

COLUMBIA UNIVERSITY

IN THE CITY OF NEW YORK

DEPARTMENT OF BIOLOGICAL SCIENCES

Editors
Journal of Neuroscience

Monday, December 22, 2014

Dear Editors,

We hereby submit the following manuscript (“Endogenous sequential cortical patterns with precise firing sequences evoked by visual stimuli”) for consideration in The Journal of Neuroscience.

In our recent work (Miller et al. PNAS 2014) we demonstrated with two-photon calcium imaging in awake freely moving mice that visual stimuli recruit intrinsically generated neuronal ensembles to represent specific drifting-grating orientations or natural scenes. The present manuscript represents the next step in that research program, describing the temporal properties of these endogenous ensembles and how they are built with precise firing sequences. Although we used mainly the same dataset as in Miller et al. 2014, we performed a completely independent analysis focusing on the multidimensional structure of network activity, extracting the spatiotemporal features of neural networks under different experimental conditions. We found that trajectories of population activity in cortical networks *in vivo* exhibit recurrent sequential patterns in the absence of visual stimulation and that the same temporal trajectories can be entrained by visual stimuli. We also can predict the future neuronal ensembles, based on the sequential activity patterns. Finally, we demonstrate that precise firing sequences occur during the sequential activity patterns.

This work is of general interest because we show how sequential ensembles defined by multidimensional neuronal activity can be used to encode temporal information from the visual environment. This agrees with the possibility that the neocortex uses temporal sequences of activity to encode information. Our description of these temporal network dynamics also opens the door for future work to directly manipulate identified neurons and induce specific behaviors.

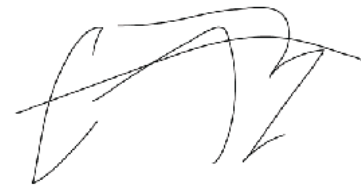
We confirm that the present manuscript has not been published elsewhere and there is no significant overlap between the present submitted manuscript and any other paper from the same authors under consideration or in press in any other journal.

We hope that the editorial committee encounters these findings of enough merit to be published in The Journal of Neuroscience.

Sincerely,



Rafael Yuste, M.D. Ph.D.
Professor of Biological Sciences and Neuroscience
Director, NeuroTechnology Center
Co-Director, Kavli Institute for Neural Circuitry
Columbia University
New York, NY 10027



Luis Carrillo-Reid, Ph.D.
Department of Biological Sciences
Columbia University
New York, NY 10027