Elucidating the Mechanism Governing Particle Alignment and Movement by DEP

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Abstract: Dielectrophoresis (DEP) has been increasingly regarded as an important technique to manipulate small particles such as biological cells in bioengineering applications. In our experiment manipulating polystyrene beads and cells, we observed some interesting phenomena with regard to alignment and movement of particles and cells. Not being able to explain these phenomena with the conventional DEP theory, we realized that an in depth elucidation of how particles interact with each other is necessary but missing in the current knowledge of DEP. We propose a new way to simulate movement of multiple particles under DEP and implement it computationally in COMSOL 4.4. The modeling results not only explain well the commonly observed pearl chain formation process, but also show very good agreement between simulation and experiment in some less common phenomena like the formation of antenna-like structure by mixed size particles. Moreover, we have modeled the process of capturing large numbers of cells in flow by DEP.

Keywords: Dielectrophoresis(DEP), particle-particle interaction, particle alignment, cell capture

1. Introduction

One of the important applications of DEP is patterning. Particles are dispersed in an electric field created by electrically biased electrodes. According to the conventional DEP theory, these particles will move toward a region with either a strong or weak field depending on the difference in dielectric property between particle and medium. However, the actual circumstances are much more complicated as particles exhibit interactive behavior instead of simply piling up in stable region. One example is that particles attract each other along electric field direction and repel each other in orthogonal direction. This kind of interaction leads to formation of pearl chain structures. Previous modeling works tried to explain the phenomenon with different methods and had made some progresses [1, 2]. However, most of the studies either investigate only the movement of a few particles or constrain the movement of particles in a two-dimensional plane, without providing a full scale pattern. Another significant application of DEP is to capture cells in flow as DEP is usually coupled with microfluidic device. Difference here is that cells also move under hydrodynamic forces. In this work, we take advantage of particle tracing module in COMSOL 4.4 and perform both 2D and 3D modeling. Results show that our 3D model can explain both patterning and cell-capture behavior well. Moreover, our models are able to successfully reproduce unique observations in our experiments such as antenna-like structure formed by mixed size particles.

2. Governing Equations

The particle tracing module includes newly added particle-particle interaction feature which allows users to self-define the type of interaction.
The DEP force on a particle can be expressed as

$$F = (\vec{P} \cdot \nabla)\vec{E} \quad (1)$$

The particle is treated as a point dipole and $\vec{P}$ stands for the dipole moment. It is determined by the permittivity and volume of the particle as well as the surrounding medium. The effect of medium can be represented by the Clausius-Mossotti factor ($f\_cm = \frac{\varepsilon_p - \varepsilon_m}{\varepsilon_p + 2\varepsilon_m}$) [3]. For single particle analysis, electric field strength E is solely determined by the local field generated by biased electrodes. When the system contains multiple particles, every particle will be affected by electric fields generated by other particles. The electric field generated by a particle (also treated as a point dipole) at certain point is:

$$E_{particle} = \frac{1}{4\pi\varepsilon_0 R^3}(3(\vec{P} \cdot \hat{R})\hat{R} - \vec{P}) \qquad (2)$$

Here R is the distance between the point and geometric center of particle and $\hat{R}$ is the unit vector along the direction pointing from center of particle to

the given point. One thing to notice is that when equation (2) is plugged into equation (1), the differential function in COMSOL cannot be used to calculate the gradient of electric field. Method of difference can solve the problem.
Aside from the DEP force, other types of forces like gravitational force, buoyancy force and hydrodynamic force are also exerted on particles.

$$F_g = vol \cdot \rho_{particle} \cdot g \qquad (3)$$

$$F_b = vol \cdot \rho_{medium} \cdot g \qquad (4)$$

$$F_h = 6\pi r \eta v \qquad (5)$$

When particles are brought down to the bottom plane under the effect of gravity or DEP, they can keep on moving in the two-dimensional plane under DEP force and hydrodynamic force. However, no wall conditions in COMSOL 4.4 can correctly describe this kind of boundary condition. To overcome this limitation, the volumetric effect of particle is included. A normal force from bottom plane is added to support the particle and keep the center of particle higher than the bottom plane by the distance of a particle's radius. The normal force can be expressed as:

$$F_n = k(d + r - qy) \cdot (qy < (d + r)) \qquad (6)$$

The normal force is linearly related to the height of the particle, where k is a proportional coefficient, d is the thickness of the insulation layer (placed on top of electrodes to keep electrodes from contacting medium) and r is the radius of the particle. qy is the height level of the particle. This equation assures that when a particle is above the bottom plane, no upward force exists and that if the particle falls below the level of $d + r$, there will be an increasing upward force to support the particle.
Due to volumetric effect, centers of particles will be separated by the distance of $2r$ when two particles are in contact. A normal force between particles is included to keep particles from overlapping. The normal force on particle i exerted by particle j is:

$$F_{ij} = k(q\alpha_i - q\alpha_j)(\exp((2r - d_{ij})/l) - 1) \cdot (2r >= d_{ij})$$
$$(\alpha = x, y, z) \quad (7)$$

d_{ij} is the distance between two particles. l is a small distance. Overlapping between particles will lead to a drastic increase in force magnitude.

3. Methods

We consider situations in both 2D plane and 3D space. The benefit of a 2D model is that it can largely reduce the computational load when the cut-planes in the third dimension can be regarded as identical. The drawback, however, is that the particle-particle interaction in the third dimension cannot be considered. Thus a 3D model becomes necessary for providing more accurate numerical analysis and for capturing more complicated processes.

3.1 2D modeling

A 2D model is built to simulate the particle alignment phenomenon on parallel electrodes. Figure 1(a) shows the geometry of our 2D model. The blue lines represent parallel electrodes at bottom. The two electrodes on both sides are biased and the middle one is grounded. The lower rectangle on top of electrodes functions as the insulating layer of polyethylene and the large rectangle above is the water layer. The smaller rectangle inside facilitates the release of particles. It eliminates the possibility that the initial heights of some particles are lower than $d + r$.

3.2 3D modeling

Two types of electrode designs are simulated in 3D modeling. For parallel electrodes, the geometry of 3D model is built by adding a third dimension with depth of 100 um on the basis of 2D model. To model the cell capturing process, a concentric electrode with two opposing fingers is designed and modeled.

4. Numerical Model

4.1 2D modeling

To simulate the particle alignment, 20 particles are released with random initial positions from the small rectangle at time 0 (Figure 1(b)). We compared the alignment patterns of particles under nDEP in two conditions: with and without particle-particle interaction. Without particle-particle interactions, particles (Figure 1(c)) form pearl chains in the center of gap and center of electrode since both are stable regions for particles under nDEP. However, when particle-particle interaction is included, only pearl chains in the center of gap can be maintained (Figure 1(d)). Chains in the center of electrode become unstable and some particles will be lift up, indicating that the effect of particle-particle interaction depends strongly on local electric field distribution.

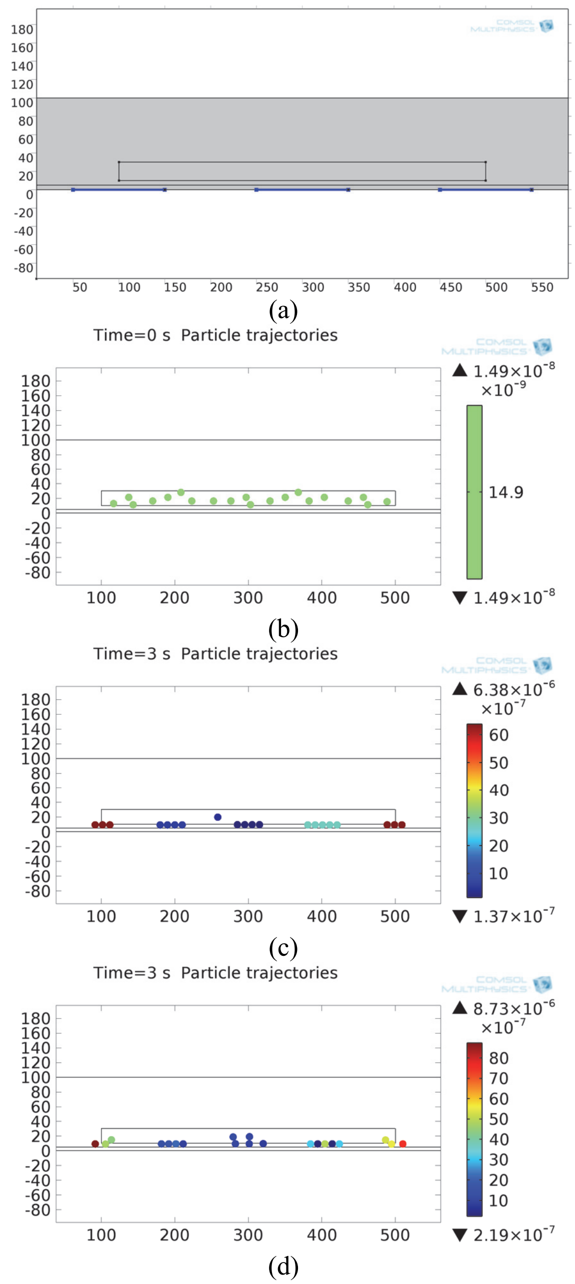


Figure 1. 2D modeling of alignment of particles in electric field generated by parallel electrodes. (a) Geometry of 2D model. (b)-(d) Particle alignment under nDEP (particle radius=5 um). (b) Initial positions of particles at 0 second. (c) Alignment pattern after 3 seconds, particle-particle interaction is not included. (d) Alignment pattern after 3 seconds, particle-particle interaction is included.

4.2 3D modeling

4.2.1 Pearl chain structure

The alignment of 50 particles under both nDEP and pDEP are studied in 3D model. Under nDEP, pearl chains reside in the center of gap between electrodes (Figure 2(b)). Different from 2D modeling results, particles on electrodes will only align along the direction perpendicular to the electric field and keep away from each other. This is because in 2D model particles are not able to rotate to assume a more stable configuration. Under pDEP, particles form chains close to the edge of electrodes (Figure 2(c)).

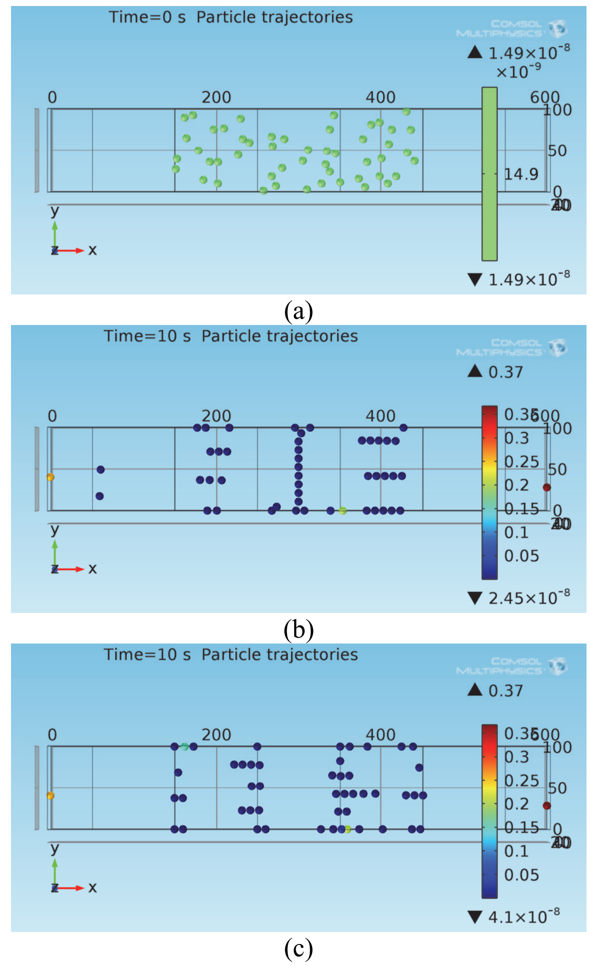
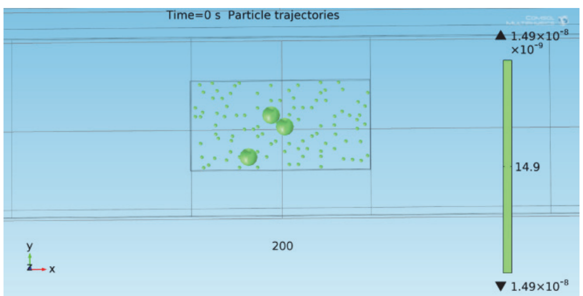


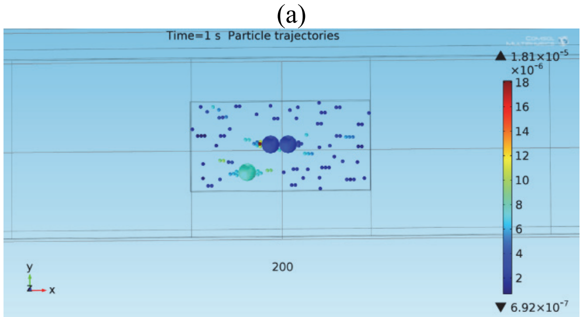
Figure 2. Alignment process of 50 particles under DEP (radius=5 um). (a) Particles are randomly released at 0 second. (b) Top view of alignment under nDEP after 10 seconds. (c) Top view of alignment under pDEP after 10 seconds.

4.2.2 Antenna-like structure

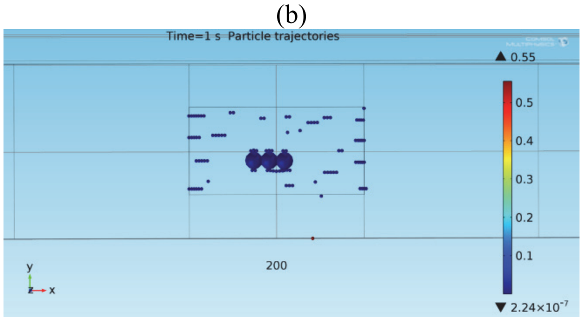
According to Arnold [4], small polystyrene beads have higher surface conductivity than large beads. In certain low frequency range, small particles undertake pDEP while large particles experience nDEP. At high frequency, both types of particles are subject to nDEP. When large particles (radius = 5um) are mixed with small particles (radius =1 um), apart from forming pearl chains comprised of particles of same size, antenna-like structures are also formed. Figure 3(b) shows that long tails of the formed antenna-like structures point in the same direction as electric field at a high frequency. At a low frequency, small particles move from left and right side of the large particles to the top and bottom side. There will be no stacking of small particles to form long tails (Figure 3(c)).



(a)



(b)



(c)

Figure 3. Simulation of the formation of antenna structure at both high and low frequency. (a) Particles released at 0 second. (b) Perpendicular antenna structure at high frequency after 1 second. (e) Parallel antenna structure at low frequency after 1 second.

4.2.3 Cell capture

Cells carried by flow in microfluidic channel can be captured by electrodes under pDEP. By treating a cell as a point dipole, we can simulate cell capture process with designed electrode pattern. 20 particles are released every 2 seconds for 5 times from the left side of the square well (Figure 4). After 15 seconds, a portion of particles are retained around the edge of electrodes (Figure 4).

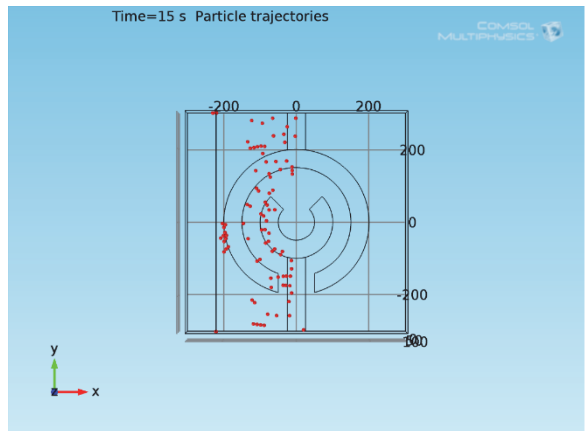
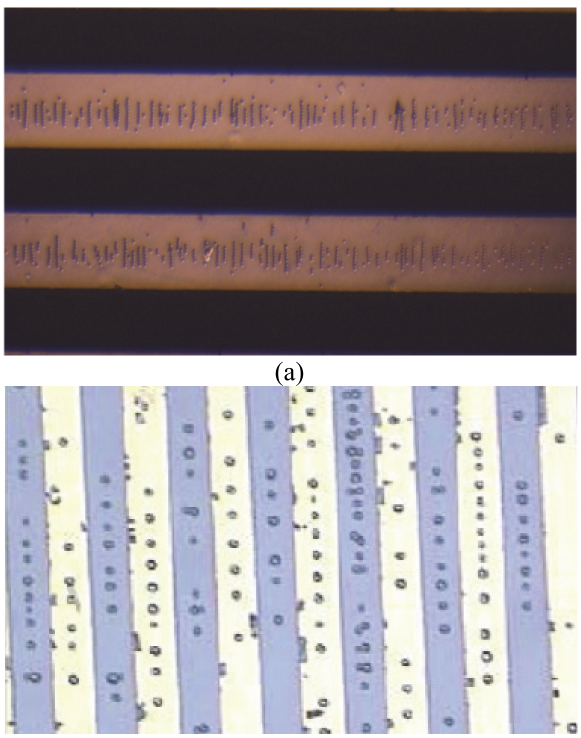


Figure 4. Capture of 100 particles released from vertical plane on the left side of the electrodes.

5. Experiment Results

5.1 Pearl chain structure

From experiments, we observed that beads would form pearl chains when the applied potential reaches a certain critical value. Chains in gaps will align along electric field direction and repel each other in orthogonal direction [5]. Above electrodes, the alignment of beads cannot be observed due to microscope limitation (Figure 5(a)) in our experiments. But in referring to the results of Chen [6], there are no pearl chain structures forming above electrodes, which verifies our 3D modeling result (Figure 5(b)).



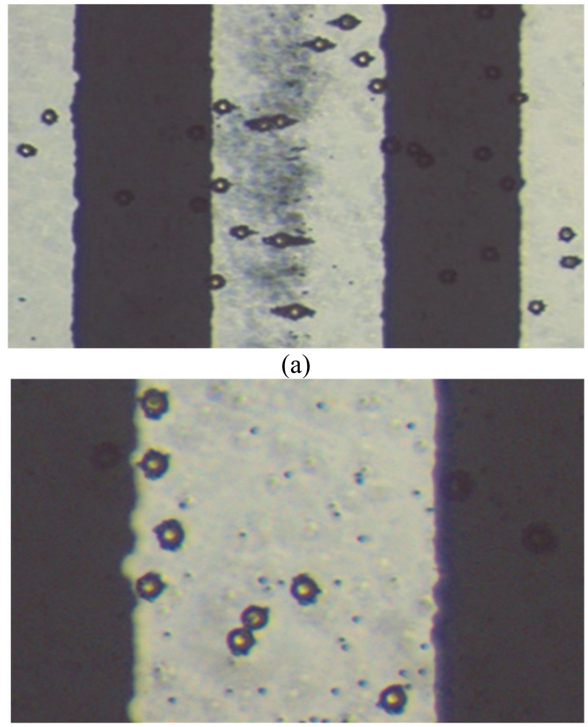
(a)

(b)

Figure 5. Alignment of polystyrene beads between interdigitated electrodes. (a) 4.5 um beads align in parallel chains at 15 V, 200 kHz. (b) 4.3 um beads settle in both the gaps between the electrodes and the centers of electrodes at 5V, 1 MHz.

5.2 Antenna-like structure

In experiments with particles of different sizes (radius=7.5 um and 1um), we observed the formation of antenna-like structures. At high frequency, the antenna structure points towards the direction perpendicular to the edge of electrode, similar to pearl chain structure (Figure 6(a)). At low frequency, the pointing direction of antenna structure is parallel to the edge of electrode (Figure 6(b)). This has been proved by our simulation results.



(a)

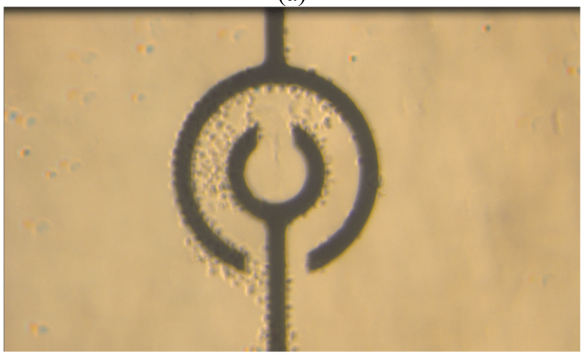
(b)

Figure 6. Images of antenna structure formed by mixed beads (radius= 7.5 um and 1 um) (a) 20 MHz (b) 100 kHz.

5.3 Cell capture

With concentric electrode, cells can be captured by pDEP. Cells will first be captured along the edge of electrode finger on the left side (Figure 7(a)). As more cells are attracted by electrode, they fill the gap and extend to the right side (Figure 7(b)). The pattern matches our simulation result.

(a)



(b)

Figure 7. Capturing breast cancer cells under 40 V, 180 kHz. (a) After 5 seconds. (b) After 30 seconds.

6. Conclusion

Alignment and movement of multiple particles under DEP are simulated using particle tracing module in COMSOL 4.4 with particle-particle interaction taken into consideration. With this work, we are able to shed important insights into the process of pearl chain formation, antenna-like structures with frequency dependent orientation, and cell capture. All our simulation results exhibit very good agreement with experimental observations, confirming the validity of our new approach to advance the DEP theory.

7. References

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8. Acknowledgement

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9. Appendix

Table 1. Parameters in model

k	Normal force coefficient	10^{-12} N/um
d	Thickness of insulation layer	5 um
r	Radius of particle	5 um
l	Selected small distance	1 um