Tuesday, April 1, 2014

Dear Editor,

We submit our manuscript “Visual stimuli recruit intrinsically generated cortical ensembles” for your consideration. Using two-photon imaging in vivo, we have mapped the spontaneous reverberating activity patterns in the primary visual cortex from awake mice at the single-cell level, and determined their relation to the activity patterns evoked by visual stimulation. We found that intrinsic, resting state cortical activity is dominated by coactive groups of neurons forming ensembles. The emergence of ensembles is not accounted for by the individual firing properties of the contributing neurons in isolation. Moreover, individual neurons flexibly contribute to multiple ensembles, vastly expanding the coding potential of the cortex. Finally, these intrinsically-generated ensembles are very similar to stimulus-evoked ensembles, with one main difference: intrinsic ensembles recur at random time intervals, while visually evoked ensembles are time-locked to stimuli. We believe that this work provides a next step in the progression of defining neuronal ensembles, rather than receptive fields of individual cells, as a functional unit in cortical microcircuits and suggests that visual stimuli recruit intrinsically generated ensembles to represent visual attributes.  
 Our results are of general interest because they demonstrate that even the most classical visual stimuli, the same one that Hubel and Wiesel used, generate group responses that are emergent properties of the circuit and that single neurons participate promiscuously in multiple groups, dynamically reorganizing their allegiance with different sets of neurons and vastly expanding the coding potential of the cortex. To describe cortical responses based on single neuron firing is no longer adequate. In fact, we argued in our 2012 justification for the Brain Activity Map that extensive interactions between cortical circuits are likely to generate emergent circuit functional states. We believe that in this paper we have identified one such emergent state, one you could call a neuronal assembly. The second reason our data are of general interest has to do with the debate of whether the brain is externally or internally driven. This runs through the middle of neuroscience (feedback vs. feedforward circuits; CPGs vs. reflexes models). Our results demonstrate that sensory stimuli recruit internally-generated patterns, in others word: the patterns are already present in the cortex before the visual stimulation.

Over the years, we have been inspired by Marcus Raichle’s work demonstrating that intrinsically active large scale brain networks are similar to evoked networks, and because of this we think he would be a great editor for this paper. Marcus Raichle kindly agreed to serve as a prearranged editor for this paper.

As reviewers we recommend Alison Barth (barth@cmu.edu), Gyorgy Buszaki (Gyorgy.Buzsaki@nyumc.org), Wolf Singer (wolf.singer@brain.mpg.de), Ed Callaway (callaway@salk.edu), Amiram Grinvald (amiram.grinvald@weizmann.ac.il), Michael Stryker (stryker@phy.ucsf.edu), Arthur Konnerth (office-konnerth@lrz.tum.de), Thomas Mrsic-Flogel (thomas.mrsic-flogel@unibas.ch), Takao Hensch (hensch@mcb.harvard.edu), Moshe Abeles (moshe.abeles@mail.biu.ac.il), Prakash Kara (kara@musc.edu), Sonja Hofer (sonja.hofer@unibas.ch), David Tank (dwtank@princeton.edu) and Rodolfo Llinas (Rodolfo.Llinas@nyumc.org). Unfortunately, Jason Kerr, Yang Dan, Massimo Scanziani, David Ferster, Ilan Lampl, Clay Reid, or Ken Harris may not be ideal because of conflict of interest.

Best,

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