FLAMMES - On-chip metasurface-based neuroimaging platform toward high-throughput drug screening in freely behaving animal

A central goal of modern neuroscience is to correlate neurological conditions, external stimuli and behavior with the activity and location of individual neuron within a large brain volume. Thus, simultaneous recording of brain activity and organism behavior are fundamental to characterize circuit alterations underlying neurological disorders and to assess potential attenuation strategies. Thanks to the high degree of morphological, genetic and behavioral resemblance with humans, zebrafish is becoming a prominent model for studying neurological disorders and screening of neurospecific compounds. Owing to reduced light scattering, small size and 3R-principle compatibility of the zebrafish larvae, parallel whole-brain neuroimaging of multiple zebrafish might pave the way of in vivo drug discovery. Recent studies report technological breakthroughs that enable monitoring of zebrafish whole brain activity with cellular resolution. Although widely used for functional imaging, larval zebrafish remains limited to manual, extremely challenging and low-throughput screening.
Here, I propose to integrate my solid background in biophysics and micro-nano optics engineering with new skills I will build at the Host Institution and Secondment for the project success. Goal of this project is to enable optical whole-brain imaging of multiple zebrafish larvae (Danio Rerio) freely behaving. First, I will demonstrate zebrafish larva neuroimaging with a novel metasurface-based optical sectioning illumination (Aim 1). Second, I will demonstrate selective plane on-chip detection synchronized with the excitation plane (Aim 2). Finally, I will prove potential parallel larvae on-chip microscopy (Aim 3). The proposed neuroimaging concept is a flexible approach to perform high-throughput drug screening based on recordings of the brain activity and characterization of the behavior outcome. Collectively, this study will provide a platform that contribute bridging the gap from bench-to-bedside.

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