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Title: OptoMEA: a new tool for combining local optical activation of compounds with distributed MEA recordings

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Since their introduction, Micro-Electrode Arrays (MEAs) have been exploited as devices providing distributed information about learning, memory and information processing in a cultured neuronal network, thus changing the field of view from single cell level (glass pipettes) to the scale of the complex network. MEAs represent a growing technology for the study of the functional activity of neuronal networks providing the possibility to gain information about the spatio-temporal dynamics of the network and to allow recordings of electrical activity over periods of time not compatible with conventional electrodes at several sites in parallel. More recently, according to the trend aimed at the reduction of animal tests, MEAs have been exploited as in vitro biosensors to monitor both acute and chronic effects of drugs on neuronal networks in physiological or pathophysiological conditions. On the contrary, the presence of stimulus artefacts and the poorly controlled spread of electrical stimuli in the culture medium limit the applicability of MEAs for neuronal stimulation. Although the problem of artefacts has been recently solved using blanking circuits, the problem of spreading of electrical signals is inherent to the use of electrical stimulations in a conductive volume. Moreover, because neurons are naturally interconnected in complex networks electrical stimuli applied to a region of the network may activate neurons of that region and also fibres of passage coming from neurons of other regions. To overcome these limitations, in addition to electrophysiological techniques, optical methods for the stimulation of neurons have been used for relatively a long time, i.e. by caged compound activation. Here we present the new OptoMEA tool where local light stimulations were obtained switching caged glutamate in the active form by UV light pulses using optical fibres exactly aligned at the MEA electrodes. This tool allows us to activate the network or to deliver other active compounds in specific regions of the network and to monitor their effects on the overall network functioning. 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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