MEASUREMENT OF HUMAN RED BLOOD CELL DEFORMABILITY IN MICRO-CHANNEL USING ELECTRIC SENSORS

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ABSTRACT

A sensor which can sequentially measure the deformability of a single red blood cell (RBC) flowing in a micro-channel using membrane electrodes is proposed in this study. The deformability of each cell is obtained by analysing the electric resistance profile which is correlated with the shape of the deformed RBC. Numerical simulation on the electric field around the electrodes and RBC is carried out to evaluate the effects of the RBC positions, the electrode size, and the channel height on the sensor sensitivity. The sensor feasibility is, then, evaluated experimently using the samples of normal human RBCs and rigidized ones.

KEYWORDS: Red Blood Cell, Deformability, Micro-sensor, Micro-flow

INTRODUCTION

Measurement of the deformability of a single red blood cell (RBC) is an important issue in terms of diagnosing initial symptoms of diseases in clinical investigation, for example, Plasmodium falciparum [1]. There are some methods in measuring the RBC deformability such as those using micro-channel and high resolution camera [2], optical tweezer [3], and rheoscope [4]. These methods, however, have problems in the measuring resolution especially when the number density of infected RBC is small, or the limitation of available sampling number of RBC. In this study, an innovative micro-sensor, which can sequentially measure the deformability of each single RBC in high accuracy and sensitivity, is proposed and evaluated.

THEORY

Figures 1 and 2 illustrate the schematic of the measuring scheme and the micro-channel applied in the present sensor, respectively. Membrane-type electrodes are attached to the bottom wall of the micro-channel, and the time-sequential signals of the electric resistance are measured under 10kHz. RBCs supplied from the inlet are

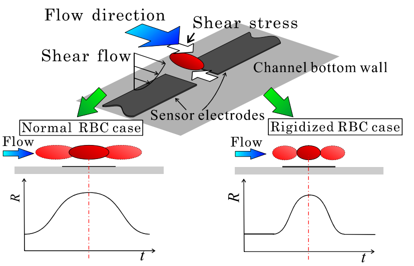

Figure 1. Concept of the measuring method of RBC deformability.

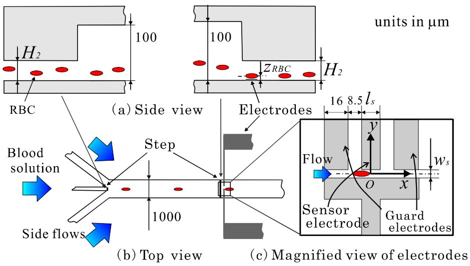

Figure 2. Schematic of the sensor (electrodes and micro-channel).

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deformed when they pass between the electrodes owing to the high shear stress of the micro-channel flow. Since the conductivity of RBC cytomembrane is negligibly small compared with the normal saline solution, the RBC interferes the current leading to significant increase in the resistance. The temporal distribution of the signal is affected by the RBC shape, which is dependent on the cell deformability under uniform shear stress. The deformability of each RBC is, thus, electrically measured by analyzing the resistance profile.

NUMERICAL

Numerical simulations solving the harmonic electric field around the electrodes and RBC, which is modelled as an isotropic sphere or ellipsoid with an frequency-dependant complex permittivity, are carried out to derive the resistance and capacitance between the electrodes. The effect of the sensor geometries are evaluated to optimize the sensor sensitivity. Furthremore, the RBC shape effect on the temporal disbtribtuion of the resistance is simulated to examine the feasibility of the sensor.

EXPERIMENTAL

The sensor size is designed on the basis of the numerical results. Namely, H_2 = 10μm, w_s = 5.2μm, l_s = 14.8μm (other parameters are shown in Fig. 1). Additionally, several techniques are applied to the sensor as follows: The channel has three inlets to control the spanwise positions of human RBCs with the sideflows. Backward- and forward-facing steps are placed upstream of the electrodes to control the RBCs height positions. Guard electrodes are attached at both sides of the sensor electrode to suppress the fringe effect of the current. Pt-nanoparticles are plated on the electrode surfaces to reduce the electric double layer effect. The sensor is tested by using samples of normal human RBCs and glutaraldehyde-treated rigidized ones.

RESULTS AND DISCUSSION

Figure 3(a) shows one of the numerical results of current density isosurfaces around the electrodes. The figure give us an insight where the RBC should flow to enhance the sensor sensitivity. Figures 3(b) ~ (e) show how the RBC position and the sensor geometries affect the resitance ($\Delta R_0 = R - R_\infty$, R_∞ = resitance of solution). The effect of applying the guard electrodes is also shown in Fig. 3(e). These figures show

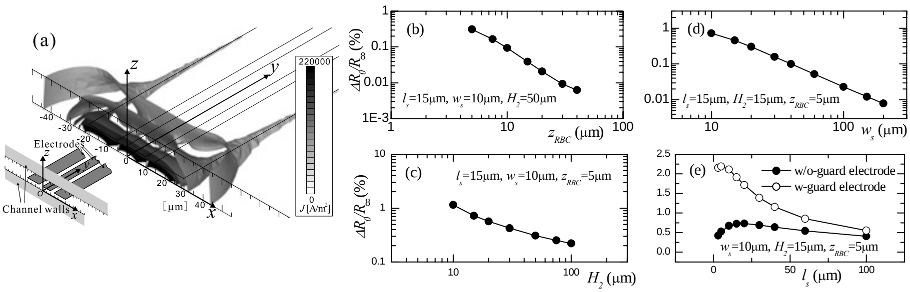

Figure 3. Numerical results: (a) Isosurfaces of current density. The effects of (b) height locations of the RBC center, (c) channel height, (d) gap width between the electrodes, and (e) width of the sensor electrode, on the sensor sensitivity.

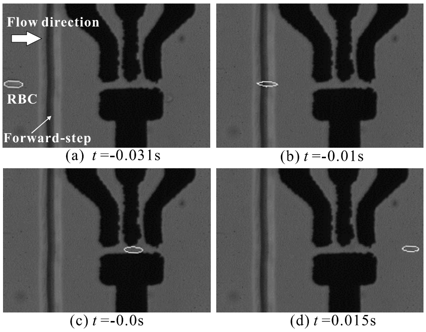

Figure 4. Snapshots of a normal RBC passing between the electrodes.

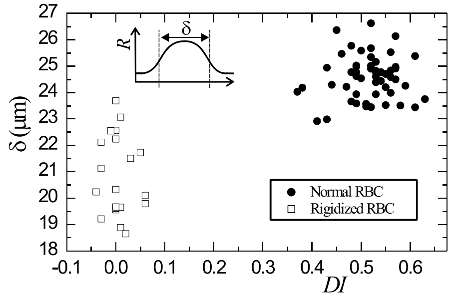

Figure 5. Relation between the half bandwidth of resistance distribution, δ, and deformation index, DI.

that the decrease in RBC height, channel height, and distance between electrodes leads to the increase of the sensor sensitivity. On the other hand, the width of the sensor electrode has an optimum value to achieve maximum sensitivity.

Figure 4 shows the snapshots of a normal RBC passing the electrodes, in which the deformation of the RBC attributed to the high shear flow is observed. Figure 5 shows the relation between the deformation index *DI* and the halfwidth δ of the signal distributions converted from the time-sequentially obtained resistance signals. *DI* is $DI = (a-b)/(a+b)$ where a and b are the major and minor axes of the RBC, respectively. A clear correlation between *DI* and δ is observed, which corresponds well with the numerical prediction (not shown in this article) and indicates the validity of the present sensor.

CONCLUSIONS

A micro-sensor which can electrically measure the deformability of single RBC passing between the electrodes was fabricated, and its feasibility was examined using normal and rigidized RBCs. A good correlation was observed between the deformation index and the half bandwidth of the electric resistance signal distributions.

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