Chapter 2
Study of the role of particle-particle dipole interaction in dielectrophoretic devices for biomarkers identification

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A three dimensional Coupled Monte Carlo-Poisson method has been used to evaluate the impact of particle-particle dipole interactions in the equilibrium distribution of a system of uncharged polarizable particles suspended in a static liquid medium under the action of an oscillating non-uniform electric field generated by polynomial electrodes. We compare the simulated distributions with experimental ones both for micro- (MDA-MB-231 breast tumor cells) and nano-(multiwall carbon nanotubes) particles. In both cases the equilibrium distributions near the electrodes are dominated by dipole interactions which locally enhance the DEP effect and promote long particles chains.

2.1 Introduction

The term "*dielectrophoresis*" [1] is used to describe the *"ponderomotive"* force exerted by a non-uniform electric field on polarizable neutral particles. Such force allows for the controlled manipulation of micro and nano-sized particles dispersed in colloidal solutions. Application fields include: cell partitioning and isolation [2], bio-structure assembling [3], nanostructure deposition [4], filtration systems for oils purification [5] etc. One of the problems that is hindering development and engineerization of DEP devices is the limited use of accurate numerical tools for their design which, in turn, is due to the computational complications arising by the

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D. Compagnone et al. (eds.), *Sensors,* Lecture Notes in Electrical Engineering 319,
DOI 10.1007/978-3-319-09617-9_2

particle-particle dipole interaction. This many-particle effect can be simulated with high accuracy solving directly the equations of motion in the few-particles limit [6] or with some strong approximations using reaction-diffusion models [7] in large systems. Recently a coupled Monte Carlo-Poisson (MC-P) method [8] has been developed which allows simulating a large number of particles in large active zones (within the experimental range), explicitly including particle-particle interactions. The MC-P method has pointed out the relevance of this inclusion in the modeling predictions for the case of 2D systems (interdigitated electrodes). We have applied this methodology to the case of polynomial electrodes comparing the simulated results with experimental distributions of micro-(tumor cells) and nano-(multi-walled nanotubes, MWCNT) particles to evaluate the role of p-p interactions and definitively demonstrate the predictive potential of this methodology.

2.2 Computational Method

A detailed description of the method can be found in refs.[8, 9], here we summarize the equations used in the implemented KMC algorithm.

In the simulated kinetics the particles are considered as hard spheres with positions r_i and a configuration energy given by:

$$E\left(\{\mathbf{r}_1,\ldots\mathbf{r}_n\}\right)=\sum_i U_{eff}(\vec{r}_i)+\sum_{i,j}\bar{U}_{ij}(\vec{r}_i,\vec{r}_j)$$

$$\bar{U}_{eff}(\vec{r})=-\frac{1}{2}\alpha_{eff}E^2_{rms}(\vec{r})$$

$$U_{ij}\cong\frac{1}{4\pi\mathrm{Re}(\varepsilon_m)}\alpha^i_{eff}\alpha^j_{eff}\frac{1-3\cos(\theta^i_{ij})\cos(\theta^j_{ij})}{R^3_{ij}}\left(\vec{E}_{rms}(\vec{r}_i)\vec{E}_{rms}(\vec{r}_j)\right) \tag{2.1}$$

where $\bar{U}_{eff}$ and $\bar{U}_{ij}$ represent the single-particle DEP energy and the dipole-dipole contribution, respectively. α_{eff} is the average polarizability of the particle defined as $\alpha_{eff}=3V\,\mathrm{Re}(\varepsilon_m)\mathrm{Re}[f_{CM}(\omega)]$. V and ω are the particle volume and electric field frequency and $f_{CM}(\omega)$ is the Clausius-Mossotti factor which fully characterizes the dielectric response of the particle in the given medium [10, 11].

The simulated particles, after an initial random distribution, were allowed to move in a cubic computational box of dimensions $1600\times1600\times1500$ μm^3 with four polynomial electrodes located at the bottom of the box (see Fig. 2.1, left) whose shapes can be described by the following parametric system:

$$\begin{gathered}D\le x\le L\\ y=\pm\sqrt{x^2+D^2}\end{gathered} \tag{2.2}$$

where D represents half the distance of opposing electrodes whereas L is related to the electrode width. In this study we sat $D=390$ μm and $L=460$ μm.

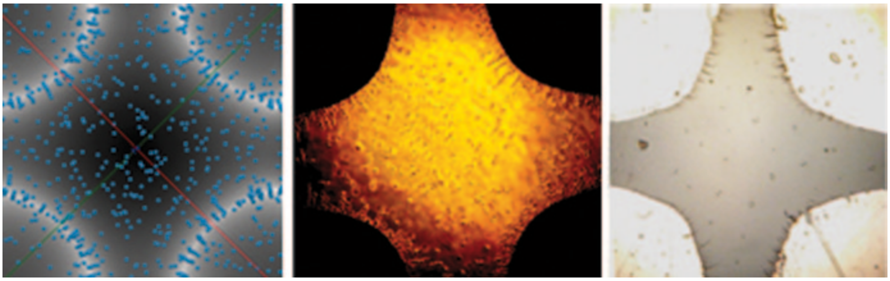

Fig 2.1 Comparison of the top view spatial distributions obtained with simulation and experiments: *left*) the Monte Carlo simulation with superimposed the intensity map of the electric field, *center*) Distribution of MDA-MB-231 after 180 s of DEP manipulation (V_{pp} = 8V f = 1000 kHz), *right*) Distribution of MWCNT after 10 min of DEP manipulation (V_{pp} = 80V f = 300 kHz)

2.3 Experimental Setup and Results

The polynomial electrode design described in the previous section, has been fabricated by deposition of 10 nm of Ti followed by 200 nm of Ni on a standard microscope glass. The electrodes were delineated by lithographic methods followed by wet etching. The device has been piloted by using a Protek 9205C signal generator which applied, consistently with simulated system, a sinusoidal voltage signal of 8V_{pp} peak-peak value at 1 MHz (DEP attractive force) for 180 s (to allow for cells equilibration). The human breast cancer cell line MDA-MB-231 used as test particles, cultured according to American Type Culture Collection (ATCC) instructions, and just before DEP tests, were suspended in a slightly conductive buffer composed of 9.5 % ultrapure sucrose, 0.3 % dextrose, and 0.1 % Pluronic F68 titrated to a conductivity of 30 mS/m (consistent with Monte Carlo simulations) with KCl. The cells, suspended in DEP buffer at concentration of 5×10^5 cells/ml were pipetted into an o-ring chamber (~ 100 μl) which was then sealed using a cover slip. In the case of MWCNT the system included further included a 1:20 step-up transformer which allows to increase the applied voltage up to ~100V_{pp} at a fixed frequency of 300 kHz. In both cases (cells and MWCNT) the sinusoidal frequencies used results in a positive DEP (i.e. particles will be attracted by electrodes edges).

2.4 Results and Conclusions

Figure 2.1 shows a comparison between the simulation and the experimental cells distribution. As can be seen the two distributions are equivalent when the statistical approach of the equilibration is considered.

The final distribution is the result of the minimization of Eq. (2.1), which, being $f_{CM}(\omega) > 0$, will induce a movement towards the regions of high intensity field (minimization of the $\bar{U}_{eff}$ term) and an aligned/chaining of the cells along the electric field lines (minimization of the $\bar{U}_{ij}$ term). From these results we can infer that particle-particle interactions compete with the dielectrophoretic force-field, which would otherwise massively trap (in p-DEP conditions) the particles in the regions where the gradient of the electric field is larger. The highest value of the cell concentration to avoid particle-particle interactions strongly depends on the electrodes and system geometry, on the particles dimensions and on the polarization factors. As a consequence a general prescription to neglect dipole-dipole interaction in the design of a device cannot be easily. For the specific considered system, an estimate for the density threshold governing the interaction free regime was suggested in ref. [9] as $\approx 3\times10^4$ cells/ml . Preliminary KMC simulations of MWCNT showed a significant quantitative discrepancy with the experimental results (Fig. 2.1, right). We could expect this results since the model (1) is reliable for spherical particles. Work is underway to evaluate the effects of polarization induced p-p interaction in the case the high aspect ratio object as the nanotubes compared to spherical particles (e.g. cells).

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http://www.springer.com/978-3-319-09616-2

Sensors
Proceedings of the Second National Conference on Sensors, Rome 19-21 February, 2014
Compagnone, D.; Baldini, F.; Di Natale, C.; Betta, G.; Siciliano, P. (Eds.)
2015, XXXVI, 453 p. 209 illus., 143 illus. in color., Hardcover
ISBN: 978-3-319-09616-2