Each submission should be accompanied by a cover letter, which should contain a brief explanation of what was previously known, the conceptual advance provided by the findings, and the significance of the findings to a broad readership. A cover letter may contain suggestions for appropriate reviewers and up to three requests for reviewer exclusions. The cover letter is confidential to the editor and will not be seen by reviewers.

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

In this paper, we built functional models of cortex from two-photon calcium imaging *in vivo* using probabilistic graphical models. 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 capture network reconfigurations induced by two-photon optogenetic stimulation. We demonstrated that our method is stable across different datasets acquired with varying experimental conditions, and our codebase will be made publicly available upon publication.

Our method is novel and significant for a broad scientific community because it provides a tool for guiding single cell targeting during specific behavior or physiological process with simultaneous optogenetics and calcium imaging, as well as studying the resulting functional changes of the network.