Modeling of the dielectrophoretic forces acting upon biological cells: A numerical comparison between Finite Element/Boundary Element Maxwell stress tensor methods and point–dipole approach

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ABSTRACT

Maxwell Stress Tensor (MST) method is investigated in this study to quantify the degree of approximation made with the point–dipole method in respect to dielectrophoresis (DEP) in micro–devices. Latex particles and biological cells immersed in aqueous buffers of various conductivities are considered. The two methods (point–dipole and MST full approaches) are compared using analytical dipolar solutions and numerical ones obtained from the Finite Element (FEM) and the Boundary Element (BEM) methods. Particular emphasis is made on the insufficiency of the point–dipole method in micro–scale issues especially when particles are located near to planar electrode.

Keywords: Boundary Element Method, Finite Element Method, Maxwell stress tensor, point–dipole approach, Micro–devices

1 INTRODUCTION

When studying DEP, two fundamentally different methods are typically used to determine the resulting DEP forces applied upon particles. The point–dipole approach, which is by far the most used method in literature [1], assumes the particle as a point–dipole. Particle is assumed here not to disturb the electric field at its vicinity and its presence is neglected for computation. For biological cell DEP micro–systems, where particles size is of the same order than electrodes gap, those assumptions become to fail. The second method, the MST full method, makes no approximation at this level and the particle presence is considered for the electric field computation. The Maxwell Stress Tensor (MST) method is used to determine, in this case, the DEP force [2].

Point–dipole approximation has been used to model the electric polarization of materials for more than two centuries. Particles forming the matter can be identified as point–dipoles when macro–scales are involved. So neglecting the particle presence allows calculating the electric field with the Laplace equation. The DEP force is then obtained from the Clausius–Mossotti expression that assumes the particle shape to be spherical. As far as biological micro–devices are concerned, none of these conditions is satisfied. However, a great deal of works done so far and connected to micro–DEP (where electrode–to–electrode distances are comparable to treated particles dimensions) do consider the point–dipole approximation as an established fact, perhaps for its easiness and straightforwardness, and hence make not enough critical of the obtained results [3].

This work is a tentative to quantifying the suitability of the point–dipole approximation to estimate the DEP forces for micro–scale devices. The dipolar, but also multipolar forces acting upon biological cells (or latex particles), deduced from the undisturbed electric field, are compared with a FEM/BEM MST force calculated by a former evaluation of the disturbed electric field. BEM technique is introduced here to make its validation in order to be able to simulate particle deformation afterwards not included in this paper.

The DEP micro–device considered in this work consists of a planar electrode near a hyperboloidal revolution electrode. The axisymmetry hence got allows studying only half of a meridian plan. The electrode gap distance equals 100μm. Latex particles experimented are of 20 μm diameter, and Chinese Hamster Ovocytes (CHO) are of 30 μm diameter. Both latex particles and CHO cells are immersed in Mannitol and in a very conductive physiological solution. The different electric properties are summarized in table 1.

Material	Relative electric permittivity, ε_r	Electric conductivity, σ S/m
Latex	2.55	2.379×10^{-3}
CHO, membrane	4	10^{-7}
CHO, cytoplasm	60	0.5
Mannitol	77.8	1.4×10^{-4}
Physiological solution	78.5	2.5

Table 1: Different electric parameters. The equivalent cellular complex permittivity formula used to compute CHO DEP is given by [4], Appendix C

2 THE POINT–DIPOLE APPROACH

This one is solely based on the electric behavior of a static configuration. Because of the skin thickness of the buffer (which is greater than the actual device size for the whole relevant frequency range), the electric field, $\mathbf{E}$, is supposed to be curl–free, *i.e.*, admits a scalar potential, ϕ, from which it derives. That quasi–static hypothesis writes down as

$$\mathbf{E} = -\nabla\phi \tag{1}$$

When no free space charge density is present, the first Maxwell law gives

$$\nabla.\mathbf{E} = 0 \tag{2}$$

Which leads then to

$$\nabla^2\phi = 0 \tag{3}$$

Taking into account the geometry of Figure 1, with no particle $\Omega^{(1)}$ for now, one can see that the problem is uniquely determined when considering the conditions, [5],

$$\begin{cases} \phi(\mathbf{x}) = V^1, & \text{for} \quad \mathbf{x} \in \Gamma_1 \\ \dfrac{\partial\phi}{\partial\mathbf{n}}(\mathbf{x}) = -E_n(\mathbf{x}) = 0 & \text{for} \quad \mathbf{x} \in \Gamma_2 \\ \phi(\mathbf{x}) = V^2, & \text{for} \quad \mathbf{x} \in \Gamma_3 \end{cases} \tag{4}$$

For FEM simulation, the problem is solved using the FEMLAB package (version 2.3a). Once this done, the electric field and its derivatives are obtained in a straightforward manner. Then, as particles are supposed to be spherical, the DEP force is computed using the formula, [1][4],

$$F_q = 4\pi\varepsilon^2 R^3 \,\mathrm{Re}\left(\frac{\overline{\varepsilon}^1 - \overline{\varepsilon}^2}{\overline{\varepsilon}^1 + 2\overline{\varepsilon}^2}\right) E_k E_{k,q} \tag{5}$$

Where R is the particle radius and $\overline{\varepsilon}^k$, $k = 1, 2$, the complex permittivity of the kth medium defined by

$$\overline{\varepsilon}^k = \varepsilon^k + \frac{\sigma^k}{i\omega} \tag{6}$$

i is the square root of –1, ω the applied external field excitation pulsation. ε^k and σ^k are the permittivity and the conductivity of the kth medium, respectively. The expression between brackets in formula (5) is called the Clausius-Mossotti factor. This factor, which is based only upon different electric properties and frequency, determines, separately from the electric field, the DEP regime as attracting to stronger electric field regions (positive DEP) or repelling from them (negative DEP).

For BEM simulation, equations are presented in section 3.2.

3 THE MST FULL APPROACH

An identical configuration as described in section 1 is involved by taking, however, the presence of the particle ($\Omega^{(1)}$) into account. That is by considering figure 1.

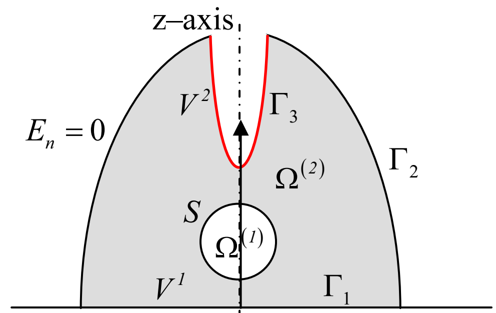

Figure 1: The configuration taken to evaluate the DEP forces by point–dipole approximation when particle is *ignored*, and by the full approach when the particle is considered.

Let us consider only a harmonic excitation, *i.e.*,

$$\begin{cases} V^1 = \overline{V}^1 e^{i\omega t} \\ V^2 = \overline{V}^2 e^{i(\omega t + \varphi)} \end{cases} \tag{7}$$

Hence, all variables will be supposed to be a $e^{i\omega t}$ time dependent, which means that $X(\mathbf{x}, t) = \overline{X}(\mathbf{x})e^{i\omega t}$ for all variable X. Therefore, the local electric Gauss theorem and the conservativeness of the electric current density, give

$$\nabla.\left(\frac{1}{i\omega}\overline{\varepsilon}^{(k)}\nabla\overline{\phi}^{(k)}\right) = 0 \tag{8}$$

3.1 FEM modeling

FEM results are obtained by solving equations (8) with FEMLAB package, which implicitly insures the continuity of the complex electric displacement vector, *i.e.*

$$\left(\overline{\varepsilon}^{(1)}\overline{\mathbf{E}}^{(1)} - \overline{\varepsilon}^{(2)}\overline{\mathbf{E}}^{(2)}\right).\mathbf{n}\Big|_S = 0 \tag{9}$$

through the interface S, in an intuitive direct manner. The other boundary conditions used are formally identical to equations (4)

3.2 BEM modeling

The following description concerns the BEM formulation. Into each medium k the complex electric potential $\overline{\phi}$ will satisfy, according to (8)

$$\nabla^2 \overline{\phi}^{(k)} = 0 \tag{10}$$

By applying the Green second identity to the later equation, the associated integral equation will be obtained, for $k = 1, 2$, as described by [6],

$$\alpha^{(k)}(\mathbf{x})\overline{\phi}^{(k)}(\mathbf{x}) = \int_{\partial\Omega^{(k)}} \left(G \frac{\partial \overline{\phi}^{(k)}}{\partial \mathbf{n}^{(k)}} - \overline{\phi}^{(k)} \frac{\partial G}{\partial \mathbf{n}^{(k)}} \right) dS'(\mathbf{x}') \tag{11}$$

$\mathbf{x}$ and $\mathbf{x}'$ are the position vectors of the observation point and the current integration one, respectively and G is the Laplace fundamental solution. $\alpha^{(k)}(\mathbf{x}) = 1$, if $\mathbf{x} \in \Omega^{(k)}$, $\alpha^{(k)}(\mathbf{x}) = \frac{1}{2}$, if $\mathbf{x} \in \partial\Omega^{(k)}$ and $\alpha^{(k)}(\mathbf{x}) = 0$, if $\mathbf{x} \notin \Omega^{(k)}$.
Let us define

$$\overline{\varpi} = \mathbf{n}.\left(\overline{\mathbf{E}}^{(1)} - \overline{\mathbf{E}}^{(2)}\right)\Big|_S \tag{12}$$

$$\overline{\delta} = \left(\mathbf{n}.\overline{\mathbf{E}}^{(2)}\right)\Big|_\Gamma \tag{13}$$

If we take the derivative of equation (11) according to the observation point, $\mathbf{x}$, combine it to equation (9), we will obtain, after manipulation, for $\mathbf{x} \in \Gamma$ ($\Gamma = \Gamma_1 \cup \Gamma_2 \cup \Gamma_3$), the main integral equation to be solved

$$\tfrac{1}{2}\overline{\varpi} = \left(\frac{\overline{\varepsilon}^{(1)} - \overline{\varepsilon}^{(2)}}{\overline{\varepsilon}^{(1)} + \overline{\varepsilon}^{(2)}} \right) \times \left[\int_S (\mathbf{n}.\nabla' G)\overline{\varpi}\, dS' - \int_\Gamma \left((\mathbf{n}.\nabla' G)\overline{\delta} + \overline{\phi}^{(2)} \left(\mathbf{n}.\nabla' \frac{\partial G}{\partial \mathbf{n}'} \right) \right) dS' \right] \tag{14}$$

This equation is solved using the CANARD BEM based programming kernel developed at IRISA, INRIA of Rennes, France, and written in FORTRAN90.

3.3 Evaluation of the DEP force by the MST

The computation of the applied DEP force upon the particle is led by using the MST method. The Maxwell tensor, for each medium k, writes as

$$T_{qj}^{(k)} = \varepsilon^{(k)} \left(E_q^{(k)} E_j^{(k)} - \tfrac{1}{2} \delta_{qj} E_l^{(k)} E_l^{(k)} \right) \tag{15}$$

(The sum for repeated indices is made).

The total force applied upon the $\Omega^{(1)}$ domain writes then down as [2]

$$F_q^{(1)} = \int_S T_{qj}^{(2)} n_j^{(1)} dS \tag{16}$$

4 RESULTS

For the point–dipole approach, BEM and FEM adequacy of the numerical obtained results is demonstrated through an analytical comparison not included in this paper. The electric potential map calculated by both methods in undisturbed configuration is shown in figure 2.

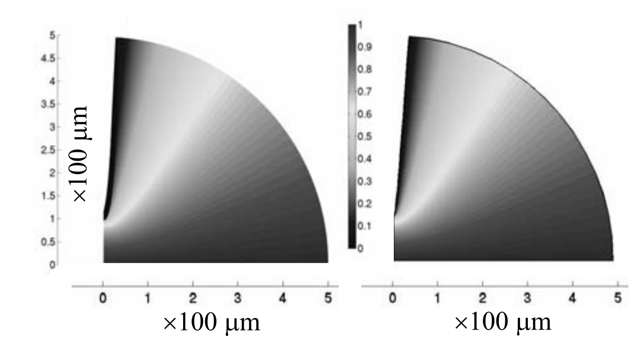

Figure 2: BEM, at left, and FEM, at right, electric potential computation mapping with no disturbing particle.

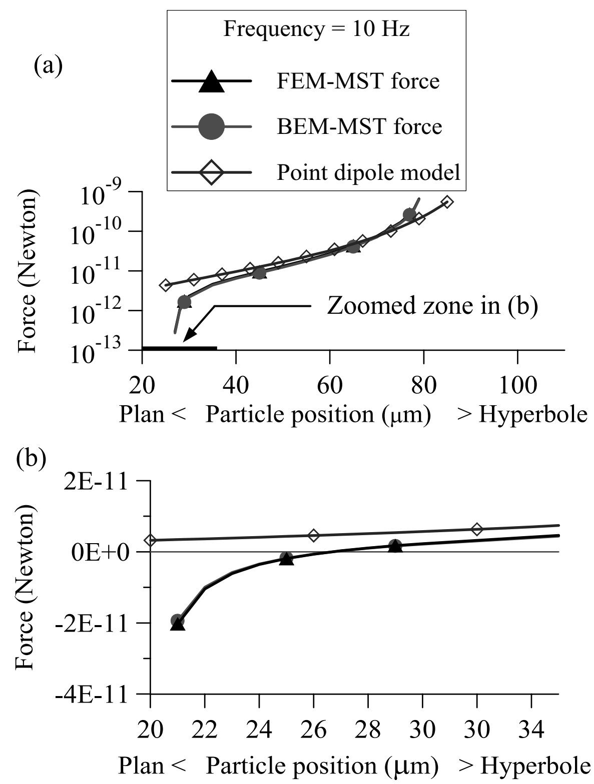

Figure 3: FEM/BEM MST force of a latex particle immersed in Mannitol at 10 Hz (radius equals 20 µm).

For the full approach, the computation is led, to evaluate the electric force applied upon latex spheres, by the MST with both BEM and FEM techniques, whilst the DEP force, deduced from the point–dipole approach, is evaluated only with FEM technique. Another computation is made on Chinese Hamster Ovary (CHO) cells with FEM technique by considering a double–layered particle model that matches up the shell like lipidic membrane surrounding the cytoplasm. Whereas BEM technique uses an equivalent homogeneous spheres model, as made by [4]. The main simulation results are shown here below.

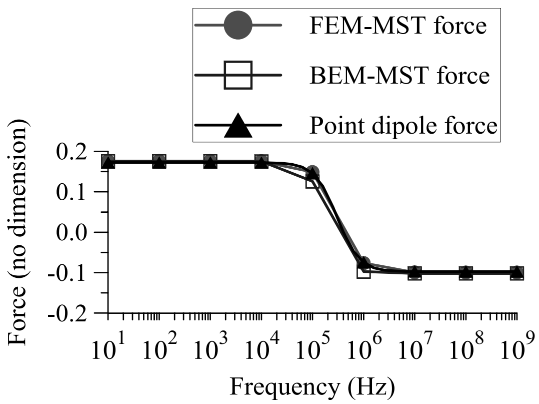

Figure 4: FEM/BEM MST and point–dipole forces at the gap center (z = 50 μm) for latex particle in Mannitol.

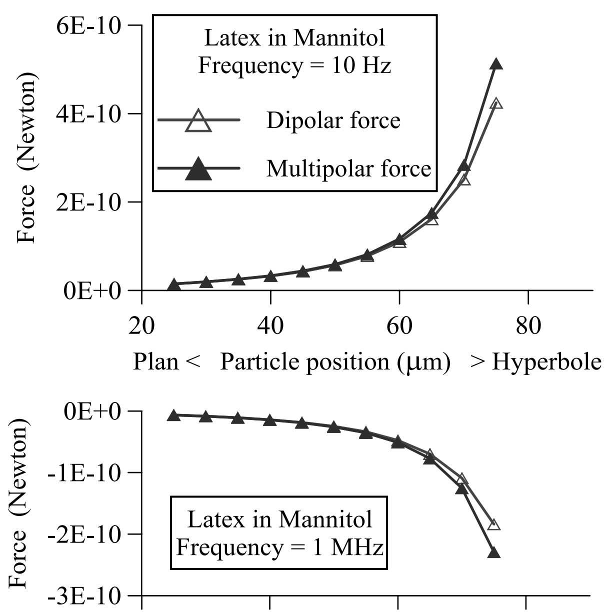

Figure 5: Multipolar forces sum (up to the fifth order), versus point–dipole force.

Latex particles and CHO cells do not perform significantly different patterns; hence for convenience only latex particle results are shown in this paper. As can be noticed by figure 3, MST FEM and BEM DEP forces exhibit satisfactory agreement. Point–dipole model shows, however, a quite different response for all frequencies and different combinatory particle–buffer experimented. The only exception (figures 3a and 4) to be mentioned is the innermost zone ($40 \le z \le 60\ \mu m$) where point–dipole approach goes with MST one. Discrepancy of the right regime (positive or negative DEP) is also noticeable near the planar electrode (figure 3b), where positive DEP should occur according to point–dipole approach. This inconsistency continues to happen even for much smaller particles, provided that they are close enough, comparing to their radius, to the planar electrode. Point–dipole DEP model mismatch could partially be explained by the multipolar effect neglected near the sharp electrode, which has tendency to increase the DEP force as can be seen in figure 5. However, this is no more sufficient near the planar electrode.

5 CONCLUSION

A survey for micro–devices regarding DEP on biological cells and latex particles was made. The comparison between DEP forces estimated by both Boundary Element/Finite Element–Maxwell Stress Tensor method and by Finite Element–point–dipole approximation showed a fundamental statement. When particle–to–electrode distance is comparable to its radius, which is the most alike situation to happen as micro–scales are concerned, the point–dipole and even multipole approaches applied to micro–devices involving biological cells, as well as synthetic particles of similar size, are not always valid. They do not only fail to estimate the DEP force magnitude order but its regime as well (as positive or negative DEP). In such a configuration, the expensive, but unavoidable, method to properly describe the DEP is to consider the immersed cells (or particles) as part of the whole micro–device.

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