Are Giant Synapses Depressed?
Modeling Study of Firing Properties of Globular Bushy Cells

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Introduction

Cochlear Nucleus (CN) is the first station in the central nervous system where processing of auditory signals takes place. It consists of several neuron types that receive direct inputs from auditory nerve fibers (ANFs) and show various firing properties. The goal of this study was to examine how synaptic depression influences firing properties of Globular Bushy Cells (GBC) that are one of the principal cells in CN.

GBC receive direct excitatory input from auditory nerve fibers through giant synapses (Endbulbs of Held). Previous studies show that such synapses are chronically depressed under in-vivo like activity levels [1]. However, it is still unclear how strong depression levels and its dependency on stimulation frequency is in-vivo. Virtually all in-vitro studies (e.g. [2]) report a strong dependency of depression on stimulation frequency. On the other hand, only a few in-vivo studies (see [3] for review) suggest no significant changes in synaptic depression.

Model Description

Our model of GBC consists of multiple ANFs converging onto the soma, which is represented as a single compartment with Hodgkin-Huxley like ion channels described in [4]. Spirou et al. (2005) [5] showed that the number of inputs greatly varies for individual GBCs in cats (9-69 for 12 studied cells). Our model (compare Fig. 1) has 45 ANF inputs from high-, medium- and low-spontaneous rate fibers. We examined two models of Endbulbs of Held: with and without synaptic depression.

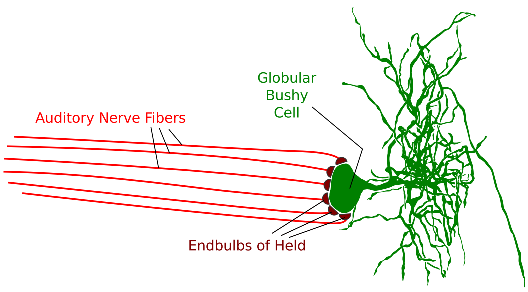

Figure 1: Schematic drawing of the optimized innervation of the GBC model: 36 high-, 5 medium- and 4 low-spontaneous rate fibers.

A depressing synapse was modeled phenomenologically with two recovery time constants and fitted to experimental data from [2]. In this experiment, ANF fibers were stimulated with electrical shocks at three different frequencies. At the same time, EPSCs were measured as shown by dots in Fig. 2. Fitting was done with a least-squares method and the results are shown as solid lines. The slow recovery time constant was set to 1000 ms (experimental constraint) and the fast component was fitted (27 ms).

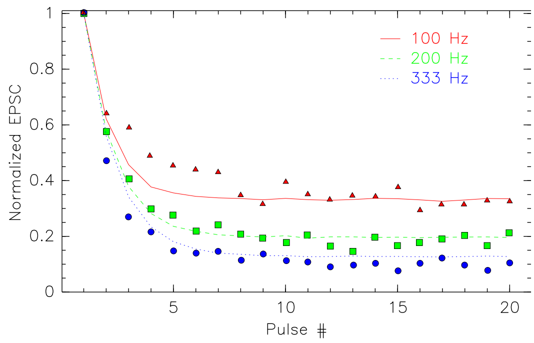

Figure 2: Relative postsynaptic currents in response to electrical shocks to the ANF at three different frequencies. Dots represent experimental data from [2] (Fig. 2d), lines show the best fit for a double exponential recovery model of synaptic depression.

Synaptic weights for the Endbulbs of Held were fitted for a single cell (CF: 600 Hz). It was stimulated 200 times by 50 ms pure tones at CF. This procedure was performed for each combination of weights corresponding to different ANF types. The optimum selection was based on assuring that spontaneous firing rate was <3 spikes/s and maximizing synchronization and entrainment. This procedure has been repeated for both depressing and non-depressing (tonic) synapse models.

Results

The synchronization index describes how precisely a neuron fires with respect to the phase of a periodic stimulus. Entrainment close to one tells that a neuron tends to fire every cycle of the input signal. GBC display extraordinary synchronization and entrainment as shown by measurement points in Fig. 3. Both synapse models show very good synchronization. However, when we look at the entrainment plot, the model with depression shows unrealistically low entrainment. The model with tonic synapse reaches high entrainment for low CF cells, which is consistent with the data.

The plots in Fig. 4 show simulated post-synaptic currents in response to pure tone stimulation. In the case of non-depressing synapses (left) EPSCs cross firing threshold (red line) almost every stimulus cycle. This results in high entrainment. In the model with depressing synapses

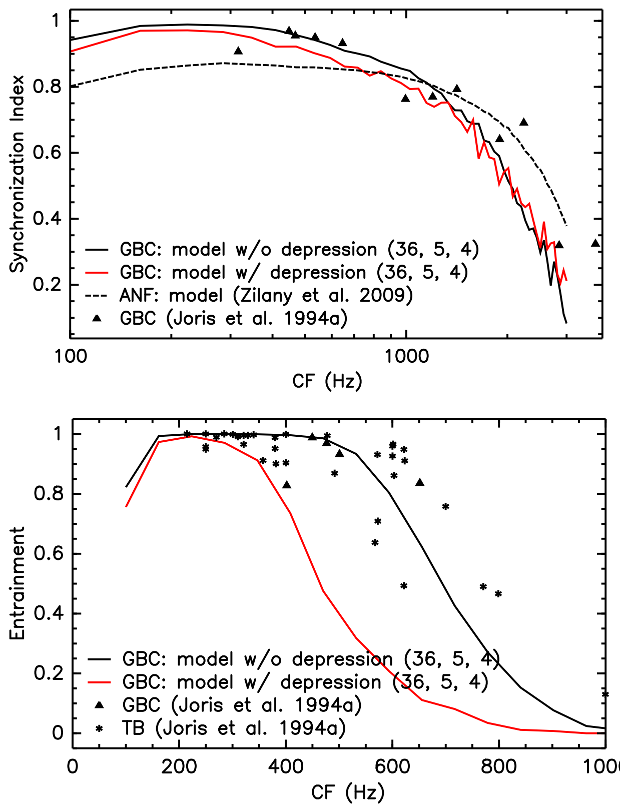

Figure 3: Synchronization index (upper panel) and entrainment (lower panel) of GBCs with depressing and tonic synapses. The highest synchronization index of the ANF was 0.86, which was significantly increased by GBC to a value of 0.95. Only the model with tonic synapse maintained high entrainment for stimulation frequencies above 300 Hz.

(right) synaptic strength decays and multiple EPSCs do not cross the threshold for spiking. In both models the spontanious rate (measured during the time before onset of the tones) is less than 3 spikes/s.

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 a single compartment model with Hodgkin-Huxley like ion channels and multiple converging ANF inputs is able to reproduce the firing properties of these neurons. Synaptic depression is not necessary to model high synchronization and entrainment. In contrast, adding synaptic depression reduces entrainment to unrealistically low values. Our finding seems to be in agreement with recent studies revealing no significant depression *in vivo* [6].

Acknowledgment

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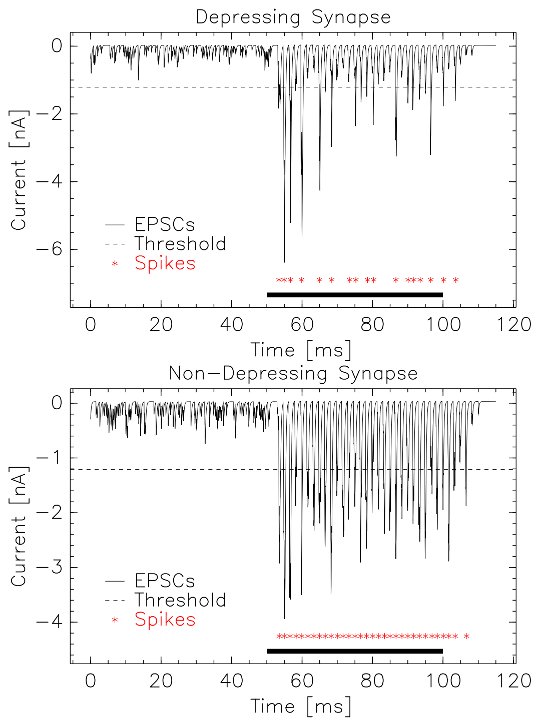

Figure 4: Synaptic currents induced by synaptic inputs into a GBC. GBC firing threshold was raised until spontaneous ANF activity caused a driven rate below 3 spikes/s. In the case of synaptic depression (upper panel), in the sustained regime, EPSC currents were too small for the GBC to reach threshold, whereas in the case without depression (lower panel), high entrainment can be sustained.

References

[1] J. Hermann, M. Pecka, H. von Gersdorff, B. Grothe, and A. Klug, "Synaptic transmission at the calyx of held under in Vivo-Like activity levels," *J Neurophysiol*, vol. 98, pp. 807–820, Aug. 2007.

[2] H. Yang and M. A. Xu-Friedman, "Impact of synaptic depression on spike timing at the endbulb of held.," *Journal of neurophysiology*, vol. 102, pp. 1699–1710, Sept. 2009.

[3] J. G. Borst, "The low synaptic release probability in vivo.," *Trends in neurosciences*, vol. 33, pp. 259–266, June 2010.

[4] J. S. Rothman and P. B. Manis, "The roles potassium currents play in regulating the electrical activity of ventral cochlear nucleus neurons," *J Neurophysiol*, vol. 89, pp. 3097–3113, June 2003.

[5] G. A. Spirou, J. Rager, and P. B. Manis, "Convergence of auditory-nerve fiber projections onto globular bushy cells," *Neuroscience*, vol. 136, no. 3, pp. 843–863, 2005.

[6] J. A. M. Lorteije, S. I. Rusu, C. Kushmerick, and J. G. G. Borst, "Reliability and precision of the mouse calyx of held synapse," *Journal of Neuroscience*, vol. 29, pp. 13770–13784, Nov. 2009.