

HIGH YIELD CELL FUSION CHIP VIA HYDRODYNAMIC APPROACH AND 3D LIQUID METAL ELECTRODES

Hung-Po Chen¹, Kuo-Wei Chang¹, Shih-Mo Yang², Jen-Pin Chen¹, Ciou-Wen Lin¹, Shilpa Sivashankar¹, Srinivasu Valagerahally Puttaswamy¹, Yen-Ta Lu³, Cheng-Hsien Liu¹

¹ Department of Power Mechanical Engineering, National Tsing-Hua University,

² Department of Electrophysics, National Chiao Tung University,

³ Department of Medical Research, Mackay Memorial Hospital, Taiwan, R.O.C.

ABSTRACT

We report a 3D microfluidic chip for cell fusion which utilizes hydrodynamic force for trapping the cells followed by fusion with the aid of electrokinetic phenomena via 3D liquid metal electrodes. This two layer microchannel design gives high cell fusion yield with higher efficiency without any cell damage.

KEYWORDS

Cell fusion, 3D microfluidic chip, 3D liquid metal electrodes

INTRODUCTION

Cell-cell interaction is a major part of research due to its importance in many biological processes like hybridoma engineering, cancer immunotherapy, and genetic information. Recently it has been possible to manipulate the microparticles by means of optics, electricity, magnetic force, and hydrodynamic force [1, 2]. However, most of these devices have a complex process for this purpose [3]. In this article, our designed cells fusion chip would trap and pair cells in series of locations. Beside, a liquid metal material is firstly integrated and applied in cell fusion application. Finally, the results of cell fusion morphology provide the evidence of our cell fusion concept.

EXPERIMENT

As shown in Fig. 1, the upper channel comprises of cell trapping locations and is placed just above the bottom channel which gives a structural advantage for trapping the cells by using the dragging force from the bottom channel.

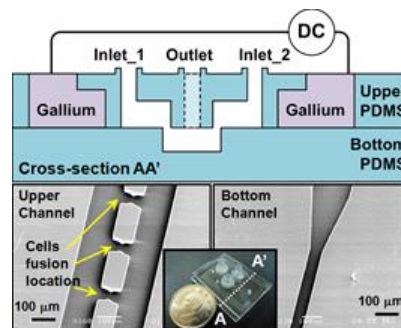


Figure 1: Cross-sectional view of the cell fusion chip with liquid metal electrodes and the SEM images of the top and bottom channel.

As shown in Fig. 2, the Gallium-based liquid metal electrodes are fully filled in the microchannels adjacent to the top channel used for trapping the cells. The three dimensional liquid metal electrodes induce uniform DC electric field through the thin PDMS wall to induce electrofusion necessary for pairing of A549 lung cancer cells.

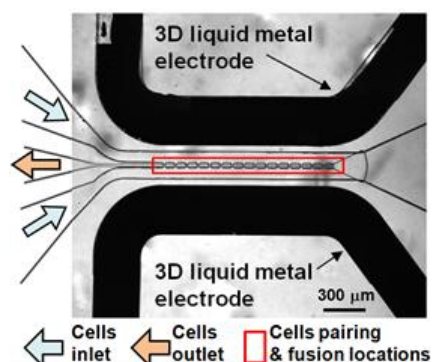


Figure 2: Top view of the cell fusion chip. Metal electrode, Gallium, fully filled in the 50 μ m height microchannel provides a 3D uniform DC electric field for cell fusion.

An equivalent electric circuit model with the correlations of flow pressure to the voltage, flow rate to the electric current and hydraulic to the electric resistance is used to illustrate the phenomenon of trapping and pairing of microparticles as shown in Fig.3. When A549 lung cancer cells injected from the inlets and withdrawing force is applied from the outlet in the bottom channel, the cells get trapped at the location, node A, because the flow resistance of the path from inlets to the location, node A, is the lowest. When the location, node A, in the top microchannel gets blocked, the path of shortest flow resistance shifts to next immediate location, node B, and the cells get trapped at this location and so on.

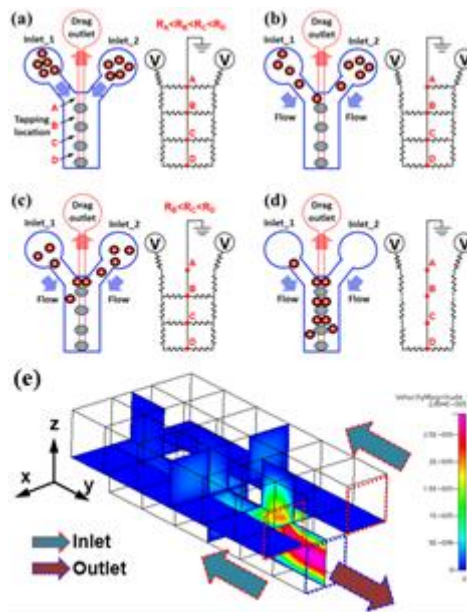


Figure 3(a)-(d) An equivalent electric circuit model of the microfluidic system in sequential steps and (e) Schematic diagram illustrating the simulation of 3D microfluidic structure.

The cells get trapped sequentially as shown in Fig. 4, the polystyrene beads, 50 μ m diameter, get trapped sequentially in the array of trapping locations.

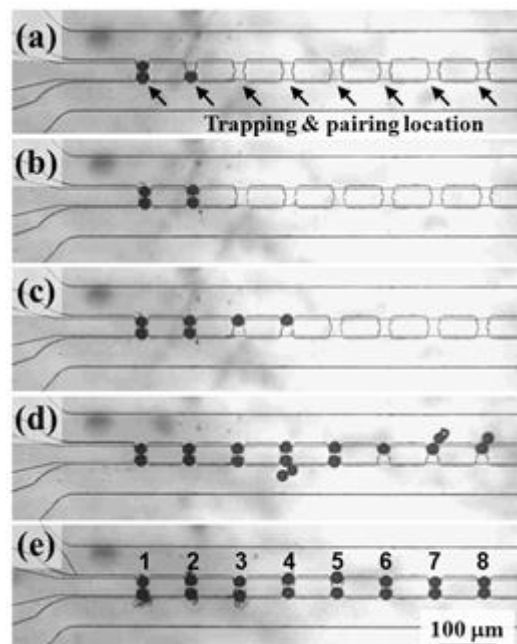


Figure 4: Top view of the two-layer channel demonstrating the high efficient trapping and pairing process of 50 μ m diameter microparticles via hydrodynamic force.

As shown in Figure 5, A549 lung cancer cells are trapped and paired in a series of cell fusion locations which have minimum flow resistance. There are twelve paired cell groups filling fifteen trapping locations.

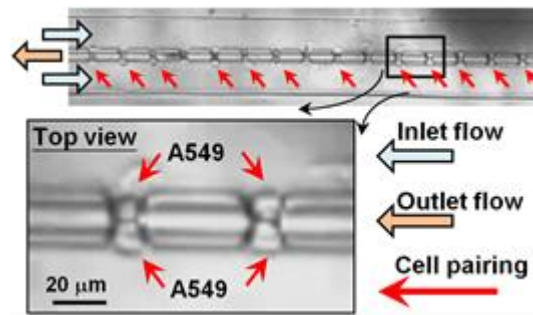


Figure 5: Paired cells of A549 lung cancer cells in each locations of two-layer microchannel. The cells suspended in liquid flow are trapped and paired efficiently via hydrodynamic force. The liquid flow also enhances cell-cell contact and increases fusion phenomenon.

After applying an external DC signal on the 3D liquid metal electrodes, it provides enough electric field through thin PDMS wall to perforate the cell membrane and fuse the two cells as shown in Fig. 6.

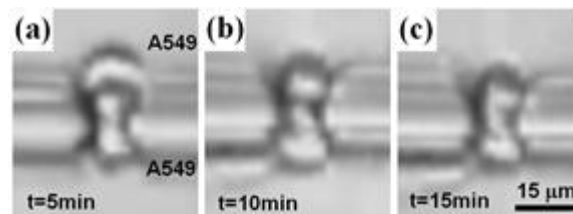


Figure 6. (a)~(c) The sequent morphology change of A549 lung cancer cells which are paired and fused in the trapping location via DC electric field of liquid metal electrodes. (c) At $t=15\text{min}$ the fused cells show only one cell membrane.

CONCLUSION

We were successful in designing a high yield cell fusion chip with 80% efficiency which utilizes hydrodynamic force for trapping the cells in two-layer microchannels. Furthermore, a 3D liquid metal electrode, Gallium, was firstly integrated to exert uniform DC field on the paired cells to allow its fusion in our microfluidic design

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CONTACT

* Hung-Po Chen, tel: +1-886-911-359-155; amidoufu@hotmail.com