Modeling Electro-manipulation of Bio/Nano Materials

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Outline

- From Immersed Boundary Method to Immersed Finite Element Method
- Applications on blood rheology and pulmonary gas diffusion
- Bio-Nano interface: measurement of cell adhesion
- IEFEM: Coupled electrokinetics and fluid-structure interaction
- Applications on dielectrophoretic assembly of nanowires
- Applications on manipulation of biomaterials
- Future work and Conclusion
Particles (Points) with Finite Mass Connected with Fibers (Springs) Form a Submerged Structure

**Challenges**

- Coupling complex nonlinear solid motions with fluid motions
- Handling very large deformation of solids
- Computational expense
Venous Valve: Experiments

- Site of deep saphenous venous thrombosis formation.
- Prevents retrograde venous flow (reflux).
- Site of sluggish blood flow.
- Decreased fibrinolytic activity.
- Muscle contraction prevents venous stasis:
  - Increases venous flow velocity.
  - Compresses veins.
- Immobilization (long distance flights, etc.) promotes venous stasis.

Courtesy of H.F. Janssen, Texas Tech University.
Comparison between experiment and simulation at 4 different time steps
Immersed Finite Element Method

Constant shear flow

Movie
Multiscale Modeling of Bio-Complexity

Organic-scale
artery

Vessel-scale
Computational angioplasty stent surgery modeling (Gay, Zhang, and Liu)

Cellular-scale
RBC aggregation
Non-Newtonian blood model

Subcellular
Bio-fibers, Fukui et al., NWU

Molecular-scale
Focal adhesion complex

Hughes et al., Texas
Liu et al., NWU

Vascular Atherogenesis and Growth of Intimal Hyperplasia (IH) (Dr. Shu Liu, NWU)

Thrombus deposition model

Cell-ECM interaction

ABIOMED Artificial heart

Self-organization of microtubules, Surrey et al.

10^{-1} m

10^{-3} m

10^{-6} m

10^{-7} \text{ - } 10^{-8} m

10^{-9} m

Actin filaments

α-actinin
talin
vinculin
paxillin
fibronectin

50 nm

1 mm

\text{100 \mu m}
Motivation

• Arterial diseases are one of leading causes of death in western countries
  - More than 700,000 die from heart failure each year in the US
  - About 6,000 patients receive support services after cardiac surgery
    with 20 to 40% survival rate

• The impact of newer mechanical circulatory support for advanced heart failure has not yet been realized
  - Further work needed to establish the role of mechanical support for myocardial recovery
  - Thrombus deposition on flexible shell surfaces is ubiquitous in human cardiovascular system
  - Lead to widespread disorders—from chronic venous insufficiency to life-threatening thromboembolic phenomena

• Thrombus deposition on mechanical valves and artificial devices severely limits the life span of these implants and contributes to various complications such as heart attack
Heart diagram

Artificial Heart (AbioCor)

From ABIOMED Inc
Survival with Artificial Heart

16 months (longest living recipient)

From ABIOMED Inc
AbioCor - Principle of Operation

AbioCor has two blood pumping chambers
• The right side pumps blood into the lungs
• The left side pumps the blood into the body

• Mimics native heart
• Responds to demand
• Few moving parts
Angioplasty

- A catheter (2 to 3 mm in diameter) with a deflated balloon on the tip is inserted through the artery in the groin or arm.
- The catheter is directed to the narrowed artery of the heart.
- The balloon is then inflated by connecting it to a special pump. The balloon is inflated and deflated several times to squeeze the plaque deposits against the wall of the artery.
- As the balloon is inflated, it compresses the fatty deposits or calcium accumulations that make up the coronary blockage.
- The deflated balloon and wire are withdrawn.

http://www.jomed.com/patientinfo/stents/stents/html/g.html
Stents are stainless steel or nytinol mesh-like devices that look similar to the spring in a pen. Their size depends on the size of the artery or vessel that has to be reopened. A major challenge for designers of coronary stents is to make them smaller, more flexible, and stronger than types used in the rest of the body.

Balloon-expanding stents are manufactured in the crimped state and expanded to the vessel diameter by inflating a balloon, thus plastically deforming the stent. The stent opens up the diseased segment into a rounder, bigger and smoother opening compared to angioplasty.
Surgical procedure

http://www.jomed.com/patientinfo/stents/stents/html/g.html
Simulation of the Stent Deployment Process

Shaded movie

Velocity profile
IFEM Applications in biological system

Blood Rheology:
- influence of blood cell aggregation on blood viscosity
- gas diffusion in pulmonary capillaries

Cell adhesion/migration on an substrate
The depletion mediated aggregation model

- Two basic models for RBC aggregation
  - Adsorption model: adsorption of plasmatic polymers at surfaces
  - Depletion model: exclusion of plasmatic polymers at surfaces

- Neu et al. (Biophysical Journal, 2003) introduced the first microscopic model for depletion mediated RBC aggregation

\[ \gamma = \mathcal{W}_D + \mathcal{W}_E \]

Depletion interaction energy (leads to attractive force)
Electrostatic energy (leads to repulsive force)

From Dennis Kunkel at http://www.denniskunkel.com/

RBC aggregation (blood cells, fibrin clot)
http://tam.northwestern.edu/wkl/liu.html
Multiphysics modeling: shear-rate dependent blood viscosity

• Blood viscosity is shear-rate dependent
  – Microscopic: Aggregation of individual cells
  – Macroscopic: Break up of the aggregates at different shear rates lead to different apparent viscosities

Shear of a RBC rouleau at different shear rates

- Low shear rate: 0.25 s\(^{-1}\) - Stick together
- Median shear rate: 0.5 s\(^{-1}\) - Partially separated
- High shear rate: 3.0 s\(^{-1}\) - Totally separated

Adhesion energy vs. time graph showing the transition from stick together to totally separated at different shear rates.

Blood viscosity is shear-rate dependent

- Microscopic: Aggregation of individual cells
- Macroscopic: Break up of the aggregates at different shear rates lead to different apparent viscosities
Calculation of effective viscosity

- Effective viscosity of blood flow:

\[ \mu_{\text{eff}} = \frac{HF}{LU_0} \]
Effective viscosity of the blood flow

- The simulated shear rate dependent viscosity of the blood flow qualitatively agrees with experimental results.

- Other simulated phenomena:
  - Fahraeus-Lindqvist effect
  - Influence of cell rigidity
Fahraeus-Lindqvist effect

- The apparent viscosity of blood flow through a tube with diameter < 0.3 mm is smaller than the bulk blood viscosity.
- Apparent viscosity decreases with decreasing diameter.
- The viscosity drop is induced by the axis migration & formation of plasma skimming layer.

Blood flow in very narrow tubes

- Effective viscosity increases for blood flow through a tube with diameter even smaller than the diameter of the RBCs.
- RBCs squeeze through the tube.

Calculated Effective Viscosity vs. tube diameter

\[ \mu_{\text{app}} / \mu_0 \]

bulk viscosity

FL effect
Movies of RBCs flow in tubes with different diameters

In-flow 10μm/s

D=11μm

D=15μm

D=30μm

D=8μm
Gas diffusion in pulmonary capillaries

Diffusive transport: \[ \alpha D \nabla^2 P = 0 \]

Gas flux: \[ \alpha D \frac{\partial P}{\partial n} \]

Diffusion capacity: \[ D_M = \int \frac{\text{flux} \cdot dA}{P_A} \]

Comparable concept in electricity:

\[ \text{conductance} = \frac{\text{electric current}}{\text{voltage}} = \frac{I}{V} = \frac{1}{R} \]
Influence of RBC dynamics on diffusion capacity

- Gas diffusion in pulmonary capillaries
- IFEM simulation shows that the gas diffusion capacity decreases as the RBC deforms

![Diagram showing nonuniform gas flux on cell surface](image)
Influence of RBC distribution on diffusion capacity

- 60μm
- uniform
- Non-uniform (random)
- cluster

Clustering of RBCs in branching capillary networks
Cell migration and adhesion

• Cell motility plays a crucial role in
  – Cell differentiation, growth
  – Wound healing, embryogenesis, vessels
generation

• Cell motility is a complex coupled
  biochemical/mechanical process

  Sensing ➔ Internal structure remodeling ➔ Directed cell movement

• External mechanical environment influences cell
  organization and initiate migration

  • Rigid surface strengthens focal adhesions
  • Soft surface weakens cell adhesions

Wolf et al., 2003

HT1080/MT1 cell-
spontaneous
mesenchymal
migration

Wolf et al., 2003

HT1080/MT1 cell-
blocked
β1 integrins
(mAb 4B4)
Cell migration is guided by external environment

Different types of external factors that influence cell organization and initiate movement

(A) Chemotaxis
- chemical attractor/repellent gradients induce direct migration towards/away from the emitter

(B) Haptotaxis.
- Spatial variations in adhesion
- inhomogeneous ligand density

(C) Topographic guidance
- Cell reacts to surface curvature & prefers to align along the axis of minimal curvature of the surface, where minimal distortion of the cytoskeleton occurs

(D) Durotaxis induced by different ECM rigidity.
- Rigid surface strengthens focal adhesions & increases traction force
- Soft surface weakens cell adhesions & allows easier detachment

(E) Mechanotaxis induced by fluid shear stress or static mechanical strain of the substrate.

(F) Contact guidance
- Cell orients along ECM fiber

Our focus

Sensing
↓
Internal structure remodeling
↓
Directed cell movement
Focus and goals of this study

- Focus of this study: DUROTAXIS
- cell’s response to the mechanical properties of its environment.

Main goals:
- develop a model capable of reproducing the path cell of migration, velocity and shape of a cell lying on an elastic substrate.
- The components considered are:
  - actin–myosin filament, adhesion sites and the cytoplasmatic membrane

Discher, 2005

Li et al., 2005
Experimental observation

- Cell migrates in the direction of increasing stiffness of the substrate

Lo et al., 2000 performed experiments with cultured 3T3 fibroblasts cells

Cell accumulation on stiffer regions of PDM Substrates. Grey et al., 2002

Cell path and cell accumulation in a stiff-radial-gradient gel, Wong et al., 2003
Cells lying on a bed of microneedles: An approach to isolate mechanical force
John L. Tan et al

- Cell lying on a bed of microneedles may sink to the bottom of the substrate
- A new solution is to cover an elastic membrane on top of the microneedles
- Force generated from the cell onto the substrate can be identified by measuring the deflection of the underlying microneedles
New design: cell on an elastic membrane

- An elastic membrane glued on an array of MEMS pillars
- An array of 5 by 5 pillars is modeled
- Membrane dimension: 5.0 x 5.0 x 1.0 um, fixed boundary
- Membrane material: PDMS
  - $E = 0.75$ MPa
  - Poisson ratio $= 0.4$

Layout bottom view

Stress distribution due a point force in the center
Bio-nano sensors for the study of cell adhesion

- Design and modeling of MEMS/NEMS devices for cellular force measurement

**HT1080/MT1 cell - spontaneous mesenchymal migration**

- The light square areas are coated with fibronectin (to enable focal adhesion)
- Measured adhesion force distribution profile at the cell-substrate interface.
- 3 patterns with different spacings

**HT1080/MT1 cell - blocked β1 integrins (mAb 4B4)**

- Force resolution: 10-300nN
- Substrates with printed fibronectin patterns
- Assembly of CNTs across parallel electrodes

Tan et al., 2002

Abel, Fukui, and Liu (NWU)

Wolf et al., 2003

Force resolution: 10-200nN

<10pN
Modeling cell response to substrate stiffness

• By regulating force at individual adhesion sites in response to the ECM resistance, cell can migrate according to the elastic properties of substrate.
Combination of experimental test and modeling

- Experimental work in progress at NWU
  - cell migrating on an elastic membrane with a gradient of width that results in a non-linear gradient of stiffness
  - Check out the minimum gradient that cells can sense

Abel, Fukui, and Liu (NWU)

The light square areas are coated with fibrinectin (to enable focal adhesion)

3 patterns with different spacings
Cell adhesion/migration on elastic substrate

Juhee Hong, Junghoon Lee, Seoul National Univ

M. Glucksberg, Abel, Liu, NWU

peaks of effective stiffness appear at pillar regions

- Cells know where pillars are through the nonuniform stiffness
- Cells align in high stiffness region, i.e., regions close to pillars
- How cells “sense” the environment?
Cell migration on an **elastic membrane** with a **gradient of stiffness** (experiment by Abel L. Thangawng)

- **Description of the experiment:** HEK cells (human epidermis keratinocytes) were plated on a PDMS (polydimethylsiloxane) membrane to study the effects of its mechanical properties on cell migration.

- Cells migrated on the membrane and **accumulated** in specific areas.

**PDMS elastic properties:**
- Young’s modulus: \( E = 750 \text{kPa} \)
- Poisson’s ratio \( \nu = 0.5 \)

Top view (left) and lateral view (up) of the PDMS membrane
Cells accumulate in 4 regions of the membrane.

**DUROTAXIS**: cells migrate to stiffer regions

Observations:

- In general, cells accumulate in the stiffest regions A and D, but some also accumulate in less stiff regions B and C.
- The patterned membrane is affecting the migration of the cells since the local and global stiffnesses of the membrane are modified by the patterns (ridges).

Blue rectangles: accumulation region  Green lines: patterned region  Red rectangles: non-accumulation region
Effective stiffness and experimental results

HYPOTHESIS: stiffness profiles explains accumulation regions

**Region D:** Cells that were originally here stay here

**Region C:** Cells accumulate here because they sense stiffer regions (B and D) to their left and right.

**Region B:** Cells get trapped here because stiffness gradient is too small to be sensed by the cells.

**Region A:** Cells accumulate in the ‘thick region’. Cells coming from the right can sense the stiffness gradient and migrate into the stiff region A.
Model of adhesion-contraction

Cell migration is a complex process that can be divided into 5 steps (Sheetz):

A: extension of the leading edge
B: adhesion to extracellular matrix contacts
C: contraction of the cytoplasm
D: release from contact sites
F: recycling membrane receptors from the rear to the front

The model that is going to be presented deals with C-D steps of cell migration: adhesion to extracellular matrix contacts, contraction of the cytoplasm and release from contact sides.
The local system of the cell membrane, focal adhesion, and stress fiber is modeled as a 1D viscoelastic model:

\[ F = K_E x + \beta \frac{dx}{dt} \]

- **F**: stress fiber contractile force
- **K_E**: effective spring constant of the stress fiber and focal adhesion
- **\( \beta \)**: viscous coefficient of cell membrane
- **x**: FA displacement along the membrane
Biophysical principles explaining Durotaxis

**Work done** in the process of interacting with the substrate:

\[
W_k(T) = \int_0^T F_k dx = \frac{F^2}{k} e^{-\frac{KT}{\beta}} = \cosh \left( \frac{K}{\beta} T \right) - 1
\]

\[
W_\beta(T) = \int_0^T F_\beta dx = \frac{F^2}{k} e^{-\frac{KT}{\beta}} = \sinh \left( \frac{K}{\beta} T \right)
\]

- **\( W_k \):** energy invested in deforming the substrate
- **\( W_\beta \):** energy invested in dragging the FA along the membrane

Efficiency of the pulling-process is defined by

\[
\alpha = \frac{W_k(T)}{W_\beta(T)} = \coth \left( \frac{k}{\beta} T \right) - \csch \left( \frac{k}{\beta} T \right)
\]

It takes less energy for the cell to move to stiffer region: DUROTAXIS
Bio-nano sensors for the study of cell adhesion

Design and modeling of MEMS/NEMS devices for cellular force measurement

Measured adhesion force distribution profile at the cell-substrate interface.

Tan et al., 2003

Hong, Lee, Abel, Fukui, Liu, cell on a elastic membrane supported by a bed of microneedles

Force resolution: 10-300nN

10-400nN

<10pN
Immersed Electrokinetic Finite Element Method:

Coupled electrokinetics and fluid-structure interaction
Nanomanufacturing of electronic/molecular devices

Carbon Nanotube Based Memory Devices

*Rueckes et al., Science*

Carbon Nanotube Assembly Method

*Electric field guided assembly of NWs*

J. Chung, U. Washington

*Cross-bar array of Si NWs with electrical connection using an e-beam lithography. Y. Huang et al., Science*

Challenge

• *A production chip requires millions of these CNT ribbons to be assembled precisely between the micro electrodes*
Challenges

- **NW assembly methods**
  - growth method: high temperature
  - chemical patterning: complex chemical modifications
  - magnetic fields: not for individual assembly
  - electric fields (e-fields): low yield, work locally
  - fluid flow: not directly positioned

- Proposed new assembly method: combine fluid flow and e-field
  - room temperature fabrication
  - high packing density with high yield
  - compatible with mass parallel integration
  - may improve density of integrated circuits (ICs) by 1000~10000 times

Dielectrophoresis

Dielectrophoretic force is proportional to polarizability.

Positive DEP

Negative DEP

Polarization of a particle under nonuniform field.
Imbalance of force on the induced dipole of a particle.
Particle is more polarizable than medium: Positive DEP.
Particle is less polarizable than medium: Negative DEP.

*Darker color means higher e-field.
Dielectrophoresis

From:
http://www.ibmm-microtech.co.uk/microeng/dielectrophoresis/dielectrophoresis.php
Dielectrophoresis (DEP) force for small particles

• Induced by dipole moment under a non-uniform electric field

• The force exerted by an electric field \( E \) on dipole moment \( p \):

\[
F = (p \cdot \nabla)E
\]

• In AC field, the time-averaged force on a particle given by the Effective Dipole Moment (EDM) theory is

\[
F_{\text{DEP}} = \Gamma \cdot \varepsilon_m \text{Re}\{K_f\} \nabla |E|^2
\]

Where the geometrical factor for a sphere is \( \Gamma = 2\pi a^3 \)

Polarization factor \( K_f = (\varepsilon_2^* - \varepsilon_1^*)/(\varepsilon_2^* + 2\varepsilon_1^*) \)

\( \varepsilon \) is the complex permittivity of the medium \( (m) \) and particle \( (p) \)
General DEP formulation

• EDM is valid only for particles much smaller than the characteristic lengths of the e-field, and only derived for spherical or oblate particles

• A general expression for the DEP force on any point of a continuous domain is given through the Maxwell Stress Tensor (MST) theory

\[
\rho_f \mathbf{E} + \mathbf{p} \cdot \nabla \mathbf{E} = \nabla \cdot (\mathbf{e} \mathbf{E}) - (\mathbf{e} \mathbf{E}) \cdot \nabla \mathbf{E} = \nabla \cdot (\mathbf{e} \mathbf{E} - \frac{1}{2} \mathbf{e} \mathbf{E} \cdot \mathbf{E} \mathbf{E})
\]

\[
\sigma^M = \varepsilon \varepsilon_0 \mathbf{E} \mathbf{E} - \frac{1}{2} \varepsilon \varepsilon_0 \mathbf{E} \cdot \mathbf{E} \mathbf{E}
\]

For an AC field of \( E(r,t) = E(r)e^{i \omega t} \)

\[
\sigma^M = \mathbf{T}_1 + \mathbf{T}_2
\]

where \( \mathbf{T}_1 = \frac{1}{4} \text{Re}(\varepsilon) ((\mathbf{E E}^* + \mathbf{E}^* \mathbf{E}) - \mathbf{E}^2 \mathbf{1}) \) is the time-averaged stress tensor

\( \mathbf{T}_2 \) is the instantaneous term that vanishes by time averaging.

The time averaged DEP force and rotational torque on an arbitrary shaped particle are:

\[
\langle \mathbf{F}_{DEP} \rangle = \int (\mathbf{T}_1 \cdot \mathbf{n}) dA \quad \quad \langle \mathbf{\tau} \rangle = \int r \mathbf{n} \times (\mathbf{T}_1 \cdot \mathbf{n}) dA
\]
Electrophoresis

Electrostatic attraction between charged particles and electrodes

Example: DNA electrophoresis
DNA electrophoresis

• Analytical technique to separate DNA upon the size using electrophoresis
• Negatively charged DNA moves toward a positive electrode.
• Due to their length, DNA molecules are separated.

Note: the leftmost and rightmost markers are a standard DNA ladders showing the number of base pairs. For example, 1kb means DNA having 1000 base-pairs.

Forces in electromechanical problems

Electrohydrodynamic (EHD) forces

- Drag force induced by flow (including electroosmotic flow)
- Electrophoretic force (EP)
- Dielectrophoresis (DEP) force
- Other factors playing minor roles
  - Brownian motion
  - Temperature change due to heat up by E field

Our study

Spherical particle 10 μm above two planar electrodes with a spacing of 20 μm, density=1g cm⁻³, viscosity=0.78Pa·s

Temperature increase ~10⁻⁴ K

http://tam.northwestern.edu/summerinstitute/Home.htm http://tam.northwestern.edu/wkl/liu.html
Equations for different factors

• DEP force

\[ F_{\text{DEP}} = 2\pi a^3 \cdot \varepsilon \text{Re}\{K_f\} \nabla |E|^2, \]

• Brownian motion

\[ |\Delta x| = 2D t = \sqrt{2k_B T t / \gamma} \]

• Thermal effect

Temperature increase:

\[ \Delta T = \frac{\sigma V^2}{2k} \]

Buoyancy force due to temperature

\[ f_{\text{therm}} = \left( \frac{\partial \rho^f}{\partial T} \right) \frac{\sigma V^2}{2k} g \]

Where \( \varepsilon \) and \( \sigma \) are the permittivity and conductivity of the medium

\( k \) is the thermal conductivity of the medium

\( \text{Re}\{K_f\} \) is the polarization factor

\( \gamma \) is the viscosity of the medium

http://tam.northwestern.edu/summerinstitute/Home.htm
http://tam.northwestern.edu/wkl/liu.html
Configuration of the problem

- Domain description
  Compressible Navier-Stokes Fluid $\Omega^f$
  Elastic Solid $\Omega^s$
  Fluid-Solid Interface $\Gamma^s$

- Primary variables
  Electric field $E$
  Velocity
    \[ \begin{align*}
      & \text{solid } v^s \quad \text{in } \Omega^s \\
      & \text{fluid } v^f \quad \text{in } \Omega^f
    \end{align*} \]
  Pressure $p^f$ in $\Omega^f$

- Major charge carriers
  - Inherent charge carriers, i.e., electrons
  - Ions in fluid
Continuum Electro-mechanics

Maxwell equations

\[ \nabla \cdot (\varepsilon \mathbf{E}) = \rho_f \]

\[ \frac{D\rho_f}{Dt} + \nabla \cdot (\sigma \mathbf{E}) = 0 \]

\[ \mathbf{E} = -\nabla \phi \]

Standard BC: \( \phi = \phi_0, \quad -\sigma \nabla \phi \cdot \mathbf{n} = 0 \)

Jump BC at interface:

\[ \mathbf{n} \cdot [\varepsilon \mathbf{E}] = s^c \quad \mathbf{n} \cdot [\gamma \mathbf{E}] = -\partial s^c / \partial t \]

- Major charge carriers: inherent carriers
  - For an AC field, \( \tilde{\phi}(x,t) = \phi^M(x) e^{j\omega t} \)
  - Particle motion time scale \( \gg 1/f : \frac{D\rho_f}{Dt} \approx \frac{\partial \rho_f}{\partial t} = j\omega \rho_f \)

Reduced Maxwell equation in complex form

\[ \nabla \cdot (\tilde{\varepsilon} \tilde{\mathbf{E}}) = 0, \quad \text{in} \ \Omega^f, \]

\[ \nabla \cdot (\tilde{\varepsilon} \tilde{\mathbf{E}}) = 0, \quad \text{in} \ \Omega^s, \]

\[ \tilde{\varepsilon} \tilde{\mathbf{E}} \cdot \mathbf{n} = \tilde{\varepsilon} \tilde{\mathbf{E}} \cdot \mathbf{n}, \quad \text{on} \ \Gamma^s \]

Where \( \tilde{\varepsilon} = \varepsilon + (\gamma / j\omega) \) : complex permittivity

- Major charge carriers: ions in fluid
  - Ions are external source of free charge
  - Solids are insulators

Maxwell equation + Species equation

\[ \rho^c = \sum_{k=1}^{N} \varepsilon_k c_k, \quad \text{in} \ \Omega^f, \]

\[ \frac{\partial c_k}{\partial t} + \mathbf{v} \cdot \nabla c_k = \nabla \cdot \left[ -\eta_k \varepsilon_k c_k \mathbf{E} + \eta_k k_B T \nabla c_k \right], \quad \text{in} \ \Omega^f \]

\[ c_k = 0, \quad \text{in} \ \Omega^s, \]

\[ \varepsilon^f \mathbf{E} \cdot \mathbf{n} = \varepsilon^s \mathbf{E}^s \cdot \mathbf{n}, \quad \text{on} \ \Gamma^s \]

\( c_k \) : concentration of kth species, \( \eta_k \) : mobility
Immersed formulation of IEFEM

- Augmented fluid momentum equation

\[
\rho^f \dot{\mathbf{v}} = \nabla \cdot \mathbf{\sigma} + \rho^f \mathbf{g} + \mathbf{\sigma}^M + \mathbf{F}, \quad \text{in } \Omega = \Omega^f \cup \Omega^s \cup \Gamma
\]

\[
\mathbf{F} = \begin{cases} 
(\rho^f - \rho^s)(\dot{\mathbf{v}}^s - \mathbf{g}) + \nabla \cdot (\mathbf{\sigma}^s - \mathbf{\sigma}^f), & \text{in } \Omega^s \\
0, & \text{in } \Omega^f
\end{cases}
\]

Maxwell stress tensor

\[
\mathbf{\sigma}^M = \frac{1}{4} \text{Re}(\mathbf{\varepsilon})(\mathbf{\varepsilon}^* \mathbf{\varepsilon}^T + \mathbf{\varepsilon}^T \mathbf{\varepsilon}^*) - |\mathbf{\varepsilon}|^2 \mathbf{I}
\]

- Augmented electric field equation

- Inherent charge carriers

\[
\nabla \cdot (\varepsilon^f \nabla \phi) + Q = 0, \quad \text{in } \Omega,
\]

\[
Q = \begin{cases} 
\nabla \cdot ((\varepsilon^s - \varepsilon^f)\nabla \phi^s), & \text{in } \Omega^s \\
0, & \text{in } \Omega \setminus \Omega^s
\end{cases}
\]

- Ions

\[
\nabla \cdot (\varepsilon^f \nabla \phi) + S = 0, \quad \text{in } \Omega.
\]

\[
S = \begin{cases} 
\nabla \cdot ((\varepsilon^s - \varepsilon^f)\nabla \phi^s), & \text{in } \Omega^s \\
-\rho^e, & \text{in } \Omega^f
\end{cases}
\]

\[
\rho^e = \sum_k \varepsilon z_k c_k, \quad \text{in } \Omega^f,
\]

\[
\frac{Dc_k}{Dt} = \nabla \cdot [\eta_k \varepsilon z_k c_k \mathbf{E} + \eta_k k_B T \nabla c_k], \quad \text{in } \Omega^f,
\]
Eulerian-to-Lagrangian (E-L) Mapping

Eulerian Coordinate

\[ \begin{align*}
\bullet \ x & \in \Omega_0^s \\
X & \\
\end{align*} \]

Lagrangian Coordinate

\[ \begin{align*}
\psi (X, t) & \equiv \psi (x (X, t), t), \quad \forall X \in \Omega_0^s \\
\end{align*} \]

• Mapping function
  – FEM shape function
  – RKPM Dirac delta function
Weak formulation of immersed system

\[
R_m(v, p, p^t, u, \bar{\phi}) \equiv \int_\Omega \rho(v - \bar{g}) \cdot \bar{w} dx + \int_\Omega \sigma : \nabla \bar{w} dx - \sum_e \int_\Omega \nabla \sigma \cdot (\eta^m v \cdot \nabla w + \eta^f \nabla q) dx
\]

\[
- \int_{\tilde{\Omega}} ((\rho - \rho^t) \left( \frac{\partial \bar{v}}{\partial t} - \bar{g} \right) + q_E \cdot \bar{E}) \cdot \frac{\partial \bar{x}}{\partial X} dX
\]

\[
+ \int_{\tilde{\Omega}} (\bar{\sigma} - \bar{\sigma}^t + \bar{\sigma}^M) \left( \nabla_x \bar{w} \left[ \frac{\partial \bar{x}}{\partial X} \right]^{-1} \right) \frac{\partial \bar{x}}{\partial X} dX = 0, \quad \forall \bar{w} \in V,
\]

\[
R_{map}(v, p, p^t, u) \equiv \int_{\tilde{\Omega}} \left( \frac{\partial x(X, t)}{\partial t} - 1 + \bar{v}(X, t) \right) \cdot w^t dX, \quad \forall w^t \in V^s
\]

\[
R_{e_{inherent}}(\bar{\phi}) \equiv \int_\Omega \bar{\varepsilon}^f \nabla \bar{\phi} \cdot \nabla m dx
\]

\[
+ \int_{\tilde{\Omega}} (\bar{\varepsilon}^s - \bar{\varepsilon}^f) \left( \nabla_x \bar{\phi} \left[ \frac{\partial \bar{x}}{\partial X} \right]^{-1} \right) \cdot \left( \nabla_x \bar{m} \left[ \frac{\partial \bar{x}}{\partial X} \right]^{-1} \right) \frac{\partial \bar{x}}{\partial X} dX, \quad \forall m \in P
\]

\[
R_{e_{ions}}(\phi) \equiv \int_\Omega \varepsilon^f \nabla \phi \cdot \nabla m dx - \int_\Omega \rho_f m dx
\]

\[
+ \int_{\tilde{\Omega}} (\varepsilon^s - \varepsilon^f) \left( \nabla_x \phi \left[ \frac{\partial \bar{x}}{\partial X} \right]^{-1} \right) \cdot \left( \nabla_x \bar{m} \left[ \frac{\partial \bar{x}}{\partial X} \right]^{-1} \right) \frac{\partial \bar{x}}{\partial X} dX, \quad \forall m \in P
\]

\[
R_{ion}(c_k) \equiv \int_\Omega [-\eta_k e z_k c_k E + \eta_k k T \nabla c_k] \cdot \nabla s_k dx
\]

\[
- \int_{\tilde{\Omega}} \left( \frac{\partial c_k}{\partial t} + v \cdot \nabla c_k \left[ \frac{\partial \bar{x}}{\partial X} \right]^{-1} \right) s_k \frac{\partial \bar{x}}{\partial X} dX
\]

\[
+ \int_{\tilde{\Omega}} \alpha c_k s_k \frac{\partial \bar{x}}{\partial X} dX, \quad \forall s_k \in S
\]
Coupling of e-field with fluid-structure interaction problems

(a) Particle, Lagrangian mesh

(b) Fluid domain, Navier-Stokes flow, Eulerian mesh

(c) Electric field, Eulerian mesh with particle domains tracked separately (electric properties different from the fluid are assigned for domains occupied by particles)

(d) Coupled electrohydrodynamic modeling of the assembly of suspended particles between micro-electrodes
Applications of IEFEM

- Trapping of a rigid spherical particle
- Assembly of rigid non-spherical particles
- Electro-manipulation of a single deformable cell
- Electro-manipulation of multiple cells
- Electric field induced stretching of DNAs
- Electrokinetic detection of viruses

DEP dominant
(major charge carrier: electrons)

DEP & Electroosmosis flow
(major charge carrier: electrons and ions)
Attraction of a rigid spherical particle

Effective Dipole theory: 
\[ \langle F_{\text{DEP}} \rangle = \Gamma \cdot \mathcal{E} \cdot \text{Re} \{ K_f \} \nabla (E^2), \]

\[ \mathcal{E} = 20 \varepsilon_0 \]
\[ \varepsilon^s = 100 \varepsilon_0 \]
\[ \sigma^f = 0.0056 \text{ s/m} \]
\[ \sigma^s = 0.0112 \text{ s/m} \]

(a) \( h = 10 \mu \text{m} \)

(b) \( h = 5 \mu \text{m} \)
3D Nanowire assembly simulation

Two steps are involved in the assembly process of NWs between semi-circular shaped electrodes

- Attraction induced by DEP force
- Alignment induce by DEP torque
NW assembly between rectangular shaped electrodes

When two NWs deposit close to each other, a third NW with a longer length may be deposited to connect the opposite two ends of the deposited NWs---because a high e-field region is created at the ends of the deposited NWs. To prevent: transport and pre-orient by fluid flow.
Snap shorts of cross-linking process
Combine a shear flow and a e-field in NW assembly

Proposed microfluidic device to combine fluid flow and e-field to assemble individual NWs
Prediction from simulation

Pre-orientation induced by shear flow before NWs enter effective zone

Precise alignment and deposition induced by e-field at effective zone
NW assembly at different shear rate

Flow direction

High shear rate
5s\(^{-1}\)

Median shear rate
2.5s\(^{-1}\)

Low shear rate
1.25s\(^{-1}\)
Comparison between simulation and experiments

Single deposition
Failure single deposition
Symmetric multiple deposition
2 NWs deposition
Design criteria: DEP force

(a) A NW aligns across a pair of parallel rectangular-shaped electrodes;

(b) Cross-sectional view: non-uniform electric field between two parallel rectangular-shaped electrodes. Electric fields near the NW are distorted. The DEP force will attract the NW toward the gap;

(c) The DEP force on a NW for various gap sizes. The nominal e-field strength (the field strength at the middle point) is kept at 0.5v/μm. DEP force is maximum at a ratio $\sim 0.79$. 
Electrodeformation of deformable particle

Electro-Deformation and Poration of Giant Vesicles under an e-field of 3 kV/cm, with a duration of 200 ms

![Electrodeformation Simulation](image)

Inner fluid (0.2M sucrose) : $\sigma_{in} = 6 \text{ mS m}^{-1}$

Outer fluid (0.2M glucose) : $\sigma_{out} = 4.5 \text{ mS m}^{-1}$

Membrane modulus : 5.7 dyn/cm

Riske et al., 2005
Dynamic process of electrodeformation

Degree of deformation (a/b) history

- Determine the electrical property of cells
- Determine the mechanical property of the membrane

- Simplified analytical model

\[ F(x) = K_E x + \beta \frac{dx}{dt} + m \frac{d^2 x}{d^2 t} \]

\[ x(t) = \frac{F}{K} (1 - e^{-\frac{Kt}{\beta}}) \]
Electrodeformation and patterning of cells

Alignment and deformation of cells induced by electric field

Zimmermann et al., 2000
Electroosmosis flow

The electroosmosis flow is driven by the electric static force applied onto the charged double layer

\[ \rho \dot{\mathbf{v}} = \nabla \cdot \mathbf{\sigma} + \rho_E \mathbf{E} = -\nabla p + \mu \nabla^2 \mathbf{v} + \rho_E \mathbf{E} \]

The charge density of the double layer is described by the zeta potential:

\[ \nabla^2 \psi = -\rho_E / \varepsilon \]

Using Debye and Huckel approximation, simplify it to be

\[ \nabla^2 \psi = \kappa^2 \psi \]

Thus, \( \psi = \psi_0 \exp(-\kappa y) \) is the solution for an infinite long channel in \( y \) direction

\( \psi \) is the potential induced by the charged ions
\( \kappa^{-1} \) is called Debye length, usually in order of nm
\( \psi_0 \) is called the zeta potential, \( y \) is the distance from the wall
Electroosmosis flow

MacInnes et al proposed a steady state solution in 2D:

$$\frac{dp}{dx} - \varepsilon E_x \frac{d^2 \psi}{dy^2} + \mu \frac{d^2 u}{dy^2} = 0$$

$$\frac{dp}{dx} - \varepsilon \kappa^2 \psi E_x + \mu \frac{d^2 u}{dy^2} = 0$$

Usually the diffuse layer very thin (<20nm) and thus, a slip boundary at the electrode surface:

$$u = \frac{1}{\mu} \frac{dp}{dx} \left( \frac{y^2}{2} - \frac{hy}{2} \right) + u_s$$

$$u_s = -\frac{\varepsilon \psi_0 E_x}{\mu}$$

The zeta potential $\psi_0 = 135$mv

Viscosity of ethenal $\mu = 1.2$ mNs/m$^2$

Permitivity of ethenal $\varepsilon = 2.1e^{-10}$ F/m
AC electroosmosis flow

The charge relaxation time of a liquid: \( \tau = \frac{\varepsilon}{\sigma} \)

- If the AC frequency \( f < \frac{1}{2\pi \tau} \), charge on electrodes and in EDL alternates according to potential sign change

- The flow direction doesn’t change with potential sign change

\( u_s(x) = -\frac{\varepsilon \psi_0 E_x}{\mu} \)
CNTs rotation induced by local electroosmosis flow

AC field 100 Hz, 0.5v/μm, parallel electrodes gap size: 5 μm
Local electroosmosis flows near the edges of electrodes induce vortices and lead to CNTs rotation
Electroosmosis flow induced aggregation (side view). The model in the literature assume the electroosmosis flow generated at each sphere are independent. The influence of neighboring spheres on the flow pattern are included here.
Experimental setup for DNA deposition

\[ \text{DNA solution} \]

\[ \text{Electrodes} \]

\[ \text{Signal Generator} \]

\[ \text{Heater} \]

\[ 1\,\Omega \text{hm} \]

\[ 22\,\mu\text{F} \]

\( \lambda \)-DNA dissolved and diluted using ultrapure water.

The DNA stock solution was heated up to 100 °C so that dsDNA denaturizes into ssDNA strand.
A single DNA molecule was stretched between two electrodes, when a composite electric field was applied. The similar results at the same experimental condition were repeatedly observed. The height of DNA was around 1nm, which shows that it is a single strand DNA (unpublished results; J. Chung).
DNA stretching with CEGA (SEM images)

A DNA molecule stretched with the electric field was observed under SEM. In a few minutes of illumination of electron beam, the DNA molecule was blown by the electron beam and observed. The similar images were observed in repeated experiments (unpublished results; J. Chung).
DNA stretching

- Bead-spring model of DNA

- AC electrokinetic-induced conformational changes of long molecules

  DNA in solution: coiled form  DNA in sequencing: stretched form
  Atomistic structure of DNA  Bead spring model of DNA

- Electrokinetic force: attraction force

- Electroosmotic flow: elongation force
DNA stretching

The stretching of a DNA chain between two semi-spherical shaped electrodes.

DNA motion driven by coupled fluid/electric field

J. Chung, UW
**Virus Detection by NEMS**

- **Virus detection**
  - Transportation of virus by nanofluidic channel
  - Selective deposition of virus according to sizes & electrical properties

Nanofracture Inc., U. Washington, NWU
NIH proposal pending

<table>
<thead>
<tr>
<th></th>
<th>Head size, nm</th>
<th>Tail size, nm</th>
<th>Total length, nm</th>
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<tbody>
<tr>
<td>Herpes simplex virus</td>
<td></td>
<td></td>
<td>250 (membrane included)</td>
</tr>
<tr>
<td>Influenza virus</td>
<td></td>
<td></td>
<td>100</td>
</tr>
<tr>
<td>Bacteriophage P22</td>
<td>60</td>
<td>20</td>
<td>80</td>
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<tr>
<td>Bacteriophage UrLambda</td>
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<tr>
<td>Inovirus</td>
<td></td>
<td></td>
<td>85–280 (length) 10–16 (diameter)</td>
</tr>
</tbody>
</table>

Illustration of using frequency-dependent DEP force to sort different types of viruses.
Virus Detection by NEMS

- Virus detection
  - Selective deposition of three virus according to electrical properties

<table>
<thead>
<tr>
<th></th>
<th>Inovirus</th>
<th>Influenza</th>
<th>Bacteriophage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Size (nm)</td>
<td>85~280 (length)</td>
<td>100 (diameter)</td>
<td>65 (in length)</td>
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<tr>
<td>Permittivity</td>
<td>70</td>
<td>3</td>
<td>30</td>
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<tr>
<td>Conductivity (mS/m)</td>
<td>8</td>
<td>80</td>
<td>3</td>
</tr>
</tbody>
</table>

Selective deposition of Influenza at 5Mhz

1MHz to select Inovirus
5MHz to select Influenza

Chung et al., UW
Electrical detection of single viruses

How do we know a virus is deposited—conductance change

Patolsky et al, PNAS, 2004
Conclusion

- Developed Immersed Electrokinetic Finite Element Method for fluid-solid interaction problems under an electric field
  - IFEM is coupled with electromechanics to model electric field guided manipulation of bio/nano materials
  - Interface is tracked automatically; no mesh update algorithm needed
- Blood rheology
  - Shear rate dependent blood viscosity
  - Cell adhesion on an elastic substrate
- Electric field guided assembly nanowires on MEMS
  - Modeled the 3D dynamic assembly process
  - Proposed and validated a new design for both high yield and high precision assembly

Future research

- DEP manipulation and sorting of cells and biomolecules
- Biocompatibility of artificial heart valves
References

References