Carbon Nanotube Cellular Probes

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There has been significant interest in single cell electrophysiology measurement systems. A single cell measurement allows for detailed analysis of the electrical charge related cellular functions and is particularly helpful in studying drug interactions. The most widely used method is patch-clamping. Cells are sucked partially onto a micro pipette to allow electrical probing of the cell, with pipettes small enough to probe the ion channels of a cell. While effective, this technique is very laborious and slow. Planer arrays of patch clamps are being developed to speed up the measurements (1). These devices rely on micro-fluidics to direct the cells to micro-needles where the cells are partially sucked onto for probing. Here we present an alternative device structure that relies on an array of nano-probes. Our probes consist of vertical single wall carbon nanotubes (SWNTs) interconnected with electrodes. The SWNTs are capable of entering the cells, allowing for probing of both the inside and outside of the cells with minimal disturbance to their motility.

The devices are fabricated by using electrophoresis to control the deposition of CNTs into predefined holes (30-50nm) within a dielectric(2) over metal interconnects. The nano structures in which the CNTs are deposited are fabricated using standard CMOS technology. This allows for high-density arrays of nanoprobes (sub 100nm spacing) that are cable of probing at the subcellular level. This allows for deeper understanding of cellular functions and signaling.

To demonstrate the capability of the devices we interrogated rat neuronal cells using impedance spectroscopy as shown in Fig. 1 and Fig. 2. Measurements were performed with and without cells on the nano-probes. At low frequencies, the impedance dropped with the presence of the rat neuron cells, suggesting that the nanotube probes are able to detect the cells. This new device can lead to newer understanding of cellular functions and help tailor newer drugs by probing not just the global effects by also local effects within a cell or groups of cells.

1. Weerakoon et al., Biomedical Circuits and Systems, IEEE Transactions on **3**, 117 (2009).

2. Goyal et al., J.of Vacuum Science and Technology B 26, 2524 (2008).

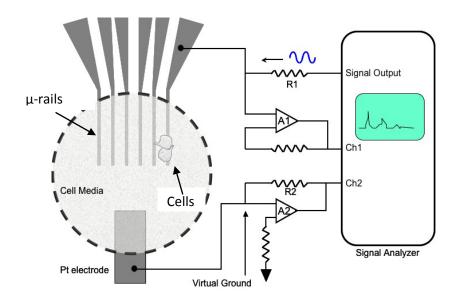


Fig 1 Schematic of the experimental setup for measuring the impedance spectrum of cells on the single wall carbon nanotube (SWNT) nanoprobes. Each micro-rail has six nano-probes spaced on 6 μ m centers. The signal analyzer outputs the ratio between Ch1 and Ch2, which gives the impedance referenced to the Pt electrode.

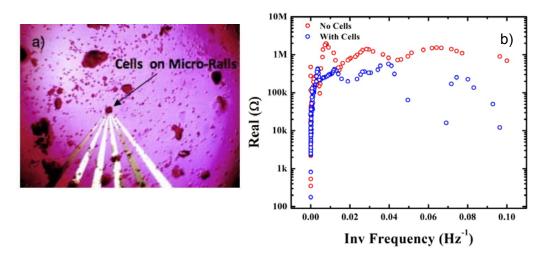


Fig 2: a) Optical micrographs comparing micro-rails with accumulated mouse neuronal cells and (b) real part of impedance spectrum of mouse neuronal cells over SWNT nanoprobe array referenced to Pt electrode versus the inverse of the frequency (to highlight the low frequency response).