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 $C_i$ ($i=1, 2, \ldots$). 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 $A_i$, $A_i$ 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.

![Diagram](image)

**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 $j, u_j$ is expressed as

$$\tau_v \frac{du_j}{dt} = -u_j + V_R + V_{S_j},$$

where $\tau_v$ is the time constant of $v$, $V_R$ is the resting potential, and $V_{S_j}$ 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

$$z_j = \delta(H(v_j - u_j) - 1),$$

where $\delta[.]$ 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

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

where $\tau_u$ is the time constant of $u$, and $U_R$ is the resting value of $u$.

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

$$V_{S_{a1}} = W_{c1a1}z_{a1} - W_{c1a2}z_{a2} + S_1,$$

$$V_{S_{a2}} = W_{c2a1}z_{a1} - W_{c2a2}z_{a2} + S_2,$$

$$V_{S_{b1}} = W_{b1a1}z_{a1},$$

$$V_{S_{b2}} = W_{b2a1}z_{a2},$$

and

$$V_{S_{c1}} = W_{c1a1}z_{a1} + W_{c1b1}z_{b1} + W_{c1a2}z_{a2} + W_{c1b2}z_{b2}.$$  

**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 $A_i$ to $B_i$ is expressed as

$$\tau_{\delta W} \frac{dW_{ji}}{dt} = -W_{ji} + \delta(z_j - \theta)$$

where $\tau_{\delta W}$ is the time constant of the plasticity. The plasticity is expressed as a proportion of the difference between the postsynaptic activity and the threshold $\theta$.

![Diagram](image)
neuron $j$ to neuron $i$ denoted by $W_{ij}$ due to homeostatic plasticity is simply expressed here as

$$\tau_w \frac{dW_{ij}}{dt} = -W_{ij} + W_{ij0} + p\zeta_i,$$

(9)

for inhibitory coupling, and

$$\tau_w \frac{dW_{ij}}{dt} = -W_{ij} + W_{ij0} - p\zeta_i,$$

(10)

for excitatory coupling, where $\tau_w$ is the time constant of $W_{ij}$, $W_{ij0}$ 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 $\tau_v=4$[ms], $\tau_u=1$[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 $W_{alc1}$.

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 $W_{a1c1}$. 
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 $W_{S_a1c_1}=0.02$ for the coupling weight from neuron $C_1$ to neuron $A_1$, and $W_{S_b}=1$ 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 $\tau_w=1\times10^6$ [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 $1\times10^5$ ms of neuron $A_1$, the membrane potential $v_{c1}$ and the number of firing $Z_{c1}$ for each period of $1\times10^5$ 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 $A_1$, $W_{a1c_1}$, respectively, from the top.

At first from $t=0$ [ms] to $t=4\times10^6$ [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 $W_{a1c_1}$ 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 $t=4\times10^6$ [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 $W_{a2c}$ does not decay to such a value since neuron $A_2$ fires occasionally. From $t=8\times10^6$ [ms] to $t=1.2\times10^7$ [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 $W_{a1c_1}$ 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 $t=8\times10^6$ [ms] to $t=1.2\times10^7$ [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 $W_{a_{1c}}$ decreases again since neuron $A_1$ does not fire. After $W_{a_{1c}}$ 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 $0 < E_1 \leq 30$. Table 1 shows the input amplitude $E_1$ 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 $W_{a_{1c}}$. Hence, both the generation of oscillation and its cessation are obtained by homeostatic plasticity of the neuronal network.

Table 1. Input amplitude $E_1$ that is required for inhibition of oscillation when only input $S_1$ is applied.

<table>
<thead>
<tr>
<th>$p$</th>
<th>0.03</th>
<th>0.05</th>
<th>0.07</th>
<th>0.08</th>
<th>0.1</th>
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<tbody>
<tr>
<td>$E_1$</td>
<td>5.55</td>
<td>3.11</td>
<td>2.13</td>
<td>1.75</td>
<td>1.35</td>
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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 $r_c=1 \times 10^6$ [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 $r=8 \times 10^6$ [ms] to $r=1.2 \times 10^7$ [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 $E_1$ that is required for inhibition of oscillation when both inputs $S_1$ and $S_2$ are applied.

<table>
<thead>
<tr>
<th>$p$</th>
<th>0.03</th>
<th>0.05</th>
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<tbody>
<tr>
<td>$E_1$, $E_2$</td>
<td>5.55</td>
<td>3.11</td>
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<td>1.75</td>
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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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