Reverse engineering of neuronal circuits using light

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One of the main challenges in neuroscience is to understand how higher brain functions arise from interactions between large numbers of individual neurons. Important computations are performed by circuits that typically consist of 10^2 – 10^7 interconnected neurons, each of which is a specialized, nonlinear signal processing device. Perhaps the most direct approach towards understanding higher neuronal computations is to measure and manipulate the activity of large numbers of defined neurons during information processing in the intact brain. Major progress towards this goal has recently been made based on the development of novel optical methods. Neurons can now be visualized in the intact brain of many animals using high-resolution imaging methods, in particular multiphoton microscopy. In combination with fluorescent activity indicators, these techniques permit neurobiologists to measure activity patterns across hundreds or even thousands of individual neurons. Moreover, "optogenetic" methods harness light-sensitive proteins such as channelrhodopsin-2 (Chr2) or halorhodopsin (HR) to excite or inhibit neurons. By combining the cell type specificity of genetic expression systems with optical stimulation techniques, this approach allows for the manipulation of neuronal activity patterns with exquisite spatial and temporal precision.

I will first provide an introduction into new optical tools and methods for the analysis of neuronal circuit function. I will then show examples of their application in zebrafish, a small genetic animal model with favorable properties for studies of neuronal circuits. The focus will be on the olfactory system where information about the identity of odors is encoded by distributed activity patterns across many neurons. Detailed analyses of dynamic neuronal activity patterns revealed that neuronal circuits perform successive transformations of odor-evoked activity patterns. These transformations result in computations such as a decorrelation and an equalization of activity patterns, which are important for pattern classification. Manipulations of these activity patterns provided insights into the underlying mechanisms and have the potential to uncover causal relationships between neuronal computations and behavioral outputs. Together, these results illustrate the power of new optical methods to analyze neuronal computations in the brain.