Co-integration of flip-tip patch clamp and microelectrode arrays for in-vitro recording of electrical acvity of heart cells

Yelkenci, Asli; Martins Da Ponte, Ronaldo; Valente, Virgilio

Publication date
2019

Document Version
Final published version

Citation (APA)
Yelkenci, A., Martins Da Ponte, R., & Valente, V. (2019). *Co-integration of flip-tip patch clamp and microelectrode arrays for in-vitro recording of electrical acvity of heart cells*. Abstract from 7th Dutch Bio-Medical Engineering Conference, Egmond aan Zee, Netherlands.

CO-INTEGRATION OF FLIP-TIP PATCH CLAMP AND MICROELECTRODE ARRAYS FOR IN-VITRO RECORDING OF ELECTRICAL ACVITY OF HEART CELLS

Asli Yelkenci*, Ronaldo Martins da Ponte and Virgilio Valente

Department of Microelectronics, Delft University of Technology, Mekelweg 4, 2628 CD and Delft, The Netherlands

ABSTRACT

The patch clamp has been widely considered the gold standard to measure intracellular ionic activity of single cells [1]. However, patch clamping is a laborious method and suffers from low throughput. To mitigate the disadvantages of patch clamping, planar patch clamp (PPC) chips with higher throughput have been recently introduced [2-3]. Yet those microfluidic chips do not allow to concurrently monitor the extracellular and the intracellular activity of the cells. Understanding of the complex cellular network activity and electrochemical processes, requires correlation between local field potentials (LFPs) of a population of cells and action potentials (APs) of single cells.

This abstract presents a novel CMOS compatible microfluidic system that integrates flip-tip planar patch clamps (FTPPCs) and microelectrode arrays (MEAs) on the same wafer, for in-vitro extra- and intra-cellular recordings of electrical activity of cardiac cells.

The device is fabricated using conventional wafer front- and back-side photolithography. The fabrication process leverages anisotropic wet etching selectivity of potassium hydroxide (KOH) and deep reactive ion etching (DRIE) to pattern FTPPCs. Before DRIE process, plasma-enhanced chemical vapor deposition (PECVD) of silicon dioxide (SiO_2) is applied as passivation layer. After DRIE process, a metallization step is performed by sputtering titanium nitride (TiN) on patterned structures. As the final step, SiO_2 is removed and backside DRIE is used to open apertures approximately with 2 µm diameter. The FTPPCs are intended to have a tip in 20 µm depth after KOH etching, and a spacing of 200 µm to ensure that mechanical stability of the device after DRIE. The planar MEAs are then patterned on the front side with 50 µm diameter and a pitch of 200 µm.

A PDMS culture chamber is attached the front-side of the wafer, while a PDMS microfluidic channel is constructed on the back-side. By applying suction through the microfluidic channels, the cells are trapped in the FTPPC apertures. Potentiostatic measurements are used to record the ionic activity of the cells intracellularly, while low-noise instrumentation amplifiers are used in combination with the MEAs, to concurrently measure LPFs.

Co-integration of PPC and MEAs on the same wafer can provide valuable insight in the correlation between single-cell activity and cellular network dynamics of heart cells in healthy and pathological states.

[1] M. E. Spira, and A. Hai, Multi-electrode array technologies for neuroscience and cardiology, *Nature Nanotechnology*, vol. 8, pp. 83-94, 2013.
[2] L. Yobas, Microsystems for cell-based electrophysiology, *Journal of Micromechanics and Microengineering*, vol. 23, no. 8 pp. 1-16, 2013.
[3] T. Urisu, Incubation type planar patch clamp as a new potential technology for developing neuronal network high throughput screening devices, *Biomedical Engineering: Applications, Basis and Communications*, vol. 28, no. 3, pp. 1-10, 2016.