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

HIROFUMI NAGASHINO[1], YOHSUKE KINOUCHI[2], ALI A. DANESH[3], ABHIJIT S. PANDYA[4]
[1]Institute of Health Biosciences, The University of Tokushima, 3-18-15 Kuramoto, Tokushima, JAPAN
[2]Institute of Technology and Science, The University of Tokushima, 2-1 Minami-Josanjima, Tokushima, JAPAN
[3]College of Education, Florida Atlantic University, 777 Glades Road, Boca Raton, Florida, USA
[4]College of Engineering and Computer Science, Florida Atlantic University, 777 Glades Road, Boca Raton, Florida, USA
[1]nagasino@medsci.tokushima-u.ac.jp http://www.tokushima-u.ac.jp
[2]kinouchi@ee.tokushima-u.ac.jp http://www.tokushima-u.ac.jp
[3] danesh@fau.edu http://www.fau.edu
[4]pandya@fau.edu http://www.fau.edu

Abstract: - Tinnitus is the perception of phantom sound in the ears or in the head. There are many therapeutic approaches for tinnitus and sound therapy is one of the techniques for its treatment. 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 by Hebbian hypothesis using a neural oscillator or coupled model neurons described by simplified Hodgkin-Huxley equations. In the present paper, a neuronal network model with synaptic plasticity by STDP (spike-timing-dependent plasticity) hypothesis is proposed for replication of the clinical results that human auditory system temporarily halts perception of tinnitus following sound therapy.

Key-Words: - tinnitus, sound therapy, neuronal network model, STDP hypothesis, oscillation, inhibition

1 Introduction

Tinnitus is the perception of phantom sound in the ears or in the head [1, 2]. For the cause of tinnitus, contribution of neural plasticity to tinnitus has been discussed [3-5]. Tinnitus has many subclasses and attempts have been made to categorize tinnitus based on its characteristics that in turn can facilitate the selection of treatment method [6]. 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 [7]. 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 [8, 9]. 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.

Next we proposed a different model [10. 11] composed of model neurons described by simplified Hodgkin-Huxley equations [12, 13]. 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.

In those models, the synaptic plasticity was modeled applying Hebbian hypothesis [14] to one of the couplings of the components in the model. Hebbian hypothesis has been adopted in a number of neural network models for many years. As a newer biologically plausible hypothesis, "spike-timing-dependent plasticity (STDP)", was proposed for the mechanism of synaptic plasticity [15, 16].

In the present paper, we propose a neuronal network model with a plastic coupling of neurons expressed by STDP equations. The structure and equations for the membrane potentials of the neurons are the same as those in the former model. 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, which explains the effect of sound therapy.

2 A neuronal network model

We propose a neuronal network model shown in Fig. 1 in which firing sequences in the nervous system are simulated. This model is a conceptually simplified system of a tinnitus generation network.

It is composed of two excitatory neurons and one inhibitory neuron as shown in Fig. 1. This model includes a positive feedback loop of the excitatory neurons E_1 and E_2 mutually coupled, and 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. 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 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) [12, 13, 17]. 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.

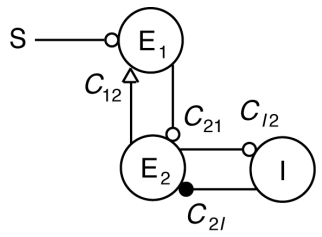

Fig. 1. Basic structure of the present model

2.1 Formulation of the model without plasticity

We describe the basic dynamics of the model as

$$\frac{dv_1}{dt} = \frac{G(v_1, m^{\infty}(v_1), n_1, h_1) + C_{12}z_2 + D + S}{C_m}, \tag{1}$$

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

$$\frac{dv_2}{dt} = \frac{G(v_2, m_2, n_2, h_2) + C_{21}z_1 - C_{2I}z_I}{C_m}, \tag{3}$$

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

$$\frac{dv_I}{dt} = \frac{G(v_I, m_I, n_I, h_I) + C_{I2}z_2}{C_m}, \tag{5}$$

and

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

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

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

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

and

$$n = 0.8(1-h) \tag{9}$$

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

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

and

$$\beta_m(v) = 4\,e^{-v/18} \tag{11}$$

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

$$\alpha_h(v) = 0.07\,e^{-v/20} \tag{12}$$

and

$$\beta_h(v) = 1\big/\{e^{(30-v)/10} + 1\}. \tag{13}$$

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 to their postsynaptic neurons is denoted by z_j and expressed as function of the membrane potential v_j as

$$z_j = \begin{cases} 1 & (v_j \geq 6) \\ 0 & (v_j < 6) \end{cases}. \tag{14}$$

In Eq. (14) the threshold value is given six in order to remove the cases where the output value 1 arises when the neurons do not fire.

The bias term D is introduced in the equation of the membrane v_1 of the neuron E_1, Eq. (1) in order to compensate for the decrease of output pulses due to the

larger threshold of output function. The bias may also be introduced in the equations of v_3 and v_I, Eqs. (3) and (5). Here it is given only to Eq. (1) to minimize the change from the previous model [10].

2.2 Formulation of plasticity

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 [15, 16] 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 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 [18]. 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_{21}, is defined as

$$t_{21} = t_2 - t_1, \tag{15}$$

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},

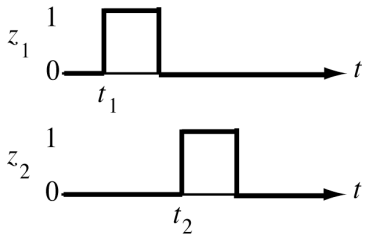

Fig. 2 Definition of firing time.

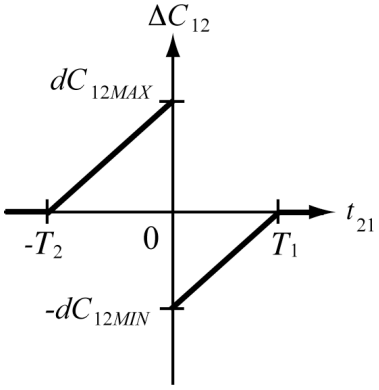

Fig. 3 Modeling of STDP hypothesis.

$$C_{12}(t + \Delta t) = C_{12}(t) + \Delta C_{12}, \tag{16}$$

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

$$\Delta C_{12} = \frac{dC_{12MIN}}{T_1} t_{21} - dC_{12MIN} \tag{17}$$

when $0 < t_{21} < T_1$,

$$\Delta C_{12} = \frac{dC_{12MAX}}{T_2} t_{21} + dC_{12MAX} \tag{18}$$

when $-T_2 < t_{21} \le 0$, and

$$\Delta C_{12} = 0 \tag{19}$$

when $t_{21} \le -T_2$ or $t_{21} \ge T_1$, which is illustrated in Fig. 3.

3 Results

We demonstrate the results of computer simulation of the model. Throughout the simulation the parameter values $D = 11$, $C_{21} = 10$, $C_{2I} = 10$, $C_{I2} = 20$ were employed.

3.1 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, which 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 $C_{12} \ge 1.9$. That is, the two states coexist when $C_{12} \ge 1.9$. The larger C_{12} brings the larger basin of the oscillatory solution in the state space of the model in the region. 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.

3.2 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 200ms to 300ms to the network that is oscillating in the simulation. The parameter values $dC_{12MAX} = 0.048$, $dC_{12MIN} = 0.001$, $T_1 = 25\,[\mathrm{ms}]$, $T_2 = 5\,[\mathrm{ms}]$ 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 for several values of C_0. The amplitude I of the input was changed by 0.1 [μA/cm^2] in the range of $0 < I \leq 10$.

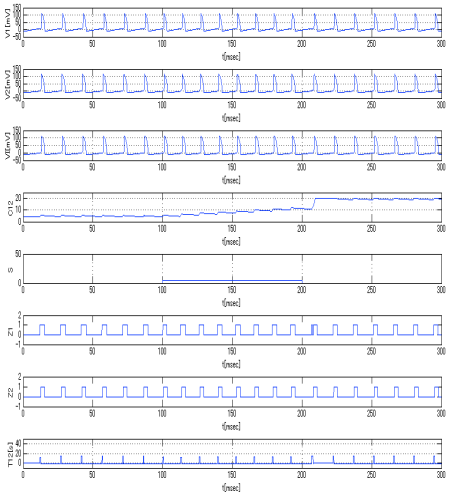

Fig. 4. An unsuccessful simulation result, $C_0 = 4$, $I = 4$[μA/cm^2],

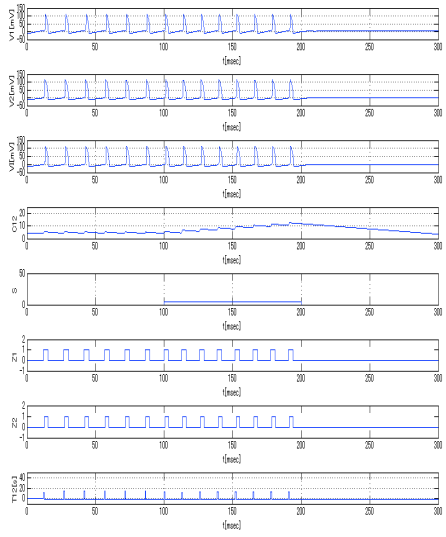

Fig. 5. A successful simulation result, $C_0 = 4$, $I = 4.5$[μA/cm^2].

Fig. 4 shows an unsuccessful result and Fig. 5 shows a successful result when $C_0 = 4$. As shown in Fig. 4 and Fig. 5, the constant input with I=4 [μA/cm^2] fails to inhibit the oscillation of the network, while the input with I=4.5 [μA/cm^2] for 100ms makes the network stop the oscillation after the input is removed. With values of I smaller than 4 [μA/cm^2] of I, the oscillation was sustained, and with values of I larger than 4.5 [μA/cm^2], the oscillation was inhibited after the input was removed.

This threshold of the input value I for the inhibition of the oscillation was larger with the smaller value of the initial value of the coupling strength C_{12}, C_0. .

We cannot state in the present model that the inhibition of oscillation is reproduced as the result of synaptic plasticity. The oscillation stops in the present model due to the change of the state of the model by the input. Hence, further investigation of modeling is necessary in order to reproduce the inhibition of oscillation by synaptic plasticity.

4 Conclusion

In this study a conceptual and computational neuronal network model with synaptic plasticity by STDP hypothesis in the human auditory system was proposed to explain the mechanisms of tinnitus and its management by sound therapy. Simulation results of this model show that oscillation of the model can be inhibited with appropriate input and model parameters, similarly to the previous neural oscillator model and the neuronal network model with conventional Hebbian hypothesis for plasticity. It means that the effect of acoustic stimuli in the sound therapy of tinnitus is replicated.

However, the change of the plastic coupling strength between neurons in the model has not been found in the simulation so far. Some change of the state condition of the model by supplying constant input to the model has been the cause of the inhibition of the oscillation. In order to demonstrate that the synaptic plasticity brings the inhibition of oscillation, further investigation of the modeling is necessary.

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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