A Computational Framework with Simplified Tonotopicity and Homeostatic Plasticity for Tinnitus Generation and Its Management by Sound Therapy

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Abstract: - An auditory perception without any external source is referred to as tinnitus. Tinnitus can be perceived in the ears or in the head. There are numerous methods for tinnitus management and sound therapy is one of the most effective techniques for tinnitus treatment. In order to investigate mechanisms of tinnitus generation and the clinical effects of sound therapy, we have proposed conceptual and computational models with plasticity using a neural oscillator and a neuronal network model. In the present paper, we propose a neuronal framework with simplified tonotopicity of the auditory system. In this framework an integrate-and-fire neuron model is employed and homeostatic plasticity is incorporated. The computer simulation results show that the present framework can demonstrate the generation of oscillation and its cessation by external input. Our simulations suggest that the present framework is promising as a modeling approach for the tinnitus generation and the effects of sound therapy on its management.

Key-Words: - tinnitus, sound therapy, neuronal framework, tonotopicity, homeostatic plasticity, oscillation, inhibition

1 Introduction

For thousands of years people have complained about perceiving intrusive sounds in their ears. The perception of auditory signals such as ringing, buzzing or roaring in the ears or head without any external source is referred to as tinnitus [1]-[7]. Tinnitus can be a symptom of ear or brain disorders. It may be associated with hearing loss or it may manifest itself without any clinically significant hearing impairment. One of the most common causes of hearing loss is noise exposure which usually results in a tonal perception of tinnitus. Other causes of tinnitus include aging, ototoxic agents, and metabolic and neurologic disorders.

Many models have been proposed for tinnitus generation. We now know that tinnitus is mainly a neuronal phenomenon. Although it may originate from a peripheral lesion such as damage to the sensory epithelium of cochlea due to noise induced hearing loss; however, the consequences of noise exposure can result in the generation of tinnitus in the more central parts of the auditory system. Neuroimaging studies, such as functional Magnetic Resonance Imaging (fMRI) [15], [16], have shown tinnitus related activities in a variety of areas within the central auditory system such as inferior colliculus of the midbrain [17], or medial geniculate body of the thalamus [18] or primary and secondary auditory cortices [19], [20].

Among the models for tinnitus generation, neurophysiological models have been favored in many studies [8], [9]. In order to understand mechanisms of tinnitus many researchers have discussed the contribution of neural plasticity to tinnitus [9]-[14]. Studies have suggested that the damage of the peripheral auditory system decreases

the activity of auditory nerve. This reduction in activity, in turn brings a shift in the balance of excitation and inhibition which is a consequence of neural plasticity. Accordingly, these activities result in an increase in spontaneous firings in the central auditory system [8], [9] which are perceived as tinnitus. However, the exact mechanism of tinnitus generation has not been identified entirely [21].

One of the promising approaches in the search for the mechanisms of tinnitus generation is computational modelling. There are several computational models that have been proposed in order to investigate mechanisms of tinnitus generation [30]-[34].

In order to replicate tinnitus generation and its management by sound therapy, we have proposed computational and dynamic models using a neural oscillator [31], [32], [35], [36] or a neuronal network [39]-[41] in the past. In those studies it was shown that our models can produce a conceptual model of tinnitus activity and inhibition of such oscillatory activities using acoustical stimuli. This inhibitory process was accomplished by utilizing neural plasticity with parameters such as coupling weights between neurons and modification of their values.

We have attempted to improvise and expand the currently proposed model compared to our previous models. We are introducing a preliminary neuronal network model which contains the tonotopic properties of the auditory system [42]. In the current model, opposed to previous models, more number of neurons has been employed. The proposed model expresses the dynamics of the neurons by an integrate-and-fire neuron model that is simpler in calculation than those in the former models.

Integrate-and-fire model of neuron [43] describes the membrane potential of a neural system in terms of the synaptic inputs and injected currents. This membrane voltage and conductances do not drive the action potential. Instead, the action potential is generated when the membrane potential reaches a threshold. Thus it models the biological plausibility and resembles McCulloch-Pitts model [44] which is widely used in artificial neural network models. Thus focusing on sub-threshold membrane properties this model allows us to understand the information processing capabilities of neurons. This in turn makes it possible to deduce other properties of output spike distribution.

In order to address the synaptic plasticity of the models, previously we employed Hebbian hypothesis [45], spike-time-dependent plasticity (STDP) [46] or homeostatic plasticity [47]. Homeostatic plasticity can account for homeostasis of activities in the nervous system [48]. In the past the role of homeostatic plasticity on tinnitus as a result of hearing loss has been investigated [49]-[53]. However, further modelling of a dynamical system for tinnitus with homeostatic plasticity is necessary. The proposed model in this paper incorporates homeostatic plasticity to address both the generation of tinnitus associated with hearing loss and its therapeutic inhibition by sound therapy.

In the current paper we demonstrate the results of computer simulations of this framework. The results of simulation show that when appropriate input and model parameters are employed, inhibition of oscillation can be replicated by utilizing the principles of homeostatic plasticity. The simulation data from this framework provide solid evidence about its effectiveness in modelling for tinnitus and the sound therapy for it.

2 A Neuronal Network Model

A neuronal network model with tonotopic structure is proposed in the current paper. The tonotopicity of the auditory system (i.e., specificity of a given tone to a specific anatomical site) is preserved in cochlea, hearing nerve and majority of the components of the central auditory pathway all the way to the auditory cortex. Fig. 1 shows the different components of the ascending central auditory pathway. The proposed model simulates the firing sequence of the nervous system. This model is a simplified network for tinnitus generation. It does not encompass all of the components that may contribute to the generation of tinnitus. In this simplified model the auditory pathway is shown only by two layers at various levels. This will give the model a flexibility to simulate tinnitus in any two levels at a time. We believe that the neural mechanism proposed here can represent components of more detailed models involving large-scale neural correlates which in turn are foundation for a neurophysiological framework of tinnitus.

It has been suggested that several regions of the brain are involved in the tinnitus. It has been pointed out that the thalamo-cortical network [54] could be critical for tinnitus generation [12], [15], [55]. The functional changes in the dorsal cochlear nucleus and the inferior colliculus in tinnitus generation have been also suggested [12], [56]. It could be stated that both positive feedback loop and negative feedback loop play important roles in regulation of auditory activities and generation of tinnitus. The model structure in our study is based on these considerations.

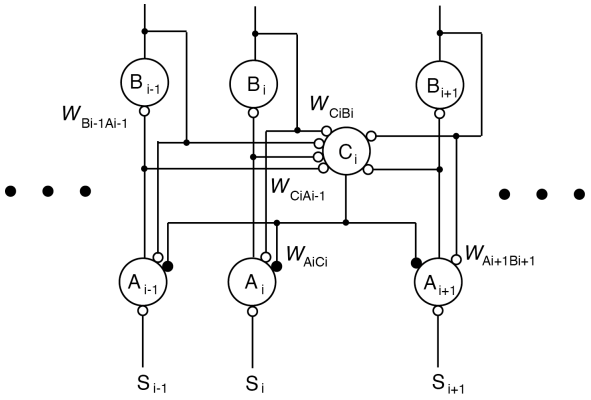

Fig. 1. A neuronal network model with two layers of excitatory neurons and a layer of inhibitory neurons.

The model is composed of two layers of excitatory neurons A_i and B_i and a layer of inhibitory neurons C_i (i=1, 2, ……). Neurons A_i and B_i are mutually coupled forming a positive feedback loop. The inhibitory neurons C_i receives input from neurons A_{i-1}, A_i, A_{i+1}, B_{i-1}, B_i and B_{i+1}. It inhibits A_{i-1}, A_i and A_{i+1} making a negative feedback loop. The negative feedback loop controls the firing rate.

The coupling weight between neurons is denoted by W_{ij}, where i and j are the index of the postsynaptic and presynaptic neurons, respectively. The output of neuron j is denoted by z_j and expressed as a threshold function of the membrane potential of the neuron. Neuron A_i receives external stimulus S_i, afferent signal due to acoustic stimuli.

Fig. 2 dipicts the simplified model which focuses on dynamical correlates involved in tinnitus generation and effect of treatment. The excitatory neurons associated with the frequency of tinnitus are represented by neurons A_1 and B_1, and those associated with other frequencies by neurons A_2 and B_2. The inhibitory neurons are represented by neuron C_1. Hence the model is composed of five neurons.

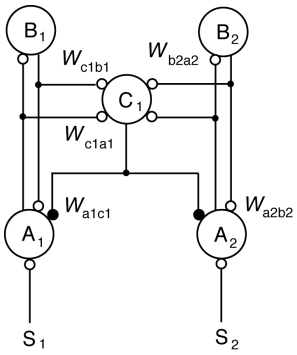

Fig. 2. A neuronal network model with simplified tonotopicity.

2.1 Formulation of the model

We express the dynamics of the model by an integrate- and-fire neuron model that is a simplified version of the model described by Burkitt [28]. Integrate-and-fire neuron models have been used widely in order to simply describe a neuron theoretically. We employed it to save the time of simulation by reducing the number of state variables for each neuron to two and describing the dynamics of them linearly. The membrane potential of a neuron j, v_j, is expressed as

$$\tau_v \frac{dv_j}{dt} = -v_j + V_R + V_{Sj}, \tag{1}$$

where τ_v is the time constant of v_j, V_R is the resting potential, and V_{Sj} is the weighted sum of input to the neuron. The neuron fires when v_j is equal to or exceeds a threshold u_j. The output of the neuron z_j is expressed as

$$z_j = \delta[H(v_j - u_j) - 1], \tag{2}$$

where δ [.] denotes the Dirac delta function and H(.) denotes the Heaviside step function. The action potential of the neuron when it fires is not expressed in the equation of v_j. After the neuron fires, the threshold u_j varies with time according to the equation

$$\tau_u \frac{du_j}{dt} = -u_j + U_R + z_j, \tag{3}$$

where τ_u is the time constant of u_j, and U_R is the resting value of u_j.

The weighted sum of input to each neuron, V_{Si}, is expressed as

$$V_{Sa1} = W_{a1b1}z_{b1} - W_{a1c1}z_{c1} + S_1, \tag{4}$$

$$V_{Sa2} = W_{a2b2}z_{b2} - W_{a2c1}z_{c1} + S_2, \tag{5}$$

$$V_{Sb1} = W_{b1a1}z_{a1}, \tag{6}$$

$$V_{Sb2} = W_{b2a2}z_{a2}, \tag{7}$$

and

$$V_{Sc1} = W_{c1a1}z_{a1} + W_{c1b1}z_{b1} + W_{c1a2}z_{a2} + W_{c1b2}z_{b2}. \tag{8}$$

2.2 Formulation of plasticity

To replicate the generation of tinnitus and the effect of sound therapy, we assume that the coupling weights between neurons have homeostatic plasticity. We introduce the plasticity to all the coupling weights between neurons [48]. We assume that the plastic coupling weights change depending on the activity of the postsynaptic neuron. The change of the inhibitory coupling weight from

neuron j to neuron i denoted by W_{ij} due to homeostatic plasticity is simply expressed here as

$$\tau_w \frac{dW_{ij}}{dt} = -W_{ij} + W_{Sij} + pz_i , \quad (9)$$

for inhibitory coupling, and

$$\tau_w \frac{dW_{ij}}{dt} = -W_{ij} + W_{Sij} - pz_i , \quad (10)$$

for excitatory coupling, where τ_w is the time constant of W_{ij}, W_{Sij} is the steady state value of W_{ij} when neuron i does not fire, and p is a parameter that is associate with the quantity of the modification of W_{ij}. The formulation is formulated in such a way that the higher the activity of neuron i is, the larger W_{ij} grows in Eq. (9), and the smaller W_{ij} grows in Eq. (10). As a result, this plasticity works as the postsynaptic neuron maintains an approximately constant firing rate.

3 Results

We demonstrate the results of computer simulation of the model by Euler's method. Throughout the simulation the parameter values τ_v=4[ms], τ_u=1[ms], V_R=0, U_R=0.1, are employed.

3.1 Analysis of the model without input or plasticity

Without input or plasticity, the neuron A_1 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 weight W_{a1c1} by 0.1 in the range $0 < W_{a1c1} \leq 2$. Other coupling weights were given the value one. The non-firing state exists for any values of the coupling weight W_{a1c1}. On the other hand, the oscillatory state exists when $W_{a1c1} \leq 0.2$. That is, the two states coexist when $W_{a1c1} \leq 0.2$. The larger W_{a1c1} brings the smaller 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.

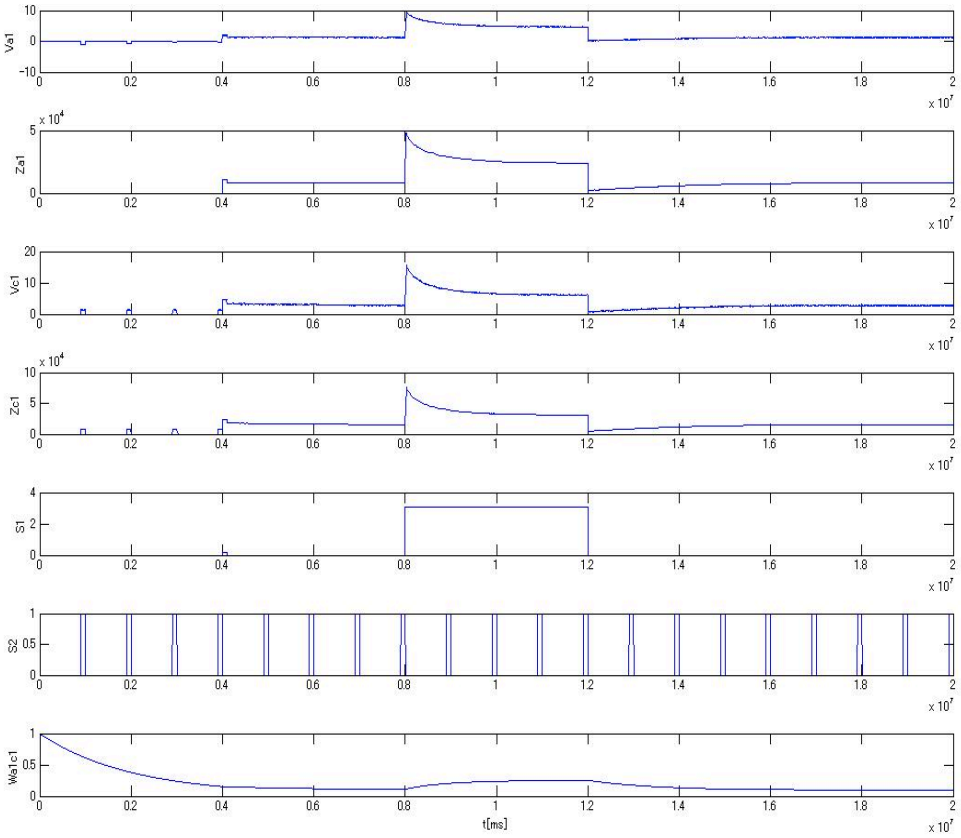

Fig. 3. A simulation result when inhibition of oscillation is not accomplished with input S_1, p=0.05, E_1=3.10. Time series of membrane potentials, outputs and input to neurons and the coupling weight W_{a1c1}.

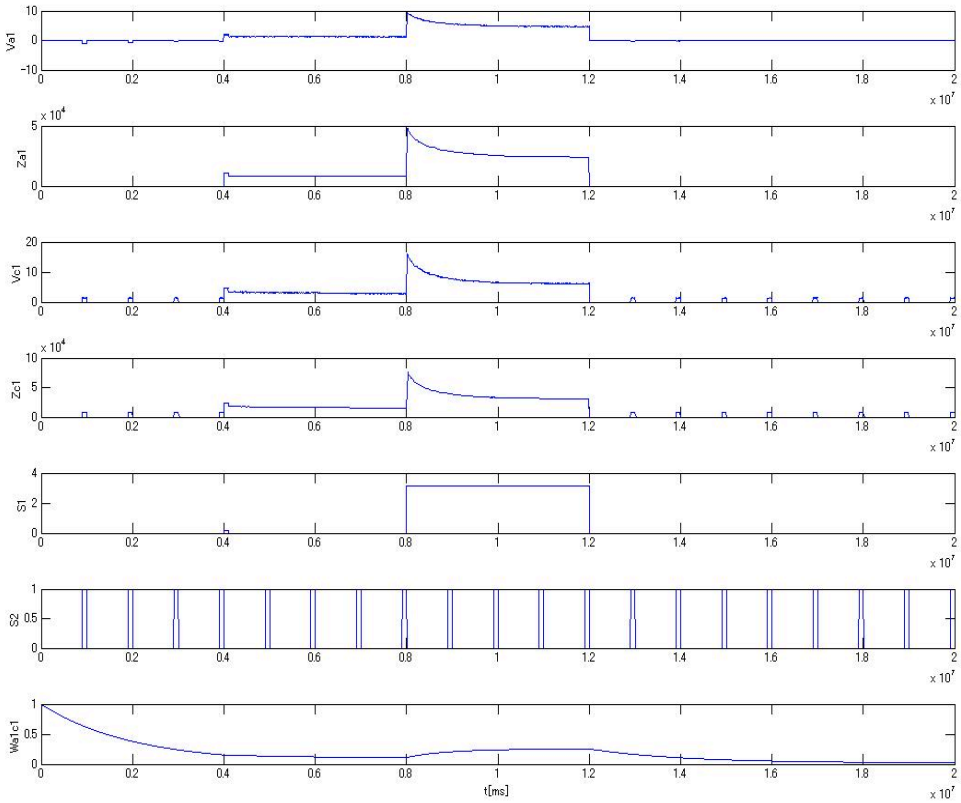

Fig. 4. A simulation result when inhibition of oscillation is accomplished with input S_1, p=0.05, E_1=3.11. Time series of membrane potentials, outputs and input to neurons and the coupling weight W_{a1c1}.

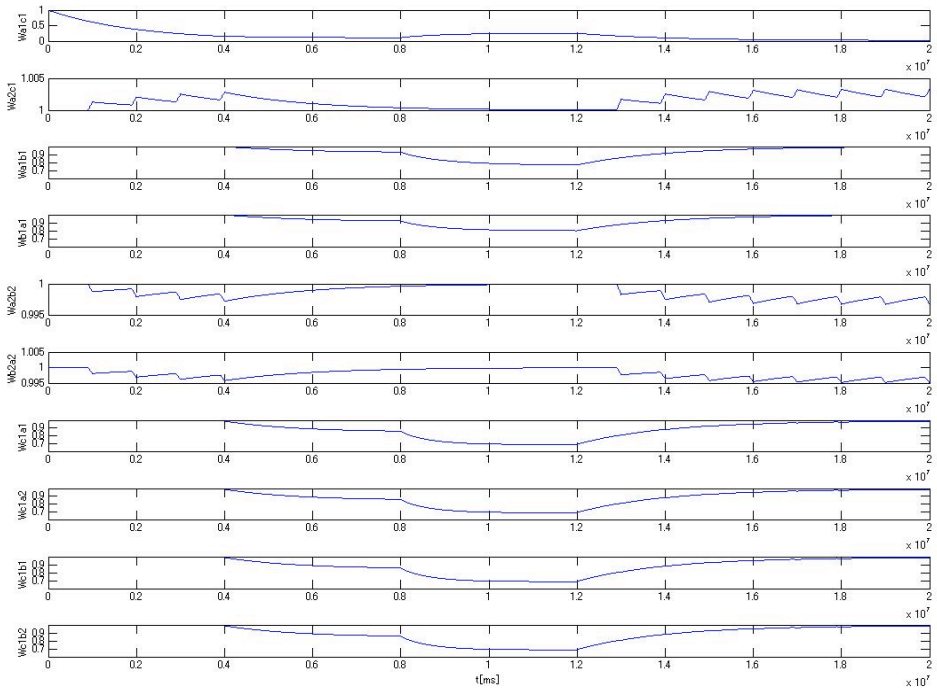

Fig. 5. Time series of coupling weights when inhibition of oscillation is accomplished with input S_1, p=0.05, E_1=3.11.

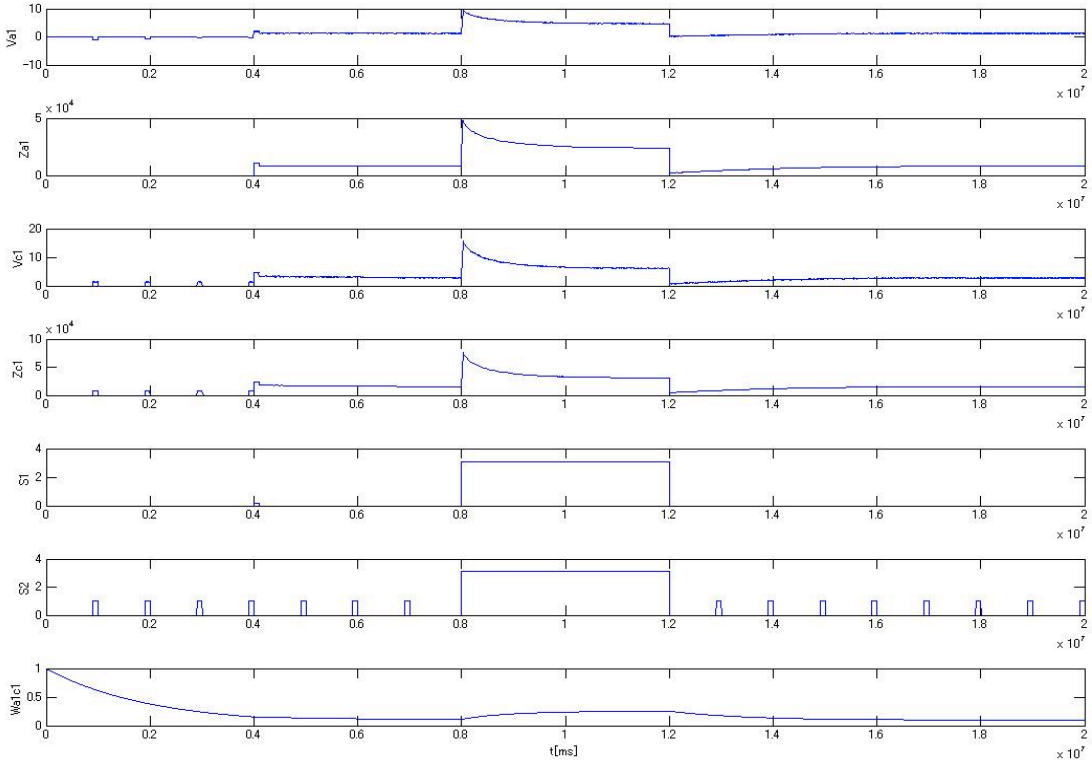

Fig. 6. A simulation result when inhibition of oscillation is not accomplished with input S_1 and S_2, p=0.05, E_1=3.10. Time series of membrane potentials, outputs and input to neurons and the coupling weight W_{a1c1}.

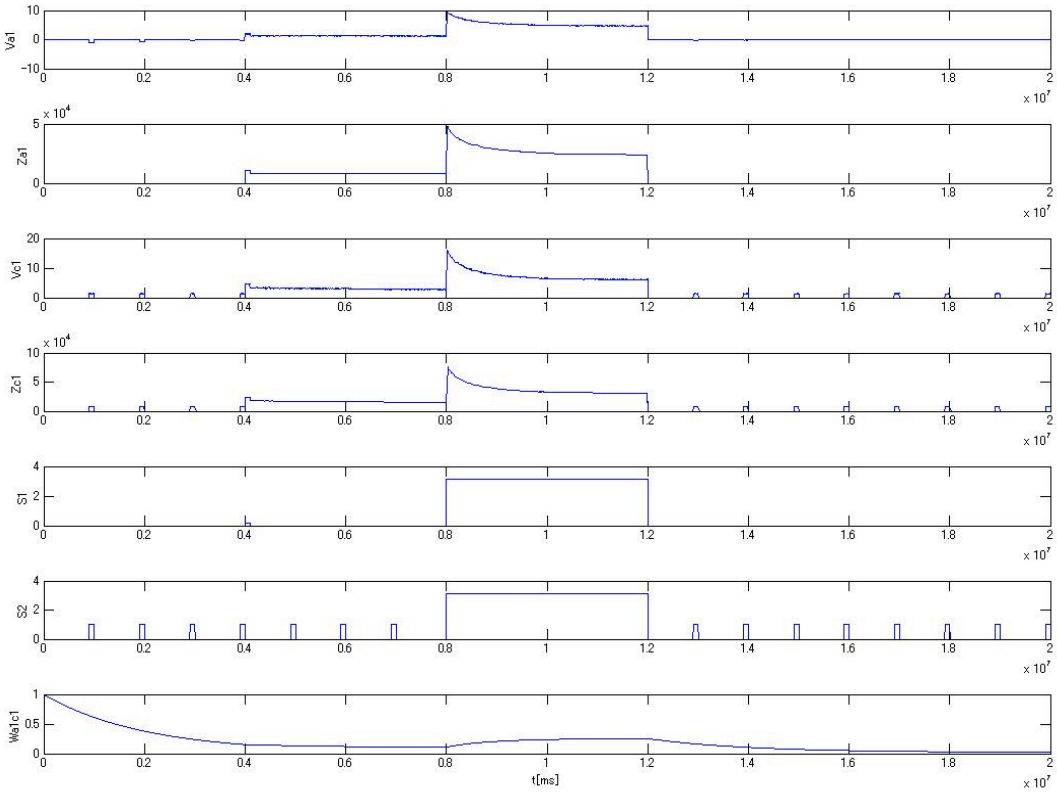

Fig. 7. A simulation result when inhibition of oscillation is not accomplished with input S_1 and S_2, p=0.05, E_1=3.11. Time series of membrane potentials, outputs and input to neurons and the coupling weight W_{a1c1}.

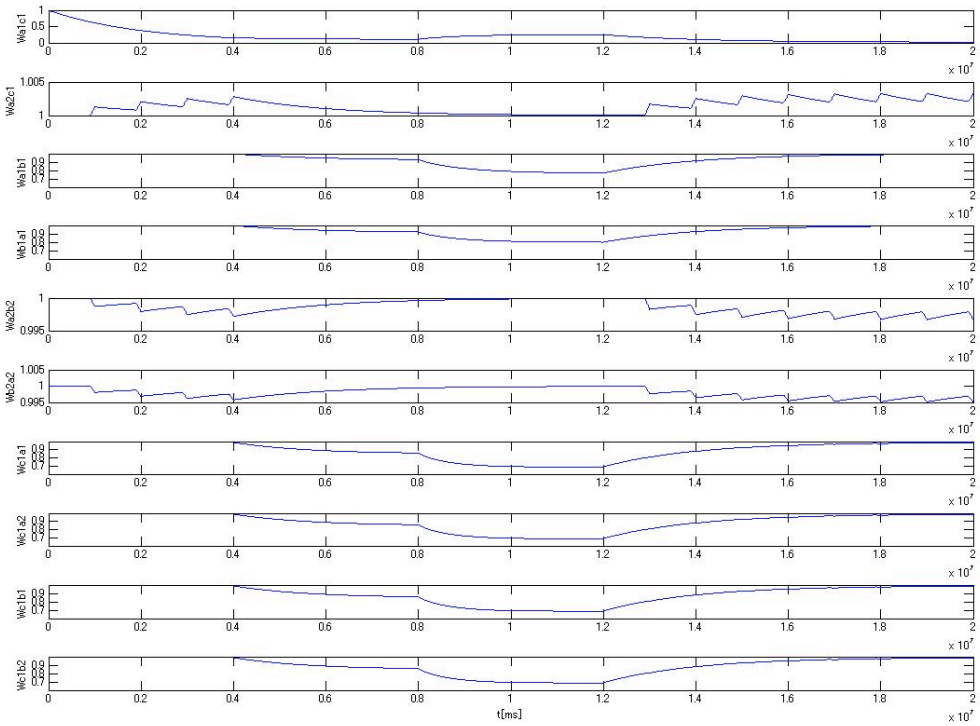

Fig. 8 Time series of coupling weights when inhibition of oscillation is accomplished with input S_1 and S_2, p=0.05, E_1= E_2=3.11.

3.2 Analysis of the model with plasticity and input S_1

The inhibition of oscillation by constant input was examined with plasticity by computer simulation with a realistic time scale. First we show the results of the simulation in which only A_1 is stimulated by constant input with amplitude E as stimulus S_1. It corresponds to the stimulation with the frequency of tinnitus, which is masking therapy. The parameter values W_{Sa1c1}=0.02 for the coupling weight from neuron C_1 to neuron A_1, and W_{Sij}=1 for other coupling weights were employed for plasticity. This value is in the range where both oscillatory and non-firing solutions exist. The initial values of all the coupling weights were given as 1. It is the value in which only non-firing solution exists.

Fig. 3 and Fig. 4 show examples of simulation results with p=0.05. The time constant of the change of the coupling weight τ_w= 1x10^6 [ms] was employed. It is comparable to the clinical process. The amplitude of input E is 22 in Fig. 3 and 23 in Fig. 4. In the figure, the rows illustrate the membrane potential v_{a1} and the number of firing Z_{a1} for each period of 1X10^{5}ms of neuron A_1, the membrane potential v_{c1} and the number of firing Z_{c1} for each period of 1X10^{5}ms of neuron C_1, input to neuron A_1, S_1, input to neuron A_2, S_2, the coupling weight from neuron C_1 to neuron A_1, W_{a1c1}, respectively, from the top.

At first from t=0[ms] to t=4x10^6 [ms] S_1=0, while S_2 has some pulses. Because it is assumed that there is no input to neuron A_1 due to hearing loss for the corresponding frequency band, while input often comes to neuron A_2 since that part is normal. The inhibitory coupling weight W_{a1c1} decreases according to homeostatic plasticity so that the firing of neuron A_1 is easier to occur. It decays to the value in which oscillatory solution also exists. At t=4x10^6 [ms] a trigger input is given to A_1. Then neurons A_1, B_1 and C_1 start firing, and the firing is sustained. The coupling weight W_{a2c1} does not decay to such a value since neuron A_2 fires occasionally. From t=8x10^6 [ms] to t=1.2x10^7 [ms] constant input E=3.10 in Fig. 3 and E=3.11 in Fig. 4, respectively, was applied to neuron A_1. Neuron A_1 fires with much higher rate for this period. Consequently the coupling weight W_{a1c1} increases according to Eq. (9). In Fig. 3 the neurons A_1 and B_1 sustain firing after the removal of constant input to A_1. In Fig. 4, where larger input was applied from t=8x10^6 [ms] to t=1.2x10^7 [ms], the neuron A_1

stops firing. The input to neuron A_1 makes the neurons A_1, B_1 and C_1 stop the autonomous oscillation after the input is removed.

However, the coupling weight W_{a1c1} decreases again since neuron A_1 does not fire. After W_{a1c1} decay to the value in which the oscillatory solution exists, neuron A_1 starts oscillation again with a trigger input. It corresponds to the regeneration of tinnitus.

The relation between the parameter p and the amplitude E_1 of the input for inhibition of oscillation was examined. The amplitude E_1 of the input was changed by 0.01 in the range of $0 < E \leq 30$. Table 1 shows the input amplitude E that is required for inhibition of oscillation with some different values of the parameter p. At large the smaller p needs the larger amplitude of input which gives higher rate of firing. The oscillation starts and stops due to change of the coupling weight W_{a1c1}. Hence, both the generation of oscillation and its cessation are obtained by homeostatic plasticity of the neuronal network.

Table 1. Input amplitude E that is required for inhibition of oscillation when only input S_1 is applied.

p	0.03	0.05	0.07	0.08	0.1
E_1	5.55	3.11	2.13	1.75	1.35

3.3 Analysis of the model with plasticity and input S_1 and S_2

Secondly we show the results of the simulation in which both A_1 and A_2 are stimulated. It corresponds to the stimulation in TRT. Fig. 6 and Fig. 7 show examples of simulation results with $\tau_w = 1\text{x}10^6$ [ms] and p=0.05. The amplitude of constant input E_1 and E_2 is 3.10 in Fig. 6 and 3.11 in Fig. 7 from $t=8\text{x}10^6$ [ms] to $t=1.2\text{x}10^7$ [ms]. Fig. 6 is an example of sustained oscillation and Fig. 7 is an example of inhibition of oscillation by input to A_1 and A_2. The time courses of the variables in the network are similar to those in the case where the input is applied to only A_1. When p=0.05, the input with the amplitude equal to or larger than 3.11 was brought inhibition of oscillation.

Table 2 shows the input amplitude E_1 and E_2 that is required for inhibition of oscillation with some different values of the parameter p. The smaller p needs the larger amplitude of input which gives higher rate of firing. The results are quite the same as the case with input to only A_1.

Fig. 8 shows the changes of all the coupling weights when inhibition of oscillation is accomplished with input S_1 and S_2, p=0.05, E_1= E_2=3.11.

Table 2. Input amplitude E that is required for inhibition of oscillation when both inputs S_1 and S_2 are applied.

p	0.03	0.05	0.07	0.08	0.1
E_1, E_2	5.55	3.11	2.13	1.75	1.35

In summary, it was suggested that the present framework is promising as a model for the role of neural plasticity on the generation of tinnitus and the effect of sound therapy.

4 Conclusion

In the present study a conceptual and computational neuronal network model with homeostatic plasticity is proposed as a dynamical system in the human auditory system. This preliminary model is tested through computer simulations for the generation of tinnitus with hearing loss and its relief by sound therapy. The model structure is an expression of interaction of any two given layers in the auditory pathway and incorporates the tonotopicity of the auditory system. In the present framework, the generation and inhibition of the oscillation is realized by the change of coupling weight between neurons as homeostatic plasticity. Results of simulations suggest that the present framework is promising as a model for the generation of tinnitus and the effect of sound therapy.

For future work we will extend the model to a layered network with tonotopic structure, examine the inhibition of oscillation by other types of input, and explore better stimulation for tinnitus management.

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