

# A Modular Platform for Cell Characterization, Handling and Sorting by Dielectrophoresis

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## Introduction

The physical manipulation of biological cells is of vital importance in the development of miniaturized systems for biological analysis. Precise cell handling is fundamental in microcytometry and cell counting applications; cell manipulation and sorting is also essential in lab-on-chip devices for molecular diagnostics applications, as it represents the preliminary stage of sample preparation, interfacing the clinical sample to the molecular domain.

Dielectrophoresis (DEP) has been reported as a promising method for cell manipulation without physical contact in lab-on-chip devices, as it exploits the dielectric properties of cells suspended in a microfluidic sample, under the action of high-gradient electric fields. The dielectrophoretic platform that has been developed offers an integrated solution for a variety of applications, customizable for specific user needs. It is composed of several functional units, organized in a first characterization module and in a series of manipulation stages that can be rearranged on a single chip, depending on the target application (Figure 1).

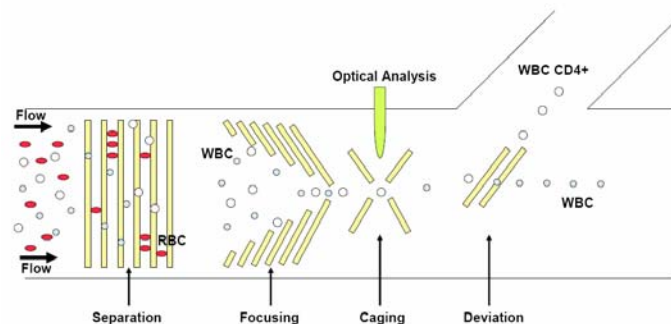


Figure 1. Schematic top view of the microchannel, showing a combination of the developed modules designed to perform a first separation between red blood cells and white blood cells, followed by the sorting of a selected white blood cells subpopulation.

## Use of COMSOL Multiphysics

The non-uniform electric fields for cell manipulation are generated by microelectrodes patterned on the silicon substrates of microfluidic channels using fabrication techniques borrowed from micro-electro-mechanical-systems (MEMS) technology. Numerical modelling has been performed using COMSOL Multiphysics to simulate the quasi-static electric field distribution and to quantify the consequent pico-Newton DEP forces acting at the cell microscale (Figure 2). Suspended cells have been modelled using both a general point-dipole approximation and a more specific 3D geometrical model, considering the dielectric properties of each cell compartment: the cytosol, the membrane and the wall, if present. Parametrical modelling has been performed in order to optimize the geometry of each functional microelectrode module (Figure 3).

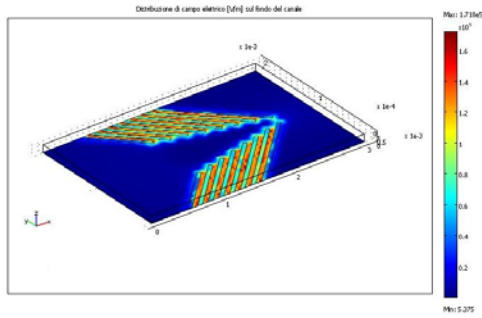


Figure 2. Electric field distribution in the focusing stage, for the alignment of the cells along the axis of the microchannel.

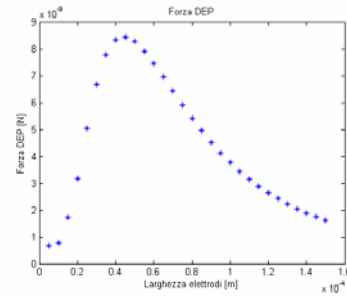


Figure 3. Parametrical modelling maximizing the DEP force acting in the multi-bar array module as function of the electrodes width.

## Results

From the measured translational and rotational velocity of cells in the subunits of the characterization stage, cell permittivity and conductivity can be determined as functions of frequency. The knowledge of the dielectric properties of different cell types is essential for the design of the electric excitation in order to obtain the desired effect in the handling or sorting modules.

The manipulation modules achieve several functionalities: the multi-bar array module can be used as a selective cell filter (Figure 4), or as a cell conveyor stage, depending on the phase shift between consecutive electrodes excitation; the focusing stage allows the alignment of a cell population along the axis of the microfluidic channel (Figure 5), where a caging module can trap cells for a subsequent in-situ fluorescence analysis of labelled membrane proteins; the deviation stage can be activated to move only selected cells in a dedicated microfluidic outlet; the spiral array module acts as a selective cell concentrator, allowing the direct observation of filtered cells at the center of the configuration.

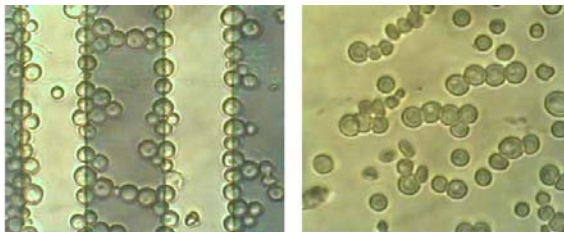


Figure 4. The multi-bar array filter traps *Saccharomyces Cerevisiae* yeast cells at the electrode edges (left side), while Sheep Red Blood (SRB) cells are levitated and transported by the fluid flow (right side). Image at 50x magnification.

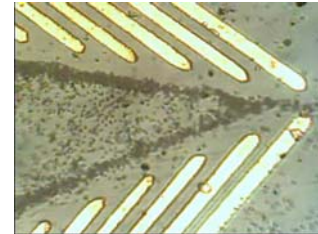


Figure 5. Focusing of *Saccharomyces Cerevisiae* yeast cells along the axis of the microfluidic channel. Image at 10x magnification.

## Conclusion

The functioning of the electrode configurations in the characterization module and in the series of manipulation stages has been demonstrated with different cells types. The experimental results and those from modelling are in close agreement. The dielectrophoretic platform represents a complete solution, allowing the dielectric characterization of the cell types of interest and their manipulation in applications in which cell handling and sorting are needed.