



Presentation Abstract

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Presentation Title: Automated patch clamping of neurons in the mammalian brain in vivo

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Abstract: In recent years, in vivo patch clamping (IVPC) has arisen as one of the most precise methods for measuring subthreshold synaptic events, as well as intrinsic channel and receptor activities in neurons in the brain. The extremely high signal-to-noise ratio and temporal precision enabled by IVPC helps with the assessment of the dynamics of neural network activity during specific behaviors or pathological states. However, IVPC has proven to be very difficult to do, and remains something of an art form, due to the laborious nature of finding cells and obtaining recordings. Accordingly, we have developed a system capable of carrying out IVPC in an automated fashion in the living mouse. A computer is interfaced with the patch clamp amplifiers via a USB data acquisition board. A piezo motor controlled through a serial port on the computer is used to move the micropipette into the brain, enabling automated detection and recording of neurons in the brain. The computer utilizes an algorithm that detects variations in micropipette impedance that are indicative of contact with a neuron, automatically adjusting pipette velocity until a cell is detected. In this algorithm, a glass micropipette ($R = 5-8 \text{ M-Ohms}$) is lowered in the brain in steps of 2-3 micrometers, while constantly monitoring impedance. When the tip of the pipette encounters a neuron, motion slows and stops. We have developed this system and successfully used it to detect and record in vivo from single neurons, in a juxtacellular or cell-attached fashion with ~35% efficiency and an average time of 10 minutes per recording.

We will also report progress towards implementing a system of electronically controlled pneumatic valves to modulate the internal pressure in the micropipette for

formation of giga-ohm seal and break-in to achieve 'whole cell' IVPC configuration, automating the final step. The whole cell configuration can currently be achieved by manually modulating micropipette pressure similar to a standard IVPC protocol. We are also working on ways of integrating the system with optogenetic stimulation and inhibition of neuron types, so that the synaptic and subthreshold impact of a given cell class can be assessed within a local or global network. Such a system will contribute to helping make IVPC a simple, widely accessible technology that enables systems neuroscientists to probe synaptic and subthreshold physiology in the mammalian brain, and to enable monitoring of individual optogenetically driven synaptic events in intact circuits. Further, automation may enable IVPC of multiple neurons in vivo simultaneously for assessment of neural synchrony and population coding at the subthreshold or synaptic level.

Disclosures: **S.B. Kodandaramaiah:** None. **E.S. Boyden:** None. **C.R. Forest:** None.

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IN VIVO

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