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Impedance Spectroscopy Based Flow Rate Monitoring in Autonomous Cell Analytical Micro-Capillary Systems

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Summary:
A hybrid polymer and silicon based, modular, autonomous microfluidic device was designed and fabricated with integrated electrode system to enable simple, robust detection of the interactions between particulate elements of cellular samples as blood and the functionalized capillary wall. The sequential filling of the specially designed capillary system can be monitored by measuring directly the electrical impedance between the integrated parallel electrode lines, thus the cell-surface interaction affected flow characteristics can be quantified. This method enables the fast and easy-to-use detection of disease specific cells from whole blood samples or screening the blood type and coagulation process in the microfluidic system.

Keywords: autonomous microfluidics, impedance spectroscopy, blood screening, coagulation

Introduction

Actual goal regarding the development of Point-of-Care (POC) diagnostic devices is to design complex biosensing solutions integrated with microfluidic systems, which are capable of extracting biomedical information immediately. The passive microfluidic systems utilizing label-free sensing principles and combined with integrated signal detection, processing and communication capabilities can revolutionize the medical diagnostic conceptions. Accordingly, a polymer based, autonomous microfluidic system was designed and fabricated to enable simple monitoring the binding of cells and other particulate elements of blood on the adequately functionalized channel walls or directly the fluidmechnical properties of the sample through the flowrate variation. Previous studies demonstrated that the fast analysis of the AB0 blood group system is feasible in a passive microfluidic system, applying respective antibody reagents and capillary blood samples with different blood groups, as the interaction between the cells and the reagents changes the local hydrodynamic resistance of the microfluidic channels [1].

Materials and Methods

The characteristics of sample flow can be examined in a specially designed, autonomous microfluidic devices. The microfluidic systems have dedicated sequential geometric structure and adequate material composition to define suitable conditions for sensitive detection of individual flow rates. The fluidic channels were fabricated by soft lithography using SU8 molding pattern with adequate heights compatible with cell sizes. Surface modified polydimethylsiloxane (PDMS) was chosen as the structural material of the microfluidic chip to solve the autonomous sample transport. The PDMS was modified by embedding amphiphilic PDMS-b-PEO molecules to achieve adequate hydrophilic behavior of the channels [2].

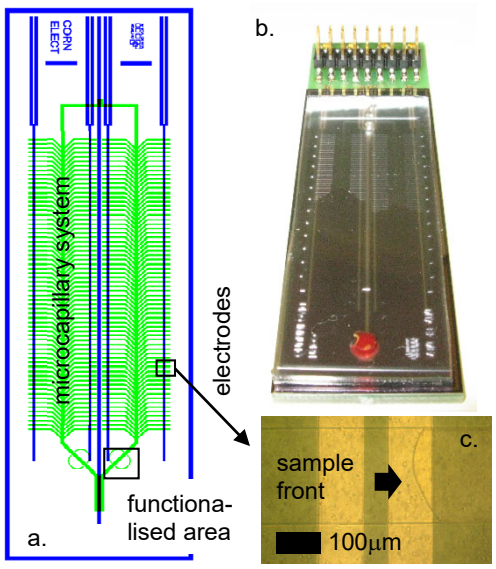

Fig. 1: Schematic architecture of the sequential micro-capillary system (a) and the assembled device during sample loading (b). The sequential resistance change measured between the parallel electrodes (c).

To monitor the sequential filling of the capillaries electrode array was designed and fabricated by micromachining technology on silicon substrate and integrated with the PDMS microfluidic system. The impedance monitoring microsystem contains parallel gold electrodes perpendicularly crossing the microfluidic side channels (Fig. 1). In this work we have demonstrated that the capillary flow in the microfluidic system can be precisely monitored by real-time impedance measurement. As analytical signal the electrical resistance changes of parallel connected fluidic channels was detected to determine fluid movement and sequential channel filling.

Results

As a preliminary functional validation the resistance of the parallel electrode pairs were monitored during capillary filling up the microfluidic system by phosphate buffer solution (PBS) as Fig. 2 demonstrates. The impedance was decreased in quantified steps as the conducting sample shunting the parallel electrodes after reaching the first side channel. Although the step time (time to fill an individual channel) was not changed significantly (Fig. 3).

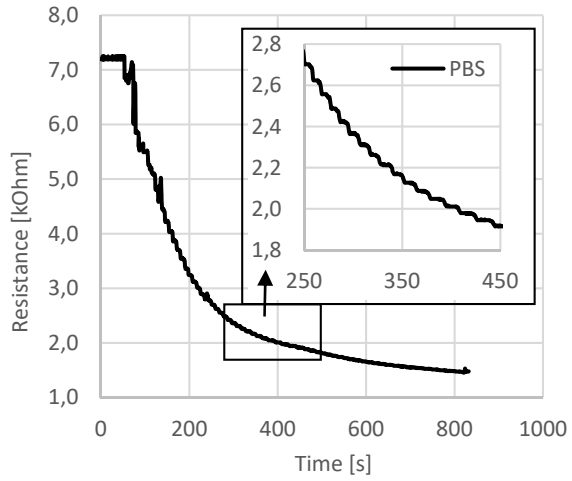

Fig. 2: Time dependent decreasing of electrode resistance clearly demonstrates the sequential filling of individual channels (by PBS).

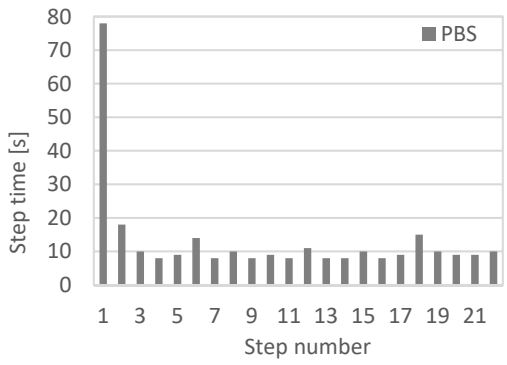

Fig. 3. The filling time of the individual side channels.

The time dependent signal clearly refers the change in sample flow rate, and can quantify the interactions between the blood cells (e.g. coagulation) or between the functionalised channel walls and the specific cells. To demonstrate its feability to quantify interaction-triggered cell binding assay, the blood flow in coagulant modified system was analysed. One of the channel was modified by $CaCl_2$ to significantly change the coagulation behavior of the injected EDTA treated blood sample. The flow characteristics were significantly different in the individual channels, and the coagulant caused flow rate deterioration and clogging as shown in Fig. 4.

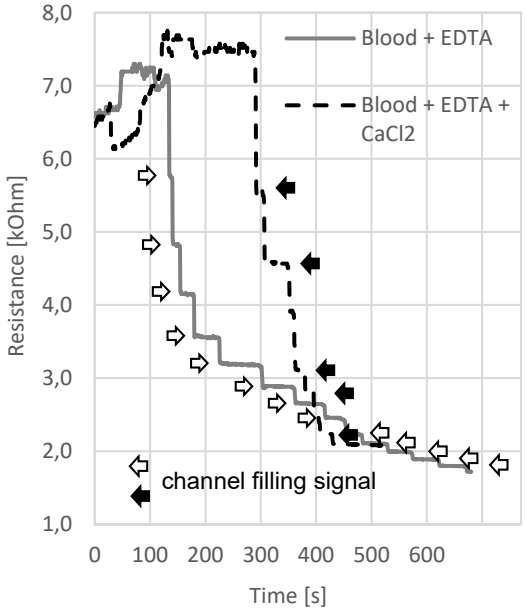

Fig. 4. The sensor signal refers to sample flow rate (step length) and the number of filled channel (step number): the $CaCl_2$ covered surface triggering the coagulation of the blood sample causing slower filling and faster clogging of channel system.

Our proof-of-concept results can provide basis for construction simple quantitative device for blood screening for different diseases.

References

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