Universal Platform for Developing an Integrated Biochip or Micro-TAS Based on Electrokinetics

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Abstract

This study developed a novel universal platform for developing integrated electrokinetics-base biochips. The purpose of the platform is to provide a standard for modulizing the experiment chip. The chip is using microscope slides (75 × 38 × 1 mm) as substrate and patterning the electrode array on the slides to connect the signal controller with ISA (Industry Standard Architecture) bus slot. The control devices are using 8255 (Programmable Peripheral Interface) IC and relays to switch the signal source and program control. Then through computer and using Microsoft Access we can test any combination of experiment procedures and the electrode patterns.

Key Word: Micro Electrode, Electrokinetics, Micro-TAS

1. Introduction

The development of electrokinetics-based biochips always needs multistations on a chip, including sampling, separation [1-2], cell lyses [3], and testing. During the process of development, each station will be individually setup and tested, after completed, and then it will be integrated into the chip. Thus before finishing the process of development, for each station we should not only design different electrodes and signals, but also consider its compatibility for integration.

In order to meet the above requirements, this platform has to be conformed to the following facts. (1) Experiment chip should be fabricated easily and low cost. (2) Experiment chip can be used repeatedly. (3) Electrode connector must be module standards. (4) Electro-signal should have multi-selection to exchange. (5) Signal of sequence must be controlled. (6) Experiment must be easy to observe and record.

Compared with related prior arts, we have not found a complete development platform. The most similar paper reported by Zhen et al. [4] brought up the prototype for standard fluidic and I/O connector. They used the silicone tube and standard IC socket for this purpose. But in some situations, the chip is hard to be built and have some optical observation limits. To satisfy the constant modification of a prototype chip, a flexible platform is needed to be developed.

2. Design and Fabrication

2.1 Experiment Chip

Considering the cost, process conditions and biological compatibility, the substrate is using a microscope slide (75 × 38 × 1 mm). The fabrication sequence of biochips is shown as below. Aluminum (6000 Å) is thermally evaporated onto
the glass slide. Photolithography and wet-etching is employed to build the electrode patterns.

In order to provide control signal to the electrode pattern of the chip, we use 8-bit ISA bus slot to be the connector, which has 31 pins on its each side. The contact specification is shown in Figure 1 (1.8 × 7 mm, pitch 2.54 mm). The slide contains 29 contactors each side. Any experiment chip connector following this standard can be used in the development platform.

A thin insulation layer (positive photoresist, 1813) is spin-coated on the electrodes for electrical insulation between the electrodes and the solution, which is to ensure that no electrochemical reaction occurs on the electrode surface. Then, the fluid channel is made of photo-resist with channel depth of 50 µm.

Cover slips are bound with fluid channel, or use conductive ITO (indium tin oxide) glass as the ground electrode, then apply the silver–glue link to bottom electrode. Figure 2 shows the fabricated chip: (1) cell manipulation, (2) ROT Measurement, (3) cell drawing, (4) cell separation.

2.2 Controller

The control device is using 8255 (Programmable Peripheral Interface) IC and relays to switch the signal and program control. Each 8255 provides three 8-bit I/O ports. According to the requirements of biochips, the control circuit can provide more than 6 kinds of input signal source and 31 output terminals. Making choice of relays must consider their contact power capacity. High electric field may burn down the switch contact. Figure 3 shows a prototype of the control circuits.

2.3 Control Software

The communication between Computer and 8255 IC is using the LPT port. Microsoft Access is employed to design the experimental procedures. The Access database table is shown as below.

<table>
<thead>
<tr>
<th>Column</th>
<th>Step</th>
<th>Function</th>
<th>Display</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Step: Experiment Step Index</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Function: Setting etch step Signal</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Display: Experiment step name</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time: Step holding time</td>
<td></td>
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</tr>
</tbody>
</table>

We define the specific grammar to program the experimental procedure, and then calculate output data. Each experiment can be specified with different procedures and signals by editing Access database. We used Microsoft Visual C++ to write the control software. Figure 4 shows the software operation interface.

When experimenting, connect up the function generator and power supply to input terminal of control circuits in Figure 3. Take account of microscope observation limit and join the ISA Bus slot and controller with 62-pins cable. Then fix it on the
3. Application

3.1 Cell Manipulation

Cell manipulation experiment is based on DEP force, which can move a particle or an object by a spatially non-uniform electrical field [1]. DEP only arises when the object has a different tendency to become electrically polarized relative to its surroundings. The direction of DEP motion is either toward higher field (positive DEP) or lower field (negative DEP). We can manipulate cells by applying variant frequency electric field.

Besides, when cells are exposed on electric field, cell membrane will make some micro-pores. If the electric field is high enough, it will cause the infeasible mechanical breakdown [3]. Therefore, we can lysis cells by applying pulse electric field.

To demonstrate the flexibility of our platform, an example of cell separation and lysis can be achieved on the same chip. The electrode connection diagram is shown in Figure 7. Pin 1 and 29 are cell-separation electrodes, using 1 MHz and 25 V AC voltage. Pin 2–9 and 28–21 are cell-translation electrodes, using 50 kHz 20 V AC voltage. Pin 10 and 20 are cell lyses electrodes,
using 1 MHz 25 V AC voltage and DC 40 V voltage. In lysising process, 20 V 1 MHz is applied for attracting cells then use DC 40 V 5 m s pulsed to lysis cells. Lysis waveform that generated by control device is shown in Figure 8.

When experiment begins, yeast will be attracted near separation electrode by positive DEP force and fluid will wash out the other sample (polystyrene beads in this case). Then moving yeast to the lysis electrode. Finally, apply lysis waveform to lysis cells. All of above experimental procedures and signal switch settings can be programmed through Microsoft Access.

Figure 9 shows the cell separation. The target cell will be attracted on the electrode surface. Figure 10 shows the cell lysis: (1) not apply any electric field, (2) two target cells are attracting to the tip of electrode, (3) applying pulse voltage, only the cell that on the outside tip of electrode begins lysising, (4) after lysising the cells. They cannot be attracted to the electrodes using the 1MHz AC voltage. But the cell that inside the electrode or attracted on the side of electrode before pulsing can still be attracted to the electrode by 1 MHz AC field.

4. Conclusions

The universal platform we proposed can provide various requirements of developing electrokinetics-base biochips or µTAS. It can increase flexibility and reliability. When finish development of the biochip, the signal generation source such as function generator can be implemented as circuit board and integrated with control circuits. By this way the universal platform can shrink into a small volume and has advantages to become a final portable product.

References


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