ONLINE ANALYSIS AND PERTURBATION OF BRAIN-WIDE ACTIVITY IN ZEBRAFISH

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In order to understand sensory-motor transformations in the brain, one needs a combination of tools for interrogating brain function, including large-scale neuronal recordings, activity perturbations, and large-scale data analysis. We combine light-sheet volumetric imaging of zebrafish brain expressing GCaMP6 sensors [1,2] with distributed computing methods [3] and two-photon excitation techniques to

a) map the tuning of most neurons in the brain of larval zebrafish to behavioral and sensory variables, and

b) perform targeted circuit perturbations to test functional roles of identified populations.

As a model of sensorimotor transformation, we use the optomotor response (OMR), in which larval zebrafish orient and swim along the direction of visual motion. Using regression analysis we identify, on a brain-wide scale, populations of neurons whose activity correlates with swimming, visual input, or both (red, green/blue, or yellow/orange, respectively, in Fig. 1). Our real-time analysis during data acquisition allows us to perform perturbations (two-photon ablations) specific to a particular sample, using its neuronal activity as a guide. Single-cell ablation accuracy is achieved by using online drift correction methods.

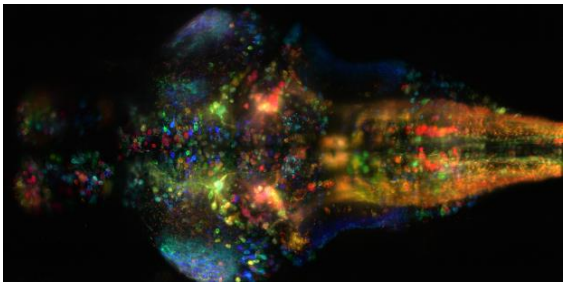

Fig. 1. Functional map of a zebrafish brain.

Changes in fish behavior and brain activity due to ablations were characterized. Several motor-correlated bilateral groups of neurons in the hindbrain, when perturbed, showed strong and reproducible effects on the behavior. Ablating these cells caused a severe reduction in swim characteristics and global brain activity.

Our method can additionally be applied with two-photon optogenetic stimulation instead of ablation. These methods, combined, establish a technique for perturbing brain activity based on whole-brain functional mapping and large-scale online data analysis.

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