Non-invasive characterization of individual neurons with Continuous dynamic photo-stimulation

Understanding information encoding by individual central neurons requires characterization of their input-output functions under near-natural input conditions, e.g. in the fluctuation driven regime, characteristic of cortical circuits. Controlling the input and registering on the order of 10,000 - 100,000 spikes as output, one can compute transfer metrics which are critical for collective network dynamics, such as dynamic gain, correlation gain or spike frequency vs current (FI-) curves. So far now such data are exclusively obtained in sharp electrode or patch-clamp recordings, where the input to the cell body and therefore to the spike trigger zone in the axon initial segment is directly controlled. Due to the limited number of spikes obtained in invasive recordings, characterization of individual neurons is often not possible, dynamic gain curves, for instance, are averaged over tens of neurons.

We recently developed an alternative, non-invasive method for neuronal characterization. Spikes are recorded by an array of extracellular electrodes. Well-defined, fluctuating stimuli are delivered via light-activated channelrhodopsins to pharmacologically isolated neurons. Careful characterization of channelrhodopsin's transfer function warrants precise control over the waveform of the induced conductance. The setup delivers orders of magnitude more data than previously possible in the field of input-output characterization.

Neuronal responses were stable, measurement of intracellular pH showed only minor acidification under continuous stimulation. Comparison of our results with dynamic gain measurements and FI-curves obtain with traditional methods establishes the equivalence of the non-invasive, high-throughput method.