ANALYSIS AND MODELING OF CELL MECHANICS

Session 1
Syllabus

Website:  
- http://faculty.washington.edu/nsniadec/ME599/W13/

Selected readings

Topics
- Introduction to Cell Biology
- Analysis of Cell Mechanics
- Cell Mechanics Modeling
- Measuring Cell Forces
- Mechanotransduction

Grading
- Homework: 50%
- Project: 50%
- No Final
<table>
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<td>Introductory - Analysis and Modeling of Cell Mechanics</td>
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<td>Introductory - Building Blocks</td>
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<td>Cell Mechanical Analysis - Atomic Force Microscopy</td>
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<td>Cellular Forces - MEMS Tools</td>
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<td>8-Mar</td>
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<td>Mechanotransduction - Introduction &amp; Examples</td>
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<td>Final Project Report Due</td>
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INTRODUCTIONS
Robert Hooke

- Micrographia (1665)
What are cells?

- The basic functional units of life (composed of numerous components with distinct mechanical characteristics)

- Origins:
  - Sea Urchin
  - Mouse
  - Seaweed
The Context of Cells

- **Organ**: 1 - 0.1 m
- **Tissue**: $10^{-2} - 10^{-3}$ m
- **Cells**: $10^{-4} - 10^{-6}$ m
- **Proteins**: $10^{-8} - 10^{-10}$ m

<table>
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<tr>
<th>Cells – Tissue</th>
<th>Grains – Materials</th>
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<tbody>
<tr>
<td>Animate</td>
<td>Inanimate</td>
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<tr>
<td>Basic Unit of Living Things</td>
<td>Basic Unit of Metal and Ceramics</td>
</tr>
<tr>
<td>Composed of Proteins</td>
<td>Composed of Atoms</td>
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<tr>
<td>Defines structure-function of tissue</td>
<td>Defines structure-strength of material</td>
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<tr>
<td>Sensitive to temperature, radiation, water, pH, nutrients, pressure, ionic strength, osmolarity, hormones, etc.</td>
<td>Sensitive to temperature, radiation, corrosion, loading</td>
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</table>
Organelles :: Subsystems

[Diagram of cellular organelles including microtubule, centrosome, chromatin (DNA), nuclear pore, extracellular matrix, vesicles, lysosome, nucleolus, nucleus, endoplasmic reticulum, mitochondrion, actin filaments, peroxisome, Golgi apparatus, intermediate filaments, plasma membrane]
What is Cell Mechanics?

- “The subject of cell mechanics encompasses a wide range of essential cellular processes, ranging from macroscopic events like the maintenance of cell shape, cell motility, adhesion, and deformation to microscopic events such as how cells sense mechanical signals and transduce them into a cascade of biochemical signals ultimately leading to a host of biological responses.”

  -- Mofrad & Kamm
Cell Mechanical Analysis

- Diameter: 30-50 µm (~3 µm for bacteria)
- Mass: 2-6 \times 10^{-8} \text{ g}
- Young's modulus: 1 – 10^5 \text{ Pa} (CSK: ~ 10^{-9} \text{ Pa})

![Graph showing Young's modulus for different experimental techniques]

- MTC: Magnetic twisting cytometry
- MA: Micropipette aspiration
- MM: Micromanipulation (compressive)
- CP: Cell poking
- AFM: Atomic force microscopy
- MBR: Magnetic bead rheometry
Modeling Cell Mechanics

- Spectrin network of RBC
- Tetramers of neo-Hookean springs
Role of Cell Mechanics

- Conflicting mindsets:
  - Mechanics treats cells as a material with properties that are time invariant
  - Mechanotransduction illustrates that cells are living, changing entities that alter themselves in response to mechanical stimuli

- Conceptual Framework:
  - *The mechanics of cells and their altered biological functions are intrinsically linked.*
  - *What are the central structure-function relationships?*
Maintenance of Cell Shape

- Cell function follows form
- Cell types:
  - motor neuron
  - osteocyte
  - hair cell
  - adipocyte
  - rods and cones
  - endothelials
  - skeletal muscle
  - smooth muscle
  - RBC
  - lymphocyte
  - epithelial (separated)
  - fibroblasts
  - sperm and egg cells

(Drawn to scale)
Cell Migration

Actin Filaments

Myosin

Focal Adhesions

Myosin complex

Actin Helix

Tropomyosin

ATP

P_i

Ca^{2+}

ADP

Mg^{2+}

actin cortex

lamellipodium

substratum

cortex under tension

actin polymerization at plus end extends lamellipodium

movement of unpolymerized actin

retraction

anchorage points
Mechanosensing

- Mechanosensation: Hair cells, touch-sensitive sensory neurons
- Mechanotransduction: mechanical stimuli that cause a biochemical response
Mechanics of Disease

- Tissue remodeling in response to stress
Active Cell Contraction

http://www.youtube.com/watch?v=ren_IQPOhJc
Tissue Engineering

1. Cell sourcing
2. Cell expansion and manipulation
3. Cell seeding and extracellular matrix expression
4. Implantation of construct
5. Full incorporation into host
Morphogenesis

Cell Shape & Migration

<table>
<thead>
<tr>
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<th>Contractility</th>
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<th>Cell-matrix</th>
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<td>Cuboidal</td>
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<td>Border cells</td>
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C

Zygote → Cleavage → Eight-cell stage → Cleavage → Blastula (hollow ball) → Blastocoel → Cross section of blastula → Gastrulation → Gastrula

Archenteron
Endoderm
Ectoderm
Blastopore

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