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A new CMOS-electrode-array-based impedance sensor integrated into an open microfluidic platform

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Motivation

Compared to traditional two-dimensional (2D) cell cultures, three-dimensional (3D) microtissues and organoids more accurately replicate in-vivo physiological conditions, e.g., cell-cell interaction and density gradients [1]. Open microfluidic hanging-drop platforms are used to culture microtissues or organoids at the air-liquid interface, while the nutrients are supplied through microfluidic channels interconnecting the hanging droplets [2]. However, tissue monitoring in the drops relies on microscope-image acquisition to characterize tissue size and growth. To provide continuous characterization of the tissue size and properties, we integrated a new complementary metal oxide semiconductor (CMOS) impedance sensor platform into the hanging-drop network for in-situ measurements.

Materials and Methods

The microfluidic hanging-drop system was fabricated from PDMS by using a double-sided molding process. To integrate the CMOS sensor into the hanging-drop platform, we first glued the CMOS chip onto a glass substrate featuring metal contact traces. We then plasma-bonded the microfluidic structure onto the substrate and connected the metal traces on the glass substrate to the CMOS chip via bond wires, which were then covered with epoxy for protection and stability. Finally, inlet and outlet holes were drilled into the glass substrate and metallic needles were aligned and affixed for fluidics inlet and outlet [3].

Results

To characterize the performance of the CMOS impedance sensor platform, we loaded a 700 um-diameter glass bead in the hanging drop below the sensor (Figure 1.a) We then acquired impedance measurements at 100 kHz using two pseudo electrodes, which were formed from the electrodes of the array at the side and at the center using a reference electrode, placed along one side of the electrode array. Impedance measurements were taken at different drop heights (Figure 1.b). As depicted in Figure 1.c, impedance values recorded from the side electrode remained essentially constant for all drop sizes, as they mostly depended on the medium conductivity. In contrast, the impedance between the center and reference electrodes significantly increased as the drop height was reduced, as the dielectric bead affected the current distribution between the electrodes.

Summary and conclusion

Here we showed the integration of a CMOS impedance sensor platform in an open-microfluidic hanging-drop network. Impedance measurements from sensing electrodes at the side and center of the array enabled us to sense the medium conductivity and the electrode-to-sample distance.

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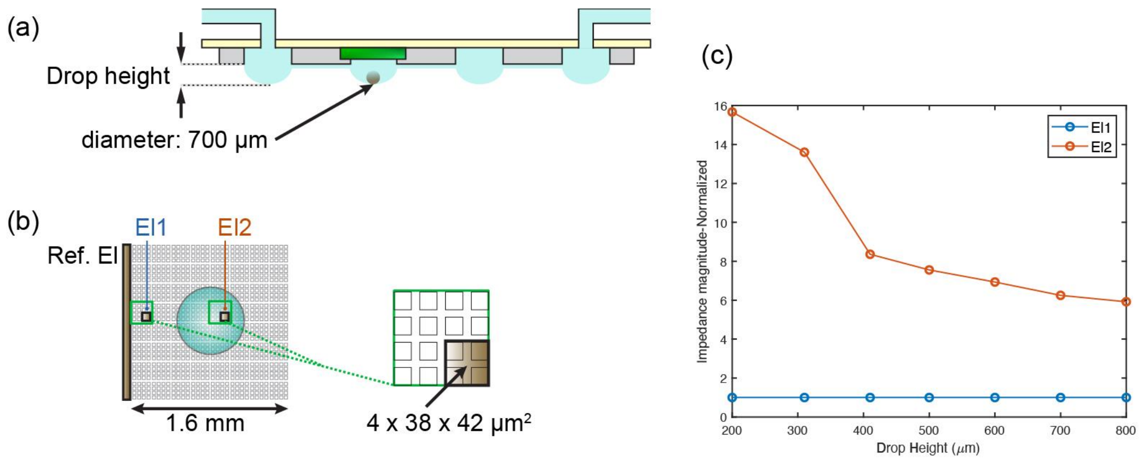

Figure 1: (a) Hanging-drop platform with a glass bead in the sensing droplet, (b) bottom view of the electrode array indicating reference and sensing pseudo-large electrodes, used for the impedance measurements, (c) impedance measurements conducted at 100 kHz at different drop heights

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