Extended Abstracts of the 2014 International Conference on Solid State Devices and Materials, Tsukuba, 2014, pp578-579

Device Technologies for Cell and Tissue Analysis

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Abstract

Microfluidics is one of the most promising device technologies that could provide the capability in high-resolution analyses in the field of cell and tissue related biological sciences. In this talk, our recent achievements to realize massively parallel single cell analysis, spatiotemporal control on culture conditions of cells and tissues are presented with some experimental results for validation.

1. Introduction

Microfluidics is one of the most promising techniques that could provide the capability in high resolution analyses in the field of cell and molecular biology, especially in the scientific domain where spatiotemporal dynamics is among the major issues, such as developmental biology, regenerative medicine, systems biology, etc.

There are numerous advantageous features of microfluidics over the conventional experimental tools, such as test tubes, dishes, etc. In this talk, some of the specific examples of the use of microfluidics to realize the high resolution analyses, such as;

1) Massively parallel single cell analyses (Fig.1),
2) Use of heterogeneous microenvironments for stem cell differentiation (Fig.2),
3) Use of various concentration waveforms to stimulate cells in vitro (Fig.3)

2. Electroactive Microwell Array

Individual cells can easily be trapped in a large array of microwells, which size is designed to be the one being occupied only by one cell at a time. The trapping procedure is reinforced by dielectrophoretic (DEP) forces generated by the pairs of embedded electrodes at the bottom of the microwells [1]. Our recent efforts to improve the trapping efficiency will be presented in details.

2. Spatially Patterned Differentiation

In order to realize heterogeneous microenvironment for cell and tissue analyses, a membrane-based microfluidic device is introduced [2]. The device consists of upper and lower channels separated by a porous membrane, on which cells are inoculated and cultured. Laminar flow streams containing soluble factors are formed in the lower channel, and the spatial pattern of the laminar flow will be transferred through the membrane, so that the cells on the membrane will be modulated accordingly.

3. Temporal Waveforms

Temporal waveforms often exhibit the different consequences in the living systems, e.g insulin-glucose dynamics in a human body [3]. Though it is so important to conduct experiments with those temporal waveforms in the concentration of specific compounds, it is so difficult to apply dynamically changing stimuli to cells or tissues by existing experimental tools.

Microfluidic technology can be a promising solution to realize such system capable of generating temporal concentration patterns of a specific molecule that can modulate cellular functions. By carefully designing the microfluidic cell culture device itself as well as the peripheral components, we developed a cell culture system capable of applying temporal concentration waveforms of signaling molecules, such as rectangular waves, triangular waves, etc.

4. Conclusions

The significant features of microfluidic approaches will be demonstrated through these examples that would be beneficial to the high-resolution analytical work in the field of cell and tissue biology and their applications.

Acknowledgements

The work presented here has been done in the frame of JST CREST and SICP project. Authors are grateful to all the collaborators and financial support to the work.

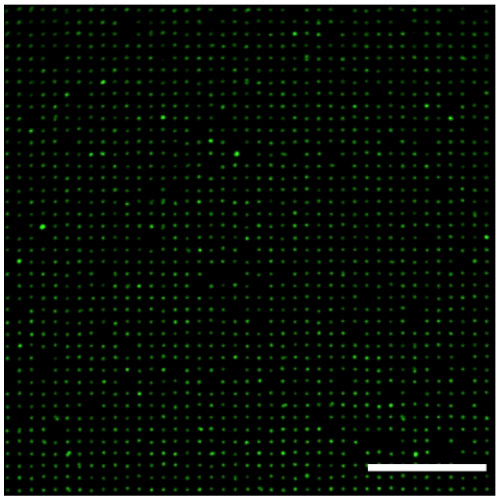

Fig. 1 A large-scale array of single cells in Electroactive Microwell Array. 1600 cells in the image. Scale bar is 500μm.

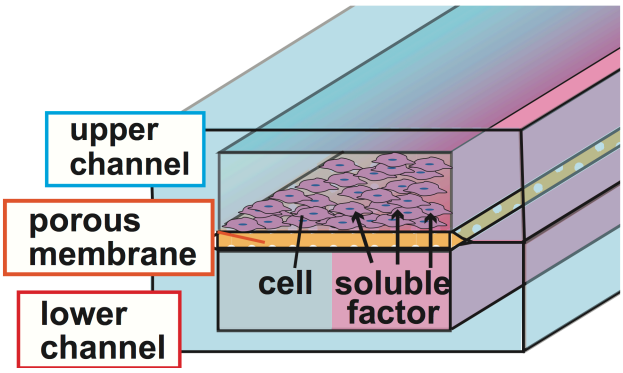

Fig. 2 A microfluidic device to realize heterogeneous conditions in space. Cells are inoculated on the membrane and the spatial pattern is formed by the laminar flow in the lower channel.

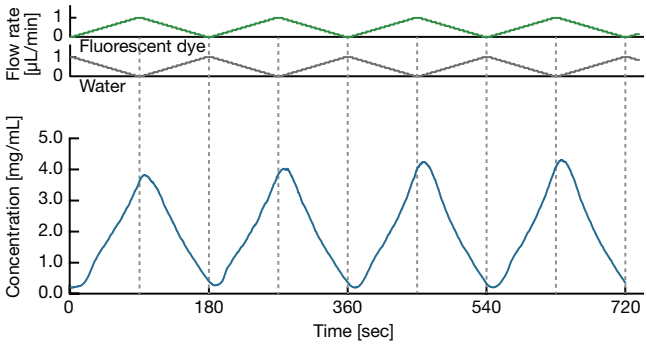

Fig. 3 A triangular wave of fluorescent dye concentration formed by the present system. This technique can be applied to other molecules to stimulate cells.

References

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