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ELECTRICAL DETECTION OF THE MECHANICAL ALTERATION OF SICKLING RED BLOOD CELLS WITHIN A MICROFLUIDIC CAPILLARY NETWORK

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ABSTRACT

In this paper we demonstrate the capability to detect red blood cells mechanical disorders, in particular the sickle cell disease, using the electrical signature of the cell transit within a microfluidic restriction mimicking the blood capillaries.

KEYWORDS: Bioimpedance, Microfluidic Restriction, Red Blood Cell Deformability, Sickle Cell Disease

INTRODUCTION

Sickle cell disease (SCD) is a genetic disorder due to a single genetic mutation that induces alteration of the red blood cell (RBC) elasticity [1]. The change of cell deformability and cell shape, due to the polymerization of haemoglobin [2], leads to vasoocclusive crises that induces organ damages [3].

In this paper, the alteration in the RBC rigidity is detected through the electrical blockage induced by the cell flow within the microfluidic restriction. The microfluidic design is based on a progressive restriction channel which hydraulic diameter decreases from 30 µm down to 5 µm (Fig. 1B). When RBCs flow through one of those microchannels, their transit time though the restriction is highly dependent on their deformability. In such conditions the sickling state of cells can be detected [4].

THEORY

To measure the transit time in the restriction, a pair of electrodes disposed at the fluidic inlet and outlet, detects the variation of the electric current (blockade amplitude) induced by the presence of the cell. A low cost dedicated device has been developed using an analog discovery card [5] associated to a homemade transimpedance amplifier on a dedicated printed circuit board. A lock-in amplifier treats the current signals that characterizes the blockade amplitude and duration. A statistical analysis on 250 successive measurements on cells is performed using Igor Software [6].

EXPERIMENTAL

The microfluidic device is fabricated by the polydimethylsiloxane (PDMS) casting on a thick resist (SU8) mold (Fig. 1A) [7]. The electrodes are patterned after Cr/Au deposition using UV photolithography. In order to achieve a reversible packaging, the PDMS microfluidic part is assembled to the quartz substrate including the electrode network, using therefore depressurization to flow the sample. A coating of the device with parylen (t = 3,5 µm) renders the PDMS non permeable and thus avoid bubbling.

For measurement, an AC voltage of 2V and 10 kHz is applied to the pair of microelectrodes. The RBC passing through the restriction is recorded by a fast camera (sample rate: 1600 fps, period: 625 µs) under microscope (objective: 10X) (Fig. 1C). For statistical analysis, around 250 cells have been analyzed for each cell type (RBCs from healthy donors or SCD patients).

RESULTS AND DISCUSSION

The cell transit time for control and SCD RBCs is presented in Fig 2A. The transit time of control RBCs is very homogeneous (average transit time: 6.48 milliseconds, with a variance of 0.47 s2), while the transit time of SCD RBCs is more dispersed (average transit time: 9.00 milliseconds, with a variance of 0.93 s2). This statistical difference reflects differences in RBC elasticity between both cell types and indicates increased RBC rigidity in

the context of SCD. The impedance module was also analyzed and is presented as a blockade amplitude diagram (see Fig. 2B).

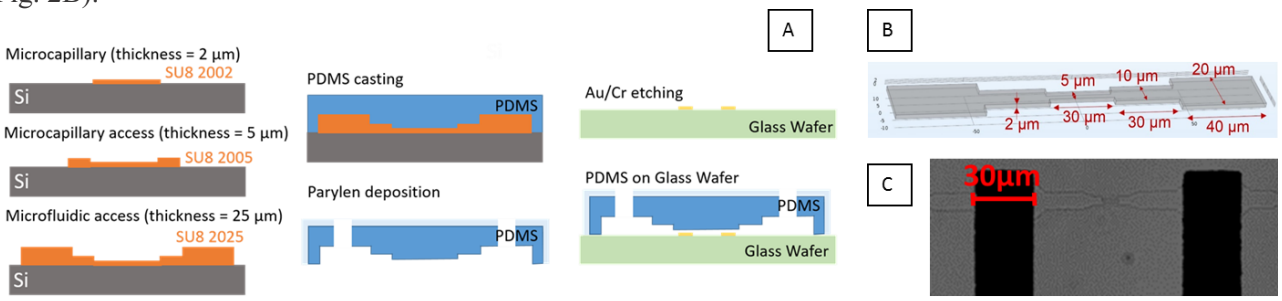


Figure 1: A. Process of microfluidic-electrical assemblage fabrication; B. Design of mimicking capillaries; C. RBC passing through the restriction by a fast camera under microscope.

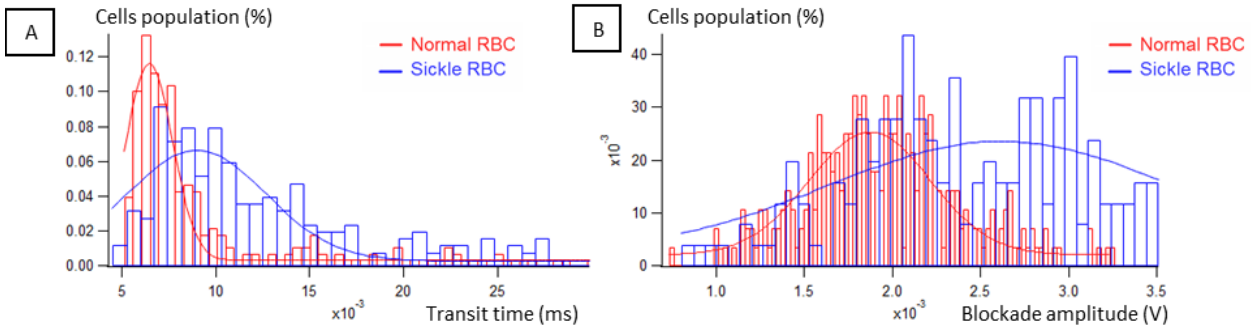


Figure 2: A. The cell transit time for either RBC or sickle cells population; B. Their blockade amplitude.

CONCLUSION

Our method, based on the electrical detection of cell deformability variation, demonstrates to be promising to discriminate normal RBCs and sickled RBCs.

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