Modeling Signal Processing in the Auditory Pathway: From Inner Ear to Brain Stem

Marek Rudnicki, Werner Hemmert
Bio-Inspired Information Processing, Technische Universität München
Emails: marek.rudnicki@tum.de, werner.hemmert@tum.de

Introduction

Sound entering our ears undergoes many transformations throughout the auditory pathway until it is perceived in the auditory cortex. The first processing stage is the auditory periphery, where pressure changes are converted to electrical potentials which are conducted by auditory nerve fibers (ANFs) to the central nervous system. ANFs converge onto several types of neurons in the cochlear nucleus (CN), which is located in the brain-stem [1].

Previously we have described a detailed model of the inner ear composed of outer- and middle ear filters, a basilar membrane, inner hair cells and ANF synapses which we tuned to human data [2]. We also included the effect of 'offset adaptation' of the synapse, which is important for temporal processing of sounds [3].

In this paper we present our modeling study of globular bushy cells (GBCs), which are one of the principal cells in the CN. They receive many inputs from ANFs through big synapses called endbulb of Held and make indirect projections to higher regions responsible for sound localization [1]. Characteristic property of GBC is their enhanced synchronization and entrainment to low frequency tones and modulated sounds. For this paper, we particularly investigated the contribution of short-term synaptic plasticity described in multiple *in vitro* studies [4] to GBC response patterns.

Bushy Cell and Endbulb of Held Models

Bushy cells were modeled as a single compartment with Hodgkin-Huxley-like ion channels. Model parameters for ion channels were taken from [5]. However, that model did not have a realistic refractory period and we had to substitute the sodium ion channel model with the one described previously in [6].

Synaptic depression has been modeled with a reservoir model of synaptic resources. From this reservoir, each presynaptic event utilizes a fraction. The reservoir then recovers with an exponential function. The postsynaptic current is proportional to the amount of resources being used. Such a model has been applied successfully in multiple studies [7]. In order to reflect the experimental data, we modeled the recovery of resources with two exponential functions. The model was fitted to the experimental data from [4] and results are shown in Fig. 1.

Taking into account the most recent electron-microscopy study about the convergence of ANFs onto bushy cells [8], we constructed two models, where each of them received 17/3/3 of high/medium/low-spontaneous rate fibers respectively. The first model had individual synapses with and the second without synaptic depression. In order to adjust synaptic weights we simulated an experiment where GBC were stimulated of stimulating at their characteristic frequency with 50 ms long 600 Hz pure tones, which were repeated every 105 ms for 200 times. This procedure was conducted for various combinations of synaptic weights. Next we calculated spike statistics (spontaneous rate, driven rate and synchronization index (SI)) for each output spike train. In order to meet physiological requirements [9], we only kept synaptic weights when spontaneous rate was < 10 spikes/s, driven rate > 470 spikes/s and SI > 0.9. None of the combinations of synaptic weights in the depressing model fulfilled the given condition. For the model without depression we recieved only a small variation of synaptic weights. The median values were 0.008 μS/0.016 μS/0.025 μS for high/medium/low-spontaneous rate fibers, respectively. Threshold value to elicit an action potential for the neuron at rest was 0.023 μS. Those values are well within physiological limits [4].

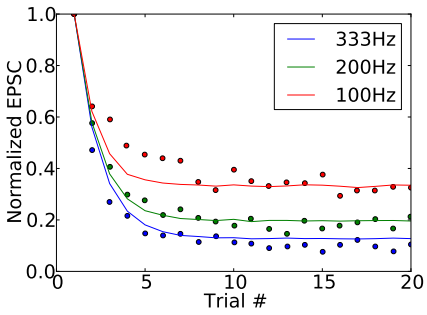

Figure 1: Relative postsynaptic currents in response to electrical shocks to the ANF at three different frequencies. Dots represent experimental data from [4] (Fig. 2d), lines show the best fit to the model.

Pure Tone Stimulation

The model has been further validated with standard pure tone simuli. Fig. 2 compares response of high-spontaneous ANFs and GBCs to a series of 500 Hz tone simulations at the characteristic frequency. The corresponding period histogram is shown in Fig. 3. Please note that GBCs tend to spike with a higher temporal precision than ANFs, what results in a higher synchronization index. Finally, the rate-intensity function simulated at 9 kHz (Fig. 4) shows low spontaneous rates of GBCs and relatively high driven rates, which is in accordance to real neurons.

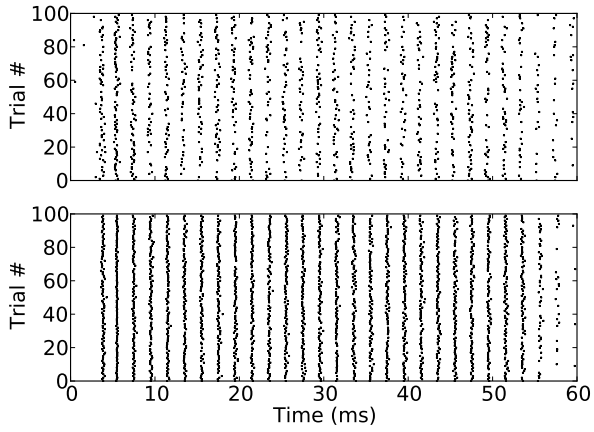

Figure 2: Raster plot of a high-spontaneous rate ANF (top) and a GBC (bottom) in response to a 500 Hz tone burst. In contrast to the ANF, the GBC can spike at almost every stimulus cycle. In addition, the ANF response exhibits larger jitter. ANF entrainment: 0.37, GBC entrainment: 0.95. Sound intensity: 60 dB_{SPL}

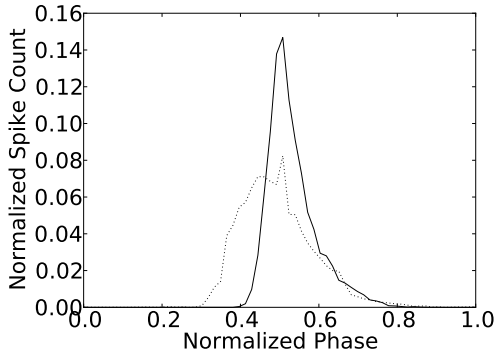

Figure 3: Period histogram of an ANF (dotted) and a GBC (solid). Stimulation frequency: 500 Hz. ANF SI: 0.86, GBC SI: 0.95. Number of bins: 64.

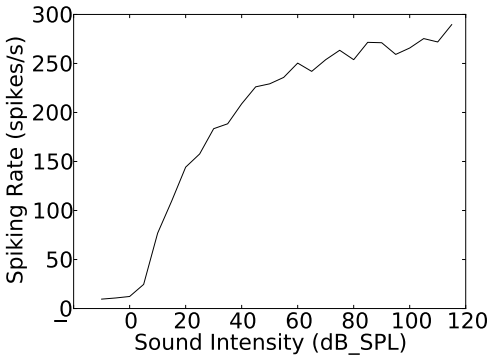

Figure 4: Rate-intensity characteristic of a simulated GBC. Spontaneous and saturation rates are correct. However dynamic range in real neurons is usually smaller than 35 dB.

Summary

We have developed a complete biophysical model for globular bushy cells from the cochlear nucleus, which reproduces their crucial temporal properties such as synchronization and entrainment. We found that incorporating synaptic depression in the model severely degrades these properties. Our finding seems to be in agreement with recent studies revealing no significant depression *in vivo* [10].

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