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Development of transparent nanowire array technology for high resolution electrophysiology of brain-on-chip.

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Neurodegenerative disorders represent a major and growing global health challenge, mainly due to the complexity of the human brain. Continuous advancements in tools to improve their functional analysis, particularly in electrophysiology, are needed to accelerate the development of safe and more effective treatments. Over the past few years, remarkable progress has been made in that regard, notably in the field of *in vitro* microelectrode arrays: the size of the sensors has been reduced and hybridised to 3D structures, such as nanowires, to promote the engulfment-like behaviour at the cell-electrode interface^{1,2}. By their configuration, this new generation of 3D nanowire electrode arrays (NEAs) allows to record the activity of a large number of neurons in an extended network with a higher throughput and higher signal resolution.

Here we present the latest development of our NEA technology, composed of an array of electrodes with core-shell metal nanowires, which aims to provide an efficient platform dedicated to the study of neuronal activity of two-dimensional, as well as three-dimensional, cell culture systems. Most technologies involving 3D nanoelectrodes are typically fabricated on opaques substrates. To address this limitation and provide optical characterization with devices conventionally used by biologists (e.g. inverted microscope), and open the possibility to couple functional characterization with morphological insights, we have developed a process on a transparent substrate. We will describe the process that allows us to create these NEAs with high aspect ratio core-shell glass-metal nanowires (Fig. 1) using a large-scale and cost-effective top-down approach, as well as detail their electrical and optical characteristic. Finally, we will demonstrate for the first time their functionality on human brain organoids (3D cell cultures based on human cells).

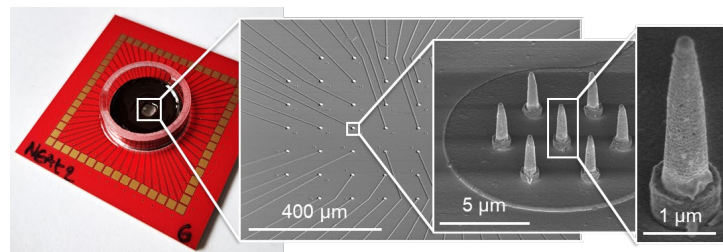


Fig. 1: Complete device, SEM images of the electrode arrays and zoom on unitary microelectrode and nanoprobe.

[1] L. Bettamin et al. *Small* 2024 & A. Casanova et al., *J. Phys.: Condens. Matter* **30**, 464001 (2018)

[2] R. Liu et al., *Nano Letters* **17** (5), 2757-2764 (2017)

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