On-chip Flow Cell Sorting System Based on High frequency Dielectrophoresis implemented on CMOS technology

R. Manczak[a], S. Saada[b], F. Hjeij[a], C. Dalmay[a], F. Lalloue[b], Mehmet Kaynak[c], A. Pothier[a]
[a] *XLIM &* [b]*EA3842 Université de Limoges, Limoges, France*
[c]*IHP microelectronic, Franckfurt Oder, Germany*

Key words: dielectrophoresis, microfluidic, cell sorting, CMOS technology

1. Introduction

Isolation and characterization of Cancer Stem Cells (CSCs) is of prime important in the development of new therapeutic treatments, especially in brain cancers. Such cells present strong therapeutic resistance and are responsible for cancer recurrence [1]. The large cell heterogeneity in tumors makes identification of such cells very huge and lead to the development of alternative analysis technics. In this context, microfluidic cell sorter based on dielectrophoresis (DEP) technics have already demonstrated capabilities in the 10 kHz to 1 MHz frequency range [2]. Increasing operating frequencies, i.e. 100 MHz to 1 GHz (Ultra High Frequency band UHF) is very interesting as intracellular properties dominate the cell response [3]. This paper presents an innovating on-chip UHF DEP cell sorting system, implemented on CMOS chip coupled to microfluidics technologies enabling integration of additional capabilities with the expected frequency range and flexibility.

2. Design and Simulation of the cell sorting system

The developed cell sorter is presented in Fig. 1(a). An array of 16 electrodes are implemented on passive layers of a CMOS chip. Opposite electrodes are biased with a high frequency signal generator whereas the overs are grounded to generate an appropriate electric field gradient. Hence, particles which experience positive DEP are attract near the edge of electrodes (high intensity areas) whereas in negative DEP, particles are repealed at the center of the channel (low intensity areas).

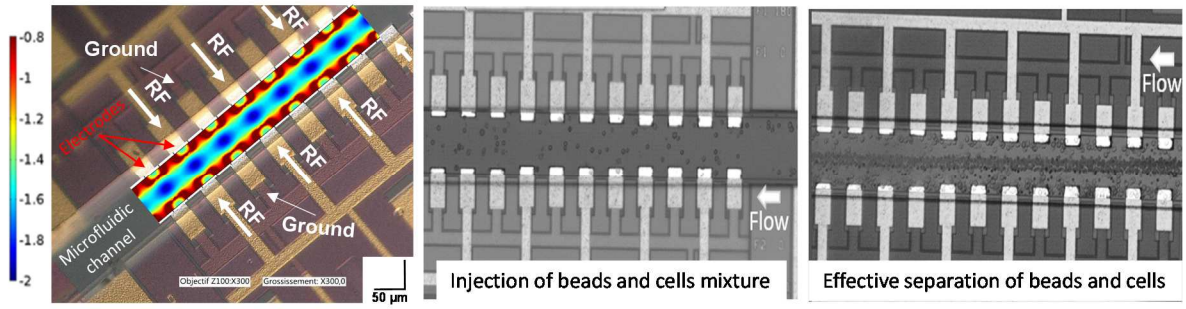

Figure 1: Photograph of the developed UHF DEP cell sorter implemented on CMOS technology with a plot of the normalized electric field (log scale) under an applied signal of 3V at 300 MHz – Photograph of the device with a mixture of LN18 cells and beads injected in the channel (b) – Photograph of the device under a 50 MHz signal applied (c).

3. Experimental Results

In order to find the appropriate working frequency to sort cells, LN18 line cells cultured with standard medium (cell line derived from malignant gliomas adult patients) have been characterized using UHF DEP characterization to determine their second cross over frequency (when the transition between positive and negative DEP occurs) around 116 MHz [3]. Then a mixture of polystyrene beads and LN18 cells are injected in the cell sorter (Fig.1(b)). Polystyrene beads exhibit negative DEP whatever the frequency range. Working at 50 MHz, lower than the cross over frequency of LN18 cells, one can see that polystyrene beads are concentrated at the center of the channel, whereas cells are located near the edges of electrodes (Fig.1(c)).

4. Conclusion

This paper demonstrates the feasibility of implemented a new type of cell sorter based on UHF DEP on CMOS technology allowing to envision to integrate power sources and active readout circuitry on chip.

References

[1] H.M. Jeon, S.H. Kim, X. Jin, J.B. Park, S.H. Kim, "Crosstalk between Glioma-Initating Cells and Endothelial Cells Drives Tumor Progression", Cancer Research, 74, 16, pp. 4482-4492 (2014).
[2] A. Valero, T. Braschler, T. Renaud, "A Miniaturized Continuous Dielectrophoretic Cell Sorter and Its Applications", Biomicrofluidics, 4, 2 (2010).
[3] F. Hjeij, C. Dalmay, B. Bessette, G. Begaud, *et al.,* "Biological Cell Discrimination Based on Their High Frequency Dielectrophoretic Signatures at UHF Frequencies", IEEE MTT-S Microwave Symposium (2017).