Lecture #1: Cell Mechanics as a Framework

What is cell mechanics?

From Mofrad & Kamm:

"The subject of cell mechanics encompasses a wide range of essential cellular processes ranging from macroscopic events like 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."

Why is cell mechanics important?

Well, let's first put things in context of human health and disease. Consider a few examples.

1) When bone cells do not experience proper mechanical stimulation, bone formation ceases and bone resorption is initiated. So, in prolonged space travel, where gravity is virtually nonexistent, astronauts face major bone loss, even with rigorouse exercise.

2) In coronary artery disease, changes in the temporal and spatial patterns of fluid shear stress on endothelial cells are linked to the formation of atherosclerotic plaques.

3) Metastatic cancer cells must be able to migrate through tissue and attach at distant sites to spread. Why certain cancers appear to metastasize preferentially to particular location is still a mystery.

4) Malaria creates subtle mechanical alteration at the cellular level. It is an infection in RBCs that increases the stickiness.

Pure definition

Cells are the fundamental building blocks of life.

- all living things are composed of cells.
- Cells are the basic unit of structure & function in living things.
- cells are produced from other cells.

There are two types of cells

1) Prokaryotic — w/o nucleus such as bacteria
2) Eukaryotic — w/ nucleus

It is characteristic for cells to

- reproduce by cell division
- metabolize raw materials into energy
- respond to external & internal stimuli

Despite their functional ~~distinctive~~ variety, the basic structural elements of most cells are the same,

- networks of filaments maintain cell shape and organize its content
- fluid sheets enclose the cells & its compartments

The layout of most cells are pretty similar → same subunits. or organelles.

Organelle	Primary Function
"control center" nucleus	DNA repository site, site of transcription
ribosome	responsible to mRNA to protein translation
"energy source" mitochondrian	energy production: glucose → ATP.
endoplasmic reticulum	site of translation & some post-translational modification & folding protein.
golgi apparatus	post translational modification & sorting protein
lysosome	degradation of carbohydrates & proteins
vesicle	intracellular transport & trafficking

DNA to RNA to protein is the "central dogma" of modern cell biology

→ Central Dogma is important to cell mechanics / mechanobiology

1) Proteins that exist to support cells structurally do not usually pre exist within the cell.

- Genes = instructions for cells to build protein via amino acids

2) Cells respond to several signals [physical forces] by altering their expression profile.

⇒ phenotype of cell depends in part on mechanical influence acting on cell

- Phenotype

A) Morphology Change.

B) ↑ Protein levels (or ↓)

C) Motion

D) Proliferation

⋮

3) What is the exact mechanism by which cells sense and respond to forces?

By studying the remarkable similarity of cell's biochemistry & biomechanics, we aim to find systematics and basic paradigms that help explain cellular form and function.

So what will we focus on?

Intro to Biopolymers

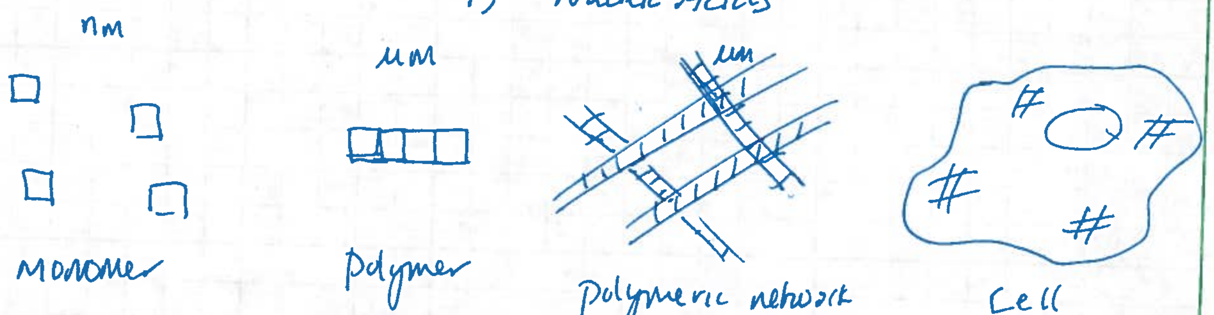
- Cells are extremely soft (almost liquid) ⇒ "SOFT MATTER"
  - → the mechanical behavior & their microstructure resemble rubber

Define rubber: Rubber consists of a network of polymeric chains that become more resistant to deformation when heated.
(kind of counter intuitive!)

→ Polymeric materials are characterized by entropy rather than energy.

Four main biopolymers
1) Carbohydrates.
2) Lipids
3) Proteins
4) Nucleic Acids

} Made of monomers & polymers.



Ex) nucleic acids, amino acids, fatty acids, Sugar ⇒
- ex) DNA/RNA, peptides/protein } genes.
- lipids, Polysaccharides, carbohydrates } not coded by genes.

- biopolymers are extremely flexible unlike steel rods
  - → upon thermal fluctuation, they may bend or jiggle

Intro to Cytoskeleton

→ the structural integrity of the cell is maintained by a complex network of tensile & compressive 1-D elements called cytoskeleton

- maintain cell shape
- protect cell
- help generate cellular motion
- enable intercellular transport
- assemble & disassemble dynamically.

→ Three main kinds of cytoskeleton filaments.

1) Actin OR microfilaments.

$d = 7nm$

→ two actin chains intertwined & close to membrane
→ tension bearing
→ together w/ myosin ⇒ contractile apparatus to generate muscular contraction of skeletal & cardiac muscle.

2) Intermediate filaments

$d = 8\text{-}12\ nm$

→ tension bearing
→ organize & maintain 3D structure of cell.

3) Microtubules

$d_o = 25nm$. $d_i = 15nm$.

→ organized by the centrosomes but reassemble.
→ Compression bearing

Intro to biomembranes

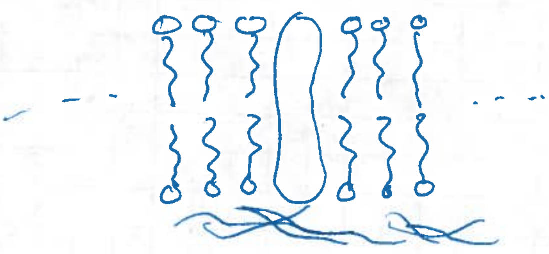
- cell membrane → $t = 4 - 5nm$
  - flexible so cell can easily adjust shape to respond to environmental changes.
  - inside cell membrane, cell almost behaves like liqu
    - → 50% H_2O
  - Cell membrane is semi-permeable
    - → controlled exchange b/w intercellular and extracellular info / components.

Passive Transport vs. **Active Transport**

- driven by concentration gradients

- requires extra energy.
  ↓
  - Regulated by ion channels, pumps, transporters exchangers, and receptors
  - Extracellular fluid:
    - charged ions like Ca^{2+}, K^+, & Na^+
    - nutrients like glucose, O_2, aminoacid vitamins
    - regulatory chemicals ⇒ steroids/hormones

ECM.



} Cell membrane is a phosphlipid bilayer

hydrophilic → o— ← hydrophobic

- it behaves similar to fatty acids or oils in water.
  - → hydrophilic polar heads typically orient towards H_2O phase while hydrophobic orients to oil phase
- internal pressure is much higher than surrounding pressure like a balloon.
  - → cell membrane strong enough not to burst.

Lecture #1: Cell Mechanics as a Frame Work | Lecture #2 Cellular Polymers

Part II: INTRO TO MECHANICS | Apply to CSK

In the field of cell mechanics, in order to understand the mechanical behavior of cells, you need to review solid mechanics, fluid mechanics and Statistical mechanics (thermodynamics).

Throughout this module, I will review relevant topic and have you relate them to biological examples. However, I thought I would review some basics right now.

From a pure mechanics POV:

Mechanical change can be described as:

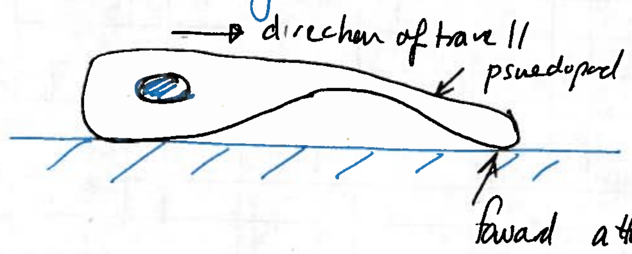
translation + rotation + deformation

⇓

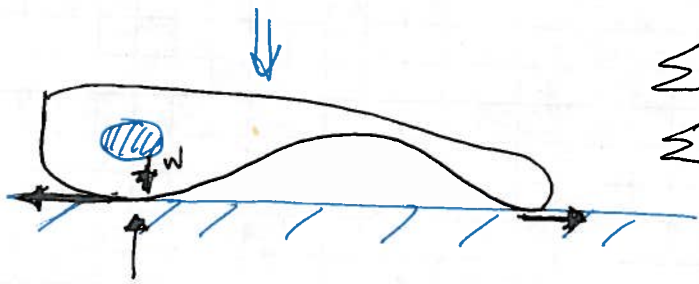
rigid body = translation + rotation + ~~deformation~~ → 0.

Fundamental tool: Free body diagrams.

Ex) Consider a crawling cell



⇓



$\sum F = ma$ → OR. $\sum F = 0$

$\sum M = I\alpha$ → $\sum M = 0$

However, rigid body mechanics is not useful for analyzing deformable bodies.

Excersise: think of your materials class or physics class

What are the 3 most important equations you applied?

Three Important Equations in Mechanics

Constitutive Equations (Physical Laws)

- stress – strain relations [$\sigma = E\varepsilon$ 1-D model]
- Hooke's law [$F = kx$ linear spring]
  [$T = \ell\theta$ torsion spring]

3-D version : $\varepsilon_x = \frac{1}{E}(\sigma_x - \nu\sigma_y - \nu\sigma_z)$

where $\nu = -\frac{\varepsilon_{trans}}{\varepsilon_{long}}$ Poisson's ratio

- Strain Energy of Hookean material.

$$W = \tfrac{1}{2}\,\sigma\varepsilon.$$

Equilibrium Equations

- momentum balance or 1-D form [$F = ma$] for rigid bodies.

or for deformable bodies. $\nabla\cdot\sigma + \rho b = \rho\frac{d^2u}{dt^2}$

Kinematic Equations

- strain : 1-D $\varepsilon = \frac{\Delta\ell}{\ell}$ or continuum $\varepsilon = \frac{du}{dx}$

Combinations

Ex) beam bending

$$y'' = \frac{M}{EI}$$

Ex) $\sigma = \frac{F}{A}$ stress