NEGATIVE DIELECTROPHORETIC FORCE BASED SEPARATION SYSTEM FOR HUMAN BREAST CANCER CELL (MCF 7) IN DILUTED RED BLOOD CELLS (RBC)

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ABSTRACT
We present a high-throughput sorting (HTS) platform based on gravitation, hydrodynamic force and negative dielectrophoretic (n-DEP) force. This platform is contrived for the separation of human breast cancer cell in diluted RBCs. As we apply the electric field to comb-type electrode (CE) array, n-DEP force acts on the particles. Accordingly, summation among gravitation, hydrodynamic force and n-DEP force determines the direction of particle movement. Based on the aforementioned principle, human breast cancer cell in diluted RBCs are separated under the condition of low voltage (10Vp-p with 500 KHz) and flow rate of 20μL/min due to draining of water.

KEYWORDS: High Throughput, Negative Dielectrophoretic (n-DEP), Cancer cell, RBCs

INTRODUCTION
For early diagnosis or analysis of tumor, separation process plays a key role in the field of cancer research. Recently, combined with microfabrication technology, various applications based on non-Newtonian force have been reported. One of the applications is Dielectrophoretically-activated cell sorting (DACS) platform, which is designed to separate target particle by discerning difference of dielectrophoretic response of particles in non-uniform electric field. Since the early principle of DACS platform for separation of yeast cells was proposed by Pethig et al., [1] the shape of microelectrode becomes a critical parameter to analyze or manipulate target particles. Based on the castellated [1], spiral [2], or partially curved [3] microelectrodes, dielectric material property (DMP) of various particles was investigated. Especially, through enrichment of CD34+ cells [1] or separation of breast cancer cells from lymphocytes [1], DACS platform is demonstrated as a tool for rare cell separation. However, in that dielectrophoretic response of particles under non-uniform electric field is dependent on low fluid flow rate in microchannel, it is difficult to realize high-throughput separation system in the microchannel. Therefore, we propose the HTS platform that comprises macro size channel (1.2mm x 0.5mm x 12.3mm) and CE array (Figure 1) that generates n-DEP force. In this system, the flow in vertical pool is derived by gravitation.

EXPERIMENTAL SETUP AND WORKING PRINCIPLE
As shown in Figure 2, we illustrate a basic principle for separation of MCF 7 cells in diluted RBCs. Owing to the vector summation among gravitation, hydrodynamic force and n-DEP force acting on the MCF 7 cells in non-uniform electric field (10Vp-p with 500 KHz), MCF 7 cells are deflected on the CE array. On the other hand, RBCs experience only...
the gravitation and hydrodynamic force except for the n-DEP force. Consequently, MCF 7 cells and RBCs are collected in outlet B and outlet A respectively.

RESULTS AND DISCUSSION

With cell mixture with ratio of $1 : 1 \times 10^5$ (MCF 7 cell to RBC), we investigate separation of MCF 7 from diluted RBCs (Figure 3_a). In order to study feasibility of separation principle, non-uniform electric field in vicinity of the electrode array is analyzed through numerical studies with a commercial code (CFD-ACE®) (Figure 3_b).

Figure 2. Basic principle of MCF 7 cell separation based on dielectrophoretic response of particle in non-uniform electric field; Gravitation (G), Hydrodynamic force (H), the first vector summation ($F_{vs}$), Negative dielectrophoretic force (D), and the second vector summation ($S_{vs}$).

Figure 3. Numerical and Experimental results for separation of human breast cancer cell (MCF7) in diluted red blood cells (RBCs); a) before separation, we prepare cell mixture with ratio of $1 : 1 \times 10^5$ (MCF 7 cell to RBC). b) numerical studies based on commercial code (CFD-ACE®); n-DEP area for dielectrophoretic deflection of particle is estimated. c-e) Experimental studies; when cell mixture (including MCF 7 cell and RBC) pass through the CE array, MCF 7 cells follow the streamline, corresponding to vector summation among n-DEP force,
As in numerical result, we confirm experimentally that the negative DEP force induced by the CE array is applicable to separate MCF 7 cell from RBCs as shown in Figure 3. Through the experiments with three different kinds of concentration (1:1.26 x 10⁴, 1:2.27 x 10⁴, and 1:6.26 x 10⁴), we confirm that this platform can separate MCF 7 cell with 71% of separation efficiency in case of the ratio of 1:6.26 x 10⁴ (Table 1).

Table 1. Counts of human breast cancer cells (MCF 7) in outlet A and outlet B before and after separation *

<table>
<thead>
<tr>
<th>Target ratio (MCF 7 : RBC)</th>
<th>Measured initial ratio (MCF 7 : RBC)</th>
<th>Separation Efficiency after separation (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Outlet A</td>
</tr>
<tr>
<td></td>
<td></td>
<td>MCF 7 c</td>
</tr>
<tr>
<td>1 : 1.0 x10⁴</td>
<td>1 : 1.26 x 10⁴</td>
<td>53</td>
</tr>
<tr>
<td>1 : 2.0 x10⁴</td>
<td>1 : 2.27 x 10⁴</td>
<td>38</td>
</tr>
<tr>
<td>1 : 6.0 x10⁴</td>
<td>1 : 6.26 x 10⁴</td>
<td>29</td>
</tr>
</tbody>
</table>

*: Applied voltage = 10Vp-p at 500KHz; Flow rate due to drain of vertical pool = 20 μL/min; Medium conductivity = 2.01 mS/cm.

CONCLUSION
For the separation of human breast cancer cell (MCF 7) in diluted RBCs, we introduced gravitation, hydrodynamic force and n-DEP force. It was found that the performance of HTS platform is dependent on the magnitude of hydrodynamic flow. Especially, we demonstrated that the lower ratio of MCF 7 in diluted RBCs mixture leads to the better efficiency of MCF 7, relatively. It is because increase of the number of MCF 7 disturbs movement of RBCs into outlet A. It can be said that hydrodynamic force due to movement of many MCF cells is dominant over summation of gravitation and n-DEP acting on RBCs. Therefore, we aim to develop an universal tool for sorting with high purity.

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