MICROFLUIDIC DIELECTRIC SPECTROSCOPY CYTOMETER: MODELLING AND OPTIMIZATION

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Introduction

Dielectric spectroscopy is a non-invasive method suitable for the characterization of living biological cells (e.g., analysis of normal and malignant white blood cells [Ermolina, 2001], or morphological inspection of erythrocytes [Asami, 2008]).

Nowadays, thanks to microfabrication techniques, it is possible to perform single-cell dielectric spectroscopy by means of microfluidic cytometers [Gawad, 2004; Morgan, 2007].

Figure 1(a) shows the schematic representation of a state-of-the-art microfluidic cytometer: ac signals applied to the top microelectrodes generate an electric field in the microchannel; when a cell passes thorough the device, an impedance variation is measured which depends on the specific cell characteristics (size, morphology and dielectric properties).

In this work an innovative design for the microfluidic cytometer is proposed by exploiting the basic principle of Electrical Impedance Tomography (EIT) [Bayford, 2006]: instead of just two pairs of opposite electrodes, two arrays of electrodes are conceived (Figure 1(b)), allowing a greater versatility in the stimulation pattern. In particular, rotating spatially-harmonic distributions of electric current can be applied at the device surface, thus enabling a thorough testing of the dielectric cell response.

Methods

The ability of the proposed device to detect cell structure and morphology is investigated by means of mathematical modelling and computer simulation. Both red blood cells of different morphology (normal erythrocytes, echinocytes, spherocytes) and cells with nucleus (e.g., white blood cells) are considered. Cell membranes are modelled as two-dimensional interfaces exhibiting a capacitive behaviour [Bisegna, 2008].

Several stimulation current patterns in the radiofrequency range are implemented as Neumann boundary condition, and the resulting surface voltage distribution is computed. The finite element method is employed, in order to take into account the complex geometrical and structural features of different cell types. Numerical computations are performed with COMSOL Multiphysics™.

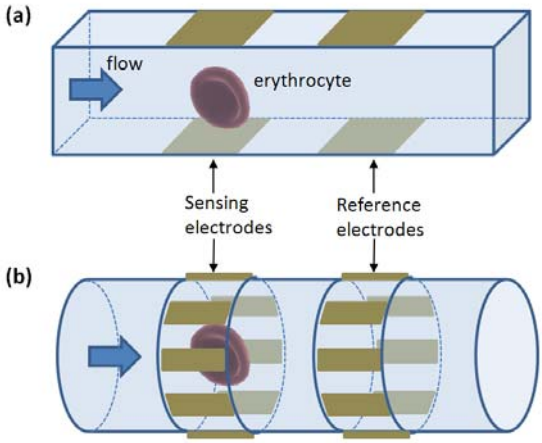

Figure 1 Schematic representation of: (a) classic microfluidic cytometer and (b) proposed device.

Results and discussion

The various stimulation patterns applied to each cell yield an ensemble of impedance spectra. Simulation results show that such an ensemble strongly depends on cell features, as dielectric properties, size, shape, nuclear-cytoplasmic ratio, and thus it constitutes a sort of cell fingerprint. As a consequence, the experimental measurement of that ensemble allows to reliably recover quantitative information on the above significant cell properties, by using reconstruction algorithms developed for EIT. The proposed design, enabling several stimulation patterns, is therefore outperforming with respect to the classic system, with very limited stimulation capability.

Future research will be devoted to the electronic design of the device and to the implementation and optimization of reconstruction algorithms. A further improvement will be obtained by substituting each strip electrode in Figure 1(b) with an array of point electrodes, thus enhancing the axial resolution.

References

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