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NEUROSCIENCE 2012

Presentation Abstract

Program#/Poster#: 208.20/DDD62

Presentation Title: The Multipatcher: A robot for automated, simultaneous whole-cell patch-clamping of multiple neurons *in vivo*

Location: Hall F-J

Presentation time: Sunday, Oct 14, 2012, 10:00 AM -11:00 AM

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Abstract: Over the last decade, in vivo whole cell patch clamping has emerged as a gold-standard method for precision measurement of the subthreshold synaptic and ion channel events that contribute to neural processing and to the pathophysiology of brain disorders. However, in vivo patch clamping is one of the more complex techniques in neuroscience, and furthermore no technology exists for in vivo patch clamping of multiple neurons in a single intact brain (in contrast to the world of extracellular recording, where tetrodes and silicon probes are in widespread use). Such a “multipatching” technology would enable the assessment of network-level effects, such as synchrony and population neural coding dynamics,that may be best understood when synaptic and intracellular dynamics are observable in the living brain. It would also work well in concert with optogenetics, for monitoring how different cells in a network respond to a given optical perturbation.
We accordingly have developed the Multipatcher, a robot for automated simultaneous whole cell patch clamp recording of multiple neurons in a single living brain. The robot has the ability to control an array of multiple patch electrodes (initially four, in the prototype we are currently exploring), that can be lowered through a craniotomy (e.g., ~2mm diameter) into the living mouse cortex to automatically establish whole cell recordings. The axial positions of the electrodes are independently controlled using programmable piezo-motors,

and the internal pressures are independently modulated using a computer controlled set of valves and regulators. For the patch algorithm, we have modified our earlier Autopatcher algorithm (S.B. Kodandaramaiah et al, Nature Methods 2012; details and updates at http://autopatcher.org) to enable each motor to lower its corresponding pipette to preset depths, hunt for neurons, and attain the whole-cell state, while additionally taking into account the tissue displacement induced by movement of multiple electrodes at once. We are exploring how multiple pipettes mechanically interact in the brain, designing novel actuators and pipettes, as well as the engineering of novel hardware to dramatically reduce the price per channel of patch clamping. We are aiming to scale multipatching towards the recording of many neurons at once, and to integrate multipatching with optogenetic network control in order to enable assessments of the synaptic basis of how specific cell types coordinate network activity.

Disclosures: **S.B. Kodandaramaiah:** None. **G. Holst:** None. **G. Talei Franzesi:** None. **A. Singer:** None. **I. Wickersham:** None. **X. Han:** None. **E.S. Boyden:** None. **C.R. Forest:** None.

Keyword(s): Autopatcher

PATCH CLAMP

optogenetics

Support: Jerry and Marge Burnett; Human Frontiers Science Program

IET A. F. Harvey Prize

McGovern Institute; MIT Media Lab

George W. Woodruff School of Mechanical Engineering, Georgia Tech

NIH Director’s New Innovator Award (1DP2OD002002) and other NIH grants

[Authors]. [Abstract Title]. Program No. XXX.XX. 2012 Neuroscience Meeting Planner. New Orleans, LA: Society for Neuroscience, 2012. Online.