A NEURAL OSCILLATOR MODEL FOR TINNITUS AND ITS MANAGEMENT BY SOUND THERAPY

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Abstract

Tinnitus is the perception of sound occurring without an external stimulus. Sound therapy is one of the most effective treatment techniques that have been employed by clinicians. To account for mechanisms of tinnitus generation and the clinical effects of sound therapy from the viewpoint of neural engineering, the authors have proposed a conceptual neural oscillator model with plasticity for the human auditory system. In this study, the authors found that this model has a bistable state, i.e., a condition where a stable oscillatory state and a stable non-oscillatory equilibrium state coexist at a certain parameter region. It was also found that the oscillation can be inhibited by supplying sinusoidal or random stimuli, which was hypothesized as sound for treatment of tinnitus, in this model. Through numerical simulations, the authors discovered that adequate noise stimulus can inhibit the oscillation. By hypothesizing that the oscillation and the equilibrium correspond to generation and inhibition of tinnitus, respectively, it can be stated that these phenomena could explain the fact that the human auditory system temporarily halts perception of tinnitus following sound therapy. This paper describes dynamical properties of the model and inhibition of the oscillation for sinusoidal stimulus and a kind of noise stimulus, which corresponds to the sound in the treatment of tinnitus.

Introduction

Tinnitus is the perception of phantom sounds in the ears or in the head. It is believed that tinnitus is an auditory phantom phenomenon resulting from neuronal activity somewhere along the auditory pathway. This phantom perception is a common condition and it can originate from many sources. Tinnitus can be perceived due to the damages in a variety of the pathologies of the auditory system. It has been shown that auditory percept can be generated by exposure to loud noise or medications which have a toxic effect on the inner ear. Additionally, tinnitus can be associated with a variety of diseases such as thyroid abnormalities, diabetes and hypertension. In some cases, tinnitus can be traced to an internally generated sound, for example, spontaneous otoacoustic emissions. However, in the overwhelming majority of serious sufferers, there is no obvious sound source to account for the tinnitus percept [1-3].

Tinnitus is a chronic disease with a reported prevalence of 10–15% [4–8]. Globally speaking, this corresponds to approximately 700 million people. The effect of tinnitus on quality of life in patients suffering from this disease should not be underestimated. It is noteworthy that an estimated 20% of patients indicate that their quality of life is significantly deteriorated. Many patients experience insomnia and depression, and in 1% of the population tinnitus seriously interferes with their life [7–9].

Attempts have been made to help those who suffer from tinnitus. The common types of tinnitus treatment include medication therapy, biofeedback, relaxation therapy, cognitive behavioral therapy and sound therapy. Although many therapies have been proposed and tried, there is no systematic and proven approach for treating tinnitus.

Despite numerous animal and human studies, the neural abnormalities underlying tinnitus are largely unknown. In some patients tinnitus can be traced to an internally generated sound such as vascular structures in pulsatile tinnitus; in the vast majority, however, no obvious sound source can be pinpointed. It has been proposed that tinnitus results from abnormal neuronal activity arising at some point along the auditory pathways which is interpreted as sound at a cortical level [10–12]. This abnormal neuronal activity is hypothesized to be the neural correlate of tinnitus, which is considered to be an auditory phantom phenomenon, similar to central neuropathic pain, due to neural plasticity in response to total or partial deafferentation somewhere along the auditory tract [10], [13–15]. Animal and human studies have provided some evidence for this theory [8], [12], [13], [16–22]. Functional MRI has been applied in a few studies, mainly case studies [23–25]. The purpose of these studies has been to visualize the entire central auditory pathway in patients with lateralized tinnitus and in patients with bilateral tinnitus to evaluate lateralization of fMRI signal change and activation clusters. The most important fMRI study shows an abnormally low percentage signal change in the inferior colliculus (IC) contralateral to the side of the perceived tinnitus [26]. Structural brain changes in tinnitus have also been discovered using MRI [27].

The role of neural plasticity in the auditory system and tinnitus has been discussed in neurophysiologic studies, and thalamocortical correlates or dorsal cochlear nucleus activities with plasticity have been investigated [28-32]. Electrophysiological studies of the auditory system have demonstrated an evidence for thalamic plasticity via top-down modulation [29]. Computational modeling of thalamocortical correlates with plasticity from the perspective toward

understanding of the tinnitus has been reported [33]. A tinnitus model based on the work by Jastreboff [11], combined with the adaptive resonance theory of cognitive sensory processing [34], has been proposed for identification of neural correlates of the tinnitus decompensation [35]. The effect of auditory selective attention on the tinnitus decompensation has also been investigated by modeling corticothalamic feedback dynamics [36], [37].

There are two typical sound therapy techniques, namely, the TM (Tinnitus Masking) technique and TRT (Tinnitus Retraining Therapy), where those who suffer from tinnitus listen to these therapeutic sounds for several hours a day [38]. In these techniques, white noise or spectrum-modified white noise are introduced to tinnitus sufferers as therapeutic sound. These sounds are usually presented via a custom-made noise (sound) generator or a tinnitus masker. It has been reported that sound therapy has a clinical effect, in a great number of cases in this management method where tinnitus perception is temporarily halted after the removal of the noise (sound) generator. This cessation of tinnitus following the presentation of a masking stimulus is referred to as residual inhibition. The mechanisms of tinnitus and its management by sound therapy, however, are not clear. Some attribute the success with sound therapy to brain plasticity [39] while others consider it a habituation process [40].

The purpose of this current study was to address mechanisms of tinnitus generation and the clinical effect of the sound therapies from the viewpoint of neural engineering. Accordingly, the authors proposed a plastic neural network model for the human auditory system. They also previously reported [41] that a certain region of the parameter hyper space exists where an oscillatory state and a non-oscillatory equilibrium state coexist. It was shown that the oscillatory state is inhibited by supplying a sinusoidal stimulus resulting in a transition to an equilibrium state [42], [43]. By hypothesizing that the oscillation and the equilibrium correspond to generation and inhibition of tinnitus, respectively, the authors demonstrated that these phenomena could explain the fact that the human auditory system temporarily halts perception of tinnitus following sound therapy. This paper illustrates inhibition of the oscillation in the proposed model using band-noise stimulus as therapeutic sound [44], [45]. In tinnitus clinics across the globe, similar noise stimuli have been employed for treatment of tinnitus by TM.

Model Description

The human auditory system consists of two divisions, a peripheral portion and a central portion. The cochlear hair cells are located in the peripheral portion and transform acoustic vibrations received by the ear into neural signals. The central auditory pathway is composed of many portions. It receives the neural auditory messages that have travelled via the auditory nerves to the cochlear nucleus, the superior olivary complex, the inferior colliculus, the medical geniculate body, and the auditory cortex. Subsequently, the brain perceives the neural signals as sound. In cases of certain tinnitus patients it has been observed that cochlear dysfunction occurs, and abnormal neural signals from the cochlea cause abnormality in the central nervous system. Consequently, tinnitus can be triggered. In addition to ascending pathway, the cochlear nucleus complex receives descending efferent fiber bundles to control the function of cochlear outer hair cells [9].

In this study, the authors proposed a conceptual neural network model to account for tinnitus generation and its inhibition from the neural engineering point of view [33]. Figure 1 shows the proposed neural oscillator model of the human auditory system.

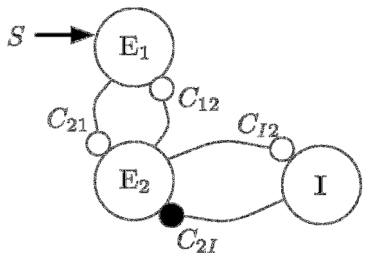

Figure 1. A Neural Oscillator Model

The human auditory 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 this 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 incoming signal, S, which is associated with an external sound signal.

The neural coupling from the j-th unit to the i-th unit is expressed by the positive constant C_{ij} ($i, j \in \{1, 2, I\}$).

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

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

and

$$\frac{dx_I}{dt} = (-x_I + C_{I2} z_2)/\tau_I \quad (3)$$

where x_j and τ_j are the internal potential and time constant of the j-th unit, respectively. The output of the j-th unit is denoted by z_j, which is given by the equation

$$z_j = \frac{2}{\pi} \tan^{-1} x_j \quad (4)$$

It was assumed that the coupling strength from the unit E_2 to the unit E_1, denoted by C_{12}, would have plasticity in such a way that it would change according to the product of the outputs of the units E_1 and E_2. This would mean that the coupling strength C_{12} would be one of the state variables in the model system. It was expressed as

$$\frac{dC_{12}}{dt} = (-C_{12} + b z_1 z_2 + C_0)/\tau_C. \quad (5)$$

The C_0, b, and τ_c are also positive constants which denote the equilibrium of C_{12} under $z_1 z_2 = 0$, the efficiency of strengthening the synaptic coupling based on Hebbian hypothesis [46], and the time constant of C_{12}, respectively.

At the present time, it is not possible to specify what regions in the brain correspond to each unit in the model. The model was hypothesized 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 include the thalamus, at which a massive corticofugal projection ends. The thalamo-cortico-thalamic loop forms an ideal positive oscillatory loop, while the thalamic interneurons and thalamic reticular GABAergic neurons likely play the role of inhibitory neurons.

The external auditory stimulus, which is represented by S in Figure 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 the 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.

Attractive Region of Non-Oscillation

The plastic system expressed by equations (1) – (5) has two attractors. An equilibrium point in the dynamical system can easily be found: (x_1, x_2, x_I, C_{12})=(0, 0, 0, C_0). The other attractor is an oscillatory orbit. Numerical analysis of the system revealed that the equilibrium exists in the range of C_0, $0 \le C_0 \le 8.06$ and the oscillatory orbit in $C_0 \ge 2.65$ [40]. Consequently, the system is bistable in $2.65 \le C_0 \le 8.06$.

Also in the system with no plasticity—that is, where the coupling strength C_{12} is not expressed by equation (5), but rather given to a constant value—there are two attractors: an equilibrium point (x_1, x_2, x_I)=(0, 0, 0) and an oscillatory orbit. The system also has the similar bistable region of C_{12} to the region of C_0 in the plastic system. Which attractor the system converges to depends on the initial values of x_1, x_2 and x_I.

In Figure 2, are shown two examples of the region of the initial values of x_1 and x_2. When coupling strength values C_{12}, C_{21}, C_{2I} and C_{I2} are help constant, the system is attracted to the non-oscillatory solution when different initial values of x_1 and x_2 are used. The parameters in equations (1) – (3) were fixed such that τ_1=0.01 seconds, τ_2=0.01 seconds, τ_I=0.02 seconds, C_{2I}=10, C_{2I}=10 and C_{I2}=20. The initial value of x_I was also fixed at zero.

The dynamics of the system are governed by equations (1) – (3). In the black region in Figure 2, if the initial x_1, x_2 values are inside the black region—excluding (0, 0)—then the system is attracted to the equilibrium point (0, 0, 0) and the oscillations subside. If the initial x_1, x_2 values are outside the black region, the oscillation occurs as the system is attracted to the oscillatory orbit.

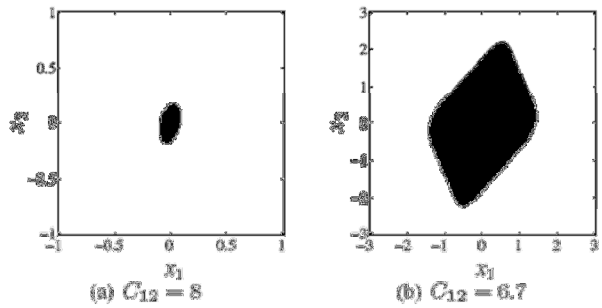

Figure 2. Regions of attraction to the equilibrium point at all constant couplings, i.e., all C_{ij} are constant. The initial value of x_I is fixed at zero

Notice that these results show dynamic properties of the non-plastic neural oscillator model, which is described by equations (1) - (3). According to the results, the model has the dynamic property that the attractive region of the non-oscillatory solution is expanded by reducing the value of C_{12}. In addition, any oscillatory behavior in this region eventually settles down in the non-oscillatory state without external stimulus according to the dynamic property of the model. Eventually, when $C_{12} < 2.65$, any initial value yields a non-oscillatory solution. Therefore, to inhibit the oscillation, it is important that the states of x_1, x_2, x_I, C_{12} change into such an attractive region of non-oscillation by external stimulus.

Inhibition of Oscillation by External Stimuli

The inhibition of oscillation by various external stimuli was examined with the model incorporating the synaptic plasticity, which is the system described by equations (1) - (5). In equation (5), the plasticity parameter values C_0=3, b=20, τ_c=0.5 seconds were employed. These parameters of plasticity were arbitrarily determined so that the simulation was performed within the appropriate time. The time scale would be much longer in the clinical situation as it is important to sufficiently expose the ears to a sufficient duration of acoustic stimulation for better inhibition or habituation.

Demonstrated here are some simulation results with sinusoidal wave and band noise as external stimuli. The stimuli were applied to the unit E_1 for the duration of $2 \le t \le 8$ seconds.

1) Sinusoidal stimulus
   Auditory stimulations can be viewed as a composite of sinusoidal signals. Hence, the first experiment was supplied an adequate sinusoidal stimulus [28]. Figure 3 shows an instance in which the oscillation was inhibited by sinusoidal stimulus defined as

$$S = 2\sqrt{2} \sin 20\pi t. \quad (6)$$

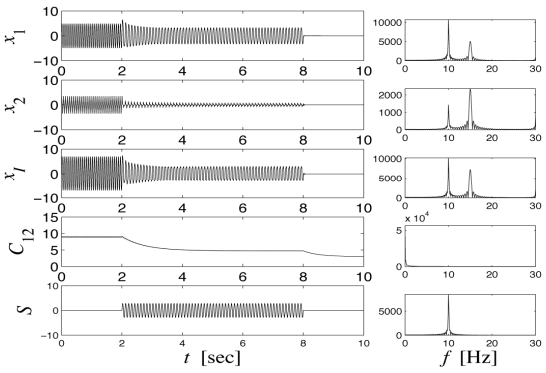

Figure 3. Inhibition of oscillation by sinusoidal stimulus

The value of the amplitude was fixed so that the root mean squared value (RMS) of the stimulus was 2.0. The timing diagrams in the left column show the waveforms of x_1, x_2, x_I, C_{12} and S, respectively; and their corresponding power spectra are illustrated in the right column.

It can be seen that by applying stimulus S starting at 2 seconds, the value of C_{12} gradually decreases and, consequently, the oscillations are inhibited. Note that the oscillation does not reoccur even after the sinusoidal stimulus stops at 8 seconds. By hypothesizing that the damping of C_{12} oscillations corresponds to what is called residual inhibition in the human auditory system for tinnitus, the phenomenon could explain the fact that the human auditory system temporarily inhibits the perception of tinnitus after sound therapy. This is a promising observation and it can help in better management of tinnitus.

The reason why the coupling strength C_{12} decreases is explained as follows. The plasticity is formulated based on the Hebbian hypothesis in equation (5). It works in such a way that the coupling strength C_{12} increases when the units E_1 and E_2 oscillate in-phase, and decreases when the oscillations of the units E_1 and E_2 are anti-phase. Without stimulus, the oscillations of the units are in-phase, while they are out-of-phase with stimulus and close to anti-phase.

2) Band-noise stimulus:
   Band-noise stimulus is typically used in the treatment of tinnitus using the TM approach [27]. In this approach, the desired noise is a band of noise with a frequency emphasis that approximates the frequency of perceived tinnitus. The frequency (pitch match) of tinnitus can range from low frequencies to high frequencies in different individuals. Most of the tinnitus sufferers perceive tinnitus at high frequencies between 2–8kHz.

In this experiment, the authors hypothesized that the fundamental frequencies of perceived tinnitus were 2, 4, 6, and 8kHz, and subsequently employed a band noise generated from Gaussian white noise through a band-pass filter which operates between each fundamental frequency with a ± 5% margin. RMS (Root Mean Square) was also adjusted to about 400.

Figures 4(a)-(d) show successful results for inhibition of the oscillations. The timing diagrams in the left column show the waveforms of x_1, x_2, x_I, C_{12} and S, from top to bottom, respectfully. Their corresponding power spectra are illustrated in the right column.

In Figures 4(a) and 4(b), oscillation of x_2 and x_I stops immediately after the noise input is applied and it brings the rapid decrease of C_{12}. In Figure 4(c), oscillation of x_2 and x_I is maintained for about 1 second. In Figure 4(d), oscillations

of x_2 and x_I are maintained almost until t=8 seconds. However, the value of C_{12} gradually decreases from the point of applying the stimulus. Eventually, the oscillations of x_2 and x_I stop. 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 during the application of noise, input unit E_1 is in an oscillating mode replicating the perception of tinnitus. After removing the input, the oscillation of the unit is in the state of non-oscillation, which replicates the state where the tinnitus is not perceived. It was observed that the oscillation was inhibited with certainty in all the simulations when 100 trials were conducted with different random sequences.

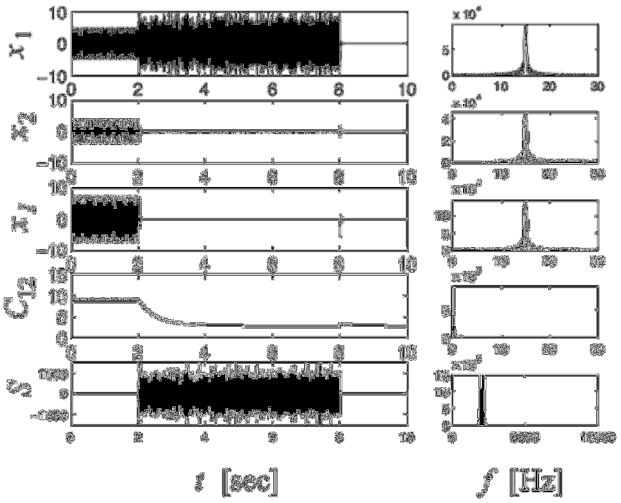

Figure 4(a). Inhibition of oscillation by band noise stimulus with the band between 2kHz ± 5% margin and 400 RMS

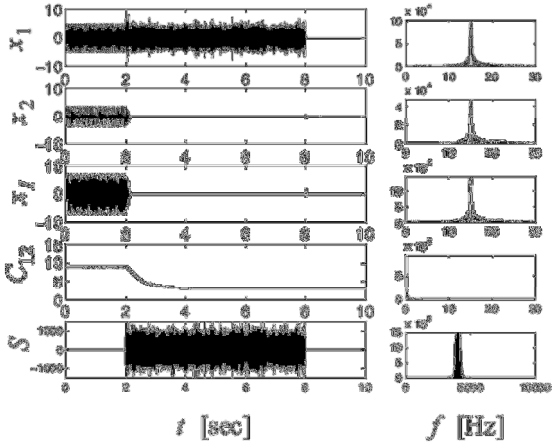

Figure 4(b). Inhibition of oscillation by band noise stimulus with the band between 4kHz ± 5% margin and 400 RMS

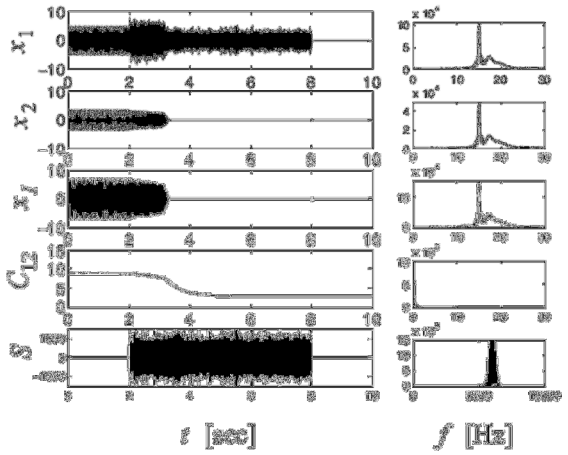

Figure 4(c). Inhibition of oscillation by band noise stimulus with the band between 6kHz ± 5% margin and 400 RMS

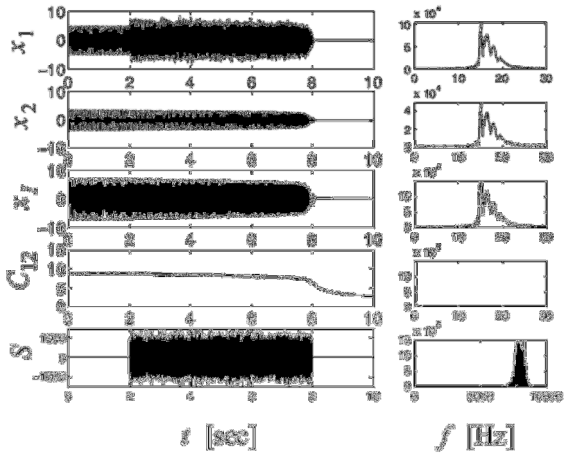

Figure 4(d). Inhibition of oscillation by band noise stimulus with the band between 8kHz ± 5% margin and 400 RMS

Figures 5(a) and 5(b) show the results for a 4kHz bandpass filter with a margin of ± 5% and an RMS adjusted to about 200. Figure 5(a) shows a successful result similar to that of Figure 4(d). Oscillations of x_2 and x_I were maintained almost until t=8 seconds. However, the value of C_{12} gradually decreased from the point of applying the stimulus. Eventually, the oscillations of x_2 and x_I stopped. On the other hand, for the same conditions, there were unsuccessful results in which the value of C_{12} was almost unchanged for the 4kHz filter and, consequently, the oscillations continued through the entire simulation time, as seen in Figure 5(b). It was observed that the oscillation was inhibited with the probability 74% when 100 different random trials were conducted.

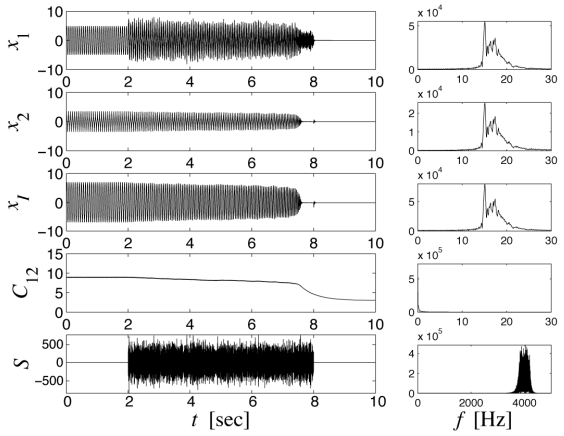

Figure 5(a). A successful experiment for inhibition of oscillation by band noise stimulus with the band between 4kHz ± 5% margin and 200 RMS

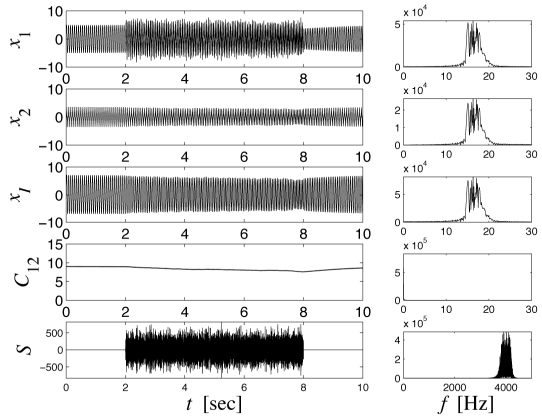

Figure 5(b). An unsuccessful experiment for inhibition of oscillation by band noise stimulus with the band between 4kHz ± 5% margin and 200 RMS

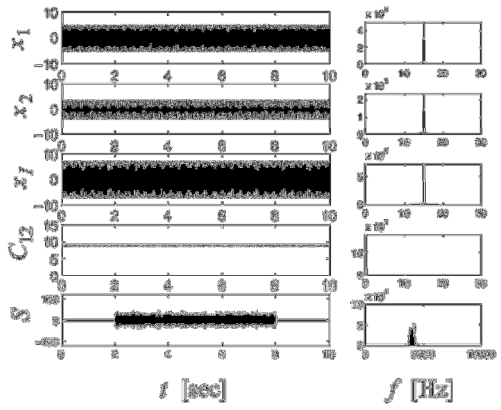

Figure 6. An unsuccessful experiment for inhibition of oscillation by band noise stimulus with the band between 4kHz ± 5% margin and 10 RMS

As seen in Figure 6, for band noise with much lower power (RMS=10), it was observed that the value of C_{12} was almost unchanged and, consequently, the oscillations continued through the entire simulation time for all the simulations that we examined with 100 different random sequences. Therefore, it can be concluded that the inhibition of the oscillations by band noise stimulus requires an appropriately higher RMS value.

For TM that uses band noise, higher amplitudes were used for the external sound in clinical practice so that the patients could not hear the sound of tinnitus [27]. It was not possible to precisely compare the RMS values of the noise in the simulation with the clinical data. However, the amplitude of the oscillation of x_1 was larger than the one that was seen before the noise was applied in Figures 4 and 5(a), and successful results were obtained. In Figure 6, the amplitude of the oscillation of x_1 was same as the one that was seen before the noise was applied and the result was unsuccessful. It corresponded to the situations when the noise was applied in clinic. Therefore, the results seem to be consistent with the practice.

Conclusions

In this study inhibition of the oscillation in the plastic neural oscillator model using sinusoidal wave and band noise was demonstrated. Through numerical simulations, it was found that band noise stimulus can inhibit the oscillation. Therefore, the finding of this experiment could explain the fact that the human auditory system temporarily halts perception of tinnitus following TM and that it is a kind of sound therapy using band noise stimuli.

It has been reported [27] that for TRT lower amplitudes were used for the stimulus so that the patients could hear the sound of tinnitus. In this current study, the simulations used the Gaussian white-noise stimulus that TRT employs. These simulation results seem to be consistent with the practice [44].

The parameters of plasticity were arbitrarily determined so that the simulation was performed within an appropriate time. The time scale would be much longer in the clinical situation. Further correspondence of the simulation data to clinical data needs to be examined.

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 better and more effective sound therapy techniques and stimuli. The present model consists of the simplest arrangement of neuronal ensembles that can produce an oscillatory state which would

resemble the perception of tinnitus. As discussed, the arrangement represents the aggregate mechanisms in the thalamo-cortico-thalamic loop and future enhancements of the model will focus on adding excitatory and inhibitory connectivity between units E_1 and I in order to capture intra-thalamic interactions.

Acknowledgments

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References

[1] E. P. Fowler, "Head noises in normal and in disordered ears: significance, measurement and treatment," Archives of Otolaryngology – Head and Neck Surgery, Vol. 39, No. 6, 1944, pp. 498-503.

[2] M. J. Penner, "An estimation of the prevalence of tinnitus caused by spontaneous otoacoustic emissions," Archives of Otolaryngology – Head and Neck Surgery, Vol. 116, No. 4, 1990, pp. 418-423.

[3] A. Sismanis and W. R. Smoker, "Pulsatile tinnitus: recent advances in diagnosis," The Laryngoscope, Vol. 104, Issue 6, 1994, pp. 681-688.

[4] A. Axelsson and A. Ringdahl, "Tinnitus – a study of its prevalence and characteristics," Br J Audiol, Vol. 23, 1989, pp. 53–62.

[5] A. J. Heller, "Classification and epidemiology of tinnitus," Otolaryngol Clin North Am, Vol. 36, 2003, pp. 239–248.

[6] J. L. Weissman and B. E. Hirsch, "Imaging of tinnitus: a review," Radiology, Vol. 2, 2000, pp. 342–349.

[7] D. De Ridder, G. De Mulder, V. Walsh, N. Muggleton, S. Sunaert and A. Moller, "Magnetic and electrical stimulation of the auditory cortex for intractable tinnitus, Case report," J Neurosurg, Vol. 100, 2004, pp. 560–564.

[8] W. Muhlnickel, W. Lutzenberger and H. Flor, "Localization of somatosensory evoked potentials in primary somatosensory cortex: a comparison between PCA and MUSIC," Brain Topogr, Vol. 11, 1999, pp. 185–191.

[9] W Meyershoff, "Tinnitus," In: Meyershoff W, Ria D (eds.) Otolaryngology head and neck surgery, WB Saunders, Philadelphia, 1992, pp. 435–446.

[10] J. J. Eggermont, "Central tinnitus," Auris Nasus Larynx, Vol. 30 [Suppl], 2003, pp. S7–S12.

[11] P. J. Jastreboff, "Phantom auditory perception (tinnitus): mechanisms of generation and perception," Neurosci Res, Vol. 8, No. 4, 1990, pp. 221-254.

[12] A. L. Giraud, S. Chery-Croze, G. Fischer, C. Fischer, A. Vighetto, M. C. Gregoire, F. Lavenne and L. Collet, "A selective imaging of tinnitus," Neuroreport, Vol. 10, 1999, pp. 1–5.

[13] W. Muhlnickel, T. Elbert, E. Taub and H. Flor, "Reorganization of auditory cortex in tinnitus," Proc Natl Acad Sci USA, Vol. 95, 1998, pp. 10340–10343.

[14] J. A. Kaltenbach, "Neurophysiologic mechanisms of tinnitus," J Am. Acad. Audiol., Vol. 11, 2000, pp. 125–137.

[15] D. De Ridder, H. Ryu, A. R. Moller, V. Nowe, P. Van de Heyning, J. Verlooy, "Functional anatomy of the human cochlear nerve and its role in microvascular decompressions for tinnitus," Neurosurgery, Vol. 54, 2004, pp. 381–388; discussion pp. 388–390.

[16] S. A. Chowdhury and N. Suga, "Reorganization of the frequency map of the auditory cortex evoked by cortical electrical stimulation in the big brown bat," J Neurophysiol, Vol. 83, 2000, pp. 1856–1863.

[17] D. Robertson and D. R. Irvine, "Plasticity of frequency organization in auditory cortex of guinea pigs with partial unilateral deafness," J Comp Neurol, Vol. 282, 1989, pp. 456–471.

[18] F. Mirz, B. Pedersen, K. Ishizu, P. Johannsen, T. Ovesen, H. Stodkilde-Jorgensen and A. Gjedde, "Positron emission tomography of cortical centers of tinnitus," Hear Res, Vol. 134, 1999, pp. 133–144.

[19] F. Mirz, A. Gjedde, K. Ishizu and C. B. Pedersen, "Cortical networks subserving the perception of tinnitus – a PET study," Acta Otolaryngol Suppl, Vol. 543, 2000, pp. 241–243.

[20] A. H. Lockwood, R. J. Salvi, M. L. Coad, M. L. Towsley, D. S. Wack and B. W. Murphy, "The functional neuroanatomy of tinnitus: evidence for limbic system links and neural plasticity," Neurology, Vol.50, 1998, pp. 114–120.

[21] W. Arnold, P. Bartenstein, E. Oestreicher, W. Romer and M. Schwaiger, "Focal metabolic activation in the predominant left auditory cortex in patients suffering from tinnitus: a PET study with [18F] deoxyglucose," ORL J Otorhinolaryngol Relat Spec, Vol. 58, 1996, pp. 195–199.

[22] A. Gardner, M. Pagani, H. Jacobsson, G. Lindberg, S. A. Larsson, A. Wagner and T. Hallstrom, "Differences in resting state regional cerebral blood flow assessed with 99mTc-HMPAO SPECT and brain atlas matching between depressed patients with and without tinnitus," Nucl Med Commun, Vol. 23, 2002, pp. 429–439.

[23] A. T. Cacace, "Expanding the biological basis of tinnitus: crossmodal origins and the role of neuroplasticity," Hear Res, Vol. 175, 2003, pp. 112–132.

[24] A. T. Cacace, J. P. Cousins, S. M. Parnes, D. Semenoff, T. Holmes, D. J. McFarland, C. Davenport, K. Stegbauer and T. J. Lovely, "Cutaneous-evoked tinnitus. I. Phenomenology, pschychophysics and

functional imaging," Audiol Neurootol, Vol. 4, 1999, pp. 247–257.
[25] M. Ballester, K. O. Lovblad, A. C. Nirkko, D. Vibert, P. Romanet, G. Schroth and R. Hausler, "Functional MRI of tinnitus – preliminary results using echo-planar imaging (abstract)," Neuroimage, Vol. 13, 2001, p. 379.
[26] J. R. Melcher, I. S. Sigalovsky, J. J. Guinan, R. A. Levine, "Lateralized tinnitus studied with functional magnetic resonance imaging: abnormal inferior colliculus activation," J Neurophysiol, Vol. 83, 2000, pp. 1058–1072.
[27] M. Muhlau, J. P. Rauschecker, E. Oestreicher, C. Gaser, M. Rottinger, A. M. Wohlshlager, F. Simon, T. Etgen, B. Conrad and D. Sander, "Structural brain changes in tinnitus," Cereberal Cortex, Vol. 16, Sept 2006, pp. 1283-1288.
[28] J. P. Rauschecker, "Auditory cortical plasticity: a comparison with other sensory systems," Trends Neurosci, Vol. 22, 1999, pp. 74-80.
[29] N. Suga and X. Ma, "Multiparametric corticofugal modulation and plasticity in the auditory system," Nat Rev Neurosci, Vol. 4, 2003, pp. 783-794.
[30] J. J. Eggermont and L. E. Roberts, "The neuroscience of tinnitus," Trends in Neurosciences, Vol. 27, No. 11, 2004, pp. 676-682.
[31] A. R. Moller, Neural plasticity and disorders of the nervous system, Cambridge: Cambridge University Press, 2006.
[32] T. Tzounopoulos, "Mechanisms of synaptic plasticity in the dorsal cochlear nucleus: plasticity-induced changes that could underlie tinnitus," American J. of Audiology, Vol. 17, Dec. 2008, pp. S170-S175.
[33] M. Dominguez, S. Becker, I. Bruce and H. Read, "A spiking neuron model of cortical correlates of sensorineural hearing loss: spontaneous firing, synchrony, and tinnitus," Neural Computation, vol. 18, 2006, pp. 2942-2958.
[34] S. Grossberg, "Linking attention to learning, expectation, and consciousness," in Neurobiol. Attention, L. Itti and J. Tsotsos, Eds., 2005, pp. 652-662.
[35] D. J. Strauss, W. Delb, R. D'Amelio, Y. F. Low and P. Falkai, "Objective quantification of the tinnitus decompensation by synchronization measures of auditory evoked single sweeps," IEEE Trans. Neural Systems and Rehabilitation Eng., Vol. 16, Feb. 2008, pp. 74-81.
[36] C. Trenado, L. Haab, W. Reith and D. J. Strauss, "Biocybernetics of attention in the tinnitus decompensation: an integrative multiscale modeling approach," J. Neurosci. Methods, Vol. 178, 2009, pp. 237-247.
[37] C. Trenado, L. Haab and D. J. Strauss, "Corticothalamic feedback dynamics for neural correlates of auditory selective attention," IEEE Trans. Neural Systems and Rehabilitation Eng., Vol. 17, Feb. 2009, pp. 46-52.
[38] J. A. Henry, M. A. Schechter, T. L. Zaugg, S. Griest, P. J. Jastreboff, J. A. Vernon, C. Kaelin, M. B. Meikle, K. S. Lyons and B. J. Stewart, "Outcomes of clinical trial: tinnitus masking versus tinnitus retraining therapy," J. Am. Acad. Audiol., Vol. 17, No. 2, 2006, pp. 104-132.
[39] P. B. Davis, "Music and the acoustic desensitization protocol for tinnitus," in Tinnitus Treatment: Clinical protocols, R. S. Tyler Ed. New York: Thieme, 2006, pp. 146-160.
[40] R. S. Hallam and L. McKenna, "Tinnitus habituation therapy," in Tinnitus Treatment: Clinical protocols, R. S. Tyler Ed. New York: Thieme, 2006, pp. 65-80.
[41] K. Fujimoto, H. Nagashino, Y. Kinouchi, A. A. Danesh and A. S. Pandya, "Analysis of a neural oscillator model with plasticity for treatment of tinnitus," in Proc. of World Congress on Medical Physics and Biomedical Engineering, Vol. 14, 2006, pp. 3413-3416.
[42] K. Fujimoto, H. Nagashino, Y. Kinouchi, A. A. Danesh and A. S. Pandya, "Oscillation and its inhibition in a neural oscillator model for tinnitus," in Proc. of the 28th IEEE EMBS Annual International Conference, 2006, pp. 5547-5550.
[43] K. Fujimoto, H. Nagashino, Y. Kinouchi, A. A. Danesh and A. S. Pandya, "A plastic neural network model for sound therapy of tinnitus," IEEJ Trans. on Electrical and Electronic Engineering, vol. 2, no. 4, 2007, pp. 488-490.
[44] K. Fujimoto, H. Nagashino, Y. Kinouchi, A. A. Danesh and A. S. Pandya, "Dynamical properties of a plastic neural network model for tinnitus therapy and inhibition of oscillation using noise stimulus," in Proc. of the 29th Annual International Conference of the IEEE EMBS, 2007, pp. 2408-2411.
[45] K. Fujimoto, H. Nagashino, Y. Kinouchi, A. A. Danesh and A. S. Pandya, "Inhibition of oscillation in a plastic neural network model for tinnitus therapy using noise stimulus," in Proc. of 2007 World Multi-Conference on Systemics, Cybernetics and Informatics, 2007, pp. 108-112.
[46] D. O. Hebb, The Organization of behavior: A neuropsychological theory. New York: John Wiley & Sons, 1949.

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