Whole-brain Ca^{2+} imaging in larval zebrafish

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To learn more on the factors that govern the development of neural circuits, both in structural and functional terms, we use whole brain two-photon imaging on larval zebrafish that express a pan-neuronal genetically-encoded calcium indicator GCaMP6s. Using a resonant scanner and piezo driven objective, we record neural activity (GCaMP6 fluorescence) from up to ~50% of the whole neuronal population (~100,000 neurons), while simultaneously conveying visual stimulation using a screen oriented towards the head-restrained larva in agarose. This experimental paradigm leverages the early-developing visual system of the zebrafish to evoke reproducible neuronal responses and behavioral outputs across individuals. Abrupt changes in illumination induce navigational tail movements, which are monitored using a high-speed camera to identify distinct behavioral modules and their neural correlates. By varying the temporal properties of visual stimuli, we also probe the neural mechanisms of habituation and anticipation. Using graph theory, functional networks are generated from spontaneous brain activity recordings, which are then paired with the zebrafish structural connectome (Kunst et al., Neuron, 2019) in order to gain fundamental insight on the interaction between structure and function in vertebrate brain networks. Our dual spontaneous/stimulus-evoked experimental framework will be used to compare fish across different developing conditions, namely germ-free fish, to observe the impact of gut microbiota on brain connectivity, sensorimotor integration and behavior.