasticity of the model. Through computer simulations this model, it is shown that oscillation can be inhibited by application of external input that can be hypothesized as sound stimulus in sound therapy. It is similar to the previous neural oscillator model and neuronal network model.

In the present model, the inhibition of the oscillation is not due to only the change of coupling strength between neurons but some change of the state condition of the model by supplying constant input to the model. In order to demonstrate in the modeling that the synaptic plasticity brings the inhibition of oscillation is realized, more investigation is necessary.

It has been pointed out that homeostatic plasticity is necessary for stability of the activities in the nervous system and it is observed in a number of systems [26]. A computational model for tinnitus-related hyperactivity through homeostatic plasticity has been proposed, and the prediction of appropriate acoustic stimulation that can reverse such hyperactivity has been presented [13]. That model is not a dynamical system. We need to develop a dynamical model incorporating not only the Hebbian plasticity but also homeostatic plasticity.

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 better and more effective sound therapy techniques and stimuli.

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