A Microfluidic Device for Long Term Study of Individual Cells

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This paper presents the original design of a microfluidic device for long-term study of individual cells. This paper describes how the microfluidic device works to handle and trap a single cell in each one of multiple channels. The vascularization networks and the special compacted shape of the device render it suitable for long-term viability of cells and biological statistical study or drug screening.

At the present time there exist a lot of devices to study groups of cells, like microarray cell chips (ref.1), or more complicated systems to study a single cell, for example optical tweezers (ref.2). A fundamental need of biologists is a system allowing the study of several cells individually for statistical and rigorous studies. This kind of studies means to be able to handle individual cells, to localize them, to assure their viability, to dispense biochemical products and to perform statistical analysis.

We answer this need proposing an original microfluidic device allowing the handling and trapping of several cells individually, typically 8 cells for the first studies.

Scope and Principle

**Scope of the project:** Biologists want to study the survival and the development of multiple tobacco cells, to test biochemical products on them. For biological statistics at least 6 cells are required.

**Principle of the project:** - Handle single tobacco cells => use of fluidic design (channel, tunnels)
- Place the cells at defined spots => create settlement places fitted to the cells
- Observe the cells => compact design

**Principle of the micro-system:** - The micro-fluidic device uses the liquid flow to transport and separates the cells.
- It consists on 4 parts: 1) inlet part for cells injection;
  2) trapping sites between the 2 channels;
  3) inner channel for cells evacuation;
  4) outer channel for liquid flow.

**Procedure of the trapping:** - Star like shape of curved inlet channels (1)
  => equiprobable repartition of cells
- The cells are first guided by the inlet channel towards the trapping sites (2); if the site is vacant, the cell enter and is stopped by a pillar
- If the site is already occupied, the following cells are evacuated through the inner circular channel (3).

Results and Discussions

- The inlet of the system is connected to an automatic syringes pump. The flow of the injected solution is typically a few ml/h. The most effective concentration of cells is 1.5x10⁶/ml in culture medium.
- The trapping of cells was successfully realized on half of the sites (8 sites on 16) for both systems. It cells is enough for the biological experiments.
- The inner channel acts well as an evacuation channel, as shown by the picture extracted from a film: one cell is entering a trapping site, while an other one is evacuated from the inner channel.
- But on some parts of the system, cells tend to cork, if the flow inside the inner channel is not fast enough, or if the cells begin to attach on the surface.

Fabrication of the micro-system

The device has been fabricated using 2 micro-machining technique, in order to test the efficiency according to the material used and to try to resolve some problems like bubbles, cells cork...

- Replica micro-molding with SU8 mold and PDMS:
- Deep-RIE etching of silicon:

Conclusions

We proposed a microfluidic device to answer the lack of tools for long-term study of single cells. The microfluidic principle involved in this device, demonstrated with vegetal cells, is easily adaptable for every type of cells and allows the handling and trapping of several single cells.

Two types of systems were realized in two different materials: PDMS and silicon, in order to test the efficiency according to the material used and to try to resolve some problems like bubbles, cells cork...

The trapping of cells was successfully obtained for both system, with the same rate (50% success), which is enough for our study. The problem of bubbles was resolved by filling the system with ethanol before introducing the cells solution. Because of its lower viscosity compared to water, ethanol removes very easily the bubbles. However still some problems of corks of cells remain. The control of liquid flow inside the channels has to be improved.

Biological studies and device optimisations are under progress.