Some Commonly Neglected Issues Which Affect DEP Applications

Vandana Pandian[1], Jozef Brcka[3], Jacques Faguet[3], Eric Lee[3], Guigen Zhang[1,2,4] *
[1]Department of Bioengineering, Clemson University, Clemson, SC 29634
[2]Department of Electrical and Computer Engineering, Clemson, SC 29634
[3]Tokyo Electron U.S. Holdings, Inc., U.S. Technology Development Center, Austin, TX 78741
[4]Instutite for Biological Interfaces of Engineering, Clemson University, Clemson, SC 29634
* guigen@clemson.edu

Abstract: Dielectrophoresis (or DEP) is an important phenomenon which is induced when a dielectric particle is placed in a non-uniform electric field. The force generated by DEP has been exploited for various micro and nano fluidics applications involved in biomedical engineering. This work identifies the problems in the literature and uses COMSOL to analyze the impact of these problems on the end results. From the analyses, it becomes clear that particle size not only affects the magnitude of the DEP force but also the conductivity of the particle. This factor, which is largely ignored, could lead to a shift in the crossover frequency. Moreover, for non-homogenous particles, such as cells, use of shell models is necessary in determining the DEP forces.

Keywords: Dielectrophoresis, cells, cross-over frequency, shell model

1. Introduction

DEP was first observed in early 20th century. However it was explained and named by Herbert A. Pohl in 1950 when he was attempting to separate particles from a polymer solution [1]. The applications of DEP remained unknown and hence not much work was done on it. In the last ten years it has been revived due to development made towards translating theoretical treatment of microparticles, nanoparticles and cells to practical applications like biosensors, bioassays. In the last three years DEP has been combined with microfluidics to help better manipulation of particles. Currently most of the work is into addressing unmet needs in tissue engineering and stem cell research [2,3].

DEP is demonstrated when dielectric particles are placed in a non-uniform electric field (both in AC and DC electric fields). This is because DEP shows higher dependence on the field gradient than the field direction. In the case of AC-DEP, which is mainly reviewed and studied in this research, fields of a particular frequency are used to manipulate particles with greater selectivity. If particles move in the direction of increasing electric field, the behavior is referred to as positive DEP (pDEP). If particles move away from high field regions, it is known as negative DEP (nDEP).

The strength of the DEP force varies with the properties of these particles and the suspension media used as well as physical parameters and electrode setup. In contrast to electrophoresis, the particles do not have to be charged. When these particles are placed in a non-uniform electric field, they will be polarized to form a dipole [4]. This leads to attraction and repulsion of particles according to the orientation of the dipole, which is dependent on the relative polarizability of the particle and medium, leading to the separation of the charges.

2. Fundamentals of DEP

2.1.1. Theoretical Explanation of DEP

The simplest theoretical model for DEP is that of a homogeneous spherical particle immersed in a dielectric medium. According to Pohl, for a homogeneous sphere of radius R in a medium with permittivity ε_m, the DEP force can be calculated as follows [5]

$$F_{DEP} = 2\pi r^3 \varepsilon_m Re(f_{CM}) \nabla |E|^2$$

where, f_{cm} is the Clausius-Mossotti (CM) factor, r is the radius of the particle and ε_m is the permittivity of the medium. When a particle has a non-spherical shape (e.g., ellipsoidal shape) the above equation can be modified to accommodate the different shape.

2.1.2. Frequency Dependence of CM factor

The CM factor introduced in the previous equation is defined in terms of complex permittivity as follows [6]

$$f_{cm} = (\varepsilon_p^* - \varepsilon_m^*)/(\varepsilon_p^* + 2\varepsilon_m^*)$$

where, ε_p^* and ε_m^* are complex permittivity of the particle and the suspension medium respectively. The calculation of the complex permittivity (ε^*) is given below [7]

$$\varepsilon_p^* = \varepsilon_p - (\sigma_p/\omega)$$

where, σ_p is the conductivity of the particle, ε_p is the permittivity of the particle, i is the imaginary unit and ω is the angular frequency. The frequency at which $Re(f_{cm})$ is zero is called the crossover frequency. The particle moves in the direction of increasing electric field when $Re(f_{cm})$ is positive, leading to pDEP. The particle moves away from the high electric field regions when $Re(f_{cm})$ is negative, leading to nDEP.

2.1.3. Polarizability

The polarizability of a particle is defined in terms of the local electric field at the particle by the following equation

$$\rho \propto E_{local}$$

where, ρ is the dipole moment and E_{local} is the local electric field. It is very important to choose the right medium to suspend the particles because the DEP force changes with the relative polarizability (depending on whether the particle is more polarizable or less polarizable than the medium) according to Maxwell-Wagner-Sillars polarization [8].

3. Common Problems in AC-DEP

3.1. Particle size

Particle size is an important factor affecting DEP because the force acting on the particle is proportional to particle's volumetric size ($4\pi r^3/3$). Thus, the DEP force is proportional to r^3, where r is the radius of the particle. However, it has to be noted that the radius also affects the conductivity of the particle, which is determined by its radius, bulk conductivity and surface conductivity. It was found that the effect of radius on conductivity has been ignored in some research works. It has been assumed in these works that the radius will affect the DEP solely by being proportional to the cube of the particle radius [9].

3.2 Shell model of Particles

In DEP and related AC electrokinetical phenomena like electrorotation and twDEP dielectric properties are usually assumed to be homogeneous. However, this assumption is not valid in the case of biological particles with which shell models are often used to define the non-uniform dielectric properties of the particles[10].

In some micro-organisms (e.g. gram positive bacteria) and other cells, the cell wall contains high concentrations of charged species and counter-ions which can form a conductive screen and effectively dominate the dielectric properties. Even if there is less charge, electrorotation measurements have shown that the cell wall plays a significant role in affecting the electrokinetic properties of the cell in low-conductivity media**.** Large sized vacuoles found in yeasts and other cells in cell require the use of a vesicle inclusion model. Thus considering the cell to be homogeneous may produce skewed results when trying to validate the experimental results with the theoretical results.

3.3 Electric Double layer

When the conductivity of particle is lower than the medium theoretically a cross-over frequency cannot exist. However a cross-over is observed in experimental setups. This is due to the presence of an electric double layer [11]. Double layer appears on the surface of an object like a solid particle, gas bubble, liquid droplet or a porous body, when it is exposed to a fluid. At lower frequencies the polarizability of the particles increases due to the presence of the ionic double layer resulting in an increase in the DEP force on the particle. It is important to consider this double layer when working with

DEP force as they affect the conductivity of the particle.

4. Use of COMSOL Multiphysics

COMSOL modeling is performed to illustrate the consequences of some of these common problems identified. Various 2D and 3D models are developed to study the factors affecting the DEP force through parametric studies.

The modeling part includes defining the parameters and variables, defining the geometry, applying and configuring the necessary physics, finding the results and plotting the graphs. Analysis of all the parameters is done using mesh plots, point graphs, surface plots and arrow diagrams. Further analysis is done using MS Excel and SigmaPlots to study the relationships between each of the factors and how these relationships affect the DEP force.

The figure below shows the electrode setup in a 3D model. The gap between the electrodes is adjusted by varying a constant ratio of the gap width to the electrode width. In the model, the electrode width is fixed and gap between the electrodes is varied by changing the ratio.

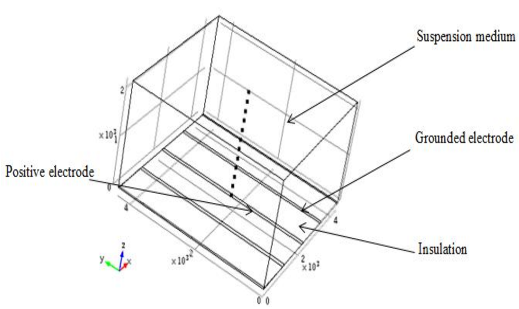

Figure 1. Model of the electrode setup used in determing the DEP force. 3D model with length, breadth and width of electrode included.

The materials used for the different components of the electrodes are crucial as they affect the DEP forces. The electrodes are made of gold and a cover layer, made of aluminum oxide, is placed on top to protect the electrodes and shield direct exposures of cells to the energized electrodes. Deionized water is used as the medium for particle suspension in this model.

The electrodes are alternately given a positive potential and grounded. The electric field is the negative gradient of the electric potential.

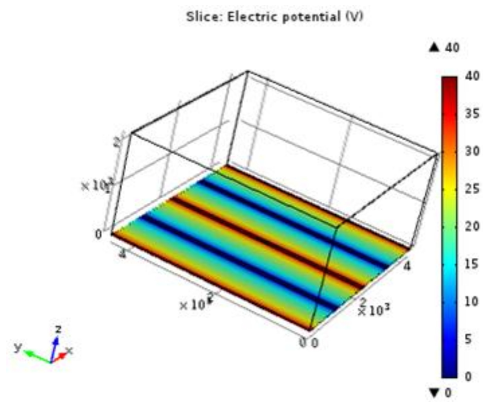

Figure 2. COMSOL model showing the electric potential applied to the electrodes.

Thus, the electrostatics physics is bound by the following equations.

$$D = \varepsilon_o E + p$$

where, *D* is the electric displacement, *E* is the external electric field and *p* is the polarisation..

$$E = -\nabla V$$

The domain for the electrode is assigned a finer mesh than the remaining region due to the expected higher electrical field gradients nearby.

Parametric sweeps are done to analyze the different factors affecting the forces acting on the particles. Four different parametric sweeps are done. The first one is for electric potential varying from 1V to 40V. The second is for the ratio (between the width of gap and width of electrode) to change the gap between the electrodes. The ratio value is swept from 0.1 to 10 with a step of 0.1.

The third parameter is the frequency which is swept for a wide range of values. The equation for force is then plotted and the magnitude of force was verified, in turn verifying the creditability of the model. Finally the radius is swept for different values and also analysis on the effect of radius on conductivity is studied.

Parametric sweep showed the trend of change of force with these parameters.

The model is designed to address the problems listed in section 3. In the parameters section of the model the conductivity of the particle is listed as a function of the radius of the particle. The radius is also defined as a variable in order to examine the effect of radius on the conductivity of particle. The following equation is used in the model to calculate the total conductivity of the particle [12].

$$k_p = k_b + 2\lambda/R$$

where, k_p is the effective particle conductivity, k_b is the bulk conductivity, λ is the surface conductivity and R is the radius of the particle.

The above equation has to be further altered to include the double layer effect. The surface conductivity λ was found to be made of a stern layer and diffuse layer. Thus the following equation is used to consider the double layer around the particle.

$$\sigma_p = \sigma_b + \frac{2(k_s+k_d)}{r}$$

where k_s and k_d are the conductivity of the diffuse layer and stern layer respectively. Effect of considering and ignoring the double layer is analyzed by plotting it on 2D graphs.

When shell models are used, the complex permittivity of particles may vary with the complex permittivity of the membrane, the core and the membrane, as

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

Where,

$v = \left(1 - \frac{d}{R}\right)^3$ and d is the thickness of outer shell, ε_p^* is the complex permittivity of the particle, ε_o^* is the complex permittivity of the outer shell or membrane, ε_i^* is the complex permittivity of the inner core, r is the inner radius and R is the outer radius [13,14].

The conductivity calculation in the presence of a double layer involves a complex dependence on polar and azimuthal angles. However a simplified calculation can be carried out by system of spherical coordinates for our research. Analytical formula is derived for calculation of the empirical constant with the capacitance of the stern and diffuse layer to facilitate the calculation.

$$\sigma_p = \sigma_b + \frac{2(k_s+k_d)}{r}$$

where k_s and k_d are the conductivity of the diffuse layer and stern layer respectively.

5. Results

Figure 3 shows the variation of DEP forces as a function of particle radius when the effect of particle size on its conductivity is considered and ignored. Clearly, ignoring this size effect results in significant differences in the prediction of DEP forces.

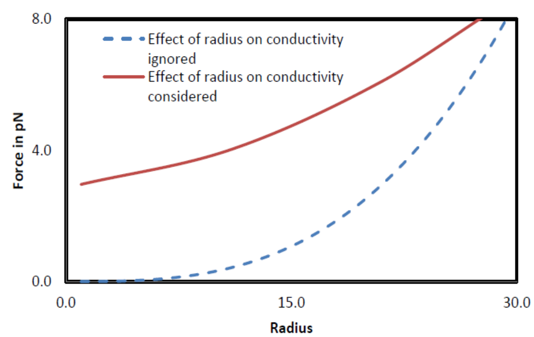

Figure 3. Change in DEP force when effect of radius on conductivity is considered and when it is neglected. (Data collected from COMSOL model)

In Figure 4 shell model was applied to E.*coli* cells and the DEP force is plotted against frequency. It shows the change of force when the shell model of cells has been ignored. It gives a cross-over frequency of about 23 kHz. If the shell model of the cells has been considered then there is a shift in the cross-over frequency to 4.2 kHz.

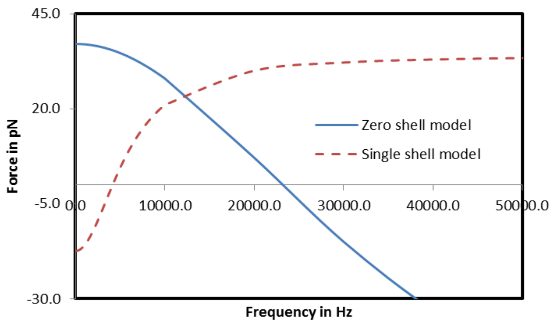

Figure 4. Differences in the variation of DEP force with frequency when a cell is treated using a single-shell and zero shell model

It can also be noted from figure 4 that the direction in which the particles travel might be different. When the cell is considered as a homogenous particle, the particles exhibit pDEP at low frequencies and then cross-over occurs. It is the other way around when the cells is considered using a shell model. The result is justified using experimental results from a publication by Pethig *et al*. according to which the cells exhibit nDEP at lower frequency and pDEP at higher frequency [15].

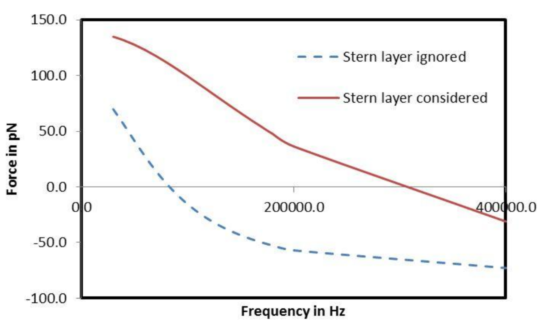

Figure 5: Shift in crossover frequency and magnitude of DEP force when the conductivity of the stern layer is included in the model

Figure 5 compares the DEP force when the stern layer conductivity is included or ignored for latex beads suspended in deionized water. It is seen that there is a considerable shift in the frequency and there is a change in the magnitude of the force as well, implying that the stern layer increases the nanocolloid conductivity to produce pDEP [16]. Due to the lack of experimental evidences to examine the distinct contribution of Stern and diffuse layer, the understanding of the polarization due to double-layer remain a subject worth of further investigation. Most of the DEP experiments focusing on colloids on monodisperse systems have not been able to explain the mutual DEP response of an individual particle affected by the presence of polarized neighbor particles in polydisperse systems and in different aggregation states [17].

6. Conclusions

DEP serves as a rapid and non-invasive technique that can be exploited for various biomedical applications like particle sorting, cell patterning, pathogen detection etc. This research identifies some common problems present in the literature. The influence of these problems is illustrated by using COMSOL multiphysics.

This work indicates that it is necessary and important to correct the problems identified. For example, not using a shell model for non-homogeneous particle could lead to a shift in the crossover frequency, and the magnitude of the DEP force would be different when the size induced conductivity change is ignored. Moreover, for manipulating particles of nano sizes, the effect of double layer would be important.

7. References

1. Pohl, H., *The Motion and Precipitation of Suspensoids in Divergent Electric Fields.* J. Appl. Phys. **22:** p. 869-871. (1951)
2. Washizu, M., Kurosawa, O. *Electrostatic manipulation of DNA in microfabricated structures.* IEEE Trans. Ind. Appl. **26**: p. 1165–1172. (1990)
3. Cummings, E.B. and Singh, A.K., *Dielectrophoresis in Microchips Containing Arrays of Insulating Posts: Theoretical and Experimental Results.* Anal. Chem. **75**: p. 4724-4731. (2003)
4. Muller, T., Fiedler, S., Schnelle, T., Ludwig, K., Jung, H., Fuhr, G., *High frequency electric fields for trapping of viruses.* Biotechnol. Tech. **10**: p. 221– 226. (1996)

5. Irimajiri, A., Hanai, T., and Inouye, A., *Dielectric theory of multi-stratified shell-model with its application to a lymphoma cell*. Journal of Theoretical Biology, **78(2)**: p. 251-269. (1979)
6. Kirby, B.J. *Micro- and Nanoscale Fluid Mechanics: Transport in Microfluidic Devices.*. Cambridge University Press. ISBN 978-0-521-11903-0.(2010)
7. Arnold, W.M., Schwan, H.P. and Zimmermann, U. *Surface Conductance and Other Properties of Latex Particles Measured by Electrorotation*. J. Phys. Chem. **91**: p. 5093-5098. (1987)
8. Hughes, M.P., Pethig, R., Wang, X-B. *Forces on Particles in Travelling Electric Fields: Computer-Aided Simulations*. J. Phys. D: Appl. Phys. **29**: p. 474-482. (1996).
9. Cui, H., Voldman,J. He, X. and Lim, K. *Separation of particles by pulsed dielectrophoresis*. Lab Chip. 2009. **9**: p. 2306–2312.
10. Einolf, C. W. and Carstensen, E. L. *Passive electrical properties of microorganisms, Low-frequency dielectric dispersion of bacteria*. 1973. Biophys. J. **(13):** p. 8-13.
11. Pethig, R., *Dielectrophoresis-Status of the theory,technology and applications.* Biomicrofluidics, 2010. **4:** p. 022811-022820.
12. O'Konski, C. *Electric properties of Macromolecules. V.theory of ionic polarization in polyelectrolytes.* J. Phys. D: Appl. Phys. 1997 **30:** p. 2470–2477.
13. Arnold, W. M. and Zimmermann, U., *Electro-rotation development of a technique for dielectric measurements on individual cells and particles.* J. Electrostat. 1998. **21**:p. 151–191.
14. Schnelle, Th., Müller, T., Fiedler, S. and Fuhr, G. *The influence of higher moments on particle behaviour in dielectrophoretic field cages*. J. Electrostat. 1999. **46**: p. 13–28.
15. Pethig, R. and Markx, G.H., *Applications of dielectrophoresis in biotechnology. Trends Biotechnol.* 1997, **15**: p. 426-432.
16. Basuray, S. and Chang, H., *Designing a sensitive and quantifiable nanocolloid assay with dielectrophoretic crossover frequencies*, Biomicrofluidics, 2010. **4**: p. 013205 1-11
17. Hoffman, P. D. and Zhu, Y. *Double-layer effects on low frequency dielectrophoresis-induced colloidal assembly*. 2008. Applied Physics Letters. **92**: p. 224103-224110

8. Acknowledgements

This work is a collaborative effort by Clemson and Tokyo Electron U.S. Holdings, Inc., U.S. Technology Development Center. We appreciate the use of Clemson’s Palmetto Cluster computing resources.