Bottom-up assembly of cells in flow with dielectrophoresis

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Key words: Cell trapping, Dielectrophoresis, Microfluidics, Bottom-up assembly

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Electrochemotherapy (ECT) consists in using electric fields to enhance the delivery of chemotherapeutic agents directly into cancer cells. However, the full development of this therapeutic approach requires a proper understanding of electric field impact on biological tissues. While in vitro studies performed on isolated cells provide useful information on how field pulses induce biological membrane permeabilization, more realistic 3D in vitro models are required to mimic the behavior of cells in a tumor or a tissue. Multicellular constructs can be used as simple models of tumor microregions for optimization of electropulsation protocols.

We present a microfluidic platform allowing dielectrophoresis-assisted formation of cell aggregates of controlled size and composition under flow. When specific experimental conditions are met (medium composition, electric field intensity and frequency), negative dielectrophoresis (nDEP) allows efficient concentration of cells towards electric field minima and subsequent aggregation. This bottom-up assembly strategy offers several advantages with respect to the targeted application: first, DEP offers precise control of cell spatial organization, which can be adjusted by optimizing electrode design. Then, rapid establishment of cell-cell interactions is allowed thanks to dipole-dipole attraction forces between neighboring cells.

The trapping geometry of our chip is composed of 8 electrodes disposed in a circle. Several parameters have been tested in simulations to find the best configurations for trapping in flow. Those configurations have been tested experimentally with both polystyrene beads and HEK cells. Figure 1 illustrates the trapping of HEK cells under flow to create a small aggregate using 3 electrodes.

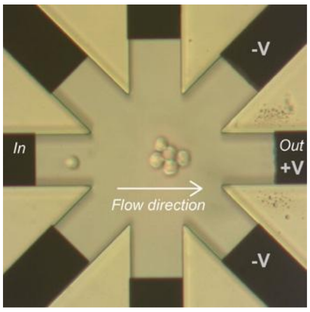

Figure 1: Trapping of HEK cells under flow.

This study demonstrates the potential of using planar electrodes and dielectrophoresis to create cell aggregates under flow. The created aggregates can be further studied with impedance spectroscopy or electrorotation and electropermeabilized using other electrodes. Both homogeneous and composite aggregates can be generated using this approach.