INHIBITION OF OSCILLATION IN A NEURAL OSCILLATOR MODEL FOR SOUND THERAPY OF TINNITUS


Abstract

Perception of continuous or intermittent sounds ringing in the ears without any external source is referred to as tinnitus. For the management of tinnitus one of the most effective approaches is sound therapy. Previously, we demonstrated a conceptual and computational plastic neural oscillator model for the mechanisms of tinnitus generation and the clinical effects of sound therapy on tinnitus. The proposed model has a stable oscillatory state and a stable equilibrium (non-oscillatory) state. It can be hypothesized that the oscillation state corresponds to the generation of tinnitus and the equilibrium state corresponds to the state in which the tinnitus is inhibited. Through numerical simulations of this model it was found that the oscillation can be inhibited by supplying band pass noise stimuli, which clinically has been used as a stimulus for treatment of tinnitus (i.e., sound therapy). The current paper describes the inhibition of the oscillation by yet two different types of noise stimuli; Gaussian white noise (GWN) and additive uniform noise. This investigation shows that only smaller RMS value of GWN input could inhibit the oscillation. When larger RMS values of GWN were employed the inhibition of oscillation was not frequent. It was observed that additive uniform noise (AUN) can inhibit the oscillation with higher possibility than GWN or BN. It is an interesting result although it does not directly suggest that...
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**Key Words**

tinnitus, sound therapy, neural oscillator, inhibition, noise, plasticity

1. Introduction

Perception of continuous or intermittent sounds ringing in the ears without any external source is referred to as tinnitus. Tinnitus is not a disease, but a symptom that can result from a wide range of underlying causes. Tinnitus can be perceived due to the damages caused by a variety of underlying pathologies of the auditory system or it may be associated with metabolic disorders. In the overwhelming majority of serious sufferers, there is no obvious sound source to account for the tinnitus percept [1-3]. As tinnitus is usually a subjective phenomenon, it is difficult to measure it using an objective test. Some techniques employ comparison of tinnitus with stimuli of known frequency and intensity, as in an audiometric test.

Results of numerous studies to pinpoint neural abnormalities underlying tinnitus have been inconclusive so far. It is believed that tinnitus originates from neuronal activities somewhere along the auditory pathway and at some point it is interpreted as sound, particularly at a cortical level [4, 5]. This neuronal activity associated with tinnitus is hypothesized to be the neural correlate of it which in turn it is perceived as an auditory phantom phenomenon. The same neuronal activity occurs in conditions such as central neuropathic pain, in response to total or partial deafferentation of the corresponding nerves [4, 6]. Animal and human studies have provided some evidence for this theory [7-9]. Some other studies have shown structural brain changes in tinnitus using MRI [10].

A number of researchers have discussed the role of plasticity in the auditory nervous system on tinnitus percept employing neurophysiologic studies. Cortical or thalamocortical correlates, or dorsal
cochlear nucleus activities with plasticity have been investigated [7-12]. Auditory electrophysiological studies have demonstrated an evidence for thalamic plasticity via top-down modulation [13]. 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 [8, 9].

Mathematical modelling of thalamocortical correlates of tinnitus has been reported [14]. A neurophysiological tinnitus model [5] combined with the adaptive resonance theory of cognitive sensory processing has been designed for identification of neural correlates of the tinnitus decompensation [15].

In order to manage tinnitus in bothersome cases, a variety of treatment approaches have been attempted. Some of the most common types of tinnitus treatment include cognitive behavioral therapy, sound therapy, medication therapy, biofeedback, neurobiofeedback and relaxation therapy. Sound therapy is one of the non-invasive and most effective clinical techniques. Although many therapies have been proposed and attempted, there is no single systematic and proven approach for curing tinnitus.

Tinnitus Masking technique (TM) and Tinnitus Retraining Therapy (TRT) are commonly prescribed sound therapy for patients of tinnitus. During those treatments tinnitus sufferers listen to therapeutic white noise or spectrum modified white noise sounds for several hours each day [16]. These sounds are usually presented via a custom-made noise (sound) generator or a tinnitus masker. A commonly observed change in tinnitus following removal of sound generators is referred to as residual inhibition. During residual inhibition tinnitus perception is temporarily halted after the removal of the noise (sound) generator. The underlying neural correlates of tinnitus cessation and its management by sound therapy are not known. Some correlate the success with sound therapy to brain plasticity [17] while others consider it a habituation process [18].

Our study addresses neural plasticity mechanisms in computational models of underlying neural circuitry that could result in synaptic changes and the effects of the sound therapy in clinic [19-23]. The
proposed neural network model incorporates plasticity based on Hebbian hypothesis [24] described with differential equations for the human auditory system. We reported [19, 20] that a certain region of the parameter hyper space exists where an oscillatory state and an equilibrium (non-oscillatory) state coexist. Many tinnitus clinics in a variety of geographical locations use band-pass noise (BN) stimuli for treatment of tinnitus by TM. Applying the same principles, we employed BN and generated a tinnitus inhibition model. It was shown that the oscillation is inhibited by giving a BN stimulus with some higher RMS value [21]. By hypothesizing that the oscillation and the equilibrium correspond to generation and inhibition of tinnitus, respectively, we demonstrated that these phenomena could explain the fact that the human auditory system temporarily halts perception of tinnitus following TM with the amplitude of the noise which masks the tinnitus perception.

On the contrary, TRT employs Gaussian white noise (GWN) and requires lower level of amplitude than what is required in TM. Due to the fact that lower amplitude is used for TRT, the patients can hear their tinnitus while listening to GWN while in TM approach the tinnitus is completely masked. This paper proposes a model of tinnitus inhibition and examines the effect of GWN input and how it inhibits the oscillation when its amplitude is relatively low. Such results correspond to the fact that in clinics across the world lower amplitude of GWN is used.

In order to explore the possibility of inhibition of oscillation by other noise, we investigated the effect of additive uniform noise (AUN) stimulus. It was observed that AUN can inhibit the oscillation with higher possibility than GWN or BN. It is an interesting observation although it does not directly suggest that AUN is better than GWN or BN in clinic.

2. A Neural Oscillator Model

In order to replicate tinnitus generation and its inhibition by a computational paradigm, we have proposed a conceptual neural network model [19]. The proposed neural oscillator model of the human
The auditory nervous system in this case is represented as a neural oscillator which consists of two excitatory units denoted by “$E_1$” and “$E_2$”, and an inhibitory unit denoted by “$I$”. The unit represents the aggregate of a neural ensemble in our model. The excitatory units $E_1$ and $E_2$ form a positive feedback loop by mutual coupling, while the units $E_2$ and I form a negative feedback loop by mutual coupling. These two loops enable the model to oscillate. This configuration is the simplest in terms of neural arrangement that could demonstrate oscillatory behavior. The unit $E_1$ receives an external signal, $S$, which is associated with the sound in clinical situations.

The neural connection from the $j$-th unit to the $i$-th unit is expressed by $C_{ij}$ ($i, j \in \{1, 2, I\}$) which are positive. The dynamics of the model is described by the simultaneous differential equations:

\[
\frac{dx_1}{dt} = (-x_1 + C_{12}z_2 + S)/\tau_1 \quad (1)
\]

\[
\frac{dx_2}{dt} = (-x_2 + C_{21}z_1 - C_{2I}z_I)/\tau_2 \quad (2)
\]

and

\[
\frac{dx_I}{dt} = (-x_I + C_{I2}z_2)/\tau_I \quad (3)
\]
where $x_j$ denotes the internal potential of the $j$-th unit and $\tau_j$ is the time constant of the dynamics of the $j$-th unit. The output of the $j$-th unit is denoted by $z_j$, which is given by the equation:

$$z_j = \frac{2}{\pi} \tan^{-1} x_j$$

(4)

The coupling strength from the unit $E_2$ to the unit $E_1$, denoted by $C_{12}$, is assumed to have plasticity and it changes according to the product of the outputs of the units $E_1$ and $E_2$. It means that the coupling strength $C_{12}$ is one of the state variables in the model system. It is expressed as:

$$\frac{dC_{12}}{dt} = (-C_{12} + b z_1 z_2 + C_0) / \tau_c$$

(5)

The $C_0$ denotes the equilibrium of $C_{12}$ under $z_1z_2 = 0$. The $b$ is the efficiency of strengthening the synaptic coupling based on Hebbian hypothesis [24]. The $\tau_c$ is the time constant of $C_{12}$. They are positive constants.

We are not able to specify the correspondence of each unit in the model to the region in the brain at present. It is assumed that the model represents tonotopic organization and depends on the frequency of tinnitus that is perceived and reported. The proposed model is likely to include the thalamus, at which a massive corticofugal projection ends, based on the anatomical structure of the auditory system. An positive feedback that brings oscillation is formed by the thalamo-cortico-thalamic loop, while a negative feedback is likely to be formed by the thalamic interneurons and thalamic reticular GABAergic neurons.

The external auditory stimulus which is represented by $S$ in Fig. 1 is received as an input in unit $E_1$ and results in generation of aggregate neuronal activity of an ensemble in the proposed model. In the auditory system such processing occurs at the peripheral nervous system and the corresponding
mechanism in terms of neural engineering is represented within unit $E_1$. Aggregate activity of thalamic interneurons and thalamic reticular GABAergic neurons are captured within the excitatory unit $E_1$ and inhibitory unit $I$. Aggregate neuronal mechanism represented within the cortex pertaining to perception of tinnitus is represented by the unit $E_2$. The thalamo-cortico-thalamic loop is represented by the excitatory links between the units $E_1$ and $E_2$ and the excitatory-inhibitory links between units $E_2$ and $I$.

3. Results and Discussion

The plastic system expressed by Eqs. (1) – (5) has two attractors. The point $(x_1, x_2, x_i, C_{12})=(0, 0, 0, C_0)$ is an equilibrium point in the dynamical system. There is another attractor, an oscillatory orbit. Numerical analysis of the system unveiled that the equilibrium exists in the range of $C_0$, $0 \leq C_0 \leq 8.06$ and the oscillatory orbit in $C_0 \geq 2.65$. Consequently, the system is bistable in $2.65 \leq C_0 \leq 8.06$.

In order to perform the simulations within appropriate time, we gave the time constant of plasticity an arbitrarily determined value. The time scale in the clinical situation is much longer than in the simulation.

Tinnitus suffers complain of tinnitus with different frequencies, 125Hz to 8kHz. The white noise that TRT uses covers such frequencies. In the simulations GWN or AUN with frequency band of 10kHz was employed.

3.1 Gaussian White Noise (GWN) Stimulus

GWN stimulus is commonly used in TRT [16]. In order to replicate such auditory stimulus, simulations were performed adding GWN with various RMS values. Here we demonstrate simulation results [22] as seen in Fig. 2 and Fig. 3. The results are probabilistic.
Figure 2. Examples of inhibition of oscillation by GWN input. RMS value of the noise is 10. (a) A successful result, (b) an unsuccessful result.

Figure 3. Examples of inhibition of oscillation by GWN input. (a) A successful result. RMS value of the noise is 20. (b) An unsuccessful result. RMS value of the noise is 100.

Fig. 2 shows the results with the noise with an RMS adjusted to 10. In Fig. 2(a) it was observed that the oscillatory states are inhibited, which coincides to the inhibition effect by GWN stimulus in clinical situations. The value of $C_{12}$ gradually decreases after the stimulus is supplied. This implies that plasticity in connectivity between various neuronal ensembles in the auditory system may play a role in the
inhibition of tinnitus. Note that for the first two seconds units $E_1$, $E_2$ and $I$ are in oscillating mode replicating perception of tinnitus. When GWN is introduced at $t=2$ [sec], the oscillations in all three units begin to subside along with reduction in $C_{12}$. At $t=8$ [sec] GWN is removed and all three units remain in non-oscillatory state replicating the effect of tinnitus inhibition in tinnitus subjects.

On the contrary, Fig. 2(b) shows an unsuccessful result in spite of the introduction of GWN which is generated under the same conditions. The value of $C_{12}$ is almost unchanged during the stimulus presentation, and consequently the oscillatory state continues through the simulation. Hence, GWN does not always inhibit the system in all cases.

Fig. 3(a) shows another successful result with RMS value of 20, and Fig. 3(b) shows another unsuccessful result with RMS value of 100.

It was observed that when 100 trials with different random sequences were conducted, the oscillation was inhibited with the probability 0% with RMS value of 0.5, 1 and 2, 18% with RMS value of 10, 6% with RMS value of 20, and 0% with RMS value of 50, 100 and 200. The oscillation was inhibited with the probability 0.3% with RMS value of 5 for 1,000 trials. The results indicate that as the RMS value increases from zero, the possibility that the oscillation is inhibited increases, but the possibility reduces and becomes zero with the larger RMS values.

It has been reported [16] that for TRT lower amplitudes are used for the stimulus so that the patients can hear the sound of tinnitus. Our results seem to be consistent with the practice.

BN is employed in TM. For TM higher amplitudes of BN are used for the external sound so that the patients do not hear the sound of tinnitus. Our results reported previously [21] also seem to be consistent with the practice, as the oscillation was inhibited with the probability 0% with RMS value of 10 and 74% with RMS value of 200.
3.2 Additive Uniform Noise (AUN) Stimulus

In order to explore the possibility of inhibition of oscillation by other noise, we investigated the inhibition using AUN stimulus. AUN is positive and given out of the uniformly distributed values. When RMS value was fixed in the range of 0.6, some simulations showed successful results for inhibition of the oscillation, while others resulted in continuation of oscillation, as shown in Fig. 4. Fig. 5(a) shows another successful result with RMS value of 5, and Fig. 5(b) shows another unsuccessful result with RMS value of 10. In Fig. 5(a), the oscillation is inhibited while the noise input is added. In Fig. 5(b), The values $x_1$ and $x_i$ are saturated to a high value while the noise input is added, and oscillation resumes after the noise input is removed.

It was observed that when 100 trials with different random sequences were conducted, the oscillation was inhibited with the probability 0% with RMS value of 0.5, 47% with RMS value of 0.6, 100% with RMS value of 1, 2 and 5, 0% with RMS value of 10, 20, 50 and 100.

The results indicate that when the RMS value is in an appropriate range, the oscillation is always inhibited. With larger or smaller RMS values, the rate of inhibition decreases. The results of the simulations revealed that AUN has a better ability in the inhibition of the oscillation compared to GWN or BN. Although this observation is an appealing result, however, it does not directly indicate that AUN would be a better inhibitor than GWN and BN in clinical settings.
Figure 4. Examples of inhibition of oscillation by AUN input. RMS value of the noise is 0.6. (a) A successful result, (b) an unsuccessful result.

Figure 5. Examples of inhibition of oscillation by AUN input. (a) A successful result. RMS value of the noise is 5. (b) An unsuccessful result. RMS value of the noise is 10.

4. Conclusions

In this study through numerical simulations, we demonstrated inhibition of the oscillation in the plastic neural oscillator model using GWN stimulus similar to the TRT stimulus that is commonly used in the clinic. We previously demonstrated the inhibition of the oscillation in the same model using BN stimulus that is employed in TM. Therefore, the findings of these experiments could explain the fact that the human auditory system temporarily halts perception of tinnitus following sound therapy of TRT and TM.

In order to explore the possible inhibition of oscillation using other noise, we examined the stimulation of the model by AUN, and also demonstrated that it can inhibit the oscillation. The results of the simulations revealed that AUN has a better ability in the inhibition of the oscillation compared to GWN or BN. Although this observation is an appealing result, however, it does not directly indicate that AUN would be a better inhibitor than GWN and BN in clinical settings.
As future work we will develop a dynamical model incorporating not only the Hebbian plasticity but also homeostatic plasticity [25] that has been evidenced in a number of nervous systems [26]. This will provide a better approach to explain the tinnitus-related hyperactivity. Our future work will also explore better stimuli for tinnitus inhibition. This in turn will result in improvement in designing better and more effective sound therapy techniques and stimuli.

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References


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