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Title:
Imaging neuronal activity in awake mice

Abstract:

One of the biggest mysteries is how behavior arises from neuronal activity and how sensory stimuli are represented in our brain. To shine some light on this mystery it is important to record neuronal activity on a cellular and subcellular level from many neurons, and to correlate the neuronal activity with behavior. In the Optical Neuroimaging Units we focus on the development and application of new methods towards this task.

Our animal model system is the mouse and for detecting the brain activity we use optical methods. To allow imaging of the brain we replace a small area of the skull by a glass cover slip which acts as a chronic cranial window to the brain. To convert the neuronal activity to an optical signal we use specifically designed genetically encoded calcium indicators which are based on the green fluorescent protein from jelly fish. The gene of this indicator is inserted into a viral vector nowadays regularly used for gene therapy. We inject the viral vector into the mouse brain before mounting the chronic cranial window. The indicator gene is under the control of specific regulatory sequences so that the indicators are only expressed in specific cell types. About 2 weeks after the injection of the viral vector into the brain the targeted neurons will start to fluoresce. To detect this fluorescence we build two-photon microscopes which are specifically optimized for in vivo imaging. This microscopy technique allows us to three-dimensionally reconstruct neurons in the living mouse with a resolution of about 1 µm. The 2-photon imaging technique is limited to about 1 mm imaging depth. For this reason we focus our research on cerebral or cerebellar cortex. 2-photon microscopy and the genetically encoded calcium indicators also allow us to record movies of the brain activity. During imaging the mice have to be head-fixed. To avoid unnecessary stress, the mouse is mounted on a treadmill to allow for running. In some of our projects we use virtual reality systems to give sensory feedback in response to running. For example, we increase sound intensity if the mouse runs toward a virtual sound source. So, even with being head fixed the mouse can perform behavioral tasks like decision making. The combination of these techniques allow us to study neuronal activity patterns of more than 600 somata of neurons or thousands of neuronal compartments simultaneously and to correlate the neuronal activity with behavior. With this data we can try to decode the neuronal activity patterns by machine learning algorithms and predict future behavior by analyzing current neuronal activity.