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Analysis and measurement of dielectrophoretic manipulation of particles and lymphocytes using rail-type electrodes

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ABSTRACT

A particle manipulation and sorting device using the dielectrophoretic (DEP) force is described in this study. The device consists of "ladder-type", "flip-type" and "oblique rail-type" electrode regions. The ladder-type and rail-type electrodes can generate a DEP force distribution that captures the particles, the DEP force of which is negative, in the area located at the center of the electrodes. The ladder-type electrode can align the particles with equal spacing in the streamwise direction. Using the flip-type electrode, which pushes the particles away, in combination with these electrodes, the direction of the particle and timing can be selected with high accuracy, reliability, and response. In the first half of this study, a numerical simulation is carried out to calculate the particle motion and evaluate the performance of the ladder-type electrode. Several models are used to investigate the influences of the non-uniformity of the electric field and the electric interaction of the surface charges and polarizations. Experiments are then carried out to demonstrate the motions of the particles and the sorting reliability. The trajectories and the probability density functions of the particles at the inlet and outlet of the electrode region showed that by using these electrodes the particles can be aligned, sorted, and guided accurately.

1. Introduction

Current technologies have been focusing on single cell analyses using microchannel flows integrated in microdevices so-called as Lab-on-a-Chip and micro total analysis systems (micro-TAS). By using the microchannel flows and microscale mechanical and electrical components integrated into these devices, individual cells can be handled, treated, and measured with high accuracy, significantly improving the analysis of biological and physical characteristics of the cells. To realize such technologies, it is essential to develop methods that can control the position of the cells and sort specific cells from others with high speed and low operating errors. Therefore, techniques for manipulating and sorting cells and microparticles in a microchannel flow have been studied extensively in the last decade by applying optical, fluid dynamic, acoustic, magnetic, and electric forces [1,2].

The dielectrophoretic (DEP) force has been one of the promising tools because it can produce a driving force to the particles or cells without changing or modifying the cells or the fluid properties compared to those using electrical charges and magnetic force which requires attachments of molecules or nano-particles to the cells. The DEP force has further advantages: it can be generated simply by patterning electrodes to the channel walls, it has a high affinity to other electrical measurements commonly used in microdevices, and it has a high response speed. Thus, the DEP force has been used in microchannels not only for sorting techniques but also for various purposes, as summarized in many review papers [3–9].

Although many types of electrodes and channels have been proposed in other studies, substantial issues remain to be solved in order to satisfy the demands of the applications, such as accuracy, sorting rate, response, and applicability under various conditions. One such problem is the significant decay of the DEP force with distance from the electrode due to the fact that the DEP force is mainly produced by the electric field gradient. Another problem is the fact that in many cases, a negative DEP force, namely a repulsion force against the electrode, is exerted on the particle or cell. It is, therefore, difficult to precisely control the particle position. Further, once the particle spanwise position is controlled, the distance between the particles flowing in the channel is still random and the particles are not aligned. To measure the cell characteristics or to sort the particle with an exact timing, it is also necessary to control the particle position in the streamwise direction. In order to overcome these problems, electrode patterns, which are not only effective but also fundamental and versatile, are developed in this study.

A schematic diagram of the electrode patterns is shown in Fig. 1. The manipulation and sorting device consists of the ladder-type

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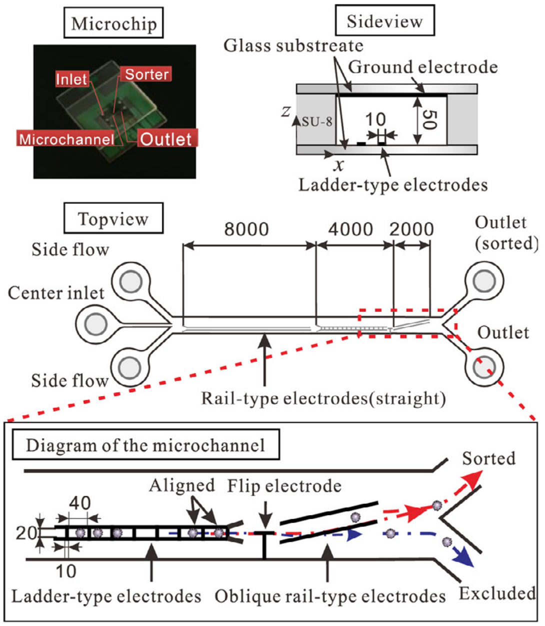
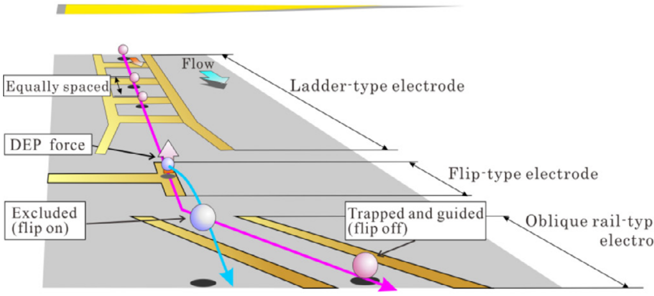


(a) Microchannel and electrodes



(b) Concept of the alignment, sorting, and guiding system

Fig. 1. (a) Schematic diagram of the microchannel and electrodes in the present microdevice. All measurements are in µm. (b) Schematic diagram showing the concept of the alignment, sorting, and guiding of particle motions in the present device.

electrode, the flip-type electrode and the oblique rail-type electrode regions. These electrodes are attached to the channel bottom wall, while the top wall consists of a grounded electrode. Having whole area of the top wall as the electrode, the alignment process of the electrodes attached to the top and bottom walls is not necessary. This can simplify the fabrication process of the microdevices and reduce the cost, which can be one of the drawbacks of applying such electrode patterns to the microchannels.

The ladder-type electrode will produce a DEP force that is exerted on the particles to make them align not only at the centerline but also with equal spacing. The flip-type electrode, operating as a gate electrode, will lift the particle when necessary by applying a voltage to the electrode, excluding it from the electrode region [10]. The remaining particles will be collected and guided along the oblique rail-type electrodes to the collection reservoir.

In the first part of this article, numerical simulation is performed to analyze the electric field, F_{DEP} distributions, and the particle motions in the rail-type and ladder-type electrodes in order to understand how the particle behaves as it flows over the electrodes. The performances of the particle position control and alignment by these electrodes will be evaluated from the results. To perform such computation, it is common to use a model based on the Clausius-Mossotti (CM) function to calculate the F_{DEP} exerted on the particles and cells. The model using the CM function is based on the assumption that the particle existence will not directly influence the electric field and that its gradient is linear. It is, therefore, important to investigate the validity of the model when considering the F_{DEP} of particles in microchannel and micro-electrodes, in which the scales of the electric field distribution and particle or cell are equivalent. Several numerical models are tested that calculate the motion of particles flowing though the rail-type electrodes where time profile of the velocity of the particle is compared with measurement results to validate the models. For the target samples, polystyrene particle and lymphocytes are discussed and compared to see the effects of the nucleus on the F_{DEP} and the model applied.

Measurement is then performed using a microchannel with ladder-type, flip-type and oblique-rail-type electrodes embedded to the walls to demonstrate the numerical scheme and the sorting system. The alignment performance of the ladder-type electrodes is evaluated by measuring how the streamwise distances of the particles changes as they flow along the electrode. Finally, the flip and oblique-rail-type electrodes are coupled with the ladder-type electrode, and the sorting performance is evaluated by discussing how high the accuracy of the particle spanwise positon can be improved by applying these electrodes in the supplementary.

2. Methods

2.1. Numerical model of the dielectrophoretic force

To calculate the dielectrophoretic force, F_{DEP}, of the particle, CM function [8], Multipole [11,12], and Force density methods were first applied and evaluated in order to validate the numerical scheme to be used in the present computation.

The means of calculating the F_{DEP} using the CM function can be defined as Eq. (1):

$$F_{DEP} = 2\pi\varepsilon_0\varepsilon_1' R^3 \mathrm{Re}[\underline{K}_{CM}]\nabla E_{rms}^2 \tag{1}$$

$$\underline{K}_{CM} = \frac{\underline{\varepsilon}_2 - \underline{\varepsilon}_1}{\underline{\varepsilon}_2 + 2\underline{\varepsilon}_1}, \quad \underline{\varepsilon} = \varepsilon_0\varepsilon' + \frac{\kappa}{i2\pi f}$$

where ε_0 is the dielectric constant of vacuum, ε' is the relative dielectric constant, κ is the electric conductivity, f is the frequency of the alternate current, K_{CM} is the CM function, R is the radius of the particle, and E_{rms} is the root mean square of the electric field intensity. The underline indicates the complex value, and the subscripts 1 and 2 show the values of fluid and solid.

Eq. (1) can be applied to a particle filled with a material of uniform property. However, the lymphocyte has a shell structure that consists of the cell membrane, cytoplasm, nuclear envelope, and nucleoplasm. To apply Eq. (1) to such shell structure, the cell is simplified on the basis of a model presented by Asami et al. [13] and Hanai [14]. In this case, the cell is assumed to be a particle with uniform properties, which is equivalent to the multilayers with different properties. The model for two layer coupling can be described as Eq. (2). The subscripts in the equation represent the values of the two layers.

$$\underline{\varepsilon}_{2,eq} = \underline{\varepsilon}_2 \frac{a^3 + 2\frac{\underline{\varepsilon}_3 - \underline{\varepsilon}_2}{\underline{\varepsilon}_3 + \underline{\varepsilon}_2}}{a^3 - \frac{\underline{\varepsilon}_3 - \underline{\varepsilon}_2}{\underline{\varepsilon}_3 + \underline{\varepsilon}_2}} \tag{2}$$

For more layers, this coupling process can be repeated from the inner side until the equivalent value of the overall layers is obtained. For example, in the present case, Eq. (2) is applied three times to couple the four layers.

The model using the CM function applies the single dipole, which is a 1st order approximation, for the external electric field. In this case, one only needs to calculate the electric field independent of the particle existence and calculate the gradient of the electric field ∇E to

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