Auditory Neuron Responses to Predicted Synaptic Input Derived from Cochlear Prosthetic Devices
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ABSTRACT
Binaural hearing enables multiple functions of the hearing system, including sound localization. In the mammalian auditory cortex, the first neurons responsible for comparing sound from the two ears are found in the Medial Superior Olive (MSO). While there have been many studies on MSO neuron physiology, details concerning how these neurons generate meaningful patterns of activity in response to synaptic input are poorly understood. In this study, we used dynamic clamping to study neurons from acute brain slices from Mongolian gerbils in vitro. Whole cell dynamic clamp provides naturalistic synaptic input that neurons are predicted to receive in vivo. We simulated synaptic input to MSO neurons evoked by acoustic stimuli at both 100 Hz (low frequency) and 1000 Hz (high frequency). We found that with lower frequency stimuli, the cells respond significantly more at ±80 degrees out of phase in comparison to 90 degrees out of phase. At the higher frequency, the opposite is true (which is the situation in vivo). We attempted to modulate this effect by changing the strength of the synapse. Neither increasing nor decreasing the strength of each synapse eliminated the out of phase spiking. We also changed the number of inputs per side, and while the sample size is small, the data show a trend toward no effect on out of phase spiking. These results suggest that inhibition may be required to process low frequencies compared to higher frequencies. We speculate that this could be a result of the interaction between stimulus frequency and the refactory period of the neuron. Future studies will include adding monaural (EEI) and binaural (EEII) inhibition to the dynamic clamp protocols in order to observe the changes to the out of phase stimuli.

INTRODUCTION
Interaural time differences are the acoustic cue animals use to localize low frequency stimuli. ITDs arise from arrival time differences at the two ears that systematically vary with sound source position in space. ITDs create frequency specific phase differences at the two ears. The second order neurons that send excitatory information to the MSO provide a precisely timed “phase locked” signal to the MSO. MSO neurons, in turn, vary their firing rate according to the degree of phase locked” signal to the MSO. MSO neurons, in turn, vary their firing rate according to the degree to which they receive coincident inputs. Coincidence detecting circuitry of the mammal

METHODS
Dynamic Clamp
Dynamic Clamp involves injecting current directly into a neuron that mimics the information that the cell would be receiving from the synaptic inputs. These inputs are synthesized computationally prior to injection. Using this method we can manipulate many factors that may influence efficient coding of ITDs including: spike rate, synchrony value, frequency, number of inputs, and length of event. In the experiments shown the spike rate was set to 250 spike/sec and the synchrony value was set to ±1 (in order to best mimic neural inputs evoked in a cochlear implant patient.)

RESULTS
Excitatory only creates sub-optimal ITD response for low frequency input
At this low frequency input, the response at ±80 degrees (completely “out-of-phase”) is stronger than at 0 degrees. This would create improper signaling from the MSO neuron.

Changing the strength of the excitation does not impact the ITD response
From this series of experiments (which had 4 inputs per ear), it is not clear if the strength of the synapse correlates with a change in the out of phase response in the low frequency input. During the high frequency input, there definitely does not seem to be any change.

CONCLUSIONS
➢ In a purely excitatory model (EE), MSO neurons have higher amounts of out of phase noise at lower frequencies
➢ Manipulating the strength of the synapse does not alleviate the out of phase “noise response”
➢ As the period of a phase in low frequency input is longer than in high frequency input, the out of phase inputs may occur outside of the refractory time of the neuron (a period in which it is difficult to cause spiking).

➢ “Phase-locked” inhibition may be more important during lower frequency signals than higher frequency signals

FUTURE
➢ We plan on getting a larger sample size for the changing number of inputs protocol

We plan on adding inhibition into the protocol, which we believe will alleviate “out-of-phase” responses