Electrochemical Bio-Lithography for Controlling Bionic Interfaces

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The controlled interface between the biomolecules and materials is one of the most important subjects for both in-vitro and in-vivo medical devices. The photolithography-based surface micromachining have been widely and successfully applied to the bio-device engineering. For example, microcontact printing method (μCP) using the poly(dimethylsiloxane) (PDMS) stamp would be the most established and convenient method to form micropatterns of a variety of materials including proteins and cells [1].

We have been studying the potential use of microelectrode techniques as the tool for surface bio-micromachining, and developed a few original techniques for controlling bionic interfaces [2]. Our patterning technique using the microelectrode can be conducted under typical physiological conditions and thus enables the multi-micropatterning with different kinds of cells, the in situ navigation of cellular growth and migration. Furthermore, the technique is simple enough to be integrated to the small and closed systems such as microfluidic devices.

In addition to the micropatterning of proteins and cells, the in-situ microcircuit formation with conducting polymers will also be presented as a potential interface to cellular networks [3].

(1) Electrochemical Bio-Lithography for Micropatterning Proteins and Cells

The micropatterns of biomolecules and living cells (~ 10 μ m) can be routinely drawn by electrochemical means. This method is based on our finding that the biophobic feature of the albumin- or heparin-coated substrate can be quickly switched into protein- and cell-adhesive by exposure to the locally generated HBrO at the microelectrode. The technique is simple enough to be integrated into the small and closed systems such as microfluidic devices, indicating the possible "on-demand" immobilization of proteins and cells just prior to the use of devices.

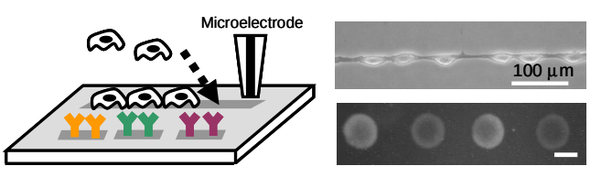

Figure 1. Electrochemical Biolithography of cells (Bovine aortic endothelial cell) and proteins (IgG).

2) In-situ Navigation of Cell Growth and Migration

Our patterning technique is mild and enables the multi-micropatterning with different kinds of cells as to give hetero-culture networks. Furthermore, the navigation of cellular growth and migration has been succeeded, since the generated oxidizing agent can selectively denature only the surface coating of albumin and heparin nearby the cells without a significant damage on the pre-existing cells.

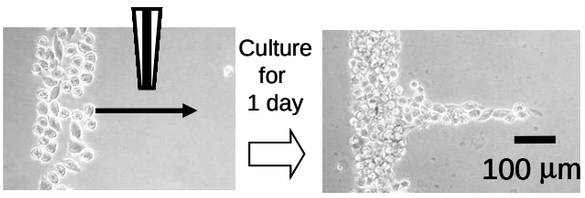

Figure 2. In situ navigation of growth of the micropatterned HeLa cells on a glass substrate.

(3) Intercellular Communication Assay for Micropatterned Cell Networks

In vitro assays using cultured cells have been conventionally carried out by measuring the activity of individual cells and cultures. In addition to such cellular activity, the function of cell-cell networks, such as synaptic junctions between neuronal cells, should also be an important measure for drug analysis.

The high-speed confocal microscope was applied to analyze the intercellular, dynamic Ca^{2+} transition along the micropatterned cardiomyocytes and PC12. The patterned cardiomyocytes connected each other via gap junctions and served as a pharmacological model of cardiac tissue. The micropatterned cells were integrated with the microfluidic devices and with the microelectrode arrays for local application of electrical and chemical stimulations. We believe the present system would be applicable for drug screening or drug assessment in near future.

(4) Ultra-Anisotropic Growth of Conducting Polymers along insulating surfaces

We have found a way to form conducting polymer microcircuit by navigating the growth of electrodeposites. The lateral growth along the surface pattern has been achieved with the anisotropic ratio of > 150. Such the soft and bio-functional circuit would serve as the interface with cellular systems.

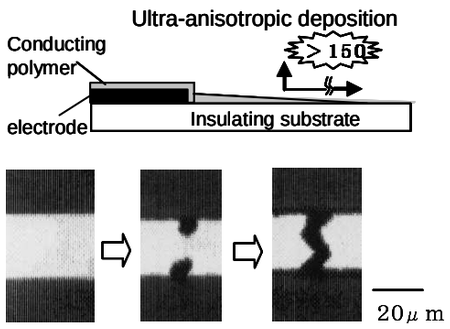

Figure 3. Ultra-anisotropic lateral growth of polypyrrole from band-electrodes along the glass surface having a zigzag hydrophobic micropattern.

References:

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