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Title: PhotoMEA: development of optical tools for the study of the functional properties of neuronal networks

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A large number of studies on neuronal physiology and plasticity have provided a detailed picture of the molecular machinery underlying the modulation of neuronal activity. On the contrary, the mechanisms controlling properties of complex neuronal networks remain poorly understood. At present, the neuronal functional properties are investigated either by a large-scale approach (i.e. MicroElectrode Array devices, MEAs) that enables the study of the general activity of a complex neuronal network, or alternatively by a micro-scale approach (i.e. intracellular or patch electrodes) suitable for the detailed analysis of the molecular mechanisms that actively contribute to the generation and modulation of the single neuron activity.
Systems based on electrodes have yielded important results in neurophysiology, but now they start to show some severe limits, such as the possibility of inducing cellular damage in the case of intracellular electrodes and the poor spatial resolution in the case of MEAs.
Optical methods for neuronal stimulation, e.g. using caged compounds, and for neuronal activity recording, e.g. using Voltage-Sensitive fluorescent Dyes (VSDs), can be useful tools to overcome these limits. Local light stimulations are obtained activating caged glutamate by UV light pulses. Single neurons or selected parts of them can be stimulated using optical fibres micro-positioned in the neuronal culture or optical waveguides micro-structured in the glass coverslip, on which the neurons are cultured, to precisely drive UV light. Optical recordings of the electrical activity from the entire network are performed using di-4-ANEPPS Voltage-Sensitive Dye and a standard epi-fluorescence microscope equipped with a dedicated large-sensor high-speed camera.
Combining these two optical methods the micro-scale approach (stimulation) meets the large-scale approach (recording). This methodology may turn out to be extremely useful for testing the ability of drugs to affect neuronal properties as well as alterations in inter- and intra-neuronal communication.

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