Detection of Filopodia and Cancer Cell Concentration by Hybrid Plasmonic and Impedance Biosensor

Shuyan Zhu, Mohammed A. Eldeeb, and Stella W. Pang
Department of Electronic Engineering
Center for Biosystems, Neuroscience, and Nanotechnology
City University of Hong Kong, Hong Kong
Email: pang@cityu.edu.hk

Metastatic cancer cells will migrate from their primary site to distant parts of body. More than 90% of death caused by cancer results from metastatic cancer. To understand cancer cell migration and invasion, most researchers used two-dimensional or three-dimensional platforms to culture cancer cells.[1] Other than external environment effect, the extension of filopodia also contributes to cancer cell migration and invasion. Filopodia are thin finger-like extension of cancer cell membrane protrusions and proved to be important in cell adhesion, migration, invasion, and cell to cell communication. However, in spite of their importance in cancer diagnostics, filopodia are rarely studied because their width is 300 nm or less which is hard to be observed by optical microscopy. In this study, a novel biosensor with hybrid plasmonic and impedance detectors were used to measure filopodia and cell concentration separately. To the best of our knowledge, this is the first study to monitor filopodia extension and cell concentration simultaneously by hybrid plasmonic and impedance biosensor.

Figure 1(a) shows the schematic of hybrid plasmonic and impedance biosensor. As shown in Fig. 1(a), gold (Au) nanodots array with 300 nm diameter, 535 nm pitch, and 20 nm thickness were used as plasmonic biosensor and SU-8 nanopillars with 500 nm height were designed to prevent cell membrane from contacting the plasmonic biosensor. The detection range of localized surface plasmon resonance is limited by its decay length which is normally less than 100 nm.[2] When the cancer cells migrated on top of the nanopillars, only the filopodia could extend onto the surface of plasmonic biosensor, and cell membrane remained on top of the nanopillars. Figure 1(b) shows the simulated electromagnetic field distribution of Au nanodots. The results show that the localized surface plasmons are enhanced around the Au dots. Figure 1(c) shows the fabrication technology of the hybrid plasmonic and impedance biosensor.

Figure 2 shows the micrograph of osteoblastic MC3T3 cells on SU-8 nanopillars with 120 nm width, 535 nm pitch, and 380 nm height. The results show that cell membrane spread on top of nanopillars and filopodia extended through the spacing between the nanopillars. Figure 3 shows the micrograph, refractive index sensitivity, and resonance peak as function of refractive index (RI) of certified RI liquids for Au nanodots plasmonic biosensor. Figure 3(b) shows that a resonance peak at 1221 nm was observed and this resonance peak was red shifted with increasing RI. The sensitivity of the Au nanodot plasmonic biosensor was 436 nm/refractive index unit. The effects of micro/nanostructures dimensions and layouts on the extensions of filopodia and the relationship between filopodia extensions for cancer and normal cells will be studied.

[1] S. F. Zhou, S. Gopalakrishnan, Y. H. Xu, J. Yang, Y. W. Lam, and S. W. Pang, *PloS one* **11**, 147801-147819, 2016.
[2] S. Zhu, H. Li, M. Yang, and S. W. Pang, *Nanoscale* **10**, 19927-19936, 2018.

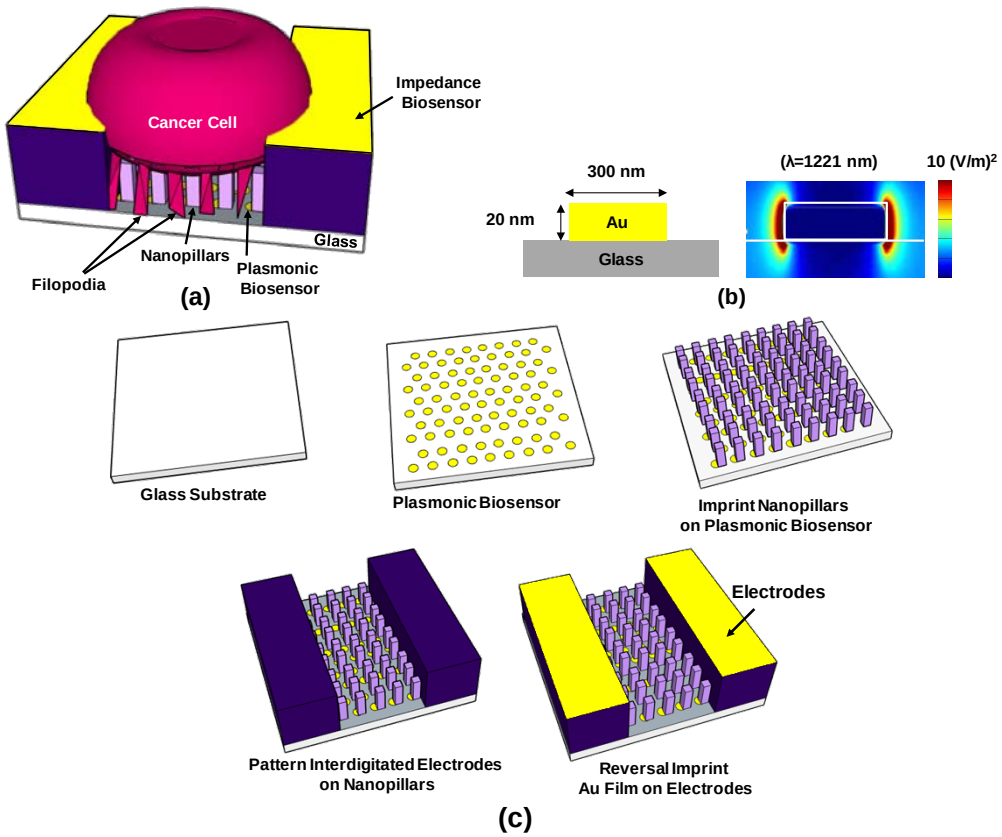

Figure 1: (a) Schematic diagram of filopodia detection by hybrid plasmonic and impedance biosensor. (b) Simulated electromagnetic field distribution of Au nanodots plasmonic biosensor. (c) Fabrication technology of hybrid plasmonic and impedance biosensor.

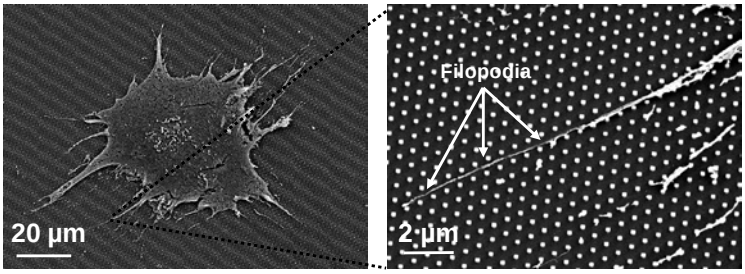

Figure 2: Micrographs of osteoblastic MC3T3 cells on SU-8 nanopillars.

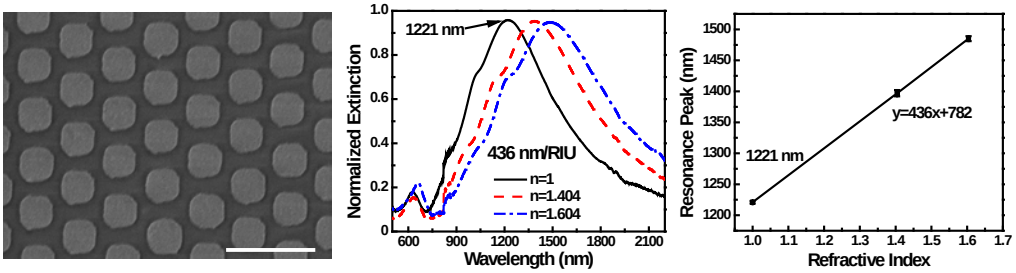

Figure 3: (a) Micrograph, (b) refractive index (RI) sensitivity, and (c) resonance peak as function of RI of certified RI liquids for Au nanodots plasmonic biosensor.