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AC Electrodynamics-Based and Label Free Discrimination

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Description

Cell characterization and manipulation are critical in biological and medical applications. Cells own important information about biological processes and environmental conditions. Cells of the same genotype in different pathological and physiological states own unique structural and morphological features. Discriminating or sorting a cell kind from a cell mixture is crucial for early stage disease diagnosis. Cell viability evaluation is of significant importance for cell toxicology assay, dose test of anticancer drugs, and other biochemical stimulations. Microfluidic chips own significant advantages including high efficiency, low cost, and easy to implement, compared to other macroscopic approaches. Various methods have been developed to analyze and discriminate cells based on a microfluidic platform, including centrifugation, filtration, chromatography, magnetic, electric, optical, and acoustic methods. Mechanical contact methods may cause a high risk of injuring cell membranes and affecting cell viability and optical methods with high optical intensities show a tendency to kill cells or bring optical damage. To mitigate side effects on cell viability, electric method has been widely exploited in microfluidics for a variety of biomedical applications among these methods. Dielectrophoresis (DEP) is the motion imparted on polarized cells subjected to a non-uniform electric field and electrorotation (ROT) occurs due to rotational torque exerted on polarized cells under a rotating electric field. These two effects relied on the relative conductive and dielectric properties of cells and the surrounding medium. DEP based devices can allow antibody independent discrimination of cells and avoid leukocyte contamination *via* the integrated evaluation of both size and dielectric properties of each cell type. ROT measures rotation speed of single cell when applying a rotational electric field and cells can be discriminated based on the cellular rotation rates. In contrast with size and antibody-based methods, these properties depend on the composition and morphology of the bioparticles and are a much specific differentiator of phenotype. DEP can be used as a unique and label-free method for manipulation and discrimination of cells without destructive consequences to the cell and several studies have demonstrated the effectiveness of DEP, since it owns excellent advantages in terms of cost, efficiency, analysis time, and sensitivity.

Based on the polynomial electrode design, the DEP and ROT frequency spectra of single cells can be measured. The electrical properties of cells change when cells transform from healthy to a pathological state. Mohktar et al., differentiated apoptotic cells from viable cells by DEP using a hollow centered circular geometry. But this chip was made up of 5 layers and the fabrication process is complex. To extend the effective DEP regions, Li et al., embedded two electrode pads in a set of asymmetric orifices on the sidewalls for investigating the DEP behaviors of yeast cells. Numerous DEP devices with 3D electrodes using double planar electrodes or electroplated gold sidewall electrodes have been exploited to characterize and manipulate cells, but these platforms are usually fabricated from glass or silicon which are subject to significant complications in the assembly process to prevent sample leakage. Yafouz et al., reported a microarray dot electrode system to discriminate between normal and dengue infected human hepatic fetal epithelial cells based on their DEP responses. Each dot electrode owns inner and out diameters and the dot electrodes are energized individually, which requires multiple connecting wires for these dot electrodes, limiting the throughput. Kim et al. developed a high density electrode array for single cell resolution measurement by incorporating with a complementary metal oxide semiconductor integrated chip. By using the impedance monitoring circuit, rapid and auto-mated single-cell detection was demonstrated using living cells of the MCF7 line. However, it contains three layers with requiring a CMOS integrated circuit and the fabrication process of this biosensor is complicated.

Bipolar Electrode (BPE) is a conductor in an ionically conductive media under an electric field which can facilitate reduction and oxidation reactions at opposite ends. BPEs have been widely used for cell trapping, electrochemical reaction, fluid mixing, showing a great potential in scalability in cell manipulations. Herein, we propose a high-throughput AC electrodynamics device for cell characterization and viability evaluation by exploiting a wireless BPE array which is scalable and easy to integrate. This work aims to discriminate the apoptotic cells from viable cells using a bipolar electrode array under a rotating electric field. The discrimination of viable and nonviable cells including yeast cells and K562 cells, was carried out by analyzing the electro-rotation speed and direction of cells, as well as the DEP responses of cells. The use of BPEs eliminates the requirement of ohmic contact to each electrode and owns benefits such as convenience and flexibility in platform design, facilitating high-throughput manipulation and analysis of cells that is unattainable by conventional ways. This work offers a new method to cell characterization and viability evaluation in various biomedical fields.

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