Oscillation and its Inhibition in A Neuronal Network Model for Tinnitus Sound Therapy

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***Abstract*—Tinnitus is the perception of phantom sounds in the ears or in the head. Sound therapy techniques for tinnitus treatment 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 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 stimuli, which is hypothesized as an afferent signal that is employed as an acoustical signal 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.**

I. Introduction

TINNITUS is the perception of phantom sounds in the ears or in the head. A mechanism of tinnitus generation has been hypothesized from the viewpoint of general neurophysiology [1]. Sound therapy techniques for tinnitus have been proposed. They have the clinical effect that the sufferers temporarily stop perceiving tinnitus after the treatment [2]. To account for mechanisms of tinnitus generation and the clinical effects of sound therapies from the viewpoint of neural engineering, we constructed a computational model using a neural oscillator for the tinnitus generation and its management by sound therapy. We attempted to explain the mechanisms of tinnitus generation conceptually and describe its inhibition using sound stimuli. It was detected that this model 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 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. 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 [3-5]. 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 [6-8]. 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 stimulus. Through numerical simulations we found out that adequate intensity of stimulus is required for inhibition of the oscillation.

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II. A Neuronal Network Model with Simplified Hodgkin-Huxley Equations

We propose a neuronal network model shown in Fig. 1 in which firing sequences in the nervous system are simulated. The model is composed of two excitatory neurons and one inhibitory neuron. 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. They form 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 of the model by a simplified version of Hodgkin-Huxley equations (HH) [6-8].

We employed it instead of HH because we can reduce the number of state variables for each neuron from four to two.

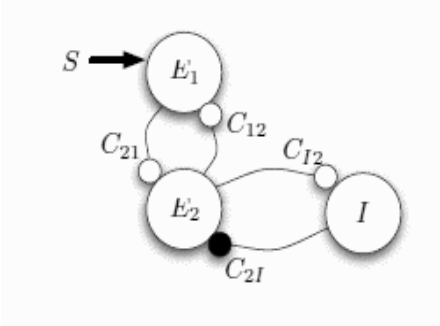


Fig. 1. A neuronal network model.

A. A 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

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

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

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

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

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

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

The parameters were fixed as C_m=1[μF/cm^2], $\bar{g}_{Na} = 120[\mathrm{mS/cm^2}]$, $\bar{g}_K = 36[\mathrm{mS/cm^2}]$, $\bar{g}_l = 0.3[\mathrm{mS/cm^2}]$, 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

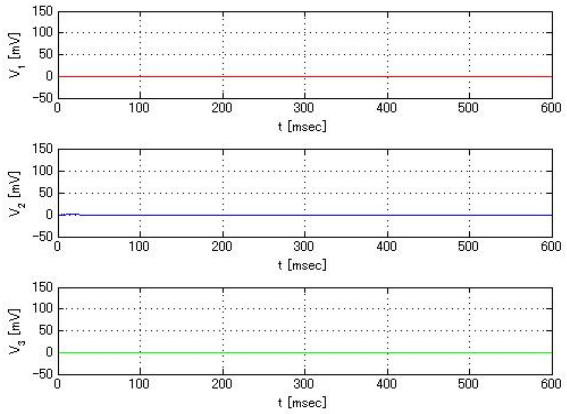
$$z_j = 1 / \{1 + e^{-(v_j - 0.5)/0.1}\} \tag{13}$$

B. A model with plasticity

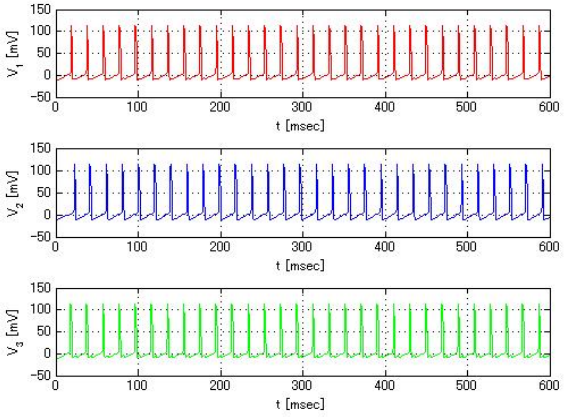
To reproduce the effect of sound therapy, we assume that the coupling strength from the neuron E_1 to the neuron E_2, C_{12}, has plasticity in such a way that it increases when the neurons E_1 and E_2 fires simultaneously, and decreases when the firings of the neurons E_1 and E_2 are not synchronized. This assumption is based on Hebbian hypothesis regarding synaptic plasticity [9]. We describe the dynamics of C_{12} as

$$\frac{dC_{12}}{dt} = \frac{-C_{12} + b(z_1 - 0.5)(z_2 - 0.5) + C_0}{\tau}, \tag{14}$$

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.



(a) Non-oscillatory state



(b) Oscillatory state

Fig. 2. Non-oscillatory state and oscillatory state in the model.

III. Analysis of The Model without Plasticity

We conducted numerical simulations of the model.

First we show the results when we changed the synaptic coefficient C_{12} one by one in the range $0 < C_{12} < 30$ as a parameter constant with time. Other parameters were fixed as C_{21}=10, C_{2I}=10, and C_{I2}=20. When $C_{12} < 2$ or $17 \le C_{12} < 30$, the model converges to the non-oscillatory steady states with all the initial states that we tried. When $2 \le C_{12} \le 16$, the model is bistable and either non-oscillatory steady states as in Fig. 2 (a) or oscillatory steady states as in Fig. 2 (b) can be obtained depending on the initial states.

IV. Analysis of The Model with Plasticity

We investigated the effect of stimulation on the model with synaptic plasticity in C_{12} using Eq. (14). We fixed the parameters in Eq. (14) as C_0=2, b=40 and τ=50[ms].

A. Constant Stimulation

First we provided the model with constant stimulation. Fig. 3 shows the result when stimulation amplitude is 5 μA/cm^2. Stimulation period is 100ms. The oscillation was inhibited by the stimulus not less than 5 μA/cm^2.

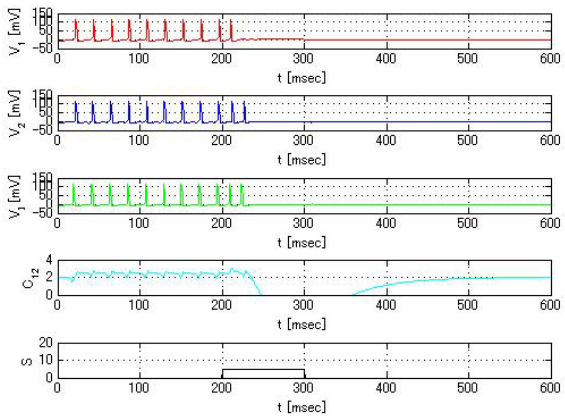


Fig. 3. A successful result for inhibition of oscillation by constant stimulus. Amplitude is 5 μA/cm^2. Stimulation period is 100ms.

B. Pulse Train Stimulation

Let us illustrate next the simulation results when pulse train is used as stimulus. Each pulse duration is 1ms. As shown in Fig. 4, the oscillation is not inhibited by the pulse train in which pulse amplitude is 5 μA/cm^2, iteration period is 10ms, and stimulation period is 100ms. By making the stimulation period longer or pulse amplitude larger, we are able to inhibit the oscillation. As shown in Figs. 5 and 6, the results are successful when stimulation period is not less than 200ms, or pulse amplitude is not less than 20 μA/cm^2.

When iteration period is 3ms, we cannot inhibit the oscillation with pulse amplitude of 5 μA/cm^2 as well as shown is Fig. 7. As shown in Fig. 8, the results are successful when pulse amplitude is not less than 13 μA/cm^2.

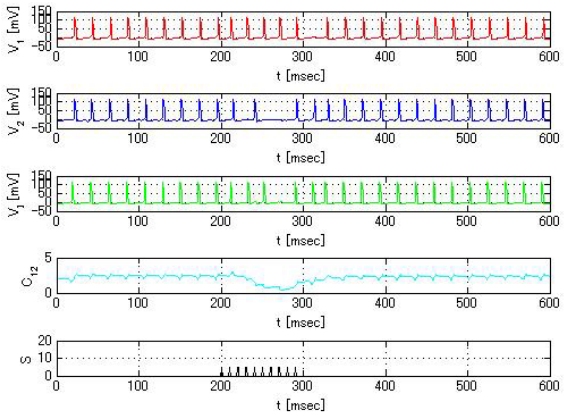


Fig. 4. An unsuccessful result for Inhibition of oscillation by pulse train stimulus. Pulse amplitude is 5 μA/cm^2. Iteration period is 10ms. Stimulation period is 100ms.

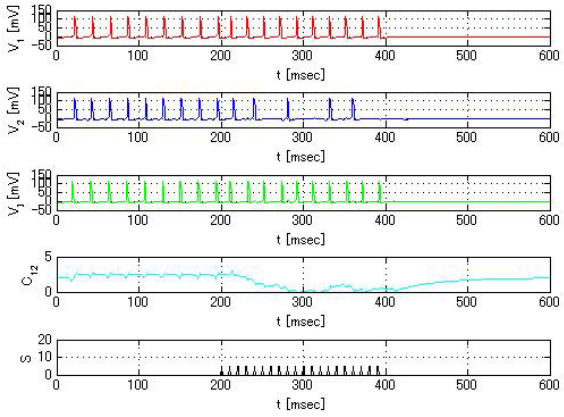


Fig. 5. A successful result for Inhibition of oscillation by pulse train stimulus. Pulse amplitude is 5 μA/cm^2. Iteration period is 10ms. Stimulation period is 200ms.

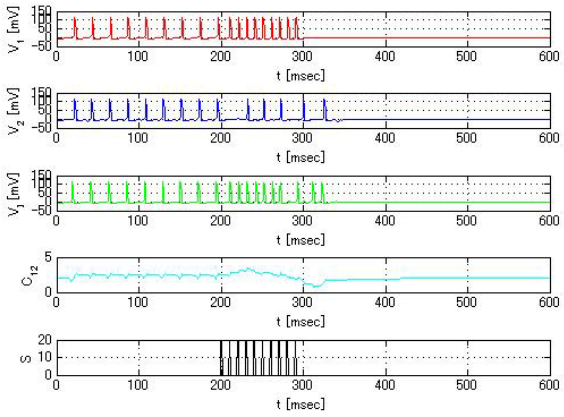


Fig. 6. A successful result for Inhibition of oscillation by pulse train stimulus. Pulse amplitude is 20 μA/cm^2. Iteration period is 10ms. Stimulation period is 100ms.

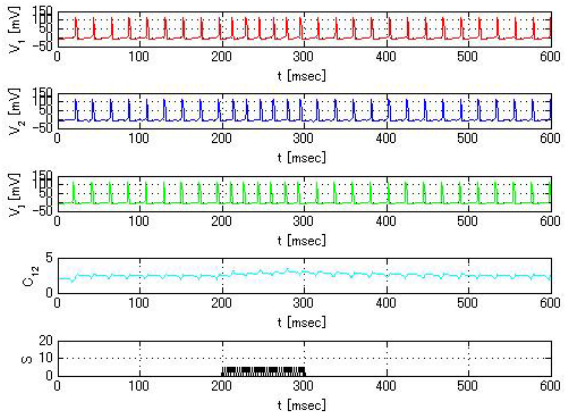


Fig. 7. An unsuccessful result for Inhibition of oscillation by pulse train stimulus. Pulse amplitude is 5 μA/cm^2 . Iteration period is 3ms. Stimulation period is 100ms.

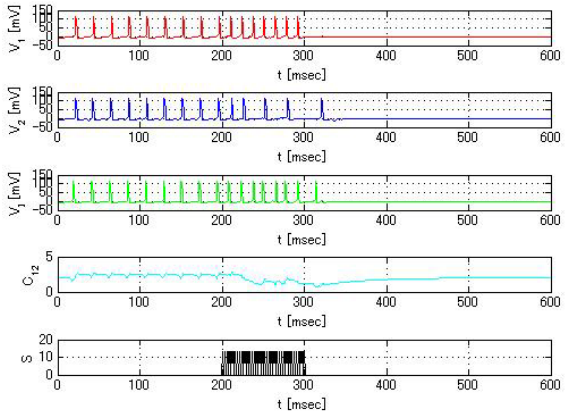


Fig. 8. A successful result for Inhibition of oscillation by pulse train stimulus. Pulse amplitude is 13 μA/cm^2 . Iteration period is 3ms. Stimulation period is 100ms.

The results show that shorter iteration period of pulse stimulus makes smaller pulse amplitude inhibit the oscillation. The effects of different values of parameters C_0 and b have not been investigated.

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. (14). Once C_{12} is decreased to the value in which only non-oscillatory solution exists and the stimulus stops, the model neurons stop firing.

V. Discussion

The parameters of plasticity were arbitrarily determined so that the simulation is performed within appropriate time. The time scale would be much longer in the clinical situation. Further correspondence of the simulation results to clinical data has not been examined.

At the present time we are not able to specify what regions in the brain correspond to each model neuron in the present stage. The model is assumed to represent tonotopic organization and depends on the perceived pitch and reported frequency of tinnitus. Based on the anatomical structure of the auditory system, the proposed model is likely to be located in the thalamus, at which a massive corticofugal project ends. The thalamo-cortico-thalamic loop forms an ideal positive oscillatory loop, while the thalamic interneurons and thalamic reticular GABAergic neurons likely to play the role as the inhibitory neuron in the present model.

VI. Conclusion

In this study a conceptual and computational neuronal network model with plasticity in the human auditory system was constructed to explain the mechanisms of tinnitus and its management by sound therapy. The model is bi-stable in a certain parameter region, where a stable oscillatory state and a stable equilibrium (non-oscillatory) state coexist. Through analysis of this model, it was shown that oscillation can be inhibited by supplying constant or pulse train stimulus to the model. For future work, we will examine the effect of noise stimulation and the reappearance of tinnitus after stimulation that occurs in clinical situations. It is required to compare the simulation results with the clinical data. Development of a more elaborate model is also required.

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