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Probing electrical activity of single neurons based on 1D nanostructures: from extra to intracellular interfacing.

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***Abstract* - The struggle against neurodegenerative diseases is one of the major challenges in the near future and the global understanding of these diseases goes through a better expertise at the single cell level of basic mechanisms involved in neuronal networks. We need to investigate closer to the cellular material and in this way, miniaturization of electronic components and emergence of nano-biotechnology open new perspectives. Indeed, we are now able to fabricate high sensitive nano-devices to follow neuronal activities. Here, we will present two different approaches to interface neurons, a first one based on a nano-FET for extracellular recordings and a second one using vertical nanowire arrays (nano-electrodes) for intracellular measurements.**

I. INTRODUCTION

Due to constant aging of the world population, neurodegenerative diseases will constitute a major issue in the near future. Neurons are basic building blocks of brain architecture and location of numerous of these diseases and to struggle against them, we need to increase our comprehension of basic mechanisms involved in a neuronal network. To have a more detailed understanding of neurons behavior, we need to reduce the scale of our study and investigate closer to the cellular material down to the cell level over the long term with in-vitro cultures. Indeed, a roadblock in the development of new therapies is related to the poor understanding of age-related diseases at the single cell level due to limits of space / time resolution of current characterization tools. In that scope, we need to develop high sensibility recording devices able to interface single cells, to increase both the recording resolution and the spatial resolution of the measures. In this context, miniaturization of electronic components and emergence of nano-biotechnology open new perspectives for addressing this kind of neurobiological issues and holds great promise to improve the resolution levels. First demonstrations have been published in this direction based on nanowireFET [1] or vertical nanowire probes [2].
In this work, we propose to co-integrate extra and intracellular approaches in a same platform, (vertical nanowire arrays and nano-FETs), to accurately compare the advantages and drawbacks of each device to interface neuron electrical activity.

II. EXTRA/INTRACELULLAR APPROACHES

The interaction between a cell and a recording electrode (active or passive), can be schematized by two junctions composed by a resistance in parallel with a capacitance (Figure 1). The first one characterizes the membrane impedance and the second one defines the electrode impedance caused by the interface between the ionic current from the cell and the electronic current in the electrode. These parameters play an important role in the recording resolution and depend on the mechanical interaction between the cell and the electrode but also the electrode characteristics. A 3D passive nanostructure, such as vertical nanowire, allows a high affinity with cell (potentially intraneuronal interfacing) but is governed by its electrode impedance, which fixes the coupling between the value of the cell potential (V_{intra}) and the measured potential (V_{mes}). On the other hand, a nano-FET enables an active transduction of the signal that is not limited by the electrode impedance but the multi-terminal configuration of the device limits the possibility of a close affinity with the cell.

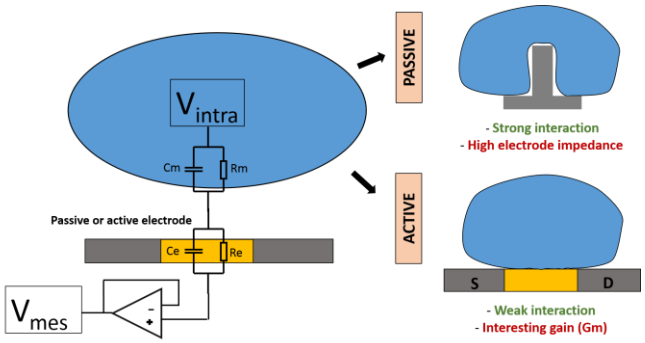


Figure 1: Electrical model of the interaction between a cell and a passive or active electrode.

III. DEVICE FABRICATION

The nanowire recording devices are created with a large scale and cost effective top-down approach combining conventional lithography tools and reactive ion etching.
Firstly, a silicon on insulator 4" wafer (Si 4µm/Buried oxide 1µm/Si wafer 400µm) has been structured by photolithography (i-line stepper), to obtain resist nanodots with diameter around 350 nm (Figure 2). The diameter has been tuned by an oxygen plasma step before the plasma etching of the silicon layer by deep reactive ionic etching. Figure 2 presents the vertical Si NW array obtained with 200 nm diameter and 3.5 µm long.

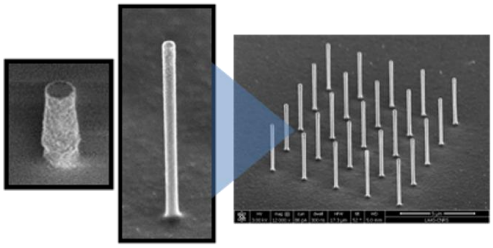


Figure 2: Resist nanodots after the photolithography step and transferred into silicon by DRIE to get 200nm diameter nanowires (H=3.5µm).

To ensure a signal recording in liquid environment, we developed a core-shell-type device (Figure 3A) with a conductive part at the center, encapsulated by a conformal silicon oxide to isolate the probing nanostructures from the culture media. The bottom part of the NWs is connected to encapsulated metallic lines to drive the potential registered at the NW level to external interface.

In parallel, silicon nano-FETs (active devices) have been developed (Figure 3B) by top down approach. The active channel is a planar NW (50 nm) connected by two source/drain extensions composed by silicided contacts on highly doped regions (boron p-type doped at 1.E19 at.cm^{-3}).

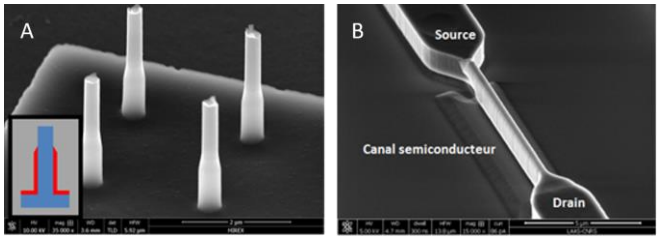


Figure 3: A) core-shell-type nanowire device for passive nanoprobes structures B) Nano-FET composed by a planar nanowire channel.

IV. RESULTS AND DISCUSSIONS

The devices have been electrically characterized in order to extract their main characteristics in liquid media. For instance, Figure 4 shows the impedance of a 9 NW array structures as function of the frequency. Considering a frequency of an action potential of neurons (1kHz), the impedance value is below $10^7\Omega$, which should lead to the high neuron/probe coupling coefficient [3].

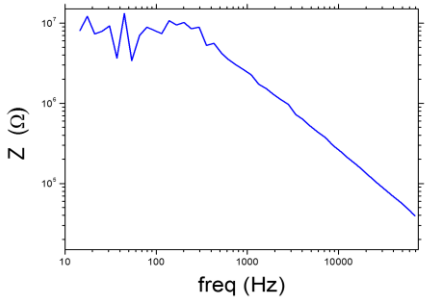


Figure 4: Impedance characterization of a 9-nanowire-array.

Nanowire-FETs have been characterized using the back-gate contact as gate electrode to get the intrinsic characteristic of the devices (I_{on}/I_{off} ratio ~ 6 decades) and then in liquid media to study their sensing behavior. In particular, Figure 5 shows a pH sensibility of the NW-FETs close to the Nernst limit (58mV/pH).

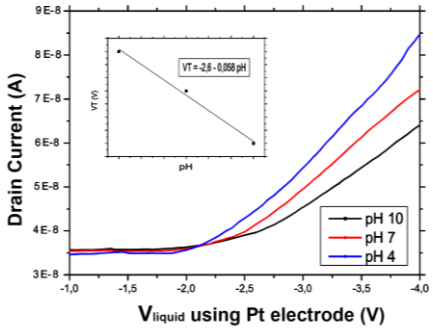


Figure 5: Current-voltage characteristics in liquid media with several pH values.

Finally, rat hippocampal and cortical neurons have been cultured on the devices and after 10 days in-vitro (10DIV), the electrical activity has been successfully recorded with both approaches. Fig. 6 shows several examples of local field potentials from few somas and action potentials from a single soma (1ms duration). We will discuss and compare these results from electrical and technical point of view.

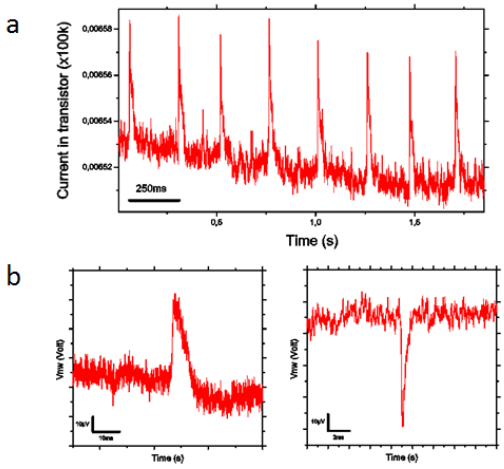


Figure 6: a) Local field potentials train by extra-cellular recording. b) A local field potential (10ms) and a action potential (1ms) with vertical nanowire approach.

V. CONCLUSION

In summary, we realized a platform based on nanowire devices combining vertical nanowires and nano-FETs to interface neurons and compare both approaches in the same culture conditions. Neuronal culture on this platform had been performed and we succeeded to accurately record neuronal activity with both devices.

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