Determination of the Dielectrophoretic Force on a Cell in a Micro Planar Electrode Structure

Jung-Hoon Choi, Sang-Wook Lee, and Yong-Kweon Kim

Abstract

The dielectrophoretic(DEP) force acting on a cell in an electric field is experimentally determined. A cell is accelerated by the DEP force in an electric field generated between micro planar electrodes. The position of the cell is measured and the velocity and acceleration of the cell are calculated based on the measured position data. The DEP force is determined from the motion equation of a moving cell in suspension. The electrode structure is fabricated by micromachining technology and the height of electrodes is 1㎛. Radish cell and yeast are used in the experiments. In the case of radish cell, the DEP force increases as voltage or frequency(1㎒~3㎒) increases. The voltage dependence can be explained that the DEP force increases when $\nabla|E|^2$ increases. The frequency dependence means that $\mathrm{Re}[\chi_{eff}]$ of radish cell is maximized in a certain frequency. In the case of yeast, the DEP force increases only as voltage increases. The reason for the voltage dependence is the same with the case of radish. The DEP force on a yeast does not vary when the frequency varies from 1㎒ to 3㎒. This result coincides with the fact that the value of calculated $\mathrm{Re}[\chi_{eff}]$ is constant in the test frequency range.

Ⅰ. Introduction

As a micromachining technology is progressed, it is applied to various fields, especially to biotechnology. In biotechnology, it is required to deal with very small particles such as biological cells, or DNA and so on. Biotechnology is suitable for the application of the micromachining technology. A well known application to the biotechnology is a micro cell manipulation device[1, 2].

In cell manipulation devices, various kinds of driving forces can be used such as the mechanical force[3], the optical pressure[4], the hydraulic pressure[5], and the dielectrophoretic force[6-8]. The dielectrophoresis(DEP) is a non-uniform field effect that yields a translational motion of dielectric particles towards where an electric field is either stronger(positive DEP) or weaker (negative DEP). In the case, a force exerted on a particle is called the dielectrophoretic force(the DEP force). The DEP force can be used in manipulating a cell, i.e., separation, capture, retention, and dielectric characterization of cells[10, 11].

When the DEP is used as a driving principle, it is necessary to know a value of the DEP force on a cell for an effective manipulation. In a conventional method, DEP force is obtained from equation (1)[12].

$$F_{DEP}=\frac{1}{3}\pi r^3\varepsilon_1\mathrm{Re}[\chi_{eff}]\nabla|E|^2 \quad (1)$$

where, r : radius of a cell, ε_1 : permittivity of suspension, $\mathrm{Re}[\chi_{eff}]$: effective polarizability of a cell

The DEP force is calculated using the determining a radius of a cell, permittivity of suspension, $\mathrm{Re}[\chi_{eff}]$, and $\nabla|E|^2$ in this method. Conductivity and permittivity of suspension, membrane and protoplasm should be known to determine $\mathrm{Re}[\chi_{eff}]$. These values are rarely known in most cases, and it needs very difficult experiments for accurate determining the values[13-15]. $\nabla|E|^2$ is calculated using FEM, because an analytic solution of $\nabla|E|^2$ exists only for a very simple electrode structure[9]. It takes a long time to calculate an electric fields three-dimensionally at each point when a cell moves. The effect of presence of a cell is increased as the size of a cell is increased. In addition, an accurate calculation of $\nabla|E|^2$ is very difficult, because modeling of a cell itself is an approximate one.

In this paper, a novel method to determine a value of the DEP force is proposed. In the proposed method, the DEP force is obtained from a motion equation of a cell. In the motion equation, a total force exerted on a cell is a sum of the DEP force and the drag force. If the total force and the drag force can be determined, the DEP force is determined from the motion equation. A procedure for determining the total force and the drag force is explained in the next chapter.

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In the proposed method, it is not necessary to know a value of $\mathrm{Re}[\chi_{eff}]$ and $\nabla|E|^2$ and a modeling of a cell. The DEP force can be determined more easily in the proposed method.

II. Determination of the DEP Force

The proposed method for determining the DEP force is as follows. The DEP force is obtained from a motion equation of a cell. The motion equation of a cell is expressed in equation (2). The assumption in the motion equation is as follows.

① No flow exists in suspension in which a cell is immersed.
② A cell is apart from a bottom and a wall.
③ Brownian motion is as small as can be neglected.
④ The motion of a cell is one-dimensional.

The total force(F_{tot}) exerted on a cell is a sum of the DEP force(F_{DEP}) generated by a non-uniformity of an applied electric field and the drag force(F_{drag}) generated by a viscosity of suspension.

$$F_{tot} = F_{DEP} - F_{drag} \tag{2}$$

$$F_{DEP} = F_{tot} + F_{drag} = ma + 6\pi\eta ru = \frac{4}{3}\pi r^3 \rho a + 6\pi\eta ru \tag{3}$$

where, r: radius of a cell, ρ: density of a cell,
η : viscosity of suspension,
u : velocity of a cell, a : acceleration of a cell

If F_{tot} and F_{drag} is determined, the DEP force can be calculated from equation (3). In determining the total force and the drag force, as shown in equation (3), the velocity and the acceleration of a moving cell should be determined. The velocity and the acceleration of a moving cell is obtained from a position of a cell versus an elapsed time.

At first, the motion of a cell is recorded with CCD camera mounted on a microscope. Fig. 1 is a schematic view of a micro electrode structure fabricated for the determination of the DEP force on a cell. When an a.c. voltage of a frequency in a range of the positive DEP is applied to the electrodes, a cell moves towards the electrodes. A displacement of a cell from an initial position versus an elapsed time is measured with a recorded motion. The situation of the experiment with a radish cell is shown in Fig. 2.

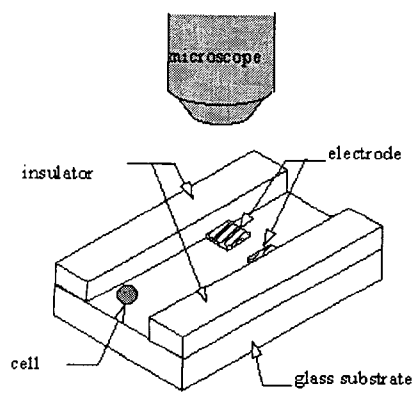


Fig. 1. Schematic view of a micro electrode structure.

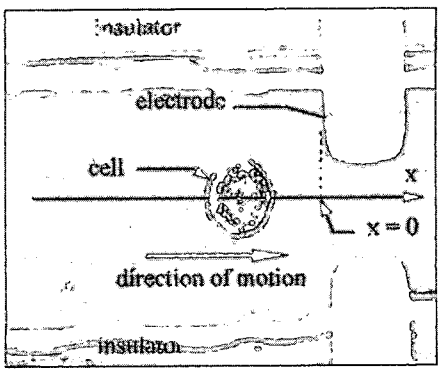


Fig. 2. Attraction of a radish cell toward electrodes.

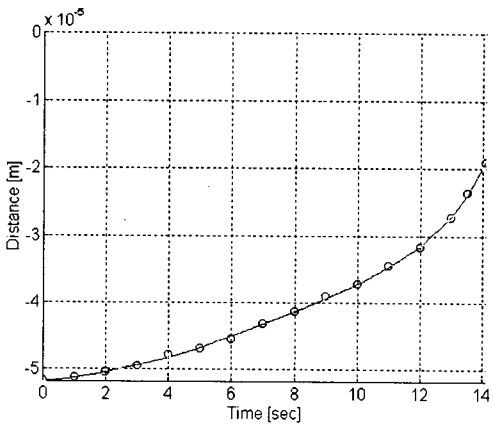


Fig. 3. Measured points and the graph of fitted function.

The measured data points for radish cells are represented as small circles in Fig. 3. The magnitude and frequency of applied voltage are peak-to-peak 9 V and 1 ㎒, respectively. The data points are fitted with a suitable function, $x(t)$. The fitting algorithm is the Nelder-Mead simplex algorithm and the used program is MATLAB. The solid line in Fig. 3 represents a plot of a fitted function.

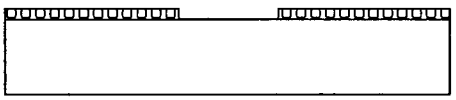
We can get a function of velocity, $u(t)$ and a function of acceleration, $a(t)$, by differentiating the fitted function, $x(t)$. The DEP force on a cell is obtained by putting $u(t)$ and $a(t)$ into equation (3).

III. Fabrication Process of the Micro Electrode Structure

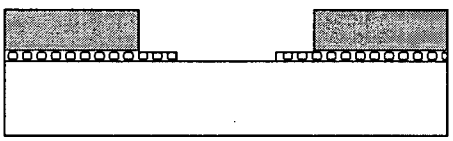
Fabrication process for the used micro electrode structure is

shown in Fig. 4. An initial substrate is Pyrex glass. The transparent Pyrex glass is good for observing cells. Aluminum with a thickness of 1 μm is evaporated thermally on the Pyrex glass substrate. Positive photoresist(AZ-1512) is spun on the aluminum layer and patterned. After patterning positive photoresist, the aluminum layer is wet-etched. The patterned aluminum layer is used as electrodes. The distance between electrodes and the width of the electrodes are 50 μm, respectively.

The flow channel is fabricated using photosensitive polyimide (Toray, UR-5100FX). The polyimide is suitable material for this purpose, because it is physically and chemically stable after curing. A thickness of polyimide layer after curing is about 20 μm, while a diameter of radish cell is about 37 μm. The polyimide process is repeated twice for the experiment of radish cell. The thickness of double layers of polyimide is about 40 μm.



(a) evaporation and patterning of aluminum



(b) coating and patterning of polyimide

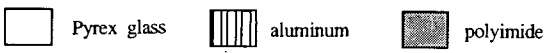
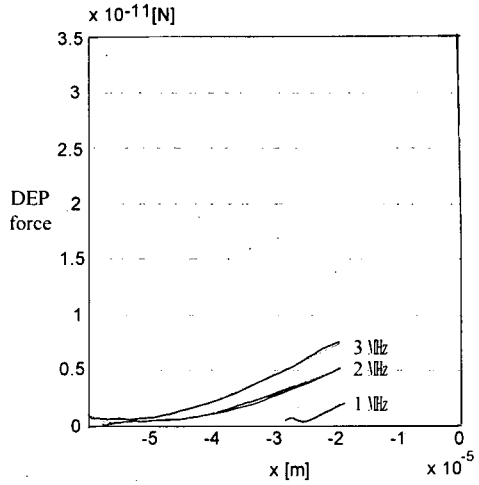


Fig. 4. Fabrication process of the micro electrode structure.

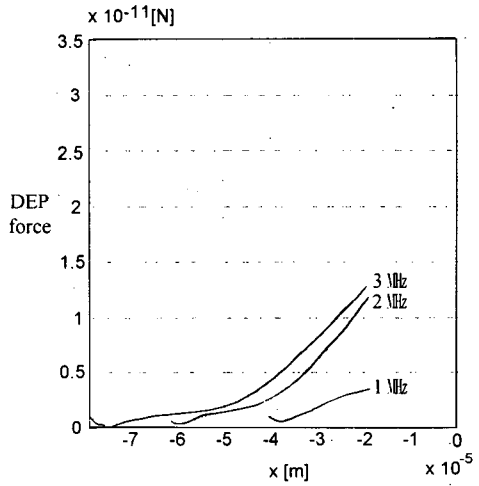
Ⅳ. Results and Discussion

A radish cell and a yeast are used in the experiment. The two kinds of cell is different in the a size of cell. A radius of a radish cell used for the experiment is 18 μm and that of yeast is 3.8 μm. Parameters of yeast are deeply investigated in genetics. The density of yeast is about 1.086 *g/ml* [16]. The viscosity of suspension is measured using Ostward viscometer for a case of yeast. The measured viscosity is 1.791×10^{-3} kg/(m · s). Density of cell and viscosity of suspension for a case of radish cell are assumed to be the same as those for yeast.

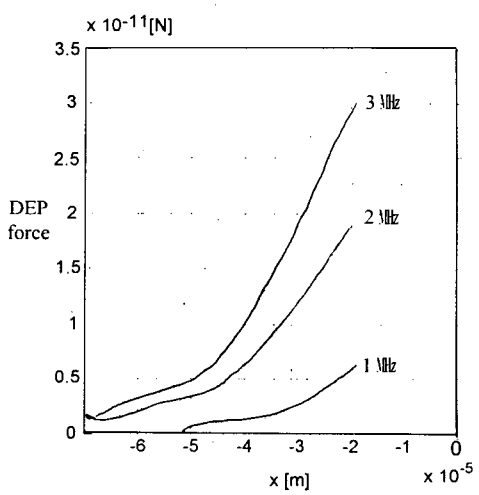
The estimated DEP force using the proposed method for a radish cell is presented in Fig. 5. In Fig. 5, y axis represents the magnitude of the DEP force and x axis represents the distance from the point depicted as x = 0 in Fig. 2 to the center of a cell. Data are collected till the edge of a cell contacts the point x = 0 in Fig. 2, and the data are presented to x = -18 μm in Fig. 5, because the radius of a radish cell used in experiment is 18 μm. Each graph contains the plots of the DEP force with frequency of 1, 2, and 3 Mhz. The DEP force exerted on radish cell is in the order of 10 *pN*.



(a) $V_{p\text{-}p}$: 5V



(b) $V_{p\text{-}p}$: 7V



(c) $V_{p\text{-}p}$: 9V

Fig. 5. The estimated DEP force for the case of radish cell.

In Fig. 5, it is noted that the DEP force on a radish cell is

increased as the magnitude and frequency of applied voltage are increased. When the magnitude of applied voltage increases, the DEP force on a radish cell increases due to $\nabla|E|^2$ as expected in equation (1). Because $\mathrm{Re}[\chi_{eff}]$ of a radish cell is increased in the range of experimented frequency, the DEP force increases due to the frequency of applied voltage.

The estimated DEP force using the proposed method for yeast are shown in Fig. 6 and Fig. 7. Fig. 6 shows the results when the magnitude of voltage is increased while the frequency is constant. Fig. 7 shows the result when the frequency is varied while the magnitude is constant. The DEP force exerted on yeast is in the order of *pN*.

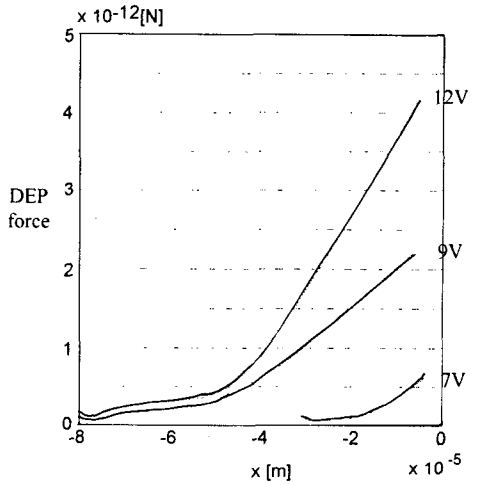
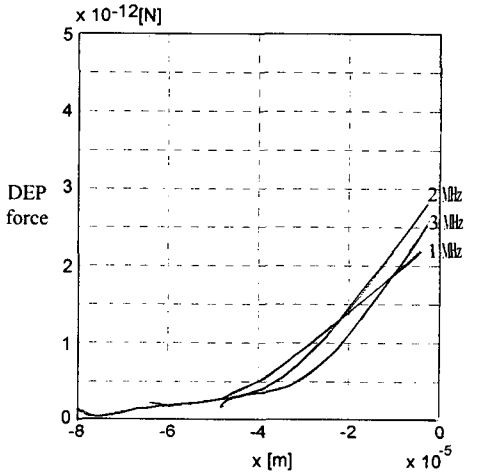


Fig. 6. The estimated DEP force for the case of yeast(Frequency : 1㎒).

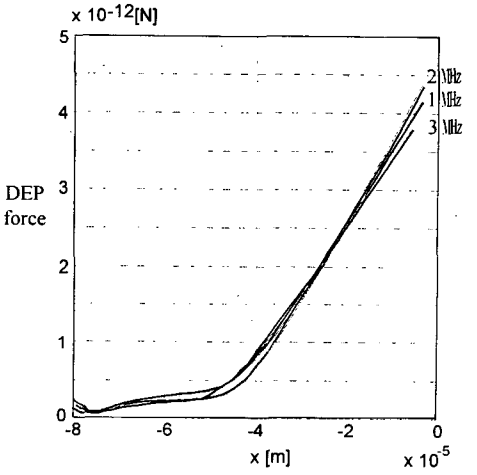
Fig. 6 shows that the DEP force on a yeast increases as the magnitude of applied voltage increases under the same frequency. The reason for this proportionality is identical to the case of radish cell. Fig. 7 shows that the DEP force on a yeast is not a strong function of the frequency in the frequency range from 1 ㎒ to 3 ㎒. This means that the effective polarizability of a yeast is almost constant in the range of experimented frequency. This result is compared with the calculated result of effective polarizability using electrical properties of yeast.

A yeast is modeled as a sphere with a single shell in the calculation of the effective polarizability of yeast [12]. The expression of an effective polarizability is known as equation (4) in this case [17]. The subscript *1* denotes suspension, the subscript *m* denotes membrane of cell, and the subscript *2* denotes protoplasm of cell. ε is the permittivity, σ is the conductivity, d is the thickness of membrane, and R is the radius of cell.

$$\mathrm{Re}[\chi_{eff}] = \frac{3(\varepsilon_r-1)}{(\varepsilon_r+2)} + \frac{-9\sigma_r}{2(\sigma_r+2)}\left\{1+\frac{\sigma_{rm}(\sigma_r+2)}{2\delta\sigma_r}\right\}^{-1}\frac{1}{1+\omega^2\tau_1^2} + \frac{-9(\varepsilon_r-\sigma_r)}{(\varepsilon_r+2)(\sigma_r+2)}\frac{1}{1+\omega^2\tau_2^2} \quad (4)$$



(a) $V_{p\text{-}p}$: 9V



(b) $V_{p\text{-}p}$: 12V

Fig. 7. The estimated DEP force for the case of yeast(under same magnitude).

where, $\varepsilon_r = \varepsilon_2/\varepsilon_1$, $\sigma_r = \sigma_2/\sigma_1$, $\sigma_{rm} = \sigma_m/\sigma_1$, $\varepsilon_{rm} = \varepsilon_m/\varepsilon_1$, $\delta = d/R$

$$\tau_1 = \left\{\frac{\sigma_m}{\varepsilon_m} + \frac{2\delta\sigma_2}{\varepsilon_m(\sigma_r+2)}\right\}^{-1}$$

$$\tau_2 = \frac{\varepsilon_2+2\varepsilon_1}{\sigma_2+2\sigma_1}\left[1+\frac{2\delta}{\varepsilon_r+2}\left\{\frac{2(\varepsilon_r-\delta_r)^2}{\varepsilon_{rm}(\sigma_r+2)} + \frac{\varepsilon_r-\sigma_r}{\sigma_r+2} - \varepsilon_{rm}\right\}\right]^{-1}$$

The effective polarizability of yeast is calculated by putting the electrical parameters of yeast into this expression. The electrical parameters of yeast are taken from Ref. 18. Table. 1 shows the electrical parameters of yeast. The graph of calculated effective polarizability is shown in Fig. 8.

Region A in Fig. 8 represents the range of frequency between 1 ㎒ and 3 ㎒. The effective polarizability in the range is almost constant. This coincides with the result from the experiment.

The DEP force on radish cell is greater than that of yeast by 10 times. The difference of permittivity and effective polarizability is not so large. The theoretical maximum value of effective

Table 1. The electrical constants of yeast.
($\varepsilon_o = 8.854\times10^{-12}$ [*F/m*])

Parameter	Value
R	4×10^{-6} [*m*]
d	10^{-8} [*m*]
ε_1	$80\varepsilon_o$ [*F/m*]
ε_m	$9\varepsilon_o$ [*F/m*]
ε_2	$60\varepsilon_o$ [*F/m*]
σ_1	10^{-2} [*mho/m*]
σ_m	10^{-6} [*mho/m*]
σ_2	1.0 [*mho/m*]

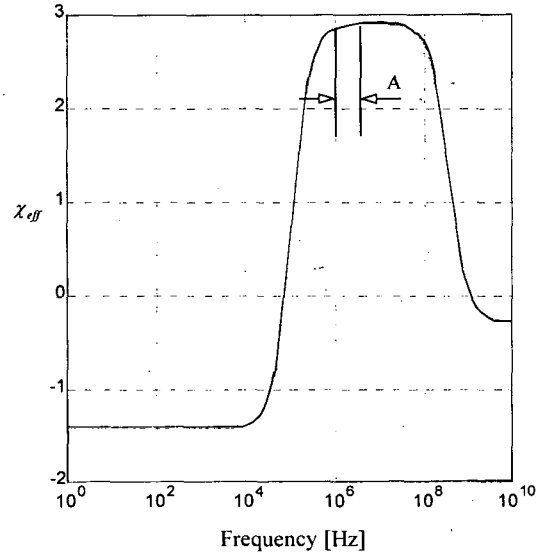


Fig. 8. Calculated effective polarizability of yeast.

polarizability is 3 in a shell model [12]. The difference in the magnitude of the DEP force is caused by the different size of cell, because the DEP force is proportional to the volume of a cell.

V. Conclusion

In this paper, the novel method for determining the DEP force on a cell is proposed. It is not necessary to know the value of of a cell, and of applied electric field in this method. The proposed method is easier to determine the DEP force than the conventional method.

Experiments are accomplished to determine the DEP force using proposed method and we fabricate a micro electrode structure for the experiment. The cells used in experiments are radish cell and yeast. The DEP force on a radish cell increases as the magnitude or the frequency(1㎒~3㎒) of the applied voltage increases. The DEP force on a yeast increases only as the magnitude of applied voltage increases. The DEP force on a yeast does not varies with the frequency of applied voltage from 1 ㎒ to 3 ㎒.

Because the DEP force increases as $\nabla|E|^2$ increases, the DEP force increases as the magnitude of applied voltage increases. The reason why the DEP force on a yeast is not affected by varying frequency is that $\mathrm{Re}[\chi_{eff}]$ of yeast is constant in the range of test frequency. This coincides with the fact that the calculated effective polarizability is constant in the test frequency range.

The experimental result using the proposed method is discussed. The DEP force can be determined more easily in the proposed method than in the conventional method. The proposed method may be used in determining the DEP force on various kinds of cell. This will be helpful to the design of the cell manipulation device and the analysis of the DEP force on a cell.

Acknowledgements

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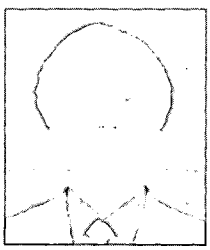

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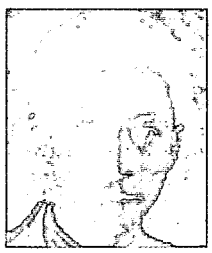

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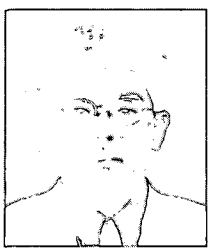

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