

Integrated microelectrode array and microfluidic platform for stimulating and recording reconstructed neuronal networks

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Compartmentalized microfluidics are devices that allow the in-vitro reconstitution of neuronal circuits using primary cultures of different neuronal populations. This configuration allows the reconstruction of axono-dendritic contacts between two cortical populations such as those found between cortical layers in vivo. In order to extend the functional analysis of reconstructed cortico-cortical networks, we developed a specific Micro Electrode Array (MEA) substrate that fits to the microfluidic geometry to stimulate and record pre- and post-synaptic neurons (Figure1). Presynaptic electrodes were disposed at the entrance of axonal channels in order to stimulate the axon initiation segment that will generate physiological action potentials and trigger release of neurotransmitter in the synaptic chamber. Postsynaptic electrodes are located under postsynaptic neuronal cell bodies. Combined with high-resolution fluorescence videomicroscopy and fast calcium imaging, this system allows monitoring intracellular dynamics, Calcium responses and synaptic transmission to different forms of neuronal activity. By combining space-time compartmentalization of neuronal populations with high-resolution videomicroscopy and electrophysiological stimulation and recording, our platform allows to decipher the cellular events that are involved in synaptic transmission and plasticity within neuronal networks. This device can be applied to virtually any type of neuronal circuits but also neuromuscular junctions.

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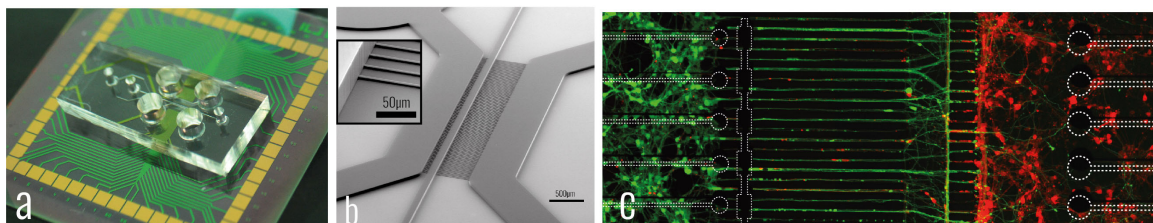


Figure 1 : Integrated multi-electrode array and microfluidics. a, Photographs of the microfluidics connected to the multi-electrode array substrate and details of the post synaptic electrodes. b, Dual thickness SU-8 mold of the microfluidic culture chamber. c, Design of the system showing the different compartments and their respective electrodes (Green, GFP- expressing cortical neurons; Red, mCherry-expressing cortical neurons).