All-optical interrogation of brain circuits using optogenetics and holography

Genetic targeting of neuronal cells with activity reporters (calcium or voltage indicators) has initiated the paradigmatic transition whereby photons have replaced electrons for reading large-scale brain activities at cellular resolution. In parallel, optogenetics has demonstrated that targeting neuronal cells with photosensitive microbial opsins, enables the transduction of photons into electrical currents of opposite polarities thus writing, through activation or inhibition, neuronal signals in a non-invasive way.

These progresses have in turn stimulated the development of sophisticated optical methods to enable "all optical" in depth brain circuits interrogation with high spatial and temporal resolution on large volumes.

Here, we will review the most significant breakthroughs of the past years, which enable reading and writing neuronal activity at the relevant spatiotemporal scale for brain circuits manipulation, with particular emphasis on the most recent advances in what we named *circuit optogenetics*: a combination of approaches including holographic light illumination, temporal focusing, opsins engineering and laser development for the control of single or multiple targets independently in space and time with single-neuron and single-spike precision, at large depths.