Electromagnetic Flux Modeling of AC Field over Planar Microarray Dot Electrodes Used in Dielectrophoretic Lab-on-Chip Device

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Abstract – **<u>Introduction</u>: Lab-on-chip devices have been proven to be advantageous in terms of selective collection, manipulation and separation of cells and particles. Numerous physical methods have been employed in the development of such devices, and alternating current (AC) electrokinetics was one of the chosen techniques due to its selectivity, efficacy, non-invasiveness, and low fabrication costs. Recently it has been shown that, by employing a specific AC electrokinetics technique called dielectrophoresis, it was possible to fabricate an addressable microarray dots in creating axisymmetrical AC fields over a planar microelectrode within a chamber containing the cell sample. Each of these dots received different input frequency values in order to create the required field with specific gradient strength, thus enabling dielectrophoretic experiments to take place in rapid succession. The objective of this study is to simulate the generation of the said electromagnetic fluxes over the microarray dots using finite element methods. <u>Materials and Methods</u>: Three different materials, namely copper, gold, and indium tin oxide were used, and simulated at different input frequencies and environment. <u>Results and Discussion</u>: The results indicate that the generated AC electric fields are satisfactory in creating the required DEP effects within a chamber height of 200 µm. Different electrode materials and environment produced no significant difference ($p>0.05$) in terms of the maximum and minimum electrical gradient strengths. Further investigation with regards to the optimal distance in between the dots is warranted in order to create consistent dielectrophoretic effects with optimal particle density.**

Keywords – **Lab-on-chip, dielectrophoresis, electromagnetic flux, dot microarray electrodes, *in silico.***

I. INTRODUCTION

Lab-on-chip devices may generally be defined as a construct consisting of multiple components such as heaters, pumps, sensors and reactors that were assembled and integrated onto a single device, with size as small as a postage stamp [1,2]. Such devices offer a number of advantages, namely in terms of fabrication costs, portability, and operational ease. The advent of the device has been boosted by the advancement of the microfabrication industry in late 1980s, leading to the development of a myriad of devices and applications with specific uses.

Among the earliest objectives of such developmental efforts were to selectively collect, manipulate and separate various particles and cells of interest. The demand for the ability to manipulate cells, particularly live mammalian cells, is always present and on the increase [2,3]. This is of particular interest to the field of medical diagnostics, including for example, the detection and isolation of malignant cells, the separation of cells according to its specific physiological properties, and single cell physical manipulation. The scope of research has even encompassed down to the level of cellular components, including genetic analysis and interpretation, and viral infection characterization [1,4].

One possible technique to be employed in a lab-on-chip was AC electrokinetics, since it allowed the physical manipulation of particles, down to individual cells, using non-invasive, low-power, and easily fabricated devices. AC electrokinetics encompasses a number of related techniques, including dielectrophoresis (DEP), electro-rotation (ROT), travelling-wave dielectrophoresis (tw-DEP), electro-osmosis, and electro-orientation [1,4,5]. Although these methods offer a number of advantages over routine cell assay methods, the uptake has been generally low due to the time-consuming processes involved. This predicament is due primarily to the limitation imposed on the number of cell assays that can be performed at any one time [1,2,6]. Recently however, it has been shown that individually-addressed, multiple microarray dot electrode is capable of conducting DEP-based cell characterization in a very short time period [7]. Although the primary objective was to overcome the said problem of extended time consumption in conducting the experiments, this capability led to the possibility of real-time monitoring and analysis of DEP events, particularly changes in the conductivity and permittivity of cellular membranes and intracellular components.

The objective of this study is thus to numerically analyze the generated AC electrical field, particularly the relative strength of the electromagnetic flux gradient, over the planar multiple microarray dot electrodes to be employed in generating DEP effects on selected cell populations. The maximum and minimum AC gradient strength generated by three different electrode materials, namely copper, gold, and indium tin oxide (ITO), will be compared and statistically analyzed.

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A. Dielectrophoresis

Dielectrophoresis (DEP) is a term used in describing an electrical phenomenon whereby a transient force is generated when a dielectric particle is immersed in a conductive medium and subjected to a non-uniform AC field. Depending on the alignment of induced dipole moments, the generated DEP force may either push towards, or pull away from, the electrical gradient [1-4]. Generally, the magnitude of DEP force is affected by the permittivity and conductivity values of the surrounding medium and the particles used.

The expression for DEP force of a homogeneous sphere may be represented by [1,2]:

$$\langle F_{DEP} \rangle = 2\pi r^3 \varepsilon_m \operatorname{Re}[K(\omega)] \nabla E^2 \tag{1}$$

where ε_0 is the free space permittivity, ε_m is the permittivity of medium surrounding the particle, r is the particle radius, $K(\omega)$ is the complex Clausius-Mossotti factor, and ∇E is the gradient strength of the applied electric field. The Clausius-Mossotti factor is generally defined as:

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

where ε^* is the specific permittivity value. Subscripts p and m are permittivity values of particles and medium, respectively. In addition, the complex permittivity is typically represented as:

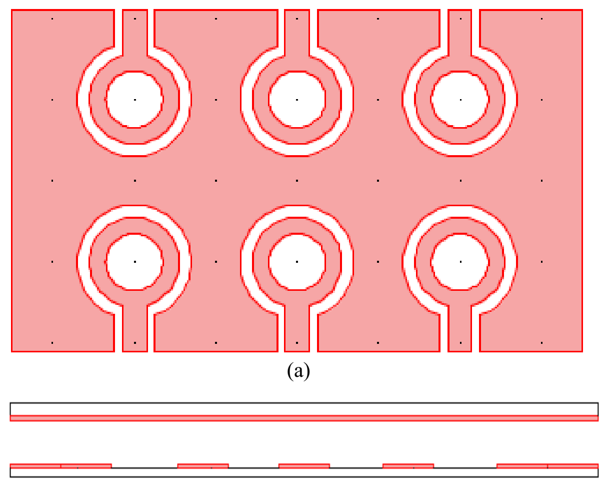
$$\varepsilon^* = \varepsilon - \frac{j\sigma}{\omega} \tag{3}$$

where ε is the permittivity, σ is the conductivity, and ω is the angular frequency. These equations indicate the interdependency of permittivity and conductivity values of both the particle and the surrounding medium, and also the gradient strength and frequency of the applied AC field. For a homogeneous sphere of a given dielectric particle, $\operatorname{Re}[K(\omega)]$ is bounded by a range of minimum and maximum values. The particle will generally be pushed away from the electrode edge when $\operatorname{Re}[K(\omega)]<0$, as the result of negative DEP (nDEP), and vice versa when $\operatorname{Re}[K(\omega)]>0$, and the effect is termed positive DEP (pDEP).

B. Electrode design

The generation of non-uniform electrical field that is of desirable strength is essential, and primarily depends on the specific electrode geometry design. Examples of planar electrode designs include the interdigitated electrodes [8], castellated inter-digitated electrodes [9,10], spiral electrodes [11,12] and polynomial electrodes [13,14]. The selection of electrode geometry is dictated by the objective of the DEP study, e.g. separation of cell populations, or physical manipulation of particles.

A single dot planar electrode has been previously shown to be capable of conducting DEP-based cell characterization at small particle concentration, due to the generation of axisymmetrical AC electric field over the electrode [15]. For the purpose of this study, multiples of similar 'dots' were designed (Figure 1) to mimic the experimental setup of Fatoyinbo *et al.* [7], to ascertain the parameters of generated AC electromagnetic field.



(a)

(b)

Fig. 1 Planar multiple microarray dot electrode used in the study viewed from (a) the top, and (b) the sides

In this study, comparison will also be made by using different materials for the electrode fabrication, namely copper, gold, and ITO. ITO currently received wide acceptance in the development of lab-on-chip devices due to its high transparency and low resistivity [4,16]. These materials also differ in terms of dielectric properties, namely conductivity and relative permittivity values.

II. METHODOLOGY

A. Finite element modeling

COMSOL Multiphysics® software (COMSOL Inc., Palo Alto, USA) was used as the finite element method (FEM) of choice for analyzing the generated electromagnetic field, both in two- and three-dimensions. In this study, the AC power electromagnetic mode was used, and the analysis will be based on partial differential equation using the Ampere's Law.

A few assumptions have been made so that it will mimic the real environment. The planar microelectrode is modeled as a rectangle of 1.75 mm x 10 µm (Figure 1). The central 'dots' were designed with a diameter of 250 µm and width of 150 µm. The potential difference applied to both positive and negative terminal is about 10 V. Various frequency values were also applied in order to estimate differences in electromagnetic fields produced.

B. *Statistical analysis*

The simulation results obtained were statistically analyzed based on the mean and standard deviation values to determine the correlation and differences (at $p<0.05$), if any.

III. RESULTS AND DISCUSSION

Figure 2 shows the electrode structure being converted into an assembly of elements prior to the finite element analyses being conducted. Figure 3 shows the generated electromagnetic fields over the electrodes fabricated from the different materials at 1 atm, when a 50 Hz signal was applied. It was found that the electromagnetic flux density is higher for materials with higher electrical conductivity and permittivity values, and the highest is recorded by copper with a mean value 4.44 mT. Gold and ITO has a mean value of 3.37 and 0.97 mT, respectively. It is worth noting that copper also recorded the widest range of electromagnetic field compared to the other two materials with a standard deviation value of $6.28\text{x}10^{-3}$ mT.

The FEM model was also simulated when the input is supplied at different frequency values, namely 50, 100, 1000, 50000, and 500000 Hz within the same environment to observe any changes in the produced electromagnetic field (Figure 4). There were no significant changes however, to the generated electromagnetic densities ($p>0.05$) when different frequencies were applied.

In addition, the FEM model was also exposed to different environments apart from the typical 1 atm air, namely in distilled water and yeast solution environment. The distilled water was assumed to have conductivity of 1.5 $\text{x}10^{-4}$ S/m and relative permittivity of 78.6, while the yeast solution was assumed to be prepared in potassium chloride medium with $5.5\text{x}10^{-4}$ S/m conductivity and 50.6 relative permittivity [17,18]. It was found that the results from these different environments were similar to when air was used, and thus do not significantly differ ($p>0.05$). This is most probably due to the values of continuity conditions when setting up the model within the software.

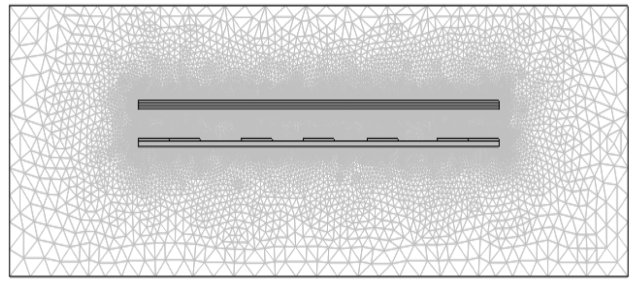


Fig. 2 The electrode structure modeled in COMSOL Multiphysics® that has been converted into an assembly of elements.

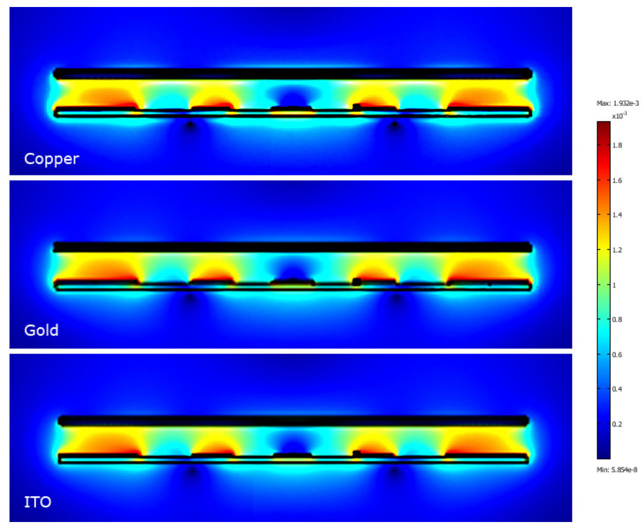


Fig. 3 Electromagnetic flux densities produced by the dot microarray electrode fabricated from different materials: (a) copper, (b) gold, and (c) ITO.

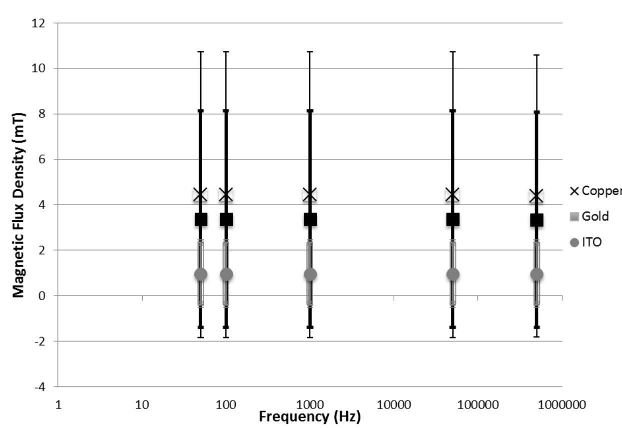


Fig. 4 The mean value of electromagnetic flux densities for each material against frequency applied.

IV. Conclusion

Although the electromagnetic flux model has been simulated previously for a single planar dot electrode [15], similar model has not been investigated hitherto for multiple dots arranged in an array that has been shown to be capable of conducting concurrent DEP experiments [7]. Results from the current study indicated that the generated AC field is satisfactory in creating the required DEP effects within a chamber height of 200 µm. Different electrode materials and environments produced no significant difference (p>0.05) in terms of the maximum and minimum electrical gradient strengths. Further studies in determining the optimal distance between the electrodes, particularly in correlation with particle density, are warranted in order to develop a consistent *in silico* models for future development of planar microelectrode-based lab-on-chip devices.

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References

1. Hughes M (2002) Strategies for dielectrophoretic separation in laboratory-on-a-chip systems. Electrophoresis 23(16), 2569.
2. Kadri NA, Fatoyinbo HO, Labeed F et al. (2011) Semi- automated dielectrophoretic cancer cell characterisation module for lab-on-chip applications. 5th Kuala Lumpur International Conference on Biomedical Engineering 2011 (Biomed 2011), 21-23 June 2011, Kuala Lumpur, Malaysia.
3. Kadri NA, Hoettges KF, Hughes MP (2009) Development of a generic multiple frequency signal generator for BioMEMS. In Dussel O, Schlegel WC. (Eds.) IFMBE Proceedings (Vol. 25), World Congress on Medical Physics and Biomedical Engineering, 7-12 September 2009, Munich, Germany.
4. Pethig R. (2010) Dielectrophoresis: Status of the theory, technology, and applications. Biomicrofluidics 4, 022811.
5. Pethig R, Markx G (1997) Applications of dielectrophoresis in biotechnology. Trends in biotechnology 15(10), 426–432.
6. Hoettges K, Hubner Y, Broche L et al. (2008) Dielectrophoresis-Activated Multiwell Plate for Label-Free High-Throughput Drug Assessment, Anal. Chem 80(6), 2063–2068.
7. Fatoyinbo HO, Kadri NA, Hoettges KF et al. (2011) Real-time quantification of biophysical changes to leukaemic cells on an addressable dielectrophoretic-dot (DEP-Dot) microarray. Electrophoresis 2011; 32(18):2541–2549
8. Suehiro J, Noutomi D, Shutou M et al. (2003) Selective detection of specific bacteria using dielectrophoretic impedance measurement method combined with an antigen-antibody reaction. Journal of Electrostatics 58(3-4), 229–246.
9. Gascoyne P, Huang Y, Pethig R et al. (1992) Dielectrophoretic separation of mammalian cells studied by computerized image analysis. Measurement Science and Technology 3, 439–445.
10. Becker F, Wang X, Huang Y et al. (1995) Separation of human breast cancer cells from blood by differential dielectric affinity. Proceedings of the National Academy of Sciences 92(3), 860.
11. Müller T, Gerardino A, Schnelle T et al. (1996) Trapping of micrometre and sub-micrometre particles by high-frequency electric fields and hydrodynamic forces. Journal of Physics D: Applied Physics 29, 340–349.
12. Wang X, Huang Y, Wang X et al. (1997) Dielectrophoretic manipulation of cells with spiral electrodes. Biophysical journal 72(4), 1887–1899.
13. Huang Y, Pethig R (1991) Electrode design for negative dielectrophoresis. Measurement Science and Technology 2, 1142–1146.
14. Hughes M, Morgan H (1998) Dielectrophoretic trapping of single sub-micrometre scale bioparticles. Journal of Physics D: Applied Physics 31, 2205.
15. Fatoyinbo H, Hoettges K, Hughes M (2008) Rapid-on-chip determination of dielectric properties of biological cells using imaging techniques in a dielectrophoresis dot microsystem. Electrophoresis 29(1), 3–10.
16. Kadri NA, Hoettges KF, Hughes MP (2008) Microelectrode Fabrication Using Indium Tin Oxide (ITO) For Microfluidic Devices Employing Dielectrophoresis. IFMBE Proceedings (Vol. 21), 4th Kuala Lumpur International Conference on Biomedical Engineering 2008 (Biomed 2008), 25-28 June 2008, Kuala Lumpur, Malaysia
17. El-Zakhem H, Lanoisellé JL, Lebovka NI et al. (2006) Behavior of yeast cells in aqueous suspension affected by pulsed electric field. Journal of Colloid and Interface Science, 300, 553–564.
18. Raicu V, Raicu G, Turcu G (1996) Dielectric properties of yeast cells as simulated by the two-shell model. Biochimica et Biophysica Acta, 1996, 143–149.

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