Submit your application to Dr. Bradley Winters

Project Title: Dendritic arbor analysis of patch-clamped lateral superior olive neuron types

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Abstract: The superior olivary complex (SOC) in the brainstem of mammals integrates information from the two ears enabling sound localization. This ability underlies selective auditory attention and is disrupted by hearing loss and in children with central auditory processing disorder (CAPD). Principal neurons of the lateral superior olive (LSO PNs) are critical for these functions. The classical view of the LSO is a homogeneous block of cells that extracts ongoing interaural level differences (ILDs), however, LSO is increasingly implicated in encoding interaural time differences (ITDs) for broadband transients and amplitude modulations. Cellular properties are fundamental to how neurons extract and encode information. ILD/ITD processing places disparate demands on neuronal properties and there is cellular diversity in the LSO that is not well-understood. It is also critical to understand how different types of information may be organized in higher processing centers of the inferior colliculus (IC).

We found that LSO PNs consist of inhibitory and excitatory cell types with different projection patterns, intrinsic membrane properties, and morphology. We will further probe the functional implications of our preliminary findings on the intrinsic membrane properties of LSO PN types by examining the synaptic drive onto these cells with the goal of finding input-output relationships that support different sound localization coding strategies. Preliminary studies show that inhibitory LSO PNs have lower activation threshold, however, cell-type specific synaptic drive could accentuate or offset these differences. We also found that excitatory LSO PNs have more complicated dendritic arbors suggesting they may integrate more synaptic inputs which could favor ILD coding. Since LSO PN dendrites mainly receive excitatory inputs, this finding suggests the hypothesis that excitatory LSO PNs receive more excitatory inputs than inhibitory LSO PNs. To test this, we will examine the number, strength, balance, short-term dynamics, and channel kinetics of synaptic inputs *ex vivo* using whole-cell patch-clamp. The recorded neurons will be filled with a marker and the brain slices fixed and mounted so that their dendritic arbors can be analyzed.

Significance: Our overarching hypothesis is that LSO PN cellular diversity supports both ILD and ITD coding and neurotransmitter system, intrinsic excitability, and projection pattern provide means to organize differentially extracted information in the IC. This project will yield foundational insights into the cellular organization of the SOC which may be disrupted by hearing loss and contribute to poorly understood disease states such as CAPD.

Goals and Objectives: The student will help us reconstruct the dendritic arbor of LSO PNs that were filled with a marker during electrophysiological recordings. This will allow us to correlate differences in synaptic drive between LSO PN types with cell morphology.

Methods: The student will image cells using a light microscope and then digitally reconstruct them using NeuroLucida software.

Data analysis: Data collected by the student will be analyzed using the NeuroLucida system and Microsoft Excel. This will produce a table of neuronal properties such as total dendritic length, number of branch points, number of primary dendrites, etc., that will be compared with previously recorded synaptic properties.

Anticipated Findings: The anticipated findings are critical to understanding the relationship between cell morphology and synaptic drive which in turn helps determine how LSO PNs integrate timing vs. level information.

Student Fellow Training/Mentoring Plan: The student will meet regularly with the PI in addition to working with other members of the lab, postdoc and other students. The student will be encouraged to observe and potentially participate in other lab activities/experiments to get a better understanding of how research labs operate. The Winters lab is part of the close-knit NEOMED Hearing Research Group which the student will have the opportunity to interact with.