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RESEARCH ARTICLE

Effect of microfluidic rectangular microelectrode geometry on bioparticles manipulation in dielectrophoretic application

[version 1; peer review: 1 approved with reservations]

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Abstract

Background: Microfluidic cell manipulation techniques have been continually developed and integrated into miniature chips as a so-called lab-on-a-chip (LOC) platform for high-throughput bioassays. Among the various mechanisms of bioparticles manipulation by electrically induced forces, dielectrophoresis (DEP) has been regarded as the most promising technique utilized in microfluidic systems. Into the micro- to nano-scale level of DEP configuration, the common challenges of undesirable side effects such as electrohydrodynamic effects, joule heating, and electrolysis that may occur in the microfluidic system has always been a hurdle which would severely limit the DEP performance.

Methods: A numerical simulation study was performed on a versatile capability of a rectangular type of dielectrophoresis microelectrode with different parametric design configuration variables (channel height: 20-50 μm ; electrode width 20-100 μm ; electrode spacing 5-50 μm).

Results: Numerical study results have shown that the ideal dimension range of design configuration for optimum DEP performance have been identified to be 40 μm in channel height, 20-40 μm in electrode width and 5-15 μm in electrode spacing, further increasing of the dimensions have shown a decrease in DEP performance consequently abridged the bioparticle manipulation.

Conclusion: This investigation of the parametric design of the rectangular geometry microelectrode has provided necessary insight to the microelectrode design information and parametric considerations for optimum DEP device fabrication and enhancement.

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1

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Any reports and responses or comments on the article can be found at the end of the article.

Keywords

Microfluidic, electrophoresis, dielectrophoresis, geometry, microelectrode, protein

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Introduction

Dielectrophoresis (DEP) has been proven as a versatile manipulation technique commonly used in a microfluidic platform¹. DEP technique is commonly used to manipulate dielectric particles in a non-uniform electric field by the induction of DEP force (F_{DEP})². Dielectrophoresis is an electrokinetic motion phenomenon occurring when a polarizable particle is put in nonuniform electric fields, and the particle mobility is influenced by the ambient electric field, as well as the characteristics of the dielectric particles or solutions³. Its versatility has provided various benefits for clinical application, laboratory diagnostics and research application⁴.

In the case of a DEP setting where target bioparticle (particle) such proteins and cells are in the submicro to nano size, the DEP force applied onto the particles will be extreme small. It is because according to the DEP equation (1), the key influence in particle motion by DEP force was determined by the electric field gradient and the particle volume, which was defined by its radius. Therefore, smaller particle will experience smaller DEP force for particle trapping or separation⁵. In order to compensate for this unchangeable particle radius variable, the microelectrodes geometry design must be optimized to provide an effective and higher performance of DEP response. To achieve of this, according to the equation (1), one of the optimizations of the microelectrodes geometry design that can be done is to design an electrode that can provide a higher electric field gradient to compensate the small particle radius⁶. Moreover, the optimization may lead to require lower voltage that can circumvent for joule heating effect, while having high throughput performance for higher particle DEP manipulation ability⁷.

$$F_{DEP} = 2\pi\epsilon_m\epsilon_0r_{ext}^3Re[f_{CM}]\nabla E_{RMS}^2 \quad (1)$$

For the case a homogeneous spherical particle in the suspension medium, the general time-averaged DEP force amplitude

can be expressed by the classical DEP force as equation (1). ϵ_m denoted as the absolute relative permittivity of suspension medium, while $\epsilon_0 = 8.854 \times 10^{-12}$ F/m is the permittivity of the vacuum, the spherical particle's radius is denoted as r or r_{ext} . E_{RMS} is the root-mean-square of the applied electric field in AC, and $Re[f_{CM}]$ is the real part of Clausius-Mossotti (CM) factor². The equation of the real part of Clausius-Mossotti factor $Re[f_{CM}]$ is given in equation (2).

$$Re[f_{CM}] = \frac{\epsilon_p^* - \epsilon_m^*}{\epsilon_p^* + 2\epsilon_m^*} \quad (2)$$

The subscripts “p” and “m” are referred to particle and medium respectively. ϵ_p^* and ϵ_m^* are the complex permittivity with respect to particle and medium which can be defined as in equation (3)⁸

$$\epsilon_p^* = \epsilon_p\epsilon_0 - j\frac{\sigma_p}{\omega}, \quad \epsilon_m^* = \epsilon_m\epsilon_0 - j\frac{\sigma_m}{\omega} \quad (3)$$

σ_p and σ_m is the electric conductivity of a particle and medium respectively. ω is angular frequency of the applied electric field defined as $\omega = \pi f$, where f is the frequency of the electric field and $j = \sqrt{-1}$.

In order to optimizing the electrode geometry and design, there are several geometrical parameters that will be affecting the electric field gradient ∇E^2 which are the width of the electrodes and the spacing between the two electrodes^{9,10}.

To further study on this, a rectangular geometry shape electrode has been designed as shown in Figure 1 which is an interdigitated castellated type design which consist of two same-sized electrodes, and these two electrodes are made up of gold material with the thickness of 0.15 μm . The two electrodes were positioned with a spacing gap between them and placed at the bottom of the microfluidic channel, the microelectrode dimension has been shown in Table 1. For 3 main variables with each parameter used to study the optimization of electric field

Figure 1. Top section view of the microfluidic channel and the rectangular microelectrode design.

Table 1. Dimension of the microfluidic and microelectrode design.

Features	Value (μm)
Channel Width	130
Channel Length	370
Electrode Length	360
Electrode Spacing	5
Electrode Thickness	0.15
A	18
B	36
C	36

gradient were: 1. the microfluidic channel height (20 μm, 30 μm, 40 μm, 50 μm), 2. the electrode width (20 μm, 40 μm, 60 μm, 80 μm, 100 μm) and 3. the electrode gap spacing (5 μm, 10 μm, 15 μm, 20 μm, 25 μm, 30 μm, 35 μm, 40 μm, 45 μm, 50 μm).

Simulation study

A Finite Element Method (FEM) simulation study was performed by using COMSOL Multiphysics version 5.5 software (RRID: RRID:SCR_014767; URL: <https://www.comsol.com/comsol-multiphysics>). A 2D space dimension FEM simulation analysis has been carried for this study with only considering the cross-section view of the microfluidic change. Electric currents (ec) physics module was added to defines the electrical potential in the fluid domain and the electric field current was governed by the Ohm's law continuity equation. The simulation study was carried out in the settings of frequency domain (AC). The governing equations for this frequency domain, electric current, electrical conductivity and relative permittivity are expressed as below:

$$\nabla \cdot J = Q_{j,v} \quad (4)$$

$$J = \sigma E + J_e \quad (5)$$

$$E = -\nabla V \quad (6)$$

$$J_C = \sigma E \quad (7)$$

$$D = \epsilon_0 \epsilon_r E \quad (8)$$

J denoted as electric current density, σ is electrical conductivity, V electrical voltage, E electrical field, D electric displacement field, ϵ_0 is the relative permittivity of air and ϵ_r is the relative permittivity of the fluid respected to the air. By solving these equations, the electric field E in the microfluidic system is calculated and the electric field E is in direct relation to the amount of DEP force according to equation (1).

The cross-section microfluidic and its rectangular geometry electrodes have been created according to the dimension in the Figure 2. Gold material were assigned for both the electrodes with the electrical conductivity, $\sigma = 44.2 \times 10^6$ S/m and relative permittivity, $\epsilon = 1$, for the medium within the microchannel was a deionized water with its electrical conductivity, $\sigma = 0.0002$ S/m and relative permittivity, $\epsilon = 78$. Under the electric currents (ec) physics module, 10 V peak to peak AC electric potential was set to be applied to the electrodes. The boundaries of one electrode have been input an electric potential $V_0 = 10V$, while the other electrode with its boundaries were input with electric potential $V_0 = -10V$. The remaining boundaries of the channel were set to be insulated. Extremely fine mesh was generated for this created model. Lastly, a study was generated with electric current model that defines the electrical potential and it is conducted in a frequency domain (AC).

The numerical results such as electrical potential distribution V_{pp} , electric field distribution V/m and electric field gradient ∇E^2 were generated from this model. This numerical study was performed with 5 different channel height (20μm, 30μm, 40μm, 50μm) and with the input of different combination parameters of electrode width and electrode spacing as according to the Table 2.

Results and Discussions

A parametric study on the geometrical parameters of rectangular shape microelectrode for DEP microfluidic platform has been conducted to identify its optimization microfluidic and electrode design for DEP manipulation of micro to nano particles. In this numerical study, an electric field gradient was generated in the model as shown in Figure 3, by further input of different design variables into the study model such channel height, electrode width and electrode spacing and its parameters to study the optimization of the rectangular microelectrode and identify its optimum design parameters. Electric field gradient ∇E_x^2 is the key identifier for an effective DEP microfluidic platform, therefore in the generation of the electric field gradient result in this cross-section microfluidic model, only the horizontal component of the electric field gradient ∇E_x^2 is considered.

According to the 3D plot result from Figure 4 has shown that the electric field gradient ∇E_x^2 is exponentially increased when the applied peak-to-peak voltage is increased. However, the electric field gradient remained unchanged to the increase of applied frequency. Although the frequency has not contributed to the electric field gradient but note that it is still an important factor that influence the particle, as the particle DEP response is highly dependent on applied frequency and which is governed by the equation (2) and equation (3)¹¹. This result has shown that the applied voltage has a substantial influence on the electric field gradient, however the applied frequency will have no effect on the electric field gradient. From the generated 3D plot of all the 4 different channel heights as shown in Figure 5, it has been shown in all the graph that the electric field gradient is gradually decreasing when the electrode spacing is increased and the electric field gradient had

Figure 2. Cross-section view of the microfluidic channel filled with suspending medium and both rectangular microelectrodes at the bottom.

Table 2. Microfluidic platform optimization variables and parameters.

No.	Variables	Parameters
1.	Channel Height	20 μm , 30 μm , 40 μm , 50 μm
2.	Electrode Width	20 μm , 40 μm , 60 μm , 80 μm , 100 μm
3.	Electrode Spacing	5 μm , 10 μm , 15 μm , 20 μm , 25 μm , 30 μm , 35 μm , 40 μm , 45 μm , 50 μm

Figure 3. Microfluidic channel and the microelectrodes model that created in the COMSOL simulation software. The result shows the electric field gradient distribution and the electric field contour.

a drop at certain point when the electrode width increased beyond 40 μm and 80 μm .

Firstly, for channel height influencing on ∇E_x^2 values are as shown in Figure 6. As observed from the graph, the difference

in channel heights (20 μm , 30 μm , 40 μm) have similar pattern and have very little difference on the electrode's ∇E_x^2 values. The ∇E_x^2 values gradually increased when the electrode spacing increased. Only the channel height of 50 μm showed lowest ∇E_x^2 values at the beginning range of electrode spacing

Figure 4. The influence on electric field gradient by the peak-to-peak voltage and frequency.

Figure 5. The 3D plots of the simulation results with the combination of the variables with its parameters. The 3D plots generated with MATLAB R2019b.

from 5 μm to 15 μm . Further to investigate, extend on channel height from 5 μm to 100 μm , with width of electrode 20 μm and electrode spacing 5 μm kept constant as shown in Figure 8. The ∇E_x^2 values have observed a fall between 40 μm to 70 μm channel height. Therefore, the optimum channel height design should be 40 μm .

For the electrode widths results as shown in Figure 7, when the channel height is 20 μm and 30 μm , the ∇E_x^2 values for different range of electrode widths are in the same pattern. It has been shown that when the electrode width exceeded 60 μm , the ∇E_x^2 values have dwindled about 64% drop in ∇E_x^2 value. For channel height 40 μm the drop in ∇E_x^2 values have started

Figure 6. Graph result of electrode spacing influence on the electric field gradient with respect to 20 μm electrode width for different channel height.

Figure 7. Graph result of electrode width influencing on electric field gradient for different channel height with respect to 5 μm electrode spacing.

Figure 8. The graph of different channel height influencing on the electric field gradient ∇E^2_x with respect to constant electrode width 20 μm and electrode spacing 5 μm .

early at 40 μm electrode width. However, the electrode widths were not much influence on the ∇E^2_x values when the channel height reached 50 μm , but it has been the least amount of ∇E^2_x values, it has about 63% less ∇E^2_x values compared to other channel, since then the ∇E^2_x values were not much fluctuated and constantly stayed within its ∇E^2_x range. The optimum design for the electrode width is within 60 μm and channel height within 30 μm .

Conclusion

Based on the simulation results, the optimum geometrical parameters for rectangular shape electrode design for the strongest DEP force was identified. In this simulation and

parametric studies were only focused on the DEP force and did not include other factors such as hydrodynamic forces, joule heating effects, particles Brownian motion in the microfluidic device. As according to this study, 1. The applied voltage has significant influence on electric field gradient, ∇E^2_x , however the frequency will not have effect on electric field gradient, nonetheless it is strongly responsible to the DEP response of the particle based on the polarizability between the medium and particle, 2. For the optimum design considerations for rectangular shape microelectrode, the electrode width is advised to fall below 60 μm and 3. the channel height should below 30 μm to obtain the strongest DEP force for particle manipulation in this microfluidic design.

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The purpose of this research is to determine the best design for manipulating biological particles by examining several parametric design configuration factors (channel height: 20-50 m; electrode width: 20-100 m; electrode spacing: 5-50 m).

I mainly have the following concerns:

Introduction:

1. The authors should clarify, on what basis did they determine these ranges, they should be related to the type of tested biological particles (i.e. normal cells, cancer cells, stem cells, or bacteria) and the manufacturing capabilities of electrodes (i.e. PCB or CMOS) and microfluidic chamber.

2. The suggested configuration of electrodes in Fig.1 is traveling wave dielectrophoresis (TwDEP):

The authors should introduce TwDEP.

The authors must revise equation 1 because TwDEP mainly depends on the imaginary part of CM.

Simulation study - The authors should clarify:

1. The reasons for gold material selection.

2. The kind of AC waveforms (i.e. sinewave, or square wave)

3. The range of the applied frequencies.

The authors based their research solely on the electric field, which is insufficient because the COMSOL software also includes a module (particle tracing for fluid flow) that determines whether

or not the electric field is capable of performing the required function (manipulation of biological particles) by calculating the dielectrophoretic force on the particles.

Also, the authors should study the fluid flow to evaluate the functionality of the channel's height.

Therefore this study is insufficient, the authors should add two modules (particle tracing for fluid flow, and creeping flow)

Is the work clearly and accurately presented and does it cite the current literature?

Yes

Is the study design appropriate and is the work technically sound?

No

Are sufficient details of methods and analysis provided to allow replication by others?

Partly

If applicable, is the statistical analysis and its interpretation appropriate?

Partly

Are all the source data underlying the results available to ensure full reproducibility?

No source data required

Are the conclusions drawn adequately supported by the results?

Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: I have 8 years of experience in a lab on a chip applications special in Dielectrophoresis

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

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