Comparison of Computational Methods for the Estimation of the Dielectrophoretic Force Acting on Biological Cells and Aggregates in Silicon Lab-on-Chip Devices

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Introduction

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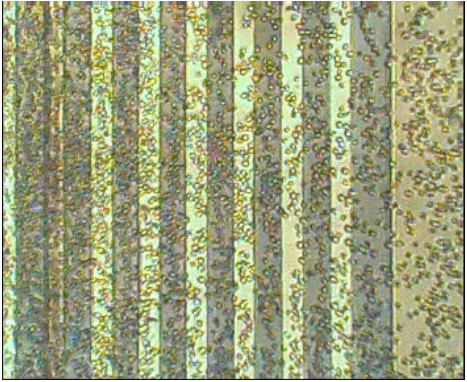

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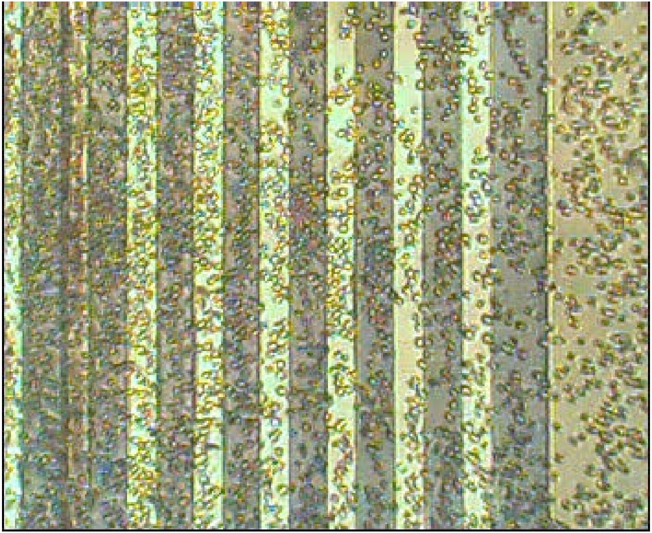

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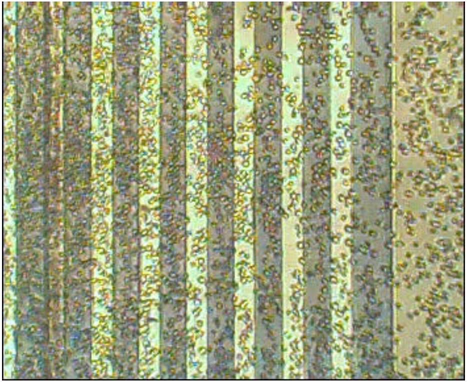
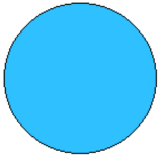


- In this work we have studied, developed and compared different methods for the force computation depending on the field non-uniformity factor and on the dimensions of the cellular aggregate

DEP Force in time constant electric fields



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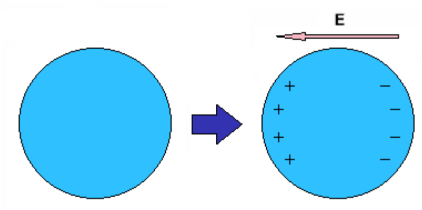

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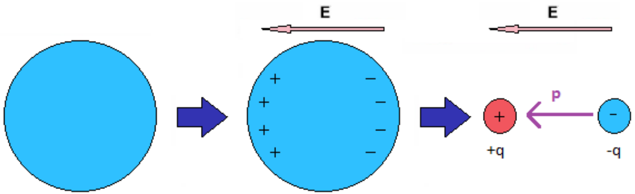

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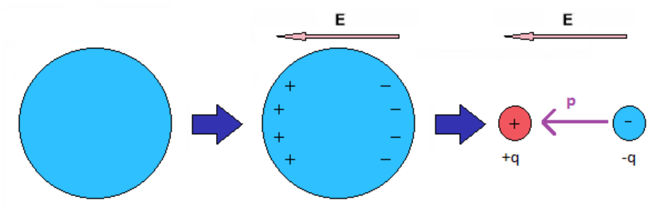
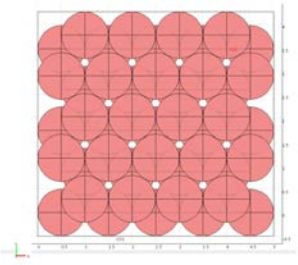


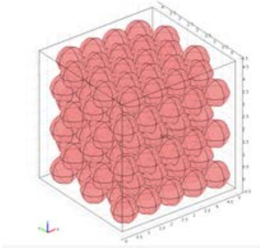
$$\langle F_{\mathrm{DEP}}\rangle_i = \underbrace{2\pi\varepsilon_m R^3 F_{\mathrm{CM}}^{(1)}\left[\nabla \boldsymbol{E}_0^2\right]_i}_{\text{Dipole approximation}}$$

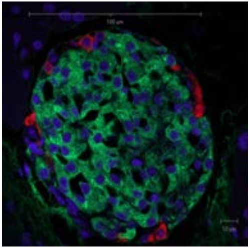
where

$$F_{\mathrm{CM}}^{(1)} = \frac{\varepsilon_p - \varepsilon_m}{\varepsilon_p + 2\varepsilon_m}$$

Cellular aggregate's model







Geometrical model of the reciprocal single cells disposition inside the aggregate and a microscope image of a mouse Langerhans islet.

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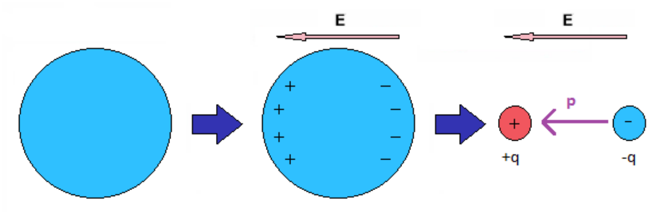

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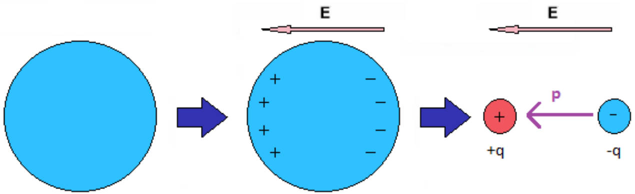

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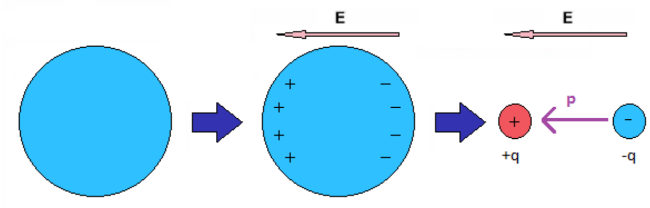

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DEP force in alternated electric fields

- $\boldsymbol{E} = E_{x,0}\cos(\omega t + \varphi_x)\boldsymbol{e}_x + E_{y,0}\cos(\omega t + \varphi_y)\boldsymbol{e}_y + E_{z,0}\cos(\omega t + \varphi_z)\boldsymbol{e}_z = \Re\left[\boldsymbol{E}_0 e^{j(\omega \boldsymbol{t} + \boldsymbol{\varphi})}\right]$

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- The DEP force approximation is:

$$\text{Dipole: } \langle \boldsymbol{F}_{\mathrm{DEP,dip}} \rangle_i = 4\pi\varepsilon_{\boldsymbol{m}} R^3 \Re\left(F_{\mathrm{CM}}^{(1)} \bar{E}_i \frac{\partial \bar{E}_i^*}{\partial x_i} + \bar{E}_j \frac{\partial \bar{E}_i^*}{\partial x_j} + \bar{E}_k \frac{\partial \bar{E}_i^*}{\partial x_k} \right)$$

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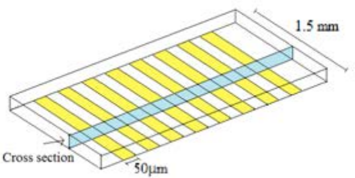
- E^*_i is the complex conjugate value of E_i

Electric field computation



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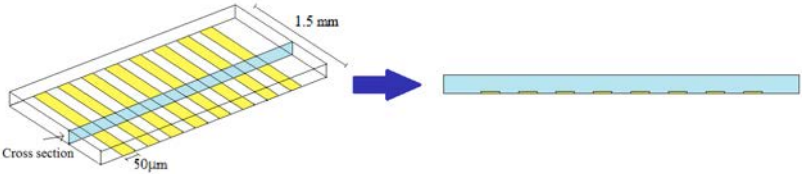

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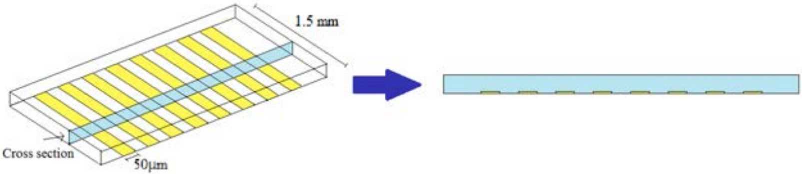

Boundary conditions for the electric potential

- electric insulation
- $V = V_0$
- $V = -V_0$

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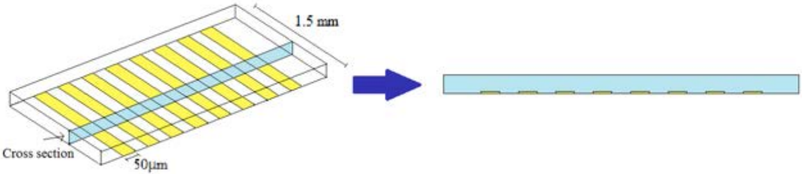

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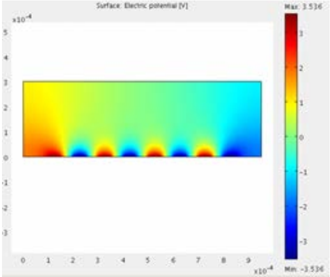
Computed electric potential



Second order derivatives computation

In the quadrupole DEP force term the second order field derivatives appear.

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A subdomain weak form equation in COMSOL Multiphysics PDE modes has been added to the existing model exploiting the Green's first identity:

$$\int_{\Omega} v \Delta \varphi = \int_{\Omega} \nabla v \cdot \nabla \varphi + \int_{\partial \Omega} v \frac{\partial \varphi}{\partial \boldsymbol{n}}$$

where

- Ω is the domain;
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we get $E1 = \frac{\partial \boldsymbol{E_x}}{\partial x}$ that can be easily differentiated.

DEP force pointwise approximations: dipole vs quadrupole

The accuracy of the dipole approximation with respect to the quadrupole one depends on the particle/aggregate's radius and on the field non-uniformity.

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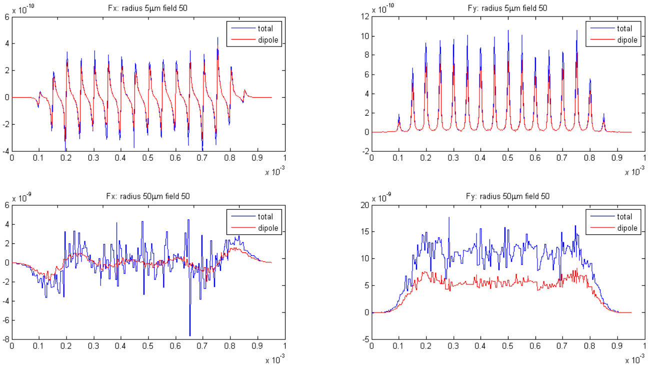
- The two approximations are computed for different values of the field non-uniformity (electrodes width between 50 and 150 μm) and of the particle's radius (5-50 μm).

DEP force pointwise approximations: dipole vs quadrupole

50 μm wide electrodes



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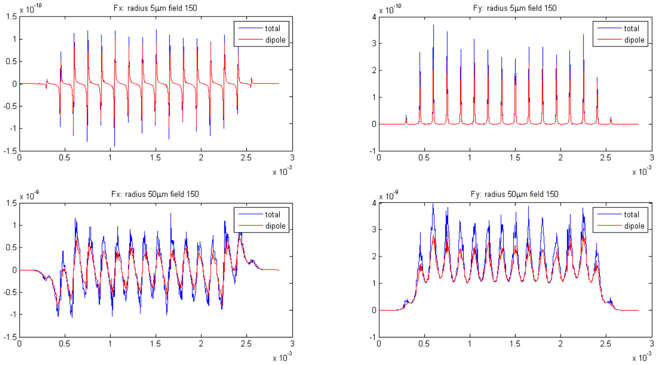
150 μm wide electrodes



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- The average of $e = \frac{|\boldsymbol{F}_{\textbf{DEP,quad}}|}{|\boldsymbol{F}_{\textbf{DEP,quad}}|+|\boldsymbol{F}_{\textbf{DEP,dip}}|}$ is computed.
- A threshold value is fixed so that, given a field non-uniformity, it is possible to define a radius value below which the dipole approximation is enough.

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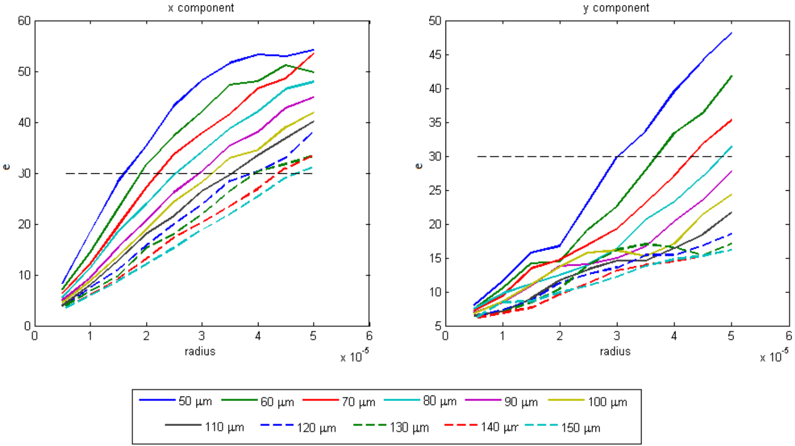

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Another method is proposed to compute the DEP force: the discrete method.

Discrete method for the force computation

In continuum area:

$\boldsymbol{F} = \int_\Omega d\boldsymbol{f}^{(d\Omega)}$ where $d\boldsymbol{f}^{(d\Omega)}$ is the "infinitesimal" force acting on the "infinitesimal" volume $d\Omega$.

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In discrete area:

$\boldsymbol{F} = \sum_{i=1}^{N} d\boldsymbol{F}_i$ where $d\boldsymbol{F}_i$ is the force acting on the i-th volume, small but finite.

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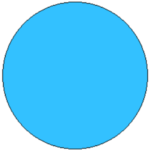

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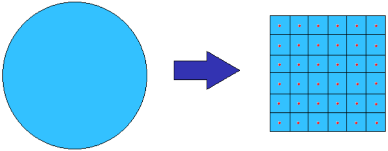
$\boldsymbol{F} = \int_\Omega d\boldsymbol{f}^{(d\Omega)}$ where $d\boldsymbol{f}^{(d\Omega)}$ is the "infinitesimal" force acting on the "infinitesimal" volume $d\Omega$.

In discrete area:

$\boldsymbol{F} = \sum_{i=1}^{N} d\boldsymbol{F}_i$ where $d\boldsymbol{F}_i$ is the force acting on the i-th volume, small but finite.



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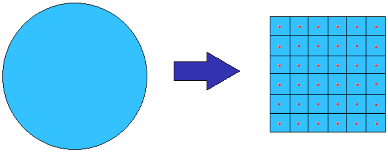

Discrete method

The force is computed in the centers of each *small volume*, enough small to use the dipole force approximation, and, then, all the contributions are summed up to give the total DEP force.

DEP force approximations: quadrupole vs discrete

To compare the quadrupole approximation with the results got with the discrete method we proceed similarly as for the comparison between the dipole and the quadrupole approximations.

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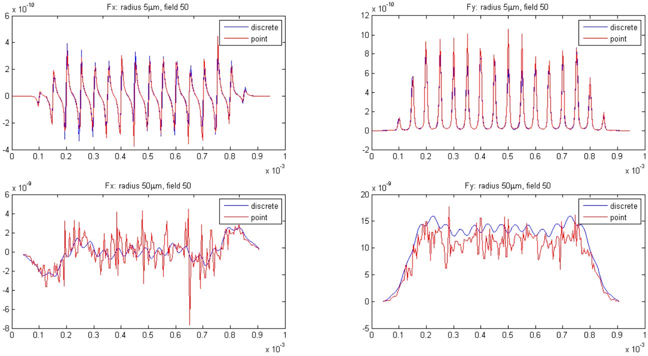
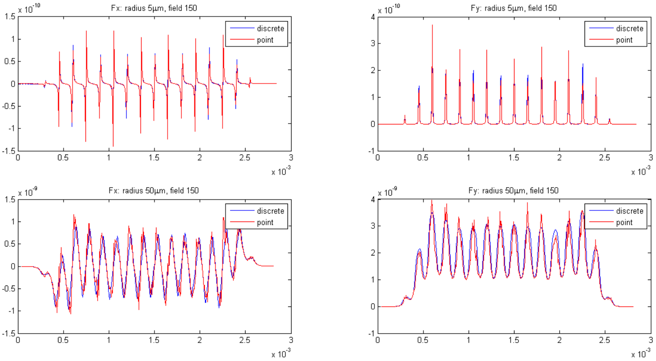
DEP force approximations: quadrupole vs discrete

50 μm wide electrodes



DEP force approximations: quadrupole vs discrete

150 μm wide electrodes



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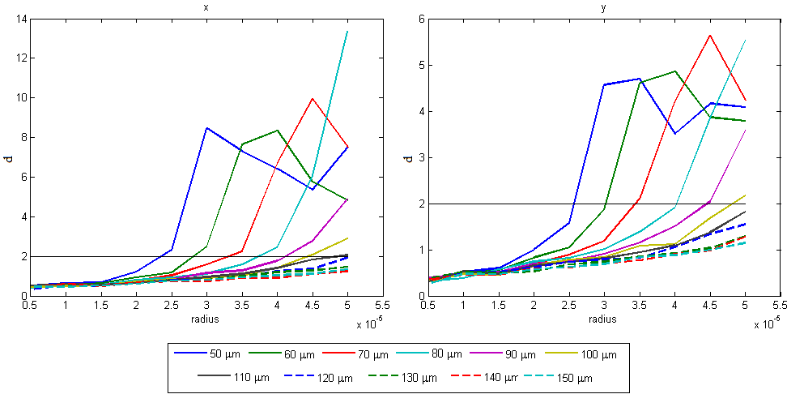
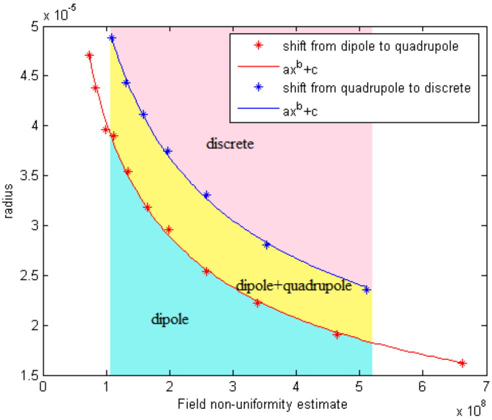
To compare the quadrupole approximation with the results got with the discrete method we proceed similarly as for the comparison between the dipole and the quadrupole approximations.

- The two DEP force approximations are computed for different values of the field non-uniformity and of the particle radius.
- Defining an appropriate function d that estimates the difference between the two approximations and a threshold value, a plot similar to the previous one is obtained.

DEP force approximations: quadrupole vs discrete



Resumptive plot



Field non-uniformity estimate: average of

$$\sqrt{\left(\frac{\partial E_x}{\partial x}\right)^2 + \left(\frac{\partial E_x}{\partial y}\right)^2 + \left(\frac{\partial E_y}{\partial x}\right)^2 + \left(\frac{\partial E_y}{\partial y}\right)^2}/4$$

Drag Force

The particles move inside a microfluidic medium and experience a drag force.

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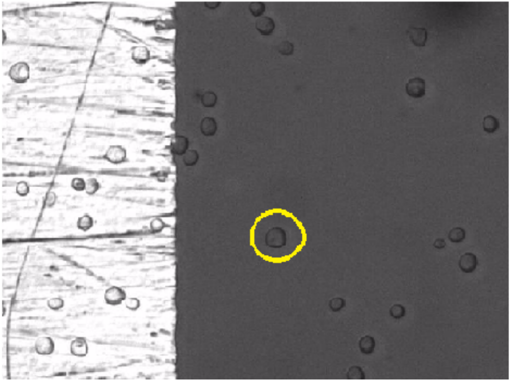
For the dimensions and velocities that appear in this kind of dielectrophoretic experiments it could be approximated as

$$F_{\text{drag}} = -6\pi\eta R v$$

where

- η is the fluid viscosity;
- R is the particle's radius;
- v is the particle's velocity.

Yeast cells in parallel electrodes configuration



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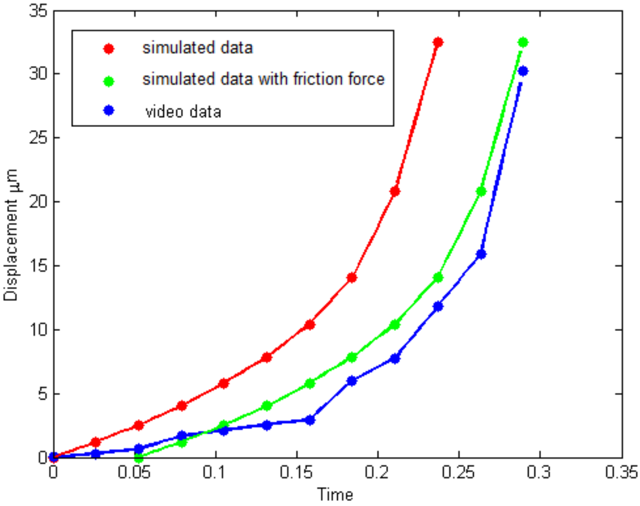

Langerhans islets in quadrupole configuration

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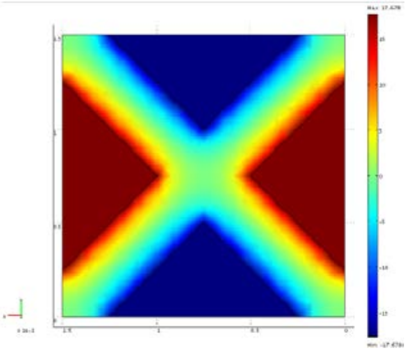

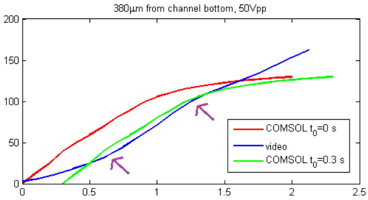

Conclusion

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Conclusion

To conclude, the major topics of this work have been:

- the definition of the discrete force;
- the comparison between different computational methods for the DEP force depending on the field non-uniformity factor and on the aggregate's dimension;
- the definition of threshold values that allow to choose which computational method to be used;
- the experimental-simulation comparison that is quite good once we consider a further friction force that postpones the simulated motion start.

Thanks for your attention!

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sarah.burgarella@st.com