Ultra-Wideband Impedance Spectroscopy of a Live Cell

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Abstract:

Accurate measurement of single-cell biophysical properties can represent helpful information on its physiological state. Electrical impedance spectroscopy (EIS) of single cells is a method for quantifying the phenotypic heterogeneity of cells. Compared to conventional optical or biochemical methods, EIS is a fast, compact, label-free, and non-invasive method. Therefore, a single cell can be trapped, characterized, and released using broad microwave frequency, by vector network analyzer (VNA). Hence, the frequency from low (kHz) up to high (GHz) can be swept through the cell to measure the subcellular features of the cell. This data will provide useful information about cell size, membrane properties, cytoplasm, and intracellular properties.

Summary of Research:

We fabricated a coplanar waveguide (CPW) electrode (Figure 1) that can be set up in a standard microscopy environment [1]. The CPW enables trapping, characterizing, and releasing a single cell and particle. Cells in an isotonic solution are moved through a microchannel equipped with electrodes in an impedance-based microfluidic channel. For this purpose, we fabricated microfluidic channels on these electrodes to guide cells through them at the minimum fluid flow and monitor the cell manipulation inside the channels which only requires one alignment step [2] (Figure 2).

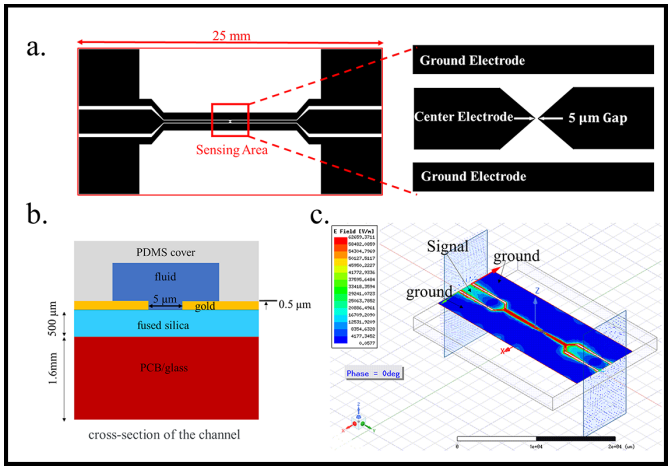

Figure 1: Coplanar waveguide (CPW) design, that includes a. a gold CPW, 2.5 cm long and 0.5 µm thick, which is deposited on a 500 µm thick fused silica substrate by an e-beam evaporator on a 1.6 mm PCB sheet. The gold CPW was covered with a 5 mm layer of PDMS. A microfluidic channel is molded onto the bottom side of the PDMS cover, intersecting the CPW. There is a 16 µm gap between the center and ground electrodes in the CPW. Besides the electrodes under the microfluidic channel, the center electrode is 200 µm wide. b. CPW cross-sectional dimensions in the channel region. c. The image shows a frequency sweeping pattern between two ports of the electrodes simulated by high-frequency structure simulator (HFSS) software.

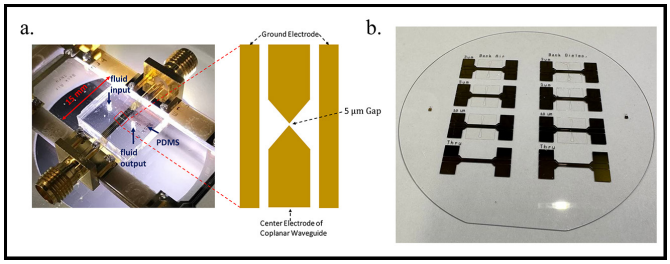

Figure 2: Microwave microfluidic device, a. The system includes a gold coplanar waveguide covered by PDMS microfluidic channel. b. Shows CPW with a different signal gap.

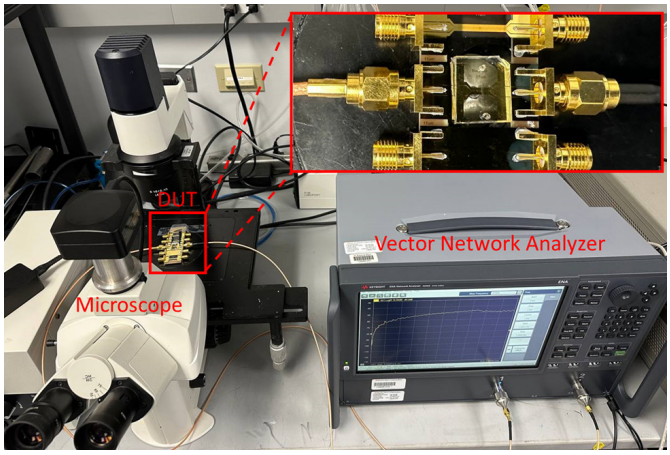

Figure 3: Shows the experimental setup. The device is placed on the microscope stage and connected to the VNA.

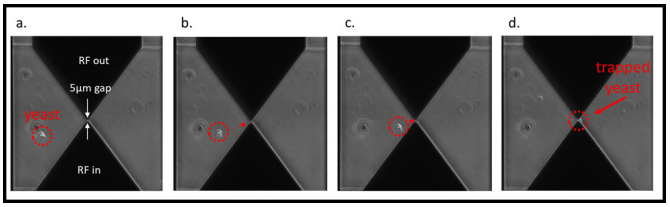

Figure 4: a-d. Shows single yeast trapped process by DEP micrograph. Yeast can be trapped and released by adjusting the frequency and power of the DEP signal from 5 MHz at 0 dBm to 30 kHz at 3 dBm.

The experimental setup is shown in Figure 3. We captured the cell using a dielectrophoresis (DEP) signal at 4 MHz and 0 dBm by VNA. The benefits of using this method are that the cells can be captured and released quickly between the two electrodes and the DEP focuses the electric field inside the cell. A yeast cell was trapped in the CPW gap by DEP and visually confirmed using a microscope. A yeast cell moves randomly in solution in the absence of DEP (Figure 4a). When DEP is applied to the solution the yeast is captured and moved toward the electrodes and immobilized by the CPW (Figures 4 b to d). When the cell is trapped between the two sharp electrode points, the majority of the radio frequency (RF) passes through the cell by way of the nucleolus. After trapping the yeast, the VNA was switched from the hold-frequency (4 MHz) to the sweep-frequency mode (30 kHz to 9 GHz) to measure the yeast's biophysical characteristics. The changes in S parameters were calculated and used to derive yeast biophysical characteristics using rapidly successive scattering parameters recorded with and without a trapped yeast.

Conclusions and Future Steps:

Impedance measurements are frequency dependent such that dispersion of a frequency spectrum can be allocated to different subcellular parts. We developed an ultra-wideband EIS device which is a non-invasive, and label-free method to characterize living single-cells. It can provide helpful information on its physiological state within the radio frequency (RF) range. This enables researchers to analyze the characterization of the cell more efficiently, instead of having to master complex tools.

For future steps, we will test the initially developed CPW electrode for validation and streamlining the sensing measurements. However, coplanar waveguides electrodes, despite having fewer fabrication complications, suffer from electric field non-uniformity with a strong electric field near the electrodes that fades away when moving away electrodes in the vertical direction. We will fabricate vertical electrodes. In this configuration, however, electric field linearity between electrodes is significantly more homogeneous with uniform electric field distribution in the entire testing region. This configuration of electrodes despite having more complexity and fabrication steps, significantly improves measurements' accuracy and signal-to-noise ratio.

References:

[1] Du, Xiaotian, Caroline Ferguson, Xiao Ma, Xuanhong Cheng, and James C. M. Hwang. 2022. "Ultra-Wideband Impedance Spectroscopy of the Nucleus in a Live Cell." IEEE Journal of Electromagnetics, RF and Microwaves in Medicine and Biology 6 (2): 267-72.

[2] Li, Hang, Caroline Multari, Cristiano Palego, Xiao Ma, Xiaotian Du, Yaqing Ning, Javier Buceta, James C. M. Hwang, and Xuanhong Cheng. 2018. "Differentiation of Live and Heat-Killed E. Coli by Microwave Impedance Spectroscopy." Sensors and Actuators. B, Chemical 255 (February): 1614-22.