

Online experiment design for mapping large-scale neural circuits

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Abstract: We consider high throughput circuit mapping experiments where subthreshold, postsynaptic responses of one neuron are recorded using whole-cell patch clamp, and optical stimulation is used to stimulate multiple genetically modified neurons per trial. In these experiments, we are interested in (i) inferring which neurons have synaptic connections with the patched neuron, and (ii) the properties of the presynaptic neurons. However, the amount of data one can collect is paltry compared to the extent of neural circuits because the preparations are short-lived. In addition, the patched neuron's responses are subject to intrinsic stochasticity due to the low spatial resolution of the optical stimulation and the biological variability in the responses of individual neurons to the optical stimulation. We propose an online procedure that automatically designs future trials during the experiment. Our procedure first focuses on detecting and eliminating disconnected cells with multi-spot stimulations, then learns properties of the connected cells with precise single-spot stimulations. To this end, we develop a robust method for fitting a physiobiologically plausible model for the observed postsynaptic events, which is used to learn the properties of the few connected cells. We derive a simplified working model that is fast to fit, which is used to detect the many disconnected cells.