Integrative Computational Modeling for Developing Means to Manipulate Biological Cells and for Solving Complex Engineering Problems

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Introduction: Computational modeling has become more widely used to guide the design of microfluidic devices for manipulating cells using Dielectrophoresis (DEP), and devise novel means for advancing the study of cellular science and engineering. Conventionally, cells are treated as volumeless points in the system, which allows study of the movement of groups of particles under the effect of field. However, this approach often neglects the distortion effect of particle on external field, as well as interactions among particles. Moreover, it ignores the complex inner structures of cell, which are the causes of distinctive cell behavior. To more accurately model the behavior of cells for better understanding of the underlying mechanism, a new numerical method, termed as 'volumetric polarization and integration method' has been developed. It has been proved to be more powerful over existing approaches when applied to explain complicated experimental observations.
In the second part, we will showcase how to use integrative modeling to solve complex engineering problems without break the Multiphysics problem into pieces. The coupling of physics in computational modeling provides more realistic guidance to experimental design.

Theoretical development:

Point dipole method:

Laplace Equation → Dipole Moment → DEP Force

$$\Delta\psi = 0 \qquad \vec{m} = 4\pi a^3 \varepsilon_m \frac{\varepsilon_p^* - \varepsilon_m^*}{\varepsilon_p^* + 2\varepsilon_m^*}\vec{E} \qquad \vec{F} = 2\pi a^3 \varepsilon_m \frac{\varepsilon_p^* - \varepsilon_m^*}{\varepsilon_p^* + 2\varepsilon_m^*}\nabla E_{rms}^2$$

MST method:

Lorentz Force Law → Volume Integration → Intermediate DEP Force → Divergence Theorem → DEP Force

$$\vec{f} = \rho\vec{E} + \vec{J}\times\vec{B} \qquad \vec{F} = \iiint_V \varepsilon_p\left(\left(\nabla\cdot\vec{E}\right)\vec{E} + (\vec{E}\cdot\nabla)\vec{E} - \frac{1}{2}\nabla E^2\right)dV$$

Volumetric polarization and integration method:

Polariztion → Force Density, Torque Density, Energy Density → Volume Integration → Force, Torque, Energy

$$\vec{P} = 3\varepsilon_m(\vec{E} - \vec{E}_{particle})$$

$$\vec{f} = (3\varepsilon_m(\vec{E} - \vec{E}_{particle})\cdot\nabla)\vec{E} \qquad \vec{F} = \oiiint (3\varepsilon_m(\vec{E} - \vec{E}_{particle})\cdot\nabla)\vec{E}\,dV$$

$$\vec{t} = 3\varepsilon_m(\vec{E} - \vec{E}_{particle})\times\vec{E} \qquad \vec{T} = \oiiint 3\varepsilon_m(\vec{E} - \vec{E}_{particle})\times\vec{E}\,dV$$

$$w = 3\varepsilon_m(\vec{E}_{particle} - \vec{E})\cdot\vec{E}\,dV \qquad W = \oiiint 3\varepsilon_m(\vec{E}_{particle} - \vec{E})\cdot\vec{E}\,dV$$

Method Validation:

Nonhomogeneous particle

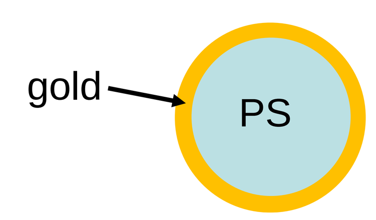


TABLE II. DEP force on gold coated particles.

	10^4 Hz	$10^{4.5}$ Hz	10^5 Hz
Volumetric-integration method (nN)	80.04	80.04	80.04
MST method (nN)	-4.24×10^4	-4.24×10^4	-4.23×10^4

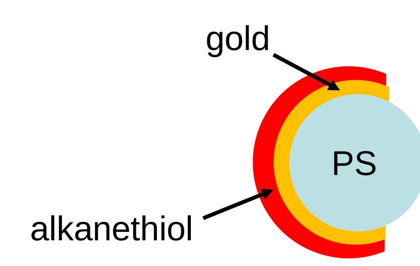


TABLE III. DEP force on Janus particles

	Volumetric-integration method						
	25 kHz	50 kHz	75 kHz	100 kHz	1 MHz	5 MHz	20 MHz
Janus particle (nN)	27.4	27.4	27.6	27.8	51.7	105	114
Janus particle with alkanethiol layer (nN)	−77.2	−17.3	2.1	10.2	32.1	77.0	97.4
	MST method						
	25 kHz	50 kHz	75 kHz	100 kHz	1 MHz	5 MHz	20 MHz
Janus particle (nN)	-1.23×10^4	-3.40×10^4	-5.08×10^4	-6.04×10^4	-8.02×10^4	-2.76×10^4	-2.95×10^3
Janus particle with alkanethiol layer (nN)	-9.63×10^4	-9.63×10^4	-9.62×10^4	-9.61×10^4	-7.32×10^4	-1.06×10^4	−667

Results:

1. Cell rotation

Self-rotation was observed for rat adipose stem cells under DEP. Modeling results suggest that the rotational movement is induced by eccentric inclusions with low conductivity inside cell.

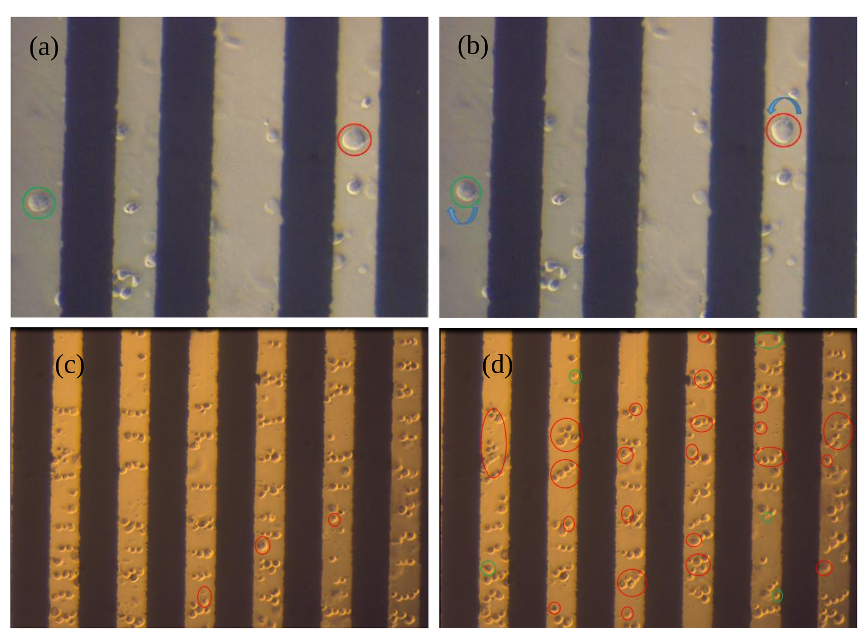


FIG.1. Rat adipose stem cells rotate in the gap regions between interdigitated electrodes. (a) Initial orientation of cells. (b) Orientation of cells after 1 second under 300 kHz, 200 V peak to peak signal. The direction of rotation is marked by arrow. (c)-(d) Rat adipose stem cells rotate under 32V peak to peak signal. Rotating cells are marked by circles (Red circles indicate cells rotate about axis perpendicular to electrode plane and green circles indicate cells rotate about axis parallel to the edge of electrode). (c): Cells rotate at 5 MHz. (d): Cells rotate at 20 MHz.

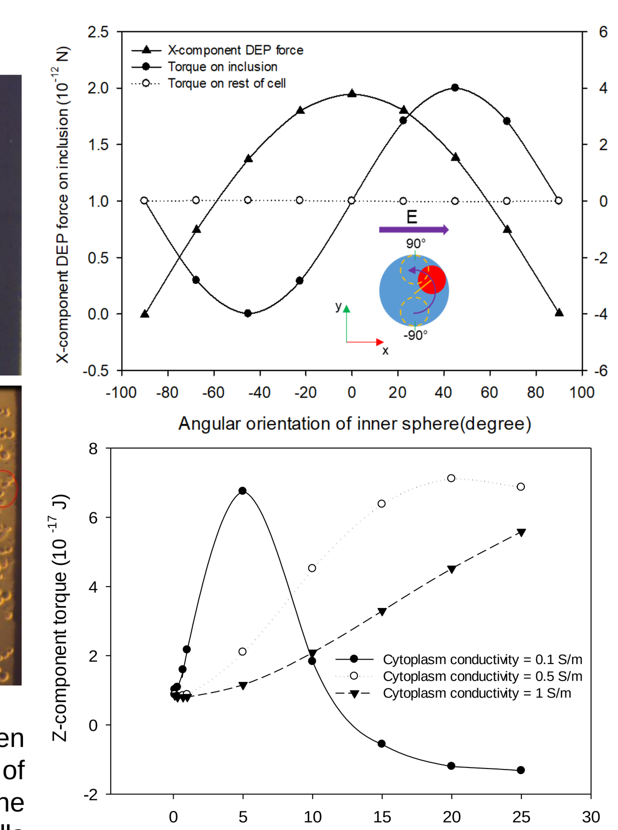
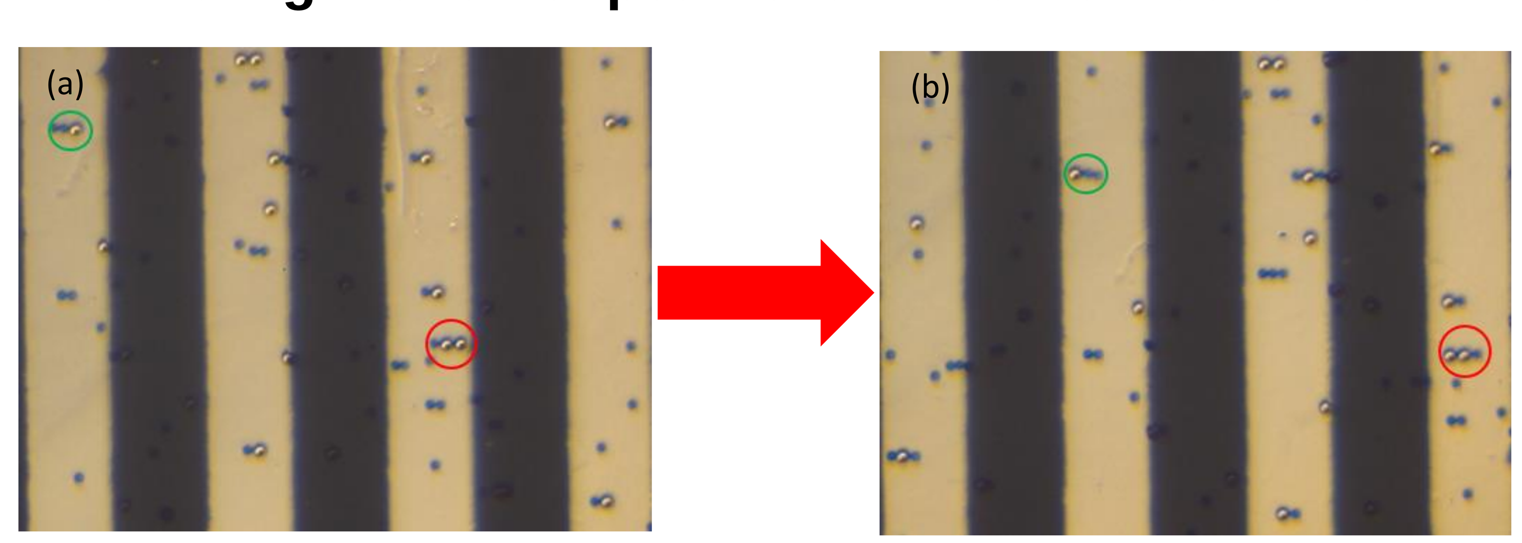


FIG.2. On top is the variation of X-component DEP force on inclusion and Z-component torque on inclusion as well as the rest of cell. On bottom is the variation of Z-component torque with frequency experienced by the whole cell for cells with different cytoplasm conductivity.

2. Tumbling motion of pearl chain in a flow condition



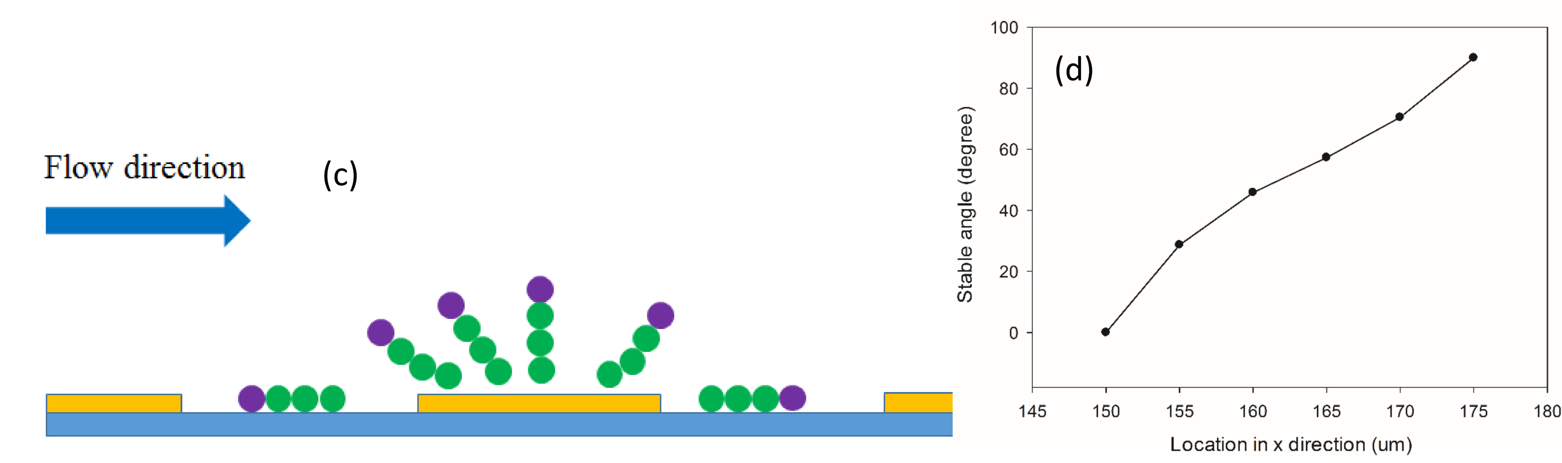


FIG.3. (a) and (b) Tumbling motion of chains of particles with different sizes. (c) Schematic illustration of the tumbling motion of a chain of particles. The trailing end of the chain gets lifted up to form an angle with the floor and stand straight at the center of electrodes, and after that the chain gradually tumbles back as it moves into the next gap region. (d) The stable angle formed by the particles with respect to the floor increases as the chain of particles moves from the edge to the center of an electrode.

3. Chemical clock in Nanopore

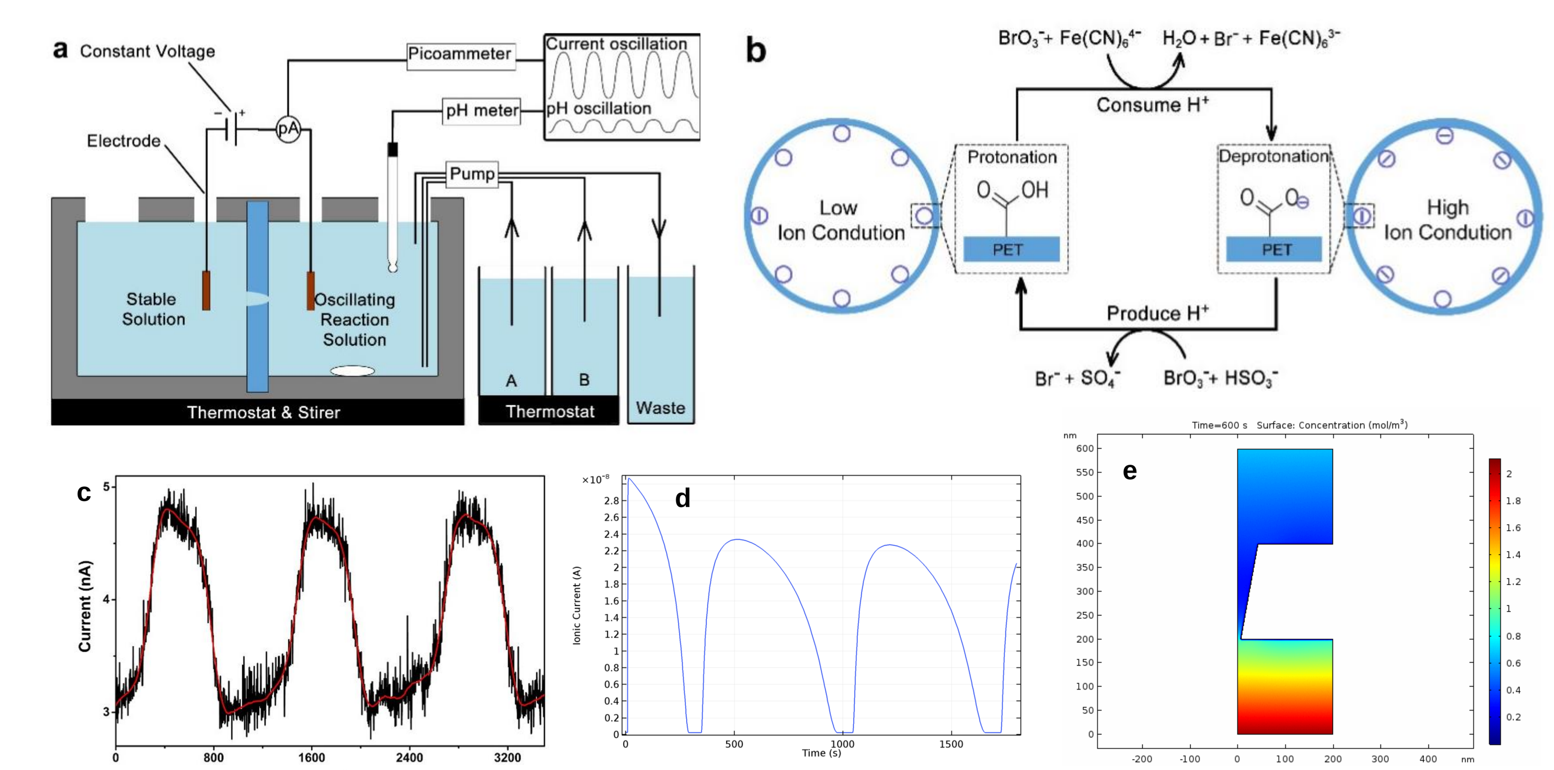


FIG.4. (a) Experimental setup of nanopore (b) Reaction on nanopore surface (c) Experimental measurement of oscillating current (d) Modeling results of periodic current (e) The concentration of SO_3^{2-}

4. Graphene interfacial ionic rectification device

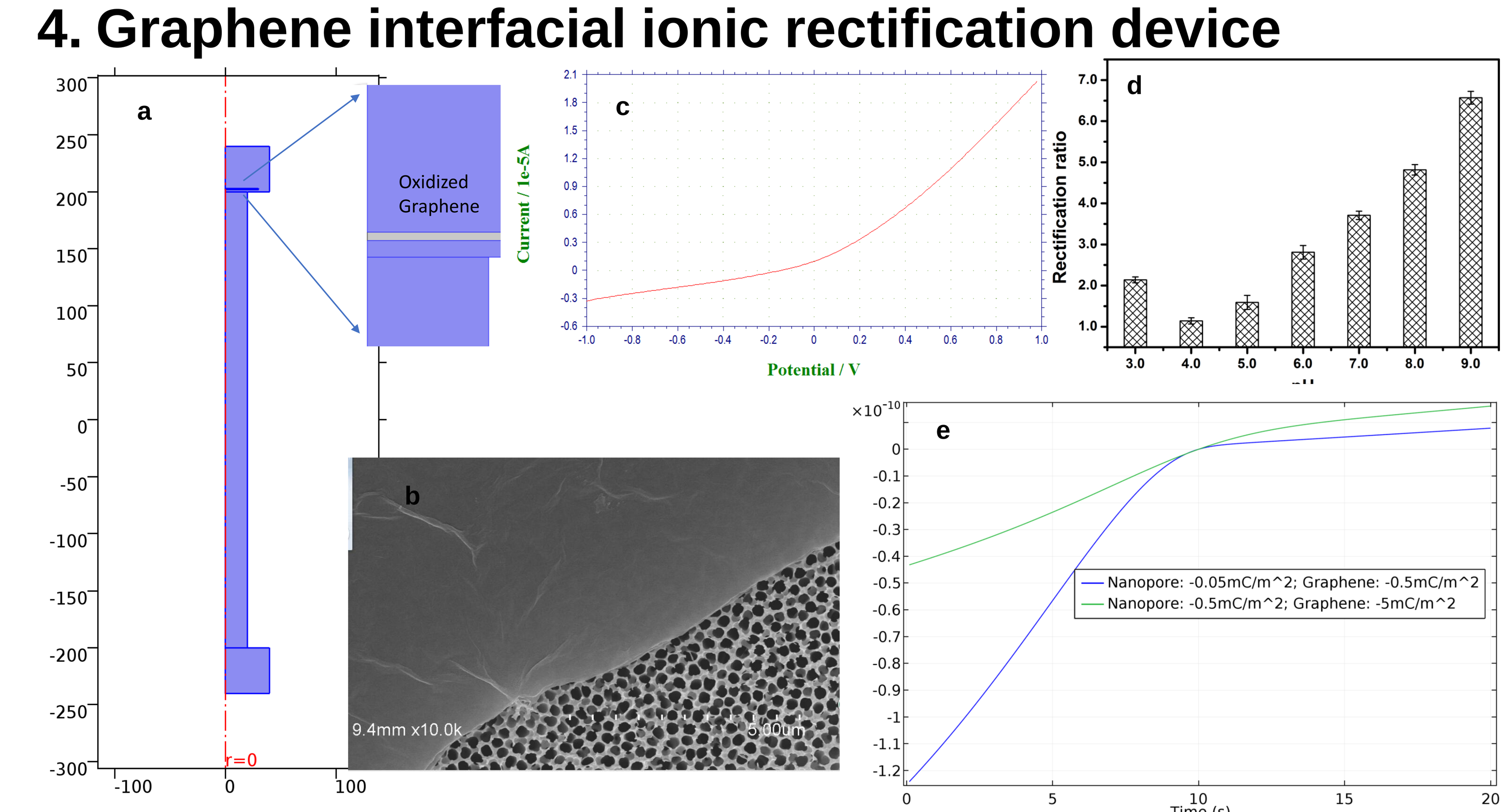


FIG.5. (a) Model geometry of the rectification device (b) Image of graphene layer and nanochannel (c) Rectifying behavior of the device (d) Impact of pH on rectification ratio (e) Modeling results of rectification with different surface charge density

Conclusion: Computational modeling provides means for examining current theory and developing new theory in order to obtain better understanding of experimental observation. It also lays the foundation for solving complex engineering problems in an integrative way.

Reference:

H. Zhang, J. Hou, R. Ou, Y. Hu, H. Wang and L. Jiang, Nanoscale, 2017, DOI: 10.1039/C7NR01343D.

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