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

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Overview

- A brief discussion on reductive vs integrative investigation

- A case study: how integrative computational modeling helps advance the understanding and application of dielectrophoresis (DEP) in various situations

- Other applications in advancing the design and development of nanopore, medical devices, novel materials, actuation devices, and coupled spectroscopic techniques, etc.
Reductive Investigation

- Reductive Engineering: reducing complex issues to small independent pieces by neglecting/discarding factors we don’t know about for simplicity and clarity.

While we have been laughing at it since childhood, we are still victims of this ‘Blind Men’ exploratory approach in our scientific endeavors.

**DNA is:**
- **AN INSULATOR**
  Dunlap et al. *PNAS* 90, 7652, 1993
- **A CONDUCTOR**
  Fink and Schoenberger, *Nature* 398, 407, 1999
- **A SEMICONDUCTOR**
- **A SUPERCONDUCTOR**
Integrative Investigation

Zen Master D. Suzuki (1870 -1966): The Zen's way of knowing a flower should not be analytically reductive, in which one would pluck the flower, bring it to a laboratory, and dissect it, because once the flower is plucked it is no longer the flower one intends to know. … Instead, one is to leave it where it is, let it be in its living state and environment, and contemplate it.

An integrative way uses non-reductive, yet analytical and investigative means to interact with the world based on computational modeling supported by experimental validation and realization.
Advancing dielectrophoresis (DEP) and expanding its application

- What is Dielectrophoresis (DEP)

Move particles with no restrictions on particle property

Orientation dependent interaction

Cell separation
Cell capture
Tissue engineering
Biofabrication
Useful DEP applications

Separation of cells based on size difference

Liver organ on chip

Single cell capture with specifically designed microwells

Pattern cells in 3D hydrogel
Analytical basis for DEP

Without computational modeling, understanding of DEP phenomena heavily relies upon the analytical method

Point dipole method

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

Advantages:

1. It is convenient to be used to determine the magnitude and direction of DEP force
2. It can be easily implemented to study the movement of a single particle

Limitations:

1. The estimated DEP force is not accurate when the field is highly non-uniform
2. Particle-particle interaction and non-homogeneity of particle are not considered
Validity of other numerical methods

Maxwell Stress Tensor (MST) method

\[ \vec{f} = \rho \vec{E} + \vec{j} \times \vec{B} \]

\[ \vec{f} = \iiint_V \epsilon_p \left( \nabla \cdot \vec{E} \right) \vec{E} + \left( \vec{E} \cdot \nabla \right) \vec{E} - \frac{1}{2} \nabla E^2 \right) dV \]

\[ \vec{F} = \iiint \frac{1}{4} \epsilon_m \left[ \left( \vec{E} \vec{E}^* + \vec{E}^* \vec{E} \right) - |E|^2 \vec{U} \right] \cdot \hat{n} dA \]

The MST method has been treated as providing the most robust and accurate solution to DEP force

Some concerns are raised about the validity of MST method, including:

- Misconception of essence of force
- Misuse of torque expression
- Validity for non-homogeneous particle
Developing and implementing a new DEP theory

A new volumetric polarization and integration method is developed to overcome deficiencies of MST method and elucidate underlying mechanism of complicated DEP phenomena.

Induced electric field

\[ \vec{E}_{\text{particle}} - \vec{E} = -\frac{1}{4\pi\varepsilon_m} \frac{Qd}{(d/2)^3} \]

Polarization

\[ \vec{P} = 3\varepsilon_m(\vec{E} - \vec{E}_{\text{particle}}) \]

Force density

\[ \vec{f} = (3\varepsilon_m(\vec{E} - \vec{E}_{\text{particle}}) \cdot \nabla)\vec{E} \]

Torque density

\[ \vec{t} = 3\varepsilon_m(\vec{E} - \vec{E}_{\text{particle}}) \times \vec{E} \]

Energy density

\[ w = 3\varepsilon_m(\vec{E}_{\text{particle}} - \vec{E}) \cdot \vec{E} \]

Force

\[ \vec{F} = \iiint (3\varepsilon_m(\vec{E} - \vec{E}_{\text{particle}}) \cdot \nabla)\vec{E} \, dV \]

Torque

\[ \vec{T} = \iiint 3\varepsilon_m(\vec{E} - \vec{E}_{\text{particle}}) \times \vec{E} \, dV \]

Energy

\[ W = \iiint 3\varepsilon_m(\vec{E}_{\text{particle}} - \vec{E}) \cdot \vec{E} \, dV \]
Some comparisons

Both the volumetric polarization and integration method and MST method are used to calculate DEP force on non-homogeneous particle.

<table>
<thead>
<tr>
<th>Volumetric-integration method (nN)</th>
<th>10^4 Hz</th>
<th>10^4.5 Hz</th>
<th>10^5 Hz</th>
</tr>
</thead>
<tbody>
<tr>
<td>MST method (nN)</td>
<td>-4.24 \times 10^4</td>
<td>-4.24 \times 10^4</td>
<td>-4.23 \times 10^4</td>
</tr>
</tbody>
</table>

TABLE III. DEP force on Janus particles

<table>
<thead>
<tr>
<th>Volumetric-integration method</th>
<th>25 kHz</th>
<th>50 kHz</th>
<th>75 kHz</th>
<th>100 kHz</th>
<th>1 MHz</th>
<th>5 MHz</th>
<th>20 MHz</th>
</tr>
</thead>
<tbody>
<tr>
<td>Janus particle (nN)</td>
<td>27.4</td>
<td>27.4</td>
<td>27.6</td>
<td>27.8</td>
<td>51.7</td>
<td>105</td>
<td>114</td>
</tr>
<tr>
<td>Janus particle with alkanethiol layer (nN)</td>
<td>-77.2</td>
<td>-17.3</td>
<td>2.1</td>
<td>10.2</td>
<td>32.1</td>
<td>77.0</td>
<td>97.4</td>
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</tbody>
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<tr>
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<th>20 MHz</th>
</tr>
</thead>
<tbody>
<tr>
<td>Janus particle (nN)</td>
<td>-1.23 \times 10^4</td>
<td>-3.40 \times 10^4</td>
<td>-5.08 \times 10^4</td>
<td>-6.04 \times 10^4</td>
<td>-8.02 \times 10^4</td>
<td>-2.76 \times 10^4</td>
<td>-2.95 \times 10^5</td>
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<tr>
<td>Janus particle with alkanethiol layer (nN)</td>
<td>-9.63 \times 10^4</td>
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<td>-9.61 \times 10^4</td>
<td>-7.32 \times 10^4</td>
<td>-1.06 \times 10^4</td>
<td>-667</td>
</tr>
</tbody>
</table>

Use of MST method for non-homogeneous particle will lead to incorrect results!
By taking interior components of cell into consideration, volumetric polarization and integration method can successfully explain rotational behavior of cell.

Direction of rotation is determined by location of inclusion.
By taking interior components of cell into consideration, volumetric polarization and integration method can successfully explain rotational behavior of cell.

Cytoplasm conductivity affects the response of rotational speed to frequency.
Pearl-chain tumbling behavior

The unique tumbling movement of pearl chains can also be explained by using the volumetric polarization and integration method.
Considering the double layer effect

Electric double layer (EDL) will affect the dielectric property of particle, but its effect is not fully understood due to lack of physical relevance in current analytical theory.

Conventional approach

\[ K_S = \sigma \mu \]  
Point dipole assumption

\[ K_{total} = K_{bulk} + \frac{2K_S}{a} \]  
(Unable to explain experimental observation)

Add correction term

\[ K_{total} = K_{bulk} + (A_1 + A_2 \kappa a) \frac{2\sigma \mu}{a} \]  
\[ K_{total} = K_{bulk} + \frac{2\sigma \mu}{a} + \frac{2\sigma_m}{\sqrt{\kappa a}} \]  
Lack physical relevance
Considering the double layer effect

The disagreement between experimental and modeling results indicate something is missing

Langmuir adsorption is used to describe the specific adsorption behavior

Surface adsorption plays a vital role in determining the crossover frequency
Other application: nanopore device
Nanopore for ionic gating
Nanopore for ionic gating

Oxidized Graphene

Isoelectric point for surface group on nanopore and graphene: pH=4
Bioengineering problems
Artificial muscle: Ionic polymer - metal composites (ipmc)

Voltage $\rightarrow$ Cation concentration gradient $\rightarrow$ Cation accumulation/depletion causes body force $\rightarrow$ bending

Concentration change along vertical direction

Deformation of ipmc
Acoustic wave actuation
Coupled WGM/SERS/SPR Spectroscopic Technique

(a) Diagram of optical setup
(b) Graph showing normalized intensity vs. wavelength

Optical fiber
Microsphere
Fusion sealed
Optical fiber
Capillary wall
Photo-detector
Laser
50/50 fiber coupler

Electric energy output (10^-8 J/m²)

4 5 6 7 8 9 10 11

y = 1e-7 - 3e-15x - 1e-15x²
R² = 1

Particle radius (nm)

y = 1e-7 - 5e-11x - 1e-11x²
R² = 1

y = 2e-7 - 1e-11x + 3e-11x²
R² = 1

y = 1e-7 - 1e-15x - 3e-15x²
R² = 0.9947

Incident laser intensity vs. wavelength

WGM alone
WGM + SERS
WGM + SERS + SPR
WGM + Nanopore
Questions?

• Let us talk, explore and collaborate …

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