Efficient chip architectures for a microfluidic cell sorter actuated by electrowetting and its electro-hydrodynamic analysis

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Abstract – We present the design and development of sorter architectures in conjunction with corresponding intelligent physical sorting algorithms for a chip-based microfluidic cell sorter actuated by the electrowetting on dielectric (EWOD) mechanism [1,8]. This microfluidic chip realizes an implementation of FACS (fluorescence activated cell sorting) [2], which operates on EWOD-manipulated droplets containing cells to be sorted.

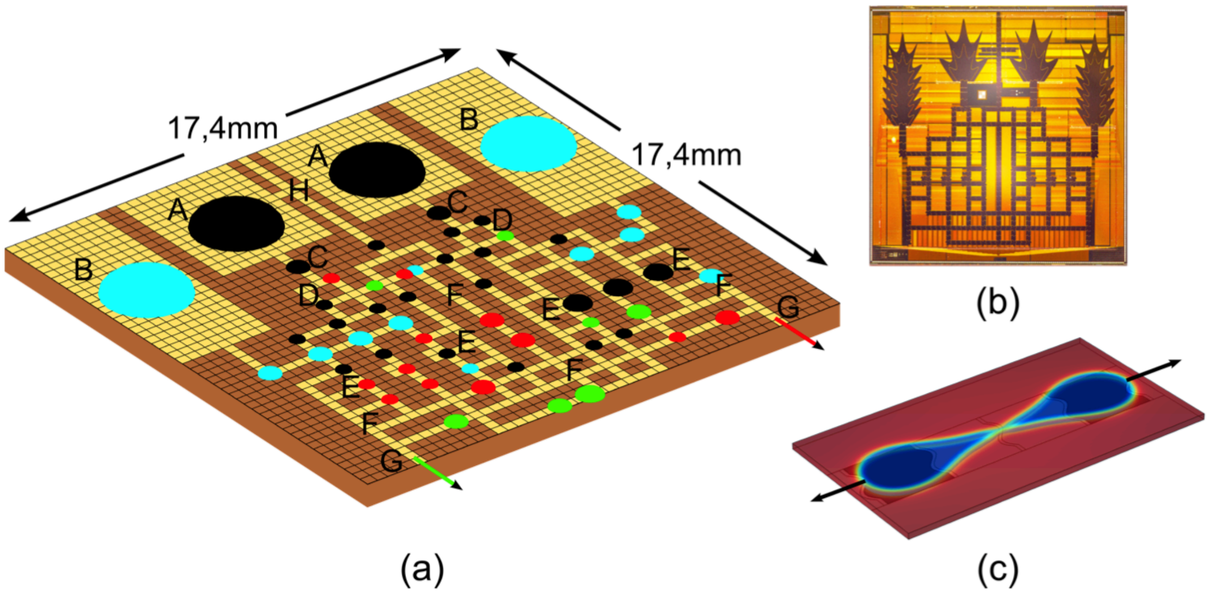

Fig.1: (a) Snapshot from simulation of «2-3-Sequential-Divider-Sorter» with cell suspension reservoirs «A», buffer solution reservoirs «B», droplets generation «C», droplets division in two parts «D», droplets mixing and division in three parts «E», logistic network for droplets removal «F», outputs for sorted droplets «G» and feedback of unsorted droplets to the reservoirs «H». Color codes: black - unsorted suspension resp. droplets; blue - pure buffer solution resp. droplets; green - sorted droplets with requested cells; red - sorted droplets with residual cells. (b) The produced microfluidic chip based on the «2-3-Sequential-Divider-Sorter». The sorter is realized on a 20 x 20 mm² multi-layer chip system – with 456 EWOD electrodes – in standard CMOS technology. (c) Snapshot from CFD simulation of the division of 11,4 nl droplet on four EWOD-electrodes (350 x 350 µm²) in the chip channel, which is filled with the silicone oil.

This novel cell chip-sorter is intended for the cytometric analysis as well as for the study of specific cell mechanisms in the research on tumor genesis such as e.g. inter alia, the development of leukemias or lymphomas. The development of the microfluidic electrowetting chip has been carried out in the framework of the EU founded (EFRE) joint research project «MINAPSO» (Mikrochip-Navigierte Parallel-Sortieranlage) [3].

The hereby produced sorter topology consists of an optimized so-called «2-3-Sequential-Divider-Sorter» with a numerically estimated throughput of sorted cells between 0,6 and 1,85 cells/clock (in consideration of the constraints of the underlying fabrication technology) [4]. The sorter is implemented on a 20 x 20 mm² multi-layer chip system (glass, ITO, teflon, tantalum pentoxide, silicon), combining standard CMOS-technologies and the corresponding microfluidic packaging [5]. Future cell sorter topologies such as the most recently developed so-called «Smart-Diffusion-Sorter» achieve even higher cell throughputs of up to 5 cells/clock [6].

For the design and optimization of the cell sorters – namely chip architectures including sorting algorithms – a simulation platform has been developed using MATLAB. With an implemented stochastic model this platform allows a time- and spatial-discrete simulation of the EWOD-manipulated cell carrying droplets on the chip area. In order to estimate the characteristic time constants resp. the dynamic behavior of the specific EWOD-based droplet operators (such as transport, division, mixing) as well as their impact on the cell throughput of the designed sorters extensive computational fluid dynamics simulations (CFD) have been performed using COMSOL Multiphysics [7,8]. These CFD simulations are also valuable in the quest for the identification of the hidden optimization potential of the realized multi-layer chip.

Inspired by the electrowetting phenomenon, our present research focuses on the so-called effect of contact angle saturation in EWOD, which is still not well understood and the corresponding debate is open. In contrast to different microscopic explanations we investigated analytically this effect on the microscopic scale using the Maxwell stress tensor e.g. to estimate the acting forces in a singular triple junction formed by the 3 adjacent media in the droplet’s contact geometry. Thus it was found that contact angle saturation of the electrically manipulated droplet emerge as a macroscopic feature of purely geometrical nature. This very surprising result is now subject of further scrutiny.

References

[1] S. K. Cho, H. Moon and C.-J. Kim, "Creating, transporting, cutting, and merging liquid droplets by electrowetting-based actuation for digital microfluidic circuits", *Journal of Microelectromechanical Systems*, vol. 12, no. 1, pp. 70-80, Feb. 2003.

[2] G. Rothe, "Technische und methodische Grundlagen der Durchflusszytometrie", in *Zelluläre Diagnostik: Grundlagen, Methoden und Klinische Anwendungen der Durchflusszytometrie*, pp. 27-70, Basel: Karger Verlag, 2006.

[3] MINAPSO (Mikrochip-Navigierte Parallel-Sortieranlage) ist ein Verbundprojekt der Universität Duisburg-Essen, dem Fraunhofer IMS und der Firma Bartels Mikrotechnik GmbH, Dortmund, welche durch die EU (EFRE) über das *Ziel-2-Programm* des Ministeriums für Wirtschaft, Energie, Industrie, Mittelstand und Handwerk des Landes Nordrhein-Westfalen im Rahmen des Innovationswettbewerbs *NanoMikro+WerkstoffePhotonik.NRW* gefördert wird.

[4] F. Schreiber, A. Rennings and D. Erni, "Optimierung von Chip-Architekturen effizienter Zellsorter basierend auf dem Elektrowetting-Verfahren", *4. Mikrosystemtechnik-Kongress 2013 (MST 2013)*, VDE und Bundesministerium für Bildung und Forschung (BMBF), Oct. 14-16, Eurogress, Aachen, Germany, paper 1.21, pp. 413-416, 2013.

[5] S. Kahnert, F. Schreiber, A. Goehlich, D. Erni, D. Greifendorf, K. Lennartz, U. Kirstein, F. Bartels, U. Janzyk, A. Rennings, R. Küppers, and H. Vogt, "Entwicklung einer Mikrochip navigierten Zellsortieranlage," *6. Mikrosystemtechnik-Kongress 2015 (MST 2015),* VDE, and Bundesministerium für Bildung und Forschung (BMBF), Oct. 26-28, Stadthalle Karlsruhe, Karlsruhe, paper 3.6, Germany, 2015.

[6] F. Schreiber, S. Kahnert, A. Goehlich, D. Greifendorf, F. Bartels, U. Michelsen, K. Lennartz, U. Kirstein, A. Rennings, R. Küppers and D. Erni, "An efficient on-chip electrowetting cell sorter architecture based on smart diffusion", *Microfluidics 2014*, EMBL Conference, July 23-25, EMBL Heidelberg, Germany, paper 133, pp. 155, 2014.

[7] F. Schreiber, S. Kahnert, A. Goehlich, D. Greifendorf, F. Bartels, U. Janzyk, K. Lennartz, U. Kirstein, A. Rennings, R. Küppers and D. Erni, "Mikrofluidik-Chip-Architekturen für eine Zell-Sortieranlage basierend auf der Elektrowetting-Technologie", *IEEE Workshop Medizinische Messtechnik 2015*, Instrumentation and Measurement Chapter IEEE Germany Section, April 17, University of Applied Sciences Ruhr-West (HRW), Muelheim an der Ruhr, Germany, 2015.

[8] F. Schreiber, S. Kahnert, A. Goehlich, D. Greifendorf, F. Bartels, U. Janzyk, K. Lennartz, U. Kirstein, A. Rennings, R. Küppers, and D. Erni, "Mikrofluidik-Chip-Architekturen für eine Zell-Sortieranlage basierend auf der Elektrowetting-Technologie," *tm – Technisches Messen*, (to appear in the May issue), 2016.