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Interdigitated electrode design and optimization for dielectrophoresis cell separation actuators

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ABSTRACT

Among all particle separation approaches, dielectrophoresis actuators which use electric properties difference between particles, have turned into strong separating tools. This way, the particles in the fluid within non-uniform electric field experience the dielectrophoresis force. The amount and direction of this force depend on the fluid and particle polarization, particle size and electric field gradient. In this paper after presenting governing equations concerning the dielectrophoresis phenomenon, a microfluidic actuator introduced in which an interdigitated electrode pattern is applied in. Voltage, pitch, and width to pitch ratio of electrode as well as channel height are of the most important geometrical parameters of this actuator whose individual effect on particles separation was investigated using finite element analysis (FEM). The simulation results showed that if the actuator is intended to work in the efficient conditions, channel height and electrodes pitch should be near to each other, height needs to be as minimum as possible while voltage as maximum as possible in order to reach to the least time duration and the highest quantity for particles separation. Then, using theoretical equations and simulation results, a flowchart is introduced to design and optimize dielectrophoresis separation actuators. Finally, experimental results for k562 cell separation, as a biological particle, from Polystyrene, as a standard particle, is presented. In the fabricated actuator recovery and purity efficiency are 93% and about 100% respectively.

1. Introduction

Selective cells manipulation as well as their separation is remarkably useful in diagnostic, pharmacy and treatment [1]. Different chemical and physical processes are widely used for cells separation. They are categorized to micro and macro dimensions. In general, when it comes to micro dimension method, since particles separating force is imposed on particles directly, more efficiency and higher purity is observed. Different principles have been used for particles separation until now [2] such as difference in density [3], size [4], deformability [5], surface properties [6] and also electrical properties [7–11]. Among all these features, dielectrophoresis actuators which use electric properties difference, have turned into strong separating tools. The important advantages of these actuators are their high ability to separate a wide range of different particles without labeling them with high efficiency and purity [12]. In addition to cell separation use, dielectrophoresis phenomenon has wide application in cell trapping [13,14], focusing [15,16] detection [4,17] and analysis [18–21]. The term dielectrophoresis was first introduced by Paul in 1978 [22]. Dielectrophoresis refers to the force imposed on a polarizable particle within a non-uniform electric field. Depending on particles electric properties and their surrounding fluid, if permittivity of particles are higher than fluid, they are absorbed by strong electric field (positive dielectrophoresis) and if permittivity of particles are lower than fluid, they are repelled from there (negative dielectrophoresis). Therefore, a dielectrophoresis system must be designed in a way that particles get enforced by non-uniform electric field. till now Different electrode patterns have been presented for making such electric field [23] such as interdigitated [24,25], polynominal [26] and castellated [27] electrode arrays. Interdigitated pattern is one of the most useful patterns for using in cell separation actuators. Several studies have been fulfilled for evaluation the effect of different parameters on this pattern. Crews et al. [28] by using numerical simulation, investigated the effect of electrodes geometry on the electric field gradient square and

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presented a new model for interdigitated electrodes [29–31]. also studied on imposed forces on particle within an interdigitated model. Morgan et al. [32] used Fourier series to present an analytical model for the generated electric field by interdigitated electrodes. By applying finite element method, Grean et al. [33] studied particle force within two and four phase stimulation. Knowing dielectrophoresis actuator design process for special application and how to optimize working condition causes increase in efficiency and capacity and lead to a remarkable contribution for designing cell sorting actuators which has not presented before. For this purpose, in this study firstly decided to study analytical theories on particles separation process. Then, a microfluidic particles separating system using dielectrophoresis with interdigitated electrode is presented. In results and discussion section not only finite element simulation result shows the effects of geometrical parameters such as pitch and widths to pitch ratio of electrodes and channel height on particles separation process, but also actuator design and optimization process is studied through a flowchart. Finally, experimental results for white blood cells (WBCs) separation from polystyrene particles are presented and efficiency of actuator is evaluated by measuring its recovery and purity.

2. Theoretical equations

When a dielectric particle is located in an electric field, it will be polarized consequently. If the exerted electric field is uniform, net force applied on particle is zero, but in case of a non-uniform electric field, the net forced will be determined as in the following equation [34]:

$$F_{DEP} = (p.\nabla)E \tag{1}$$

In the above equation, p stands for particle bipolar moment and E counts for electric field intensity. Effective particle bipolar moment in an alternating electric field is calculated upon the following equation [34]:

$$P^* = v\alpha^* E \tag{2}$$

In the above equations, P^* is complex conjugate of P, v counts for particle volume and α stands for particle complex polarization. As a result, using equations (1) and (2), average dielectrophoresis force is concluded in equation (3):

$$F_{DEP} = \frac{1}{4} Re[\alpha^*]\nabla|E|^2 \tag{3}$$

In the mentioned equation $Re[\alpha^*]$ represents the real part of particle polarization. If the particle is considered as a sphere, polarization for a uniform particle is determined by equation (4) as in the following [34]:

$$\alpha^*(\omega) = 3\varepsilon_m f_{CM}(\omega) \tag{4}$$

$\omega = 2\pi f$ stands for the applied electric field angular frequency, f_{CM} represents Clausius-Mossotti factor which will be explained in the following and also ε^* is complex permittivity coefficient determined by the following equation:

$$\varepsilon_x^* = \varepsilon_0\varepsilon_x - j\left(\frac{\sigma_x}{\omega}\right) \text{ , } x = p \text{ or } m \tag{5}$$

In which $\varepsilon_0 = 8.854 \times 10^{-12}\ F/m$ count for vacuum permittivity coefficient and also σ_x and ε_x refer to electrical conductivity and relative permittivity coefficients respectively. In case the particle is uniform, Clausius-Mossotti factor is obtained through equation (6). While, if the particle consists of a membrane layer like many cells, ε_p in equation (6) should be determined according to equation (7) in the following:

$$f_{CM} = \frac{\varepsilon_p^* - \varepsilon_m^*}{\varepsilon_p^* + 2\varepsilon_m^*} \tag{6}$$

$$\varepsilon_p^* = \varepsilon_{mem}^* = \frac{\left(\frac{r+d}{r}\right)^3 + 2\left(\frac{\varepsilon_{int}^* - \varepsilon_{mem}^*}{\varepsilon_{int}^* + 2\varepsilon_{mem}^*}\right)}{\left(\frac{r+d}{r}\right)^3 - \left(\frac{\varepsilon_{int}^* - \varepsilon_{mem}^*}{\varepsilon_{int}^* + 2\varepsilon_{mem}^*}\right)} \tag{7}$$

Where r and d is radius of internal layer and membrane thickness respectively. By using equations (4)–(7) in equation (3), force exerted on particle obtain by equation (8) in which electric field is replaced by effective electric field.

$$F_{DEP} = \frac{1}{2}\pi\varepsilon_m a^3 Re(f_{CM})\nabla|E_{rms}|^2 \tag{8}$$

As it is observed in equation (8), force on particle depends on particle radius, Clausius-Mossotti factor and gradient of electric field square. Clausius-Mossotti factor determines the direction and intensity of the force on particle. As shows equation (6), the sign of this factor and its amount depend on particle and the surrounding fluid polarization; the more the distance between these two, the higher the force on particle. If particle polarization is more than the surrounding fluid, the Clausius-Mossotti factor will be positive and the particle will be affected by positive dielectrophoresis therefore the particles will be absorbed by the region with maximum electric field gradient, while if the fluid polarization is higher, negative dielectrophoresis is expected to occur and so they will be repel from there. Fig. 1 demonstrates the general simulation done by COMSOL Multiphysics 5 which is shows electric filed line and the way a particle is moved by positive and negative dielectrophoresis.

Particles in the fluid are under the forces including gravity, buoyancy and drag as well as dielectrophoresis force. Equation (9) shows the interaction of gravity and buoyancy forces. In this equation, p refers to density, r counts for radius and g stands for gravity acceleration [20].

$$F_g = \left(\rho_p - \rho_m\right)\left(\frac{4}{3}\pi r^3\right)(g) \tag{9}$$

Equation (10) shows the drag force of a spherical particle placed in fluid. In this equation v is fluid velocity difference vector and η stands for fluid viscosity [35].

$$F_{Dreag} = 6\pi\eta r v \tag{10}$$

3. Design

3.1. Electric field frequency selection

In order to use dielectrophoresis force for separation, the actuator should be designed in a way that different force exert on the target particle in comparison with the other ones. Consequently particle separation in a microfluidic system within fluid movement would be possible. Therefore, since Clausius-Mossotti factor depends on frequency, the frequency of electric field should be selected in a way that positive dielectrophoresis force is imposed on one particle and negative one on the others. This kind of field imposition causes some of the particles enforced by positive dielectrophoresis move towards electrodes and the others get steered away from them and wash with fluid movement. Fig. 2 shows the