Microfluidic Sensor for Noncontact Detection of Cell Flow in a Microchannel

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Abstract

A microfluidic sensor for detection of cells flowing in a microchannel is presented. The sensor consists of a PDMS (PolyDiMethylSiloxane) layer with two planar microreservoirs connected by a microchannel. The bottom sides of the microreservoirs are faced to two sensing electrodes realized on a PCB (Printed Circuit Board). A noncontact measurement is ensured by an insulator layer between the electrodes and the fluid. Particles flowing in the microchannel cause changes in the conductivity of the narrow path formed by the fluid, producing variations in the impedance between the electrodes. A tailored electronic interface based on a DDS (Direct Digital Synthesis) device is proposed to measure the impedance variations. In the experimental tests, the cell flow is detected by changes in the effective capacitance and conductance between electrodes. These preliminary results are promising for biological measurements such as counting and sizing of cells in different matrices.

Keywords: microfluidic sensor; impedance sensing; cell flow detection; cell counting;

1. Introduction

Characterization and counting of cells in biological samples is a relevant task in an increasing number of research activities such as in bio-medical, food, agriculture and environmental fields. Beside the application of conventional microbiological and biochemical techniques, often time consuming and
expensive, cells detection can also be carried out by means of physical methods; for instance, cells can be
seen as flow discontinuities with respect to a support fluid in which they are transported. Among the
various techniques, cell analyses based on impedance measurements have been widely used in systems
involving microfluidic devices [1].

In this work a microfluidic sensor for the detection of cells flowing in a microchannel is presented. The
sensor consists of a PDMS (PolyDiMethylSiloxane) layer with two microreservoirs connected by a
microchannel and sensing electrodes realized on a PCB (Printed Circuit Board). A noncontact
measurement is ensured by an insulator layer, placed between the electrodes and the fluid, in order to
avoid the galvanic contact. The insulator layer allows to avoid the issues associated to double-layer
capacitances [2] and degradation of electrodes, offering advantages in terms of measurement repeatability
and lifetime of the device. The sensor has been connected to a tailored electronic interface to measure the
impedance variations between the electrodes. The ability of the sensor to detect the flow of cells has been
tested by streaming cell suspensions in the microchannel and comparing the changes in the measured
impedance variations with evidence of visual observation.

2. Microfluidic sensor

2.1. Sensor description

The device is fabricated by means of a hybrid low-cost technique, by combining the PDMS soft
lithography and the PCB milling. As shown in Figs. 1a and 1b, a rectangular microchannel with
100 μm x 50 μm cross section and 1 mm length is used as the connection of two microreservoirs obtained
in a PDMS layer. The bottom sides of the microreservoirs are respectively faced to two electrode plates
realized on a PCB, and the joining microchannel is placed across a slit in the PCB. An insulator layer is
placed between the fluid and the electrodes in order to avoid galvanic contact. Pictures of the device and
the microchannel are shown in Fig. 1c.

The suspending medium containing the cells is injected into one of the microreservoirs, flowed
through the microchannel, and finally ejected from the other microreservoir. By this way the complete
system composed by the microchannel and microreservoirs is filled with the suspending medium and the
cells flow through the microchannel.

![Fig. 1.](image-url)

Fig. 1. (a) Device 3D sketch; (b) sensor layout: top view and magnification of the microchannel region with transversal and axial
cross sections; (c) picture of the PDMS layer on the PCB and microscope pictures of the microchannel top view and cross-section.
The flowing cells cause changes in the conductivity of the narrow path formed by the fluid in the microchannel, causing variations in the impedance between the sensing electrodes. By this way, a Coulter counter configuration is obtained, yet exploiting a contactless detection technique [3-4].

2.2. Electronic interface

The electrodes on the sensor are connected to a tailored electronic interface in order to measure the impedance variations. As shown in Fig. 2, the electronic interface is based on a high sensitivity transimpedance amplifier and a DDS (Direct Digital Synthesis) device [5]. The DDS device is used to generate the excitation signal and two reference in-phase and quadrature signals with respect to the excitation signal, for the demodulation. A configuration of the transimpedance amplifier based on a T-network of capacitors, which exhibits an effective feedback capacitance \( C_{Eq} \approx 1 \) pF, is used. By an in-phase and quadrature demodulation of the transimpedance amplifier output signal, the impedance variations can be detected in two output DC signals, \( V_{M,f} \) and \( V_{M,q} \), proportional to the effective capacitance variations and effective conductance variations, respectively.

3. Experimental results

In the experimental tests a DMEM (Dulbecco’s Modified Eagle Medium) solution containing mammal fibroblasts has been flowed into the microchannel between the two microreservoirs. Mammal fibroblasts are connective tissue cells; the size of the employed cells ranges from about 10 to 20 \( \mu \)m diameter. In the experimental procedures, a flow-rate of 5 nL/s has been realized by using a syringe pump; this corresponds to a flow velocity in the microchannel of about 1 cm/s. Since both the plastic layer and the PDMS are transparent, the flow rate in the microchannel can be visually observed by a microscope through the slit in the PCB. By this way, the flow of cells can be detected by the sensor and compared with the visual observations as a reference.

Based on the results obtained from a modeling of the electrical behavior of the adopted cells [1] in the suspending medium, the electronic interface has been set to operate at an appropriate excitation frequency \( f_p = 400 \) kHz and with capacitance and conductance sensitivities of \( \frac{\partial V_{M,f}}{\partial C} \approx 0.3 \) V/fF and \( \frac{\partial V_{M,q}}{\partial G} \approx 0.1 \) V/nS, respectively. As shown in Figs. 3a and 3b, the system detects the flow of both clusters and single cells with variations in the signals associated to the effective capacitance and conductance between electrodes.

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Fig. 2. Block diagram of the electronic interface connected to the microfluidic sensor.
The flow of the cell cluster is detected with spikes on the output signals, well beyond the noise level. Variations of the effective capacitance and conductance of about 0.9 fF and 1 nS, respectively, have been obtained for a cluster of 5-6 cells with an average diameter of 15 μm each. On the other hand, the flow of a single cell with a diameter of about 20 μm generates spikes, slightly higher than the noise level, associated to variations of about 0.2 fF and 0.2 nS. In both cases, the duration of the signal spikes of about 0.1 s is in good agreement with the transit time of the flowing cells.

4. Conclusions

A microfluidic sensor for the detection of the flow of cells in a microchannel is proposed. The detection is made by measuring the impedance variations generated by the flowing cells. The sensing electrodes are insulated from the fluid in the microchannel, thereby preventing sample contamination and the degradation of the electrodes. In the experimental tests the sensor has demonstrated the ability to detect the flow of both cell clusters and single cells. These preliminary results are promising for biological measurements such as counting and sizing of cells in different matrices, by using a low-cost and time-saving portable solution.

References