Dr. Mariela Zirlinger

Scientific Editor

Neuron

Wednesday, December 21, 2016

Dear Dr. Zirlinger,

We submit our manuscript “Conditional random fields for single cell targeting of cortical ensembles” as a NeuroResource for your consideration.

In this paper, we developed a method to identify single neuron targets for optogenetic manipulations. We used a type of probabilistic graphical models, built functional models of cortical neurons from two-photon calcium imaging *in vivo*. With these models, we demonstrated that we are able to find neuronal ensembles corresponding to specific stimuli, and to identify the important cells within the ensemble that are capable of changing the ensemble activity. Moreover, our method can characterize network-level changes induced by two-photon optogenetic stimulation. Our method also show robust performance under various experimental conditions.

Our method is novel and significant for a broad scientific community because it provides a tool for manipulating the network activity via single important neurons, as well as quantifying the resulting functional changes of the network. Neuronal ensembles have been proposed to form the substrate of various physiological and behavioral processes, and recent advance in our group demonstrates the possibility of optically manipulating ensemble activity with single cell precision in awake animals (Carrillo-Reid et al., 2016). However, there is still a lack of effective approaches to identify the relevant ensembles and the critical neurons therein. Traditional models such as Ising models suit well for capturing pairwise interactions of observed neuronal activity, while our approach, the conditional random field models, allows for modeling complex interactions with a general graph structure. To our knowledge, this is the first time that conditional probabilistic graphical models with general structures are applied in identifying functional ensembles and critical neurons. This opens the new direction of using conditional graphical models to study complex real-world neuronal networks.

Our approach will guide the design of single cell optogenetic manipulation in closed loop experiments. This allows us to investigate the role of a specific population of neurons during behavioral events, and offers the possibility to alter behavior or treat pathological disorders at microcircuit level with single cell resolution.

As reviewers, we recommend Ed Bullmore, Olaf Sporns, Danielle Bassett, who are experts in graph theory, and William Bialek, who is specialized in network analysis.

Sincerely,