BIOCHIP DEVELOPMENT FOR BIOLOGICAL CELLS MANIPULATION USING DEP

Siti Nursyahirah Ahmad Latfi[1], and Fahmi Samsuri[2]

[1] Electrical and Electronic Engineering Faculty, Pekan, Pahang, Malaysia, and siti_ierah90@yahoo.com

[2] Electrical and Electronic Engineering Faculty, Pekan, Pahang,, Malaysia,, and fahmi@ump.edu.my

ABSTRACT

Biochip is a technology platform that has become the medium of researchers in carrying out the analysis of biological cells such as sorting, trapping and screening of biological within a few seconds. To conduct analysis on biological cells, appropriate manipulation techniques are required. In this research, a Dielectrophoresis force (DEP) manipulation technique was used by applying non-uniform AC electric fields generated by the microeletrodes designed. For carrying out on one of the main objectives of this study, COMSOL Multiphysics 4.4 software was used in this study in which the ring planar microarray microelectrodes pattern was designed to investigate the distribution of the electric field resulting from the microelectrodes designed. Results show the highest electric field strength occurs at the end of the microelectrode tip at the same time the lowest electric field region can be seen at the microcavity centre. Cell trapping may also occur in the central part of the micro-cavities with negative dielectrophoresis (nDEP) in which cells will become interested in the low electric field.

Keywords: Biochip, Dielectrophoresis (DEP), and Microelectrode design.

INTRODUCTION

This study aims to explore the development of biochip in which capable of analyzing biological cells by using the dielectrophoresis (DEP) force. Biochip is one technology that is now in the spotlight and many researchers use them to analyze the cells. Biochip technology allows researchers conducted various studies in the simultaneously, in addition to achieving higher throughput and speed. The use of biochip helped the researchers in conducting research on living cells to understand and study the complex properties of the cell, in addition to obtaining important analyses that may help in the treatment of human diseases for the present and the future [1].

Dielectrophoresis (DEP) is one technique to manipulate cells, where the study of the DEP force initiated in 1950 by Herbert Pohl [2]. Many manipulation techniques such as optical [3], magnetic and acoustic [4] have been used in cell analysis; however the DEP force manipulation technique offers a non-contact trapping method on a biochip platform and together with the advantages of strong controllability, easy operation, high efficiency and slight damage to target [5]. This makes the DEP manipulation techniques preferred in the present study. The DEP manipulation technique is gaining researchers in manipulating cells where it can be used for trapping, separate and sort different types of particles and has been used in research on platelets [6], yeast cells [7], and cancer cells [8].

Force that generated by a non-uniform electric field that exerted to dielectric particle produces dielectrophoresis (DEP) phenomenal. Model of conventional dielectrophoresis was first established by Pohl on the basis of classical Maxwell electromagnetic field theory. To acquire DEP force acting on a spherical particle, the following equation was used [9].

$$F_{DEP} = 2\pi r^3 \varepsilon_m \,\mathrm{Re}[K(\omega)]\Delta \mathrm{E}^2 \quad (1)$$

Where r is the radius of particle, ε_m is the absolute permittivity of media and ΔE is the electric field gradient. Re$[K(\omega)]$ is the real part of the Clausius-Mossoti (CM) factor with value range between -0.5 and 1. It mentions to positive dielectrophoresis (pDEP) when $\mathrm{Re}[K(\omega)]\rangle 0$, particles move toward high electric field region and negative dielectrophoresis (nDEP) when $\mathrm{Re}[K(\omega)]\langle 0$, particles move to low electric field region. $[K(\omega)]$ is defined as:

$$[K(\omega)] = \frac{\varepsilon_p^* - \varepsilon_m^*}{\varepsilon_p^* + 2\varepsilon_m^*} \quad (2)$$

where ε_p^* is the particle complex permittivity and ε_m^* is the medium complex permittivity, which related to applied AC electric field angular frequency ω and conductivity σ :

$$\varepsilon^* = \varepsilon - j\frac{\sigma}{\omega} \quad (3)$$

where ε is the permittivity and j is the imaginary number which is $j = \sqrt{-1}$.

Various microelectrode designs have been developed by researchers for trapping and handling of small particles using DEP forces which capable of manipulating the cells. Biochip microelectrode design plays an important role in generating required DEP force. The different electrode design will produce different DEP force strength and different electromagnetic field (EM) pattern.

METHODOLOGY

COMSOL Multiphysics 4.4 software was used in this study in which the planar microarray ring

microelectrodes pattern was designed for carrying out a study on one of the main objectives of this study, which is to investigate the distribution of the electric field resulting from the microelectrodes designed. Figure-1 illustrates the structure and the main components of the biochip. Biochip structure is based on [10], wherein the patterned microelectrode and microcavity fabricated on different layers. Microcavity etched within the Biochip surface to trapping the cells at known positions on the substrate's surface. For this design, microcavity was etched in the middle of the microelectrode.

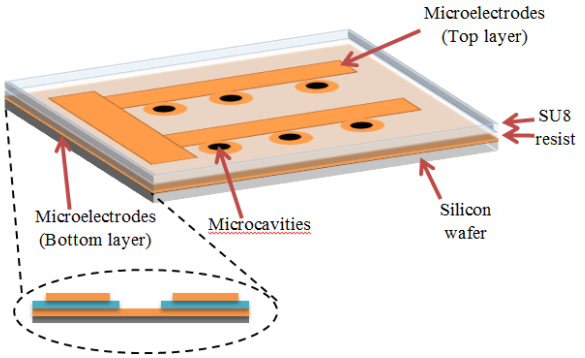


Figure-1. 3D illustration of the Biochip design.

Various microelectrode geometries have evolved by researchers to handle different tasks in the cell analysis, where the general objectives of the study will determine the electrode geometry used. Figure-2 shows the preliminary microelectrode design. Microelectrode geometry design conducted in parallel with the design simulation by using AC/DC module of COMSOL Multiphysics 4.4 software.

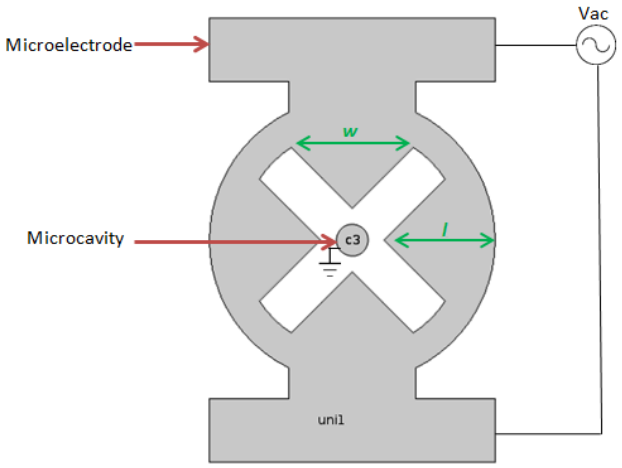


Figure-2. Preliminary microelectrode design.

The patterned microelectrode with tip length, $l = 40\mu m$, width, $w = 40\mu m$ and radius, $r = 45\mu m$ and micro-cavities with radius, $r = 5\mu m$ was given material properties of gold and SU8 with both permittivity, $\varepsilon_r = 1$. For the suspending medium, was given the material properties of deionized water (DI water) with permittivity, $\varepsilon_r = 78$ and conductivity, $\sigma = 1.7mS/m$.

By using a physics-controlled mesh with extra fine element size, meshing stage was done for the entire geometry as shown in Figure-3. The simulation was conducted using a frequency of 1MHz and supplied voltage (AC potential φ) 10Vpp. Microcavity simulations carried out by providing either 0V or -10V (180° phase different from microelectrode AC potential) and comparisons will be made. The results of it will be shown in the results and discussion section.

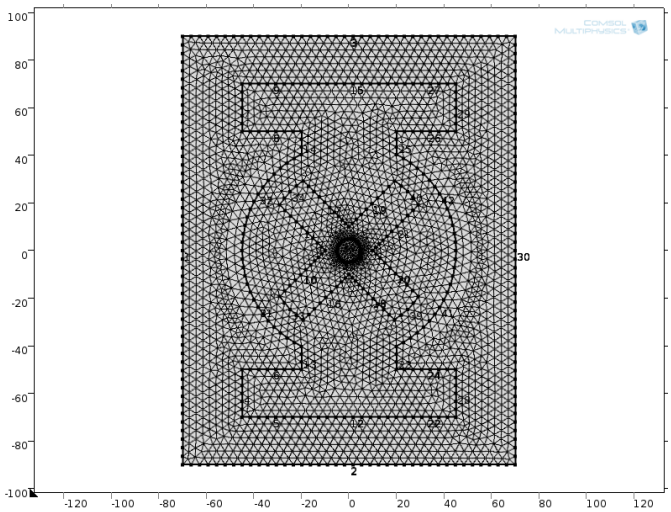
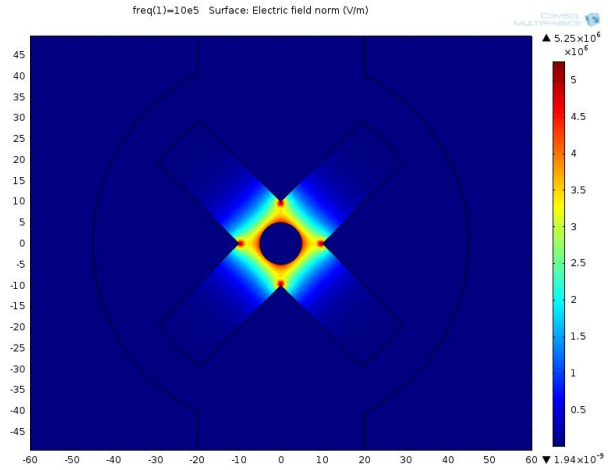


Figure-3. Meshing stage in COMSOL Multiphysics 4.4.

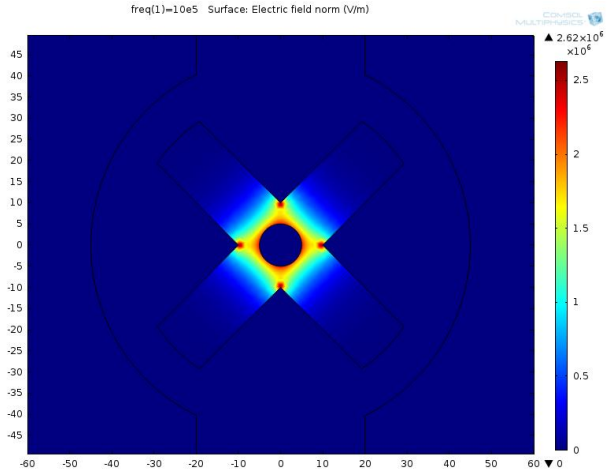
RESULT AND DISCUSSION

The simulation was conducted on the model after incorporating all the parameters such as assigning material properties and setting boundary condition for plotted the distribution of electric field strength (V/m) as shown in Figure-4 and Figure-5.

Figure-4(a) and Figure-4(b) also illustrates the differences in the distribution of electric field strength value in which microcavity supplied with -10V (180° phase different from microelectrode AC potential) generate approximately $5.25\times10^6 V/m$ at the region of high electric field while micro-cavities supplied with 0V (no phase different) generate approximately $2.62\times10^6 V/m$ at the region of high electric field. This indicates that the distribution of the electric field strength is higher when microcavity was set to -10V with 180° phase different from microelectrode potential, which is in concession with the findings in [10].

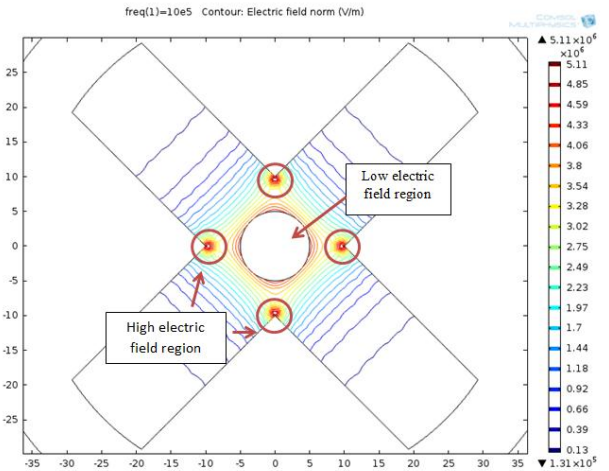


(a)

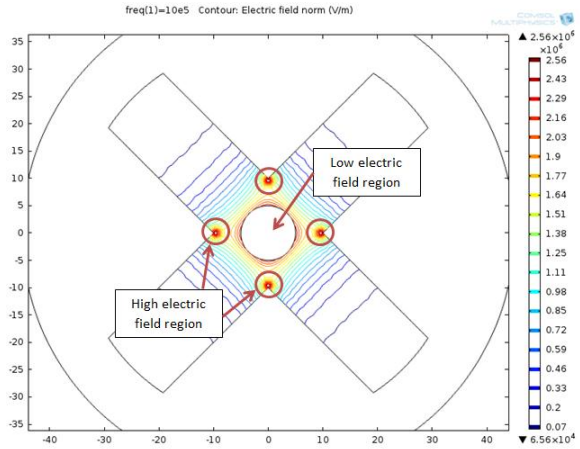


(b)

Figure-4. Electric field strength distribution (V/m) over (a) -10V of microcavity and (b) 0V of micro-cavities.



(a)



(b)

Figure-5. Trapping region over (a) -10V of microcavity and (b) 0V of micro-cavities.

Figure-5 (a) and (b) illustrates the trapping region for the microelectrodes. The simulation results show a high electric field strength distribution high in the area between the edge of the micro-cavities and end of microelectrode tip. The highest electric field strength occurs at the end of the microelectrode tip at the same time the lowest electric field region can be seen at the microcavity centre. Therefore, the DEP force expected to be higher at the end of microelectrode tip instead at the middle of microcavity. Particles movement will rely upon Clausius Mossotti factor where the particle will repel from the region of high electric field and attracted in the region of low electric field (middle of microcavity) for negative dielectrophoresis (nDEP) trapping, and vice versa for positive dielectrophoresis (pDEP).

CONCLUSION

The electric field intensity distribution analysis was conducted using the simulation software COMSOL Multiphysics 4.4 on micro-electrodes are built. Based on the results obtained, the resulting electric field strength is high between the microelectrodes tip and edge of the micro-cavities. Cell trapping may also occur in the central part of the micro-cavities with negative dielectrophoresis (nDEP) in which cells will become interested in the low electric field. Also, when using positive dielectrophoresis (pDEP), cells would be interested at the edge of micro-cavities where the high electric field region occurs. With simulation and analysis obtained, designed microelectrode able to trap the cells.

REFERENCES

[1] F. Samsuri and J. J. Evans, "Biochip development using Nanoimprint Lithography (NIL) and metallic thermal evaporation techniques for biological cells manipulation using DEP," pp. 382–387, 2011.

[2] H. a Pohl and J. S. Crane, "Dielectrophoresis of cells.," *Biophys. J.*, vol. 11, no. 9, pp. 711–727, 1971.

[3] N. Neve, S. S. Kohles, S. R. Winn, and D. C. Tretheway, “Manipulation of suspended single cells by microfluidics and optical tweezers,” *Cell. Mol. Bioeng.*, vol. 3, no. 3, pp. 213–228, 2010.

[4] T. Lilliehorn, U. Simu, M. Nilsson, M. Almqvist, T. Stepinski, T. Laurell, J. Nilsson, and S. Johansson, “Trapping of microparticles in the near field of an ultrasonic transducer,” *Ultrasonics*, vol. 43, no. 5, pp. 293–303, 2005.

[5] C. Qian, H. Huang, L. Chen, X. Li, Z. Ge, T. Chen, Z. Yang, and L. Sun, “Dielectrophoresis for bioparticle manipulation.,” *Int. J. Mol. Sci.*, vol. 15, no. 10, pp. 18281–309, Jan. 2014.

[6] N. Piacentini, G. Mernier, R. Tornay, and P. Renaud, “Separation of platelets from other blood cells in continuous-flow by dielectrophoresis field-flow-fractionation,” *Biomicrofluidics*, vol. 5, no. 3, pp. 1–8, 2011.

[7] S. Patel, D. Showers, P. Vedantam, T. Tzeng, and S. Qian, “Microfluidic separation of live and dead yeast cells using reservoir-based dielectrophoresis Microfluidic separation of live and dead yeast cells using reservoir-based dielectrophoresis,” vol. 034102, pp. 1–12, 2012.

[8] C. H. Chuang, Y. W. Huang, and Y. T. Wu, “System-level biochip for impedance sensing and programmable manipulation of bladder cancer cells,” *Sensors*, vol. 11, no. 11, pp. 11021–11035, 2011.

[9] J. Cao, P. Cheng, and F. Hong, “A numerical analysis of forces imposed on particles in conventional dielectrophoresis in microchannels with interdigitated electrodes,” *J. Electrostat.*, vol. 66, no. 11–12, pp. 620–626, 2008.

[10] S. N. Ibrahim, L. Murray, V. Nock, J. J. Evans, and M. M. Alkaisi, “The quadrupole microelectrode design on a multilayer biochip for dielectrophoretic trapping of single cells,” *Microelectron. Eng.*, vol. 97, pp. 369–374, Sep. 2012.