Modeling of Entrainment and Synchronization in Globular Bushy Cells using Depressing and Non-Depressing Synapses

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ABSTRACT

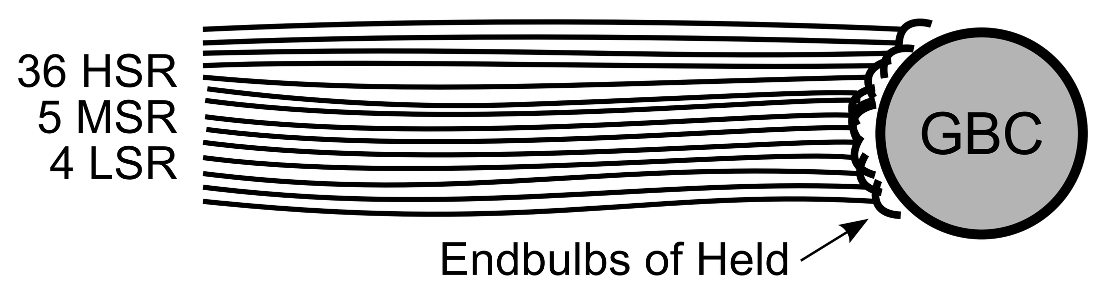
Cochlear Nucleus (CN) is the first station in the central nervous system where processing of auditory signals takes place. It consists of several neuron types that receive direct inputs from auditory nerve fibers (ANFs) and show various firing properties. The goal of this study is to develop a model of Globular Bushy Cells (GBC) that are one of the principle cells in CN. They fire action potentials with high temporal precision and with good entrainment for low pure tone stimuli. We examine how those firing properties are influenced by introducing depression into synapses that has been reported in many in-vitro studies (Yang and Xu-Friedman 2009). We compare those results with a model without synaptic depression as observed in-vivo (Borst 2010). Our model of GBCs is a point neuron with Hodgkin-Huxley type ion channels (HPAC, Kht, Klt) described previously by Rothman and Manis (2003). It receives several excitatory inputs from an inner ear model simulating responses of ANFs. ANF activity drives endbulb of Held synapses located directly on the GBC soma. Short-term depression is modeled phenomenologically using extended exponential recovery model from Tsodyks and Merkram (1997). Simulations show that for both synaptic models synchronization improved (SI > 0.9) at low stimulation frequencies compared to synchronization of ANFs. However, high entrainment levels where achieved only by the model without synaptic depression. This model was also able to reproduce experimental results obtained from pure tone stimulations: PSTH, ISIH and receptive field maps.We conclude that the model of GBC with converging ANF excitatory inputs captures basic properties of those cells. Additionally, the results suggest that depression in-vivo is much lower than in-vitro conditions. In the future, the model will allow us to study the response of GBCs to complex natural stimuli like speech.

Introduction

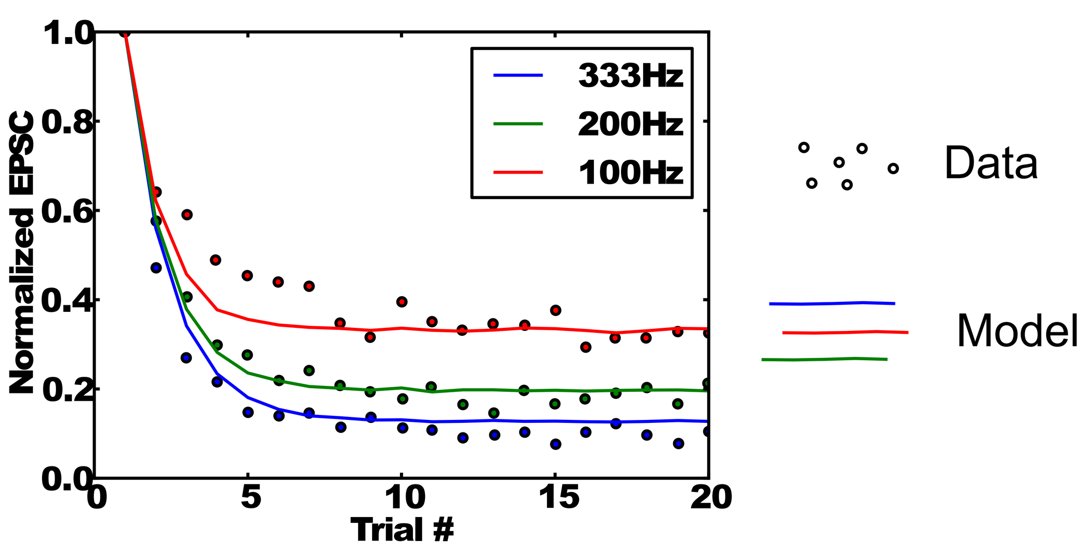
Globular Bushy Cells (GBC) are one of the principal cells in Cochlear Nucleus. They receive direct excitatory input from auditory nerve fibers through giant synapses. Previous studies show that such synapses are chronically depressed under in-vivo like activity levels (Herman et al. 2007). However, it is still unclear how strong depression levels and its dependency on stimulation frequency is in-vivo. Virtually all in-vitro studies (Wand and Manis 2008, Yang and Xu-Friedman 2009) report a strong dependency of depression on stimulation frequency. On the other hand, only a few in-vivo studies (see Borst 2010 for review) suggest no significant changes in synaptic depression. The goal of this work is to develop a model of GBC that captures key features (high synchronization and entrainment) and compare how synapses with and without depression determine those properties.

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 by Rothman and Manis (2003). Spirou et al. (2005) showed that the number of inputs greatly varies for individual GBCs in cats (9-69 for 12 studied cells). Our model 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.

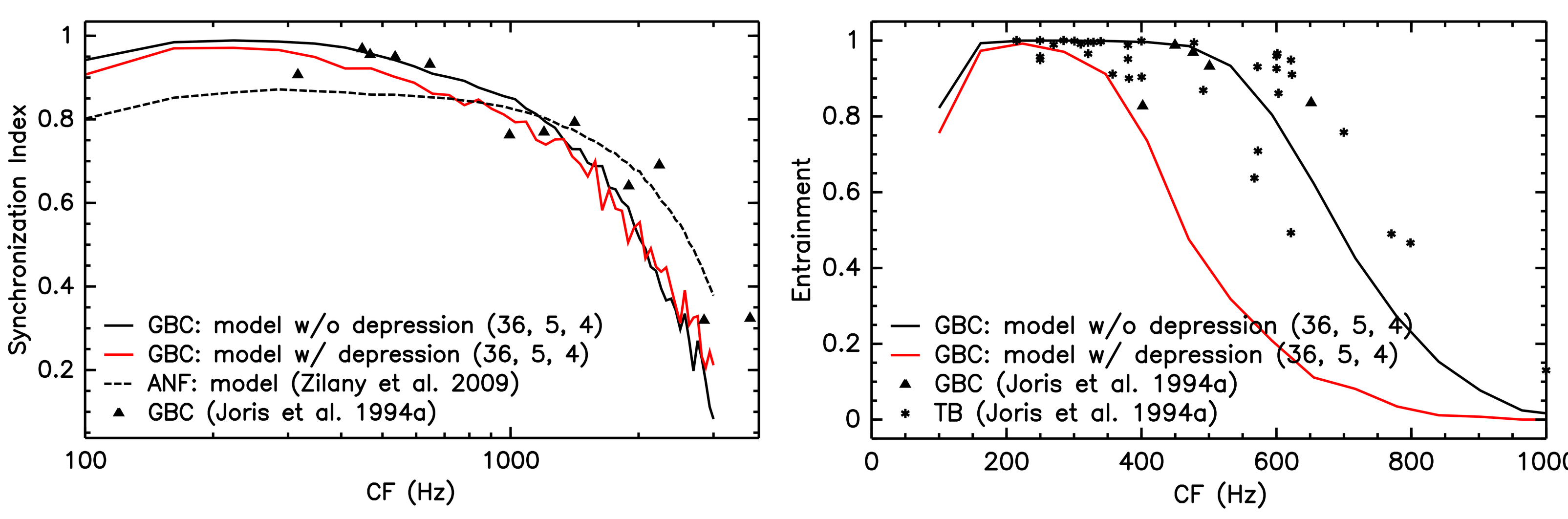


A depressing synapse was modeled phenomenologically with two recovery time constants and fitted to experimental data from Yang and Xu-Friedman (2009). In this experiment, ANF fibers were stimulated with electrical shocks at three different frequencies. At the same time, EPSCs were measured as shown by dots in figure below.



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). Synaptic weights for the Endbulbs of Held were fitted for a single cell (CF: 600Hz). 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 sp/s and maximizing synchronization and entrainment. This procedure has been repeated for both depressing and non-depressing synapse models.

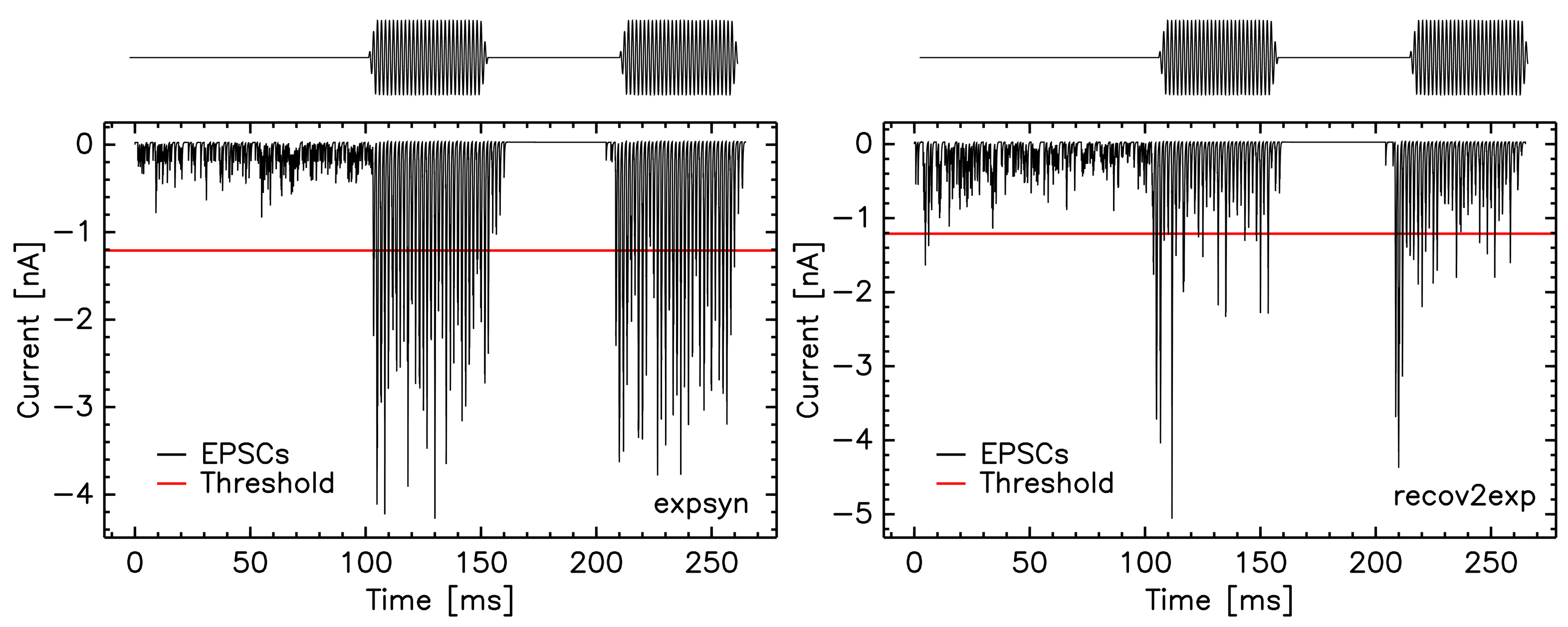
Synchronization and Entrainment



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 the plots above. Both synapse models show very good synchronization. However, when we look at the entrainment plot, the model w/ depression shows unrealistically low entrainment. The model w/ o synaptic depression reaches high entrainment for low CF cells, which is consistent with the data.

EPSCs

The plots below 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 (right) synaptic strength decays and multiple EPSCs do not cross the threshold for spiking. In both models the spontanius rate (time before the first tone) is less than 3 sp/s.



Conclusions

- A single compartment HH model with multiple converging ANF inputs is able to reproduce firing properties of GBCs.
- Synaptic depression is not necessary to model high synchronization and entrainment. In contrast, adding synaptic depression reduces entrainment to unrealistically low values.

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