Microfabricated Impedance Sensor for Single Cell Migration Monitoring and Differentiation

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Cell migration detection is essential for both fundamental biological research and clinical diagnostics. As cell cluster measurements often obscure the differences between individual cells, sensing approaches capable of resolving single cell dynamics become increasingly desirable. However, implementing single cell migration detection using electrical cell–substrate impedance sensing (ECIS) remains challenging, as conventional ECIS systems typically employ large size electrodes that monitor group of cells behaviors with limited spatial resolution and sensitivity due to small cell–electrode contact area for single cell.

To address these limitations, a microfabricated ECIS sensor was proposed for single cell migration detection and cell type differentiation, as shown in Fig. 1 (a). The proposed sensor consisted of two miniaturized electrode pairs at the bottom of SU8 microchannels. The electrode dimensions were comparable to a single cell to enhance spatial resolution. The 10/120 nm thick NiCr/Au electrodes were fabricated by thermal evaporation and lift-off technology. SU8 microchannels with 20 μm width were designed for single cell migration and defined by photolithography, as shown in Fig. 1(b). To promote cell adhesion in channels, the bottom and sidewalls of the microchannels were selectively coated with (3-aminopropyl)triethoxysilane (APTES) plus fibronectin (FN).

The developed sensor enabled detection of single nasopharyngeal epithelial (NP460) cells migrating across the electrode pair, as shown in Fig. 2(a). When a single NP460 cell traversed the electrodes from 50 to 70 min, the cell body partially blocked the current path and led to a transient increase in impedance. Besides demonstrating detection of single cell migration, the device was evaluated for label-free cell type differentiation. The impedance signatures from NP460 and osteoblast MC3T3 cells were compared. As shown in Fig. 2(b), NP460 cells showed shorter duration of increased impedance magnitude than MC3T3 cells, indicating faster movement of NP460 cells. In addition, NP460 cells induced smaller real part peak impedance changes as shown in Fig. 2(c), suggesting impedance signal changes depended on cell types. Micrographs of cells in SU8 microchannels were captured and their spread areas were shown in Fig. 3, indicating NP460 cells had smaller spreading area than MC3T3 cells. Collectively, these results demonstrated that impedance sensing by electrodes can capture intrinsic differences in cell motility and morphology, highlighting the potential of the proposed sensor for label-free cell monitoring and differentiation of single cell migration dynamics.

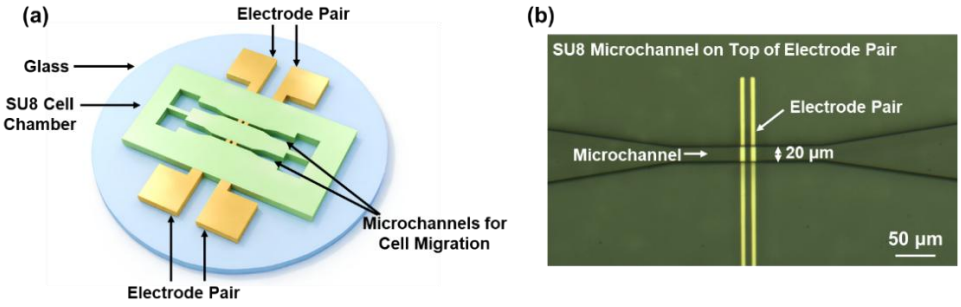

Figure 1: (a) Schematic of microfabricated impedance sensor containing two electrode pairs with SU8 microchannels on top. (b) Micrograph of fabricated SU8 microchannel on top of electrode pair.

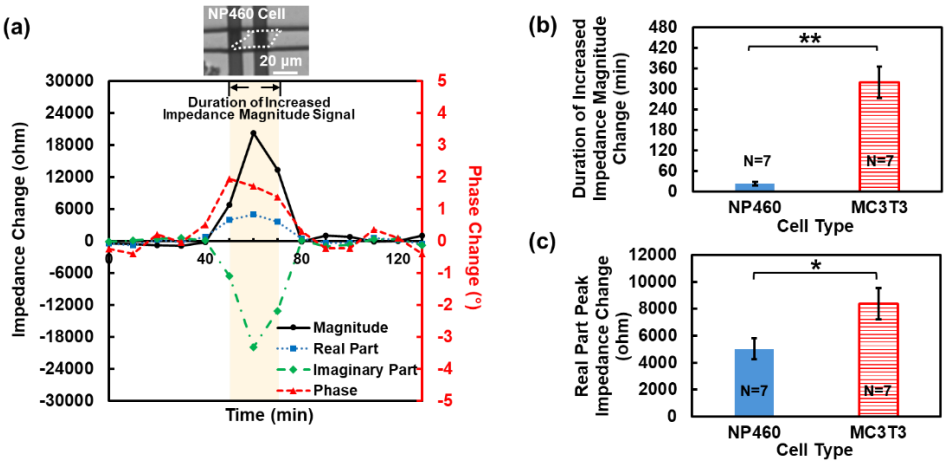

Figure 2: (a) Impedance monitoring of NP460 cell migration in microchannel with (3-aminopropyl)triethoxysilane (APTES) plus fibronectin (FN) coating. Impedance magnitude increased when single NP460 cell migrated across electrode pair. (b) NP460 cells induced shorter duration of increased impedance magnitude compared to MC3T3 cells. (c) NP460 cells induced lower real part peak impedance changes. One-way ANOVA and Tukey's *post hoc* test with *p <0.05 and **p <0.01.

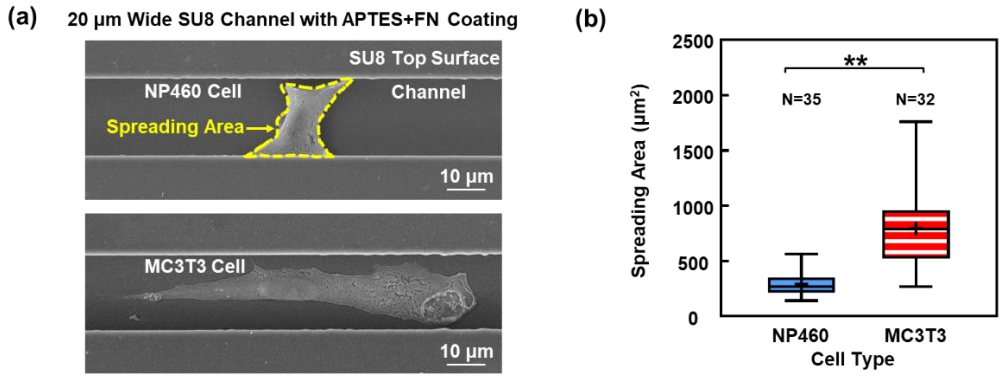

Figure 3: (a) Micrographs of MC3T3 and NP460 cells in 20 µm wide SU8 channels. (b) NP460 cells had smaller spreading area compared to MC3T3 cells. One-way ANOVA and Tukey's *post hoc* test with **p <0.01.