Session 1

ANALYSIS AND MODELING OF CELL MECHANICS

Syllabus

Prof. Nate Sniadecki

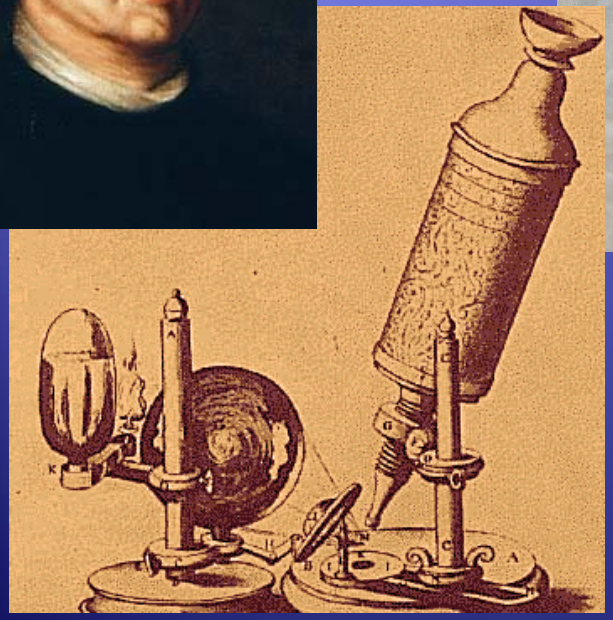
- Website:
  - http://faculty.washington.edu/nsniadec/ME599/W13/
- Selected readings
- Topics
  - Introduction to Cell Biology
  - Analysis of Cell Mechanics
  - Cell Mechanics Modeling
  - Measuring Cell Forces
  - Mechanotransduction
- Grading
  - Homework: 50%
  - Project: 50%
  - No Final

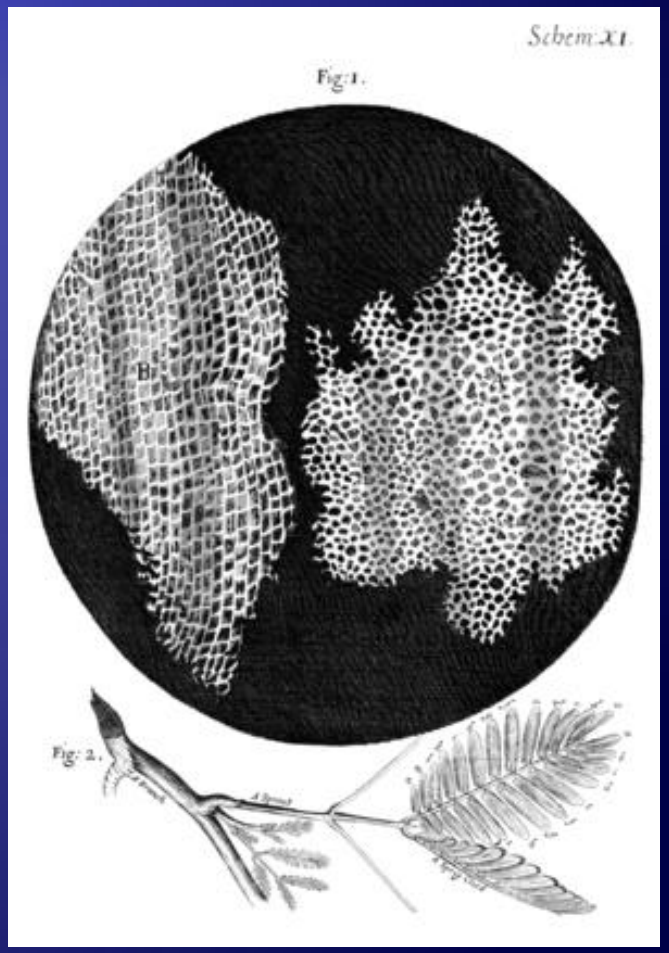
Date	Day	#	Topic
7-Jan	M	1	Introductory - Analysis and Modeling of Cell Mechanics
9-Jan	W	2	Introductory - Building Blocks
11-Jan	F	3	Introductory - Nucleus
14-Jan	M	4	Introductory - Cytoskeleton
16-Jan	W	4	Introductory - Cytoskeleton
18-Jan	F	5	Introductory - Extracellular Matrix
21-Jan	M	--	*No Class (MLK Day)*
23-Jan	W	6	Cell Mechanical Analysis - Microneedles
25-Jan	F	7	Cell Mechanical Analysis - Micropipette Aspiration
28-Jan	M	8	Cell Mechanical Analysis - Atomic Force Microscopy
30-Jan	W	9	Cell Mechanical Analysis - Microrheology
1-Feb	F	--	*No Class*
4-Feb	M	--	*No Class*
6-Feb	W	--	*No Class*
8-Feb	F	10	Cell Mechanical Analysis - Magnetic Twisting Cytometry
11-Feb	M	11	Cell Mechanical Analysis - Optical Tweezers
13-Feb	W	12	Modeling Cell Mechanics - Lumped Parameter Viscoelastic Models
15-Feb	F	13	Modeling Cell Mechanics - Pure Lipid systems
18-Feb	M	14	Modeling Cell Mechanics - Tensegrity
20-Feb	W	15	Modeling Cell Mechanics - Foams
22-Feb	F	16	Modeling Cell Mechanics - Polymer Networks
25-Feb	M	17	Modeling Cell Mechanics - Soft Glassy Material
27-Feb	W	18	Modeling Cell Mechanics - Computational Models
1-Mar	F	19	Cellular Forces - Adhesions and Traction
4-Mar	M	20	Cellular Forces - Traction Force Microscopy
6-Mar	W	21	Cellular Forces - MEMS Tools
8-Mar	F	22	Mechanotransduction - Introduction & Examples
11-Mar	M	23	Mechanotransduction - Whole Cell Analysis
13-Mar	W	24	Mechanotransduction - Nanoscale Analysis
15-Mar	F	25	Mechanotransduction - Mechanisms
18-Mar	M	--	**Final Project Report Due**

INTRODUCTIONS

Robert Hooke

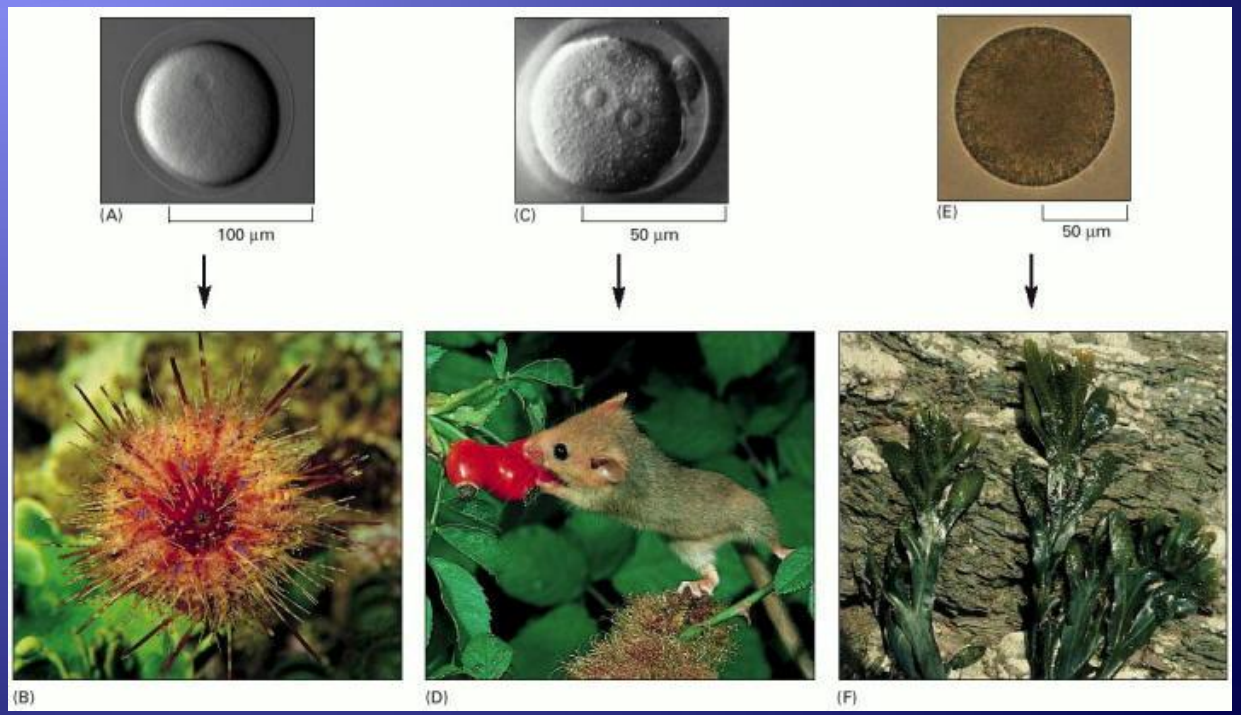
- Micrographia (1665)
  http://archive.nlm.nih.gov/proj/ttp/flash/hooke/hooke.html





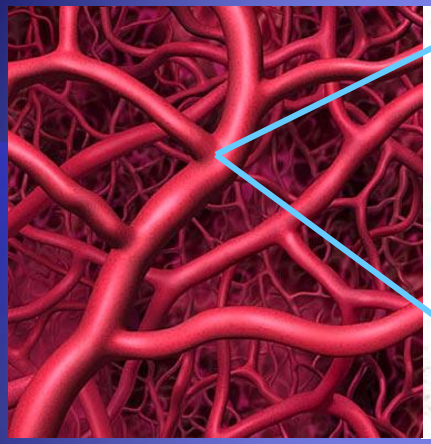
What are cells?

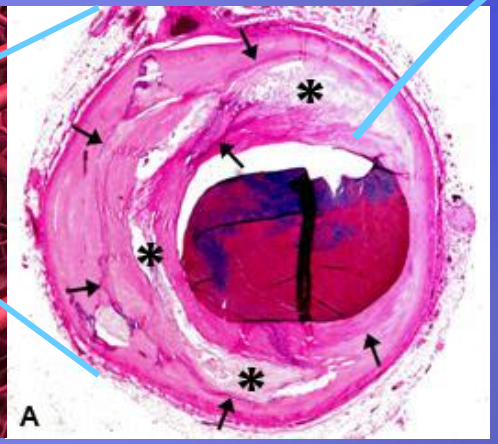
- The basic functional units of life (composed of numerous components with distinct mechanical characteristics)
- Origins:

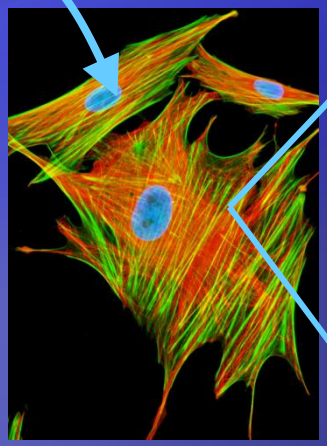


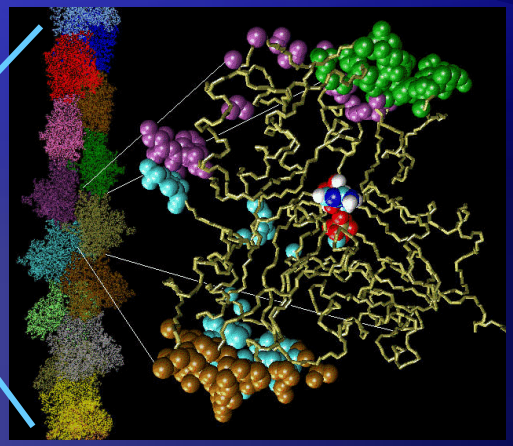
Sea Urchin Mouse Seaweed

The Context of Cells









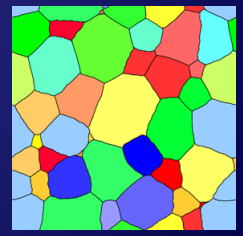
Organ — 1 - 0.1 m

Tissue — 10^{-2} - 10^{-3} m

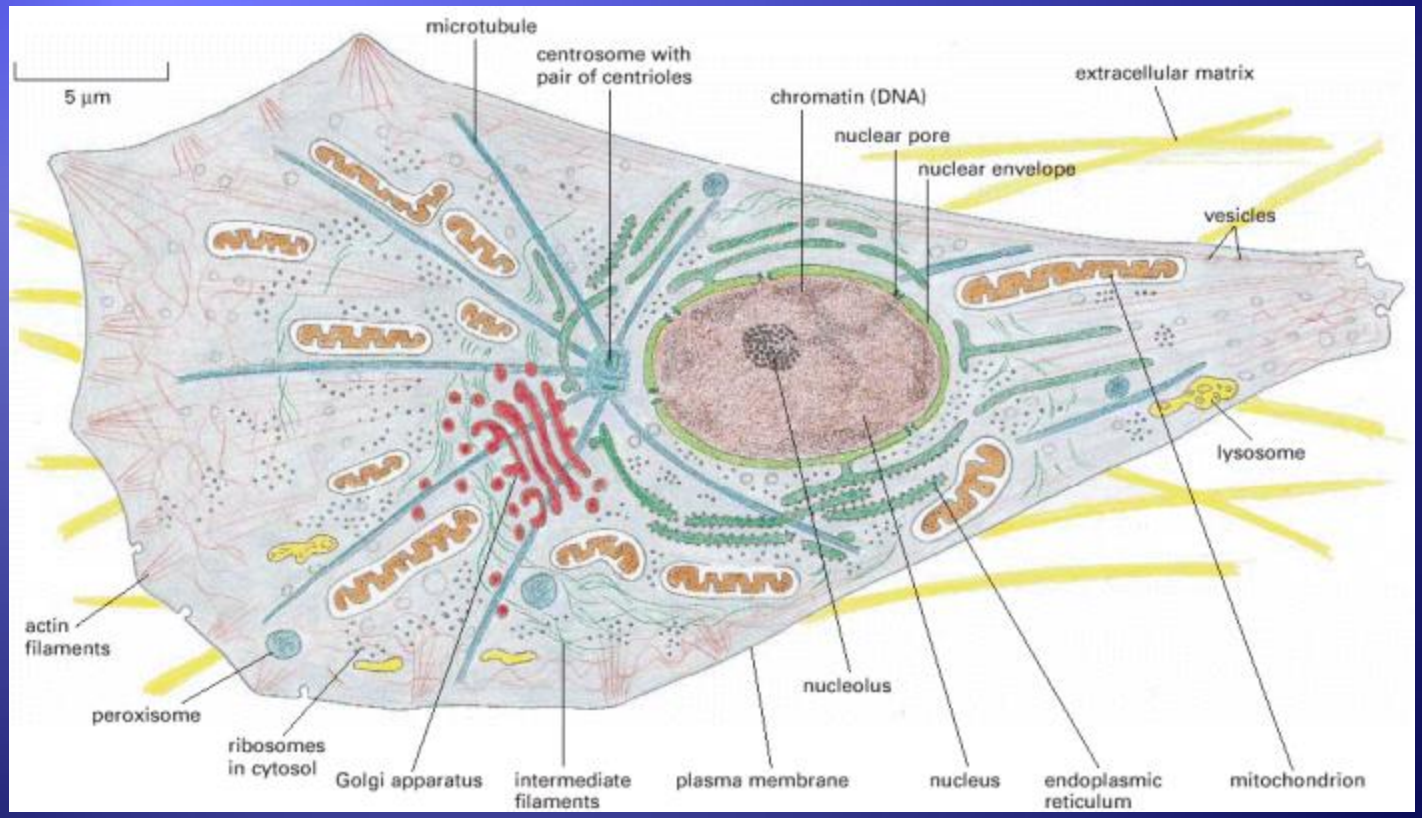
Cells — 10^{-4} - 10^{-6} m

Proteins — 10^{-8} - 10^{-10} m

Cells – Tissue	Grains – Materials
Animate	Inanimate
Basic Unit of Living Things	Basic Unit of Metal and Ceramics
Composed of Proteins	Composed of Atoms
Defines structure-function of tissue	Defines structure-strength of material
Sensitive to temperature, radiation, water, pH, nutrients, pressure, ionic strength, osmolarity, hormones, etc.	Sensitive to temperature, radiation, corrosion, loading



Organelles :: Subsystems



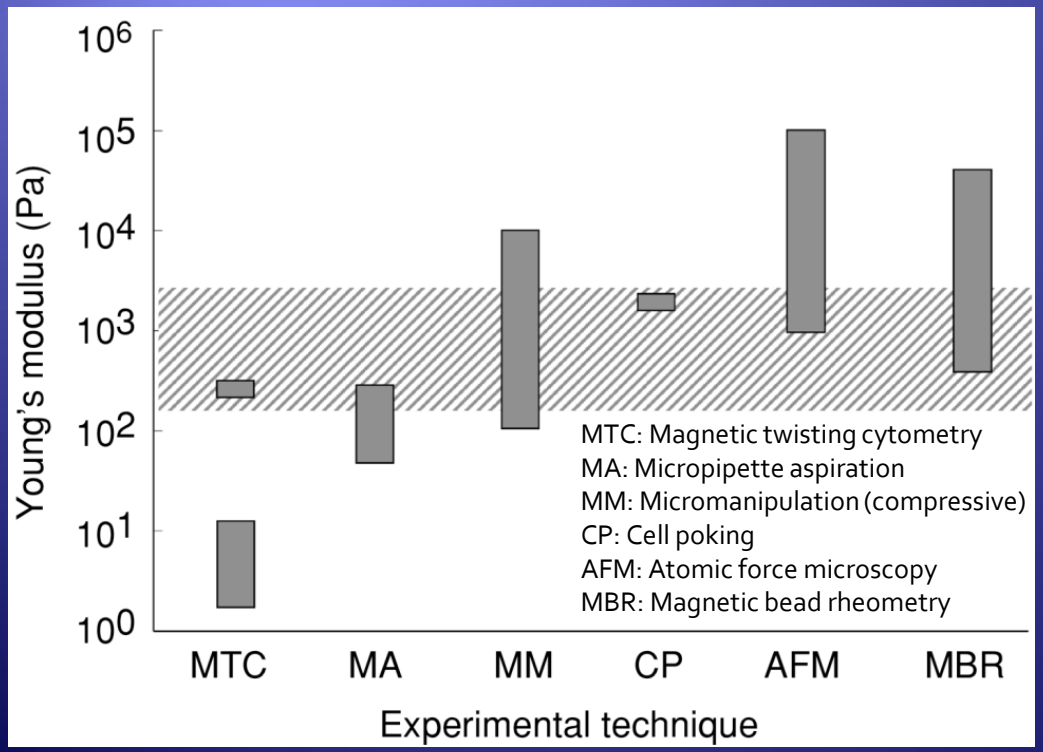
What is Cell Mechanics?

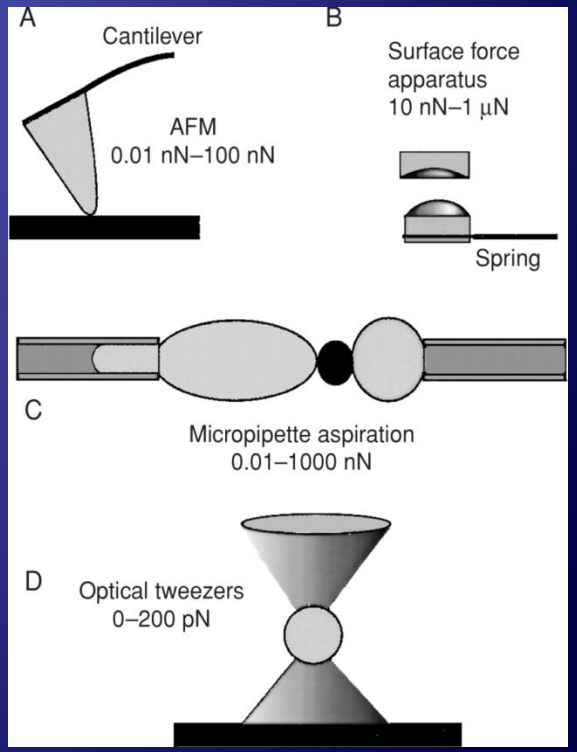
- "The subject of cell mechanics encompasses a wide range of essential cellular processes, ranging from macroscopic events like the maintenance of cell shape, cell motility, adhesion, and deformation to microscopic events such as how cells sense mechanical signals and transduce them into a cascade of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

-- Mofrad & Kamm

Cell Mechanical Analysis

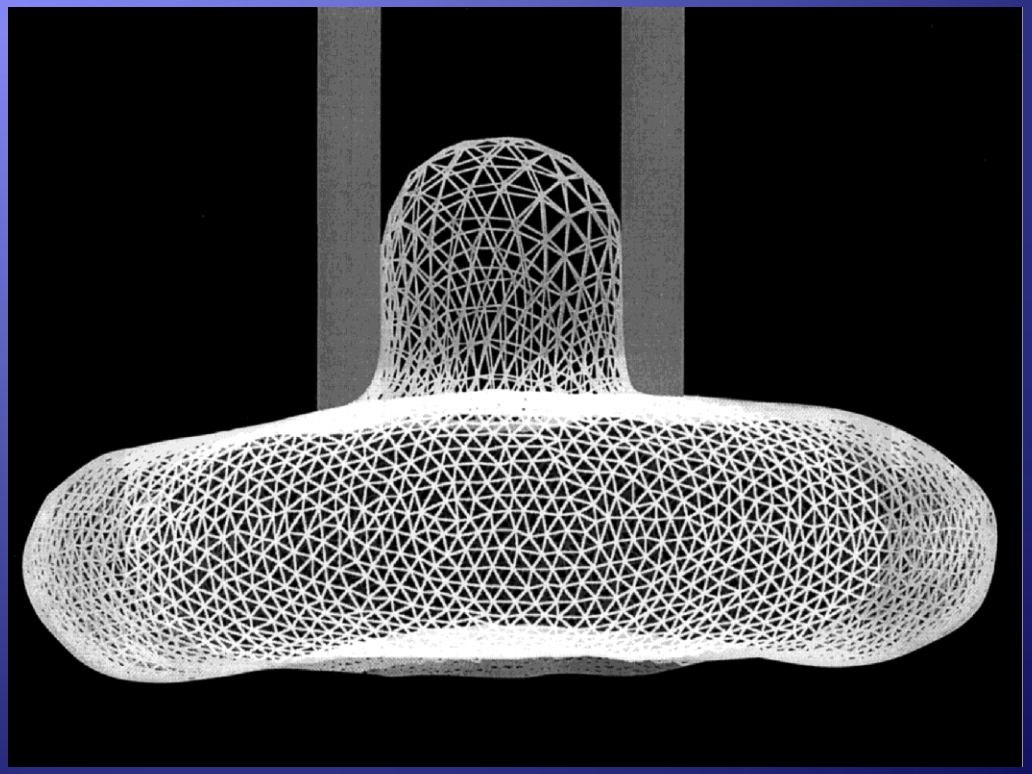
- Diameter: 30-50 μm (~3 μm for bacteria)
- Mass: 2-6 x 10^{-8} g
- Young's modulus: 1 – 10^5 Pa (CSK: ~ 10^{-9} Pa)





Modeling Cell Mechanics

- Spectrin network of RBC
- Tetramers of neo-Hookean springs

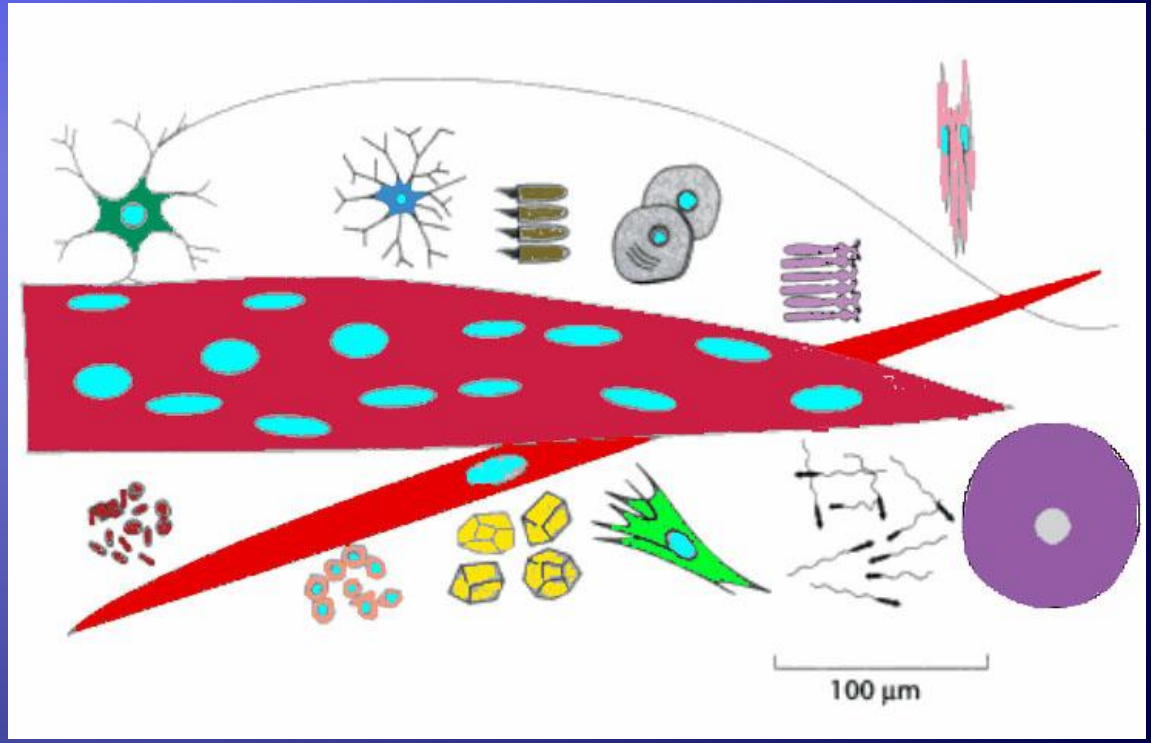


Role of Cell Mechanics

- 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?*

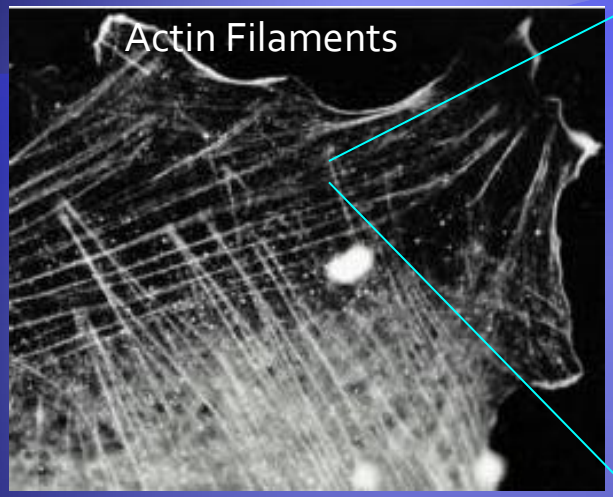
Maintenance of Cell Shape

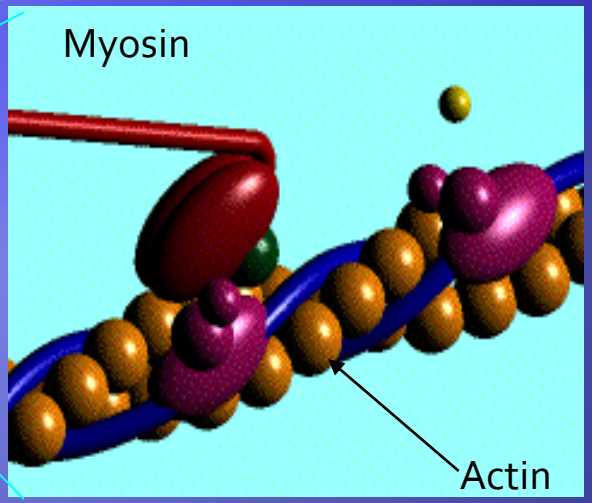
- Cell function follows form
- Cell types:
  - motor neuron
  - osteocyte
  - hair cell
  - adipocyte
  - rods and cones
  - endothelials
  - skeletal muscle
  - smooth muscle
  - RBC
  - lymphocyte
  - epithelial (separated)
  - fibroblasts
  - sperm and egg cells

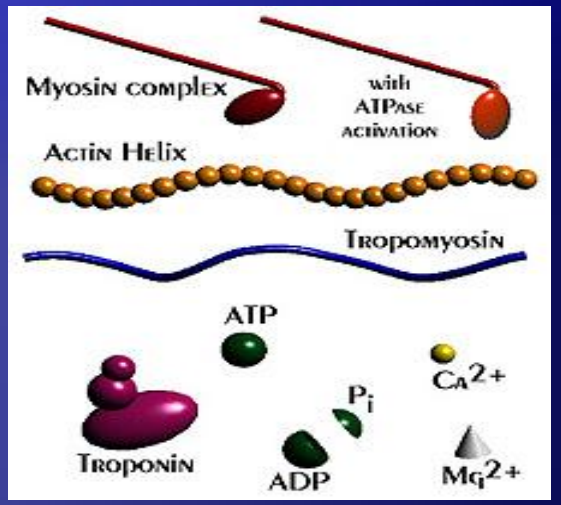


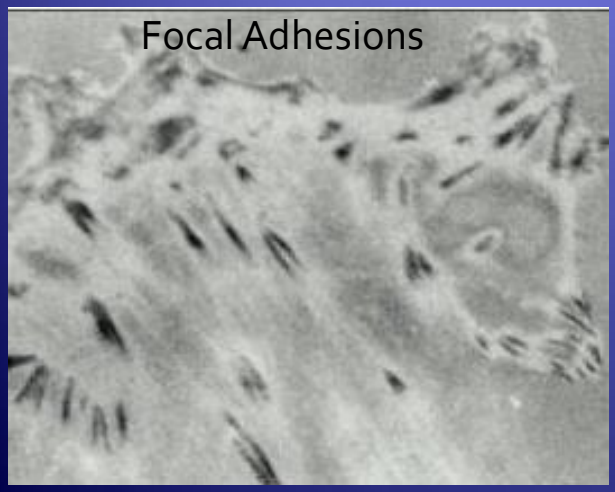
(Drawn to scale)

Cell Migration

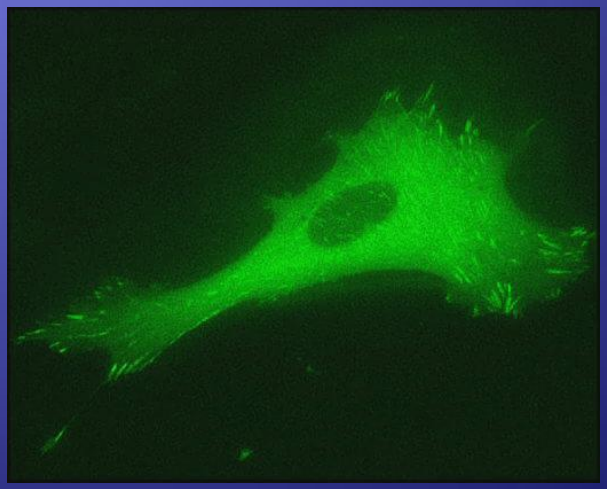








10 µm



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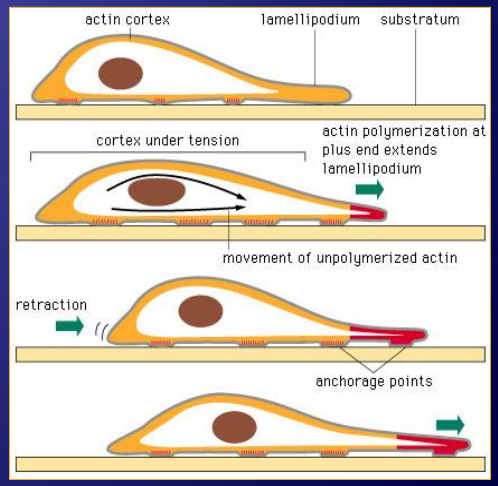
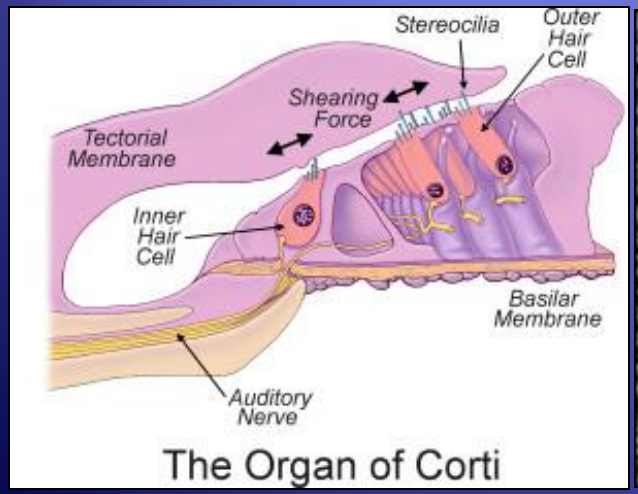
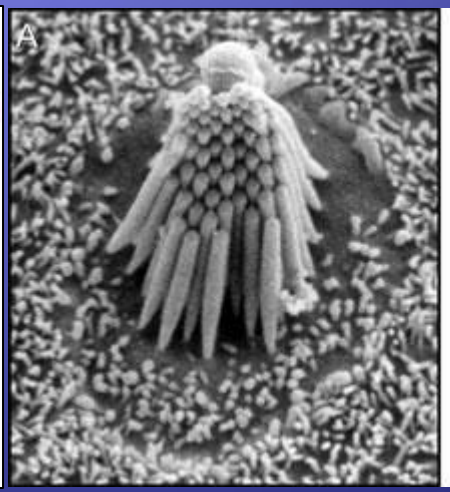
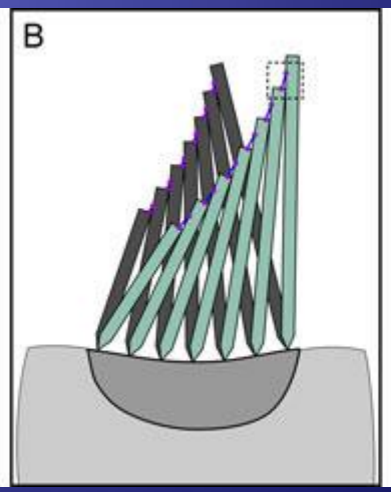


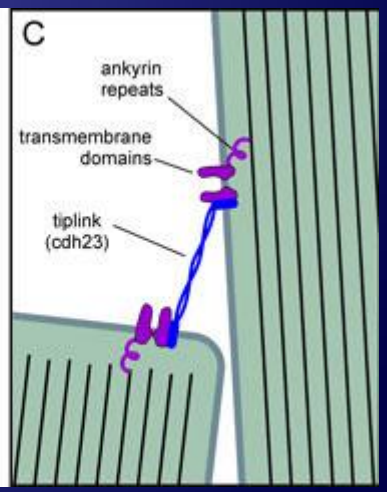
Mechanosensing

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



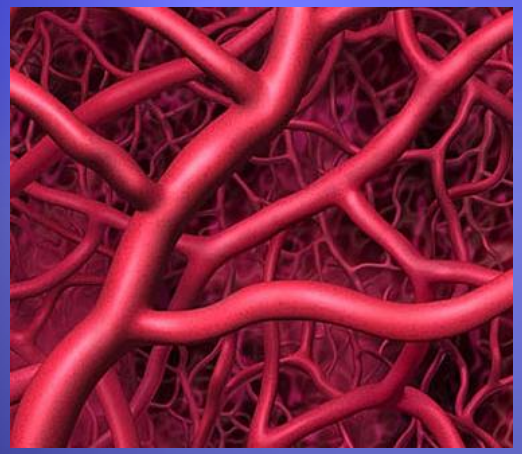


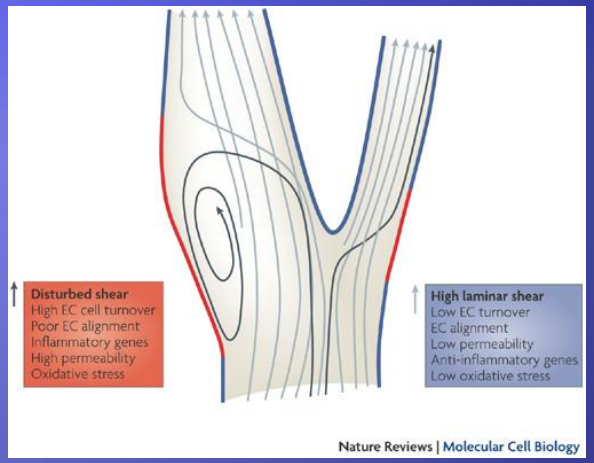


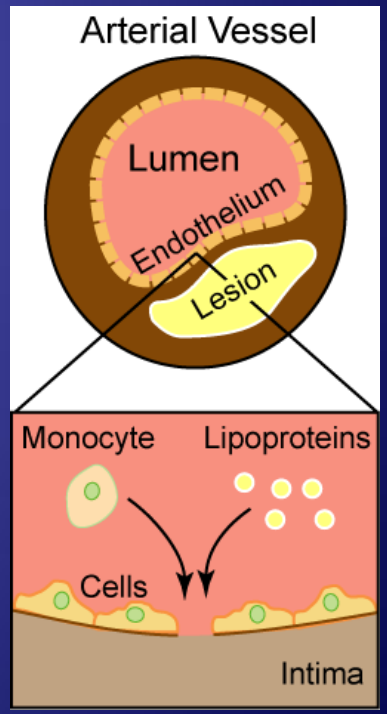


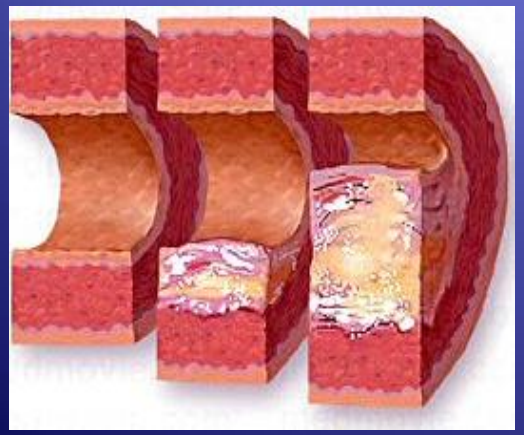
Mechanics of Disease

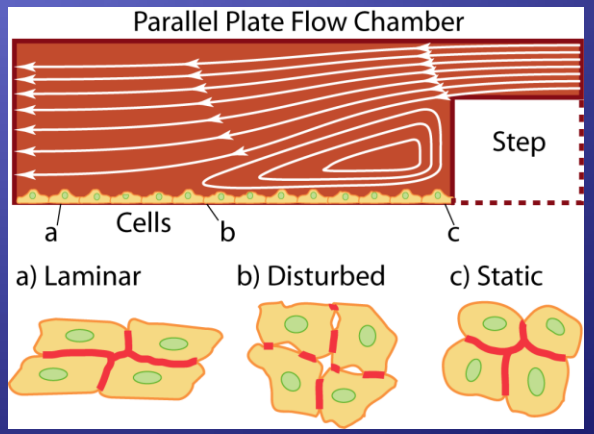
- Tissue remodeling in response to stress



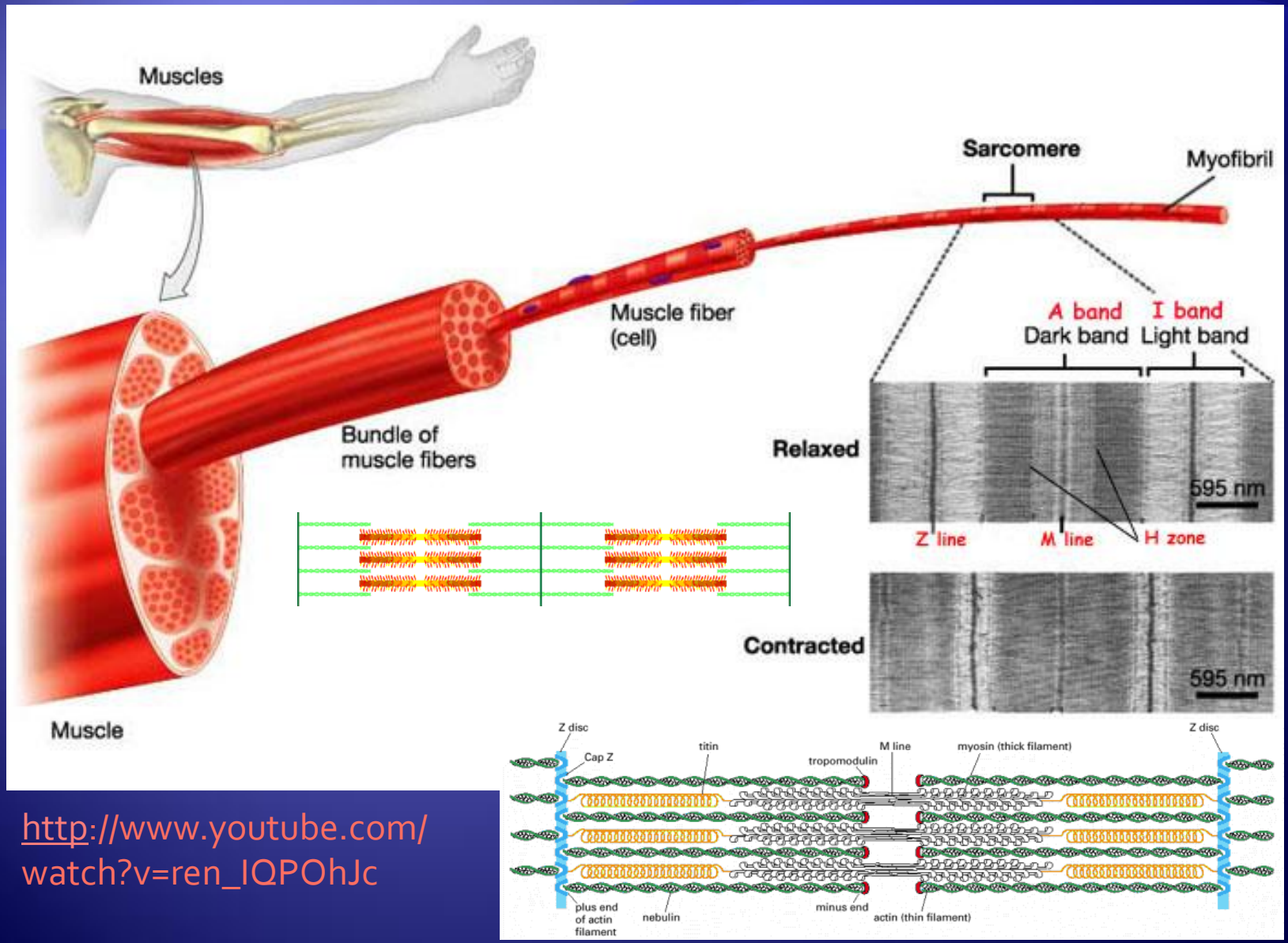






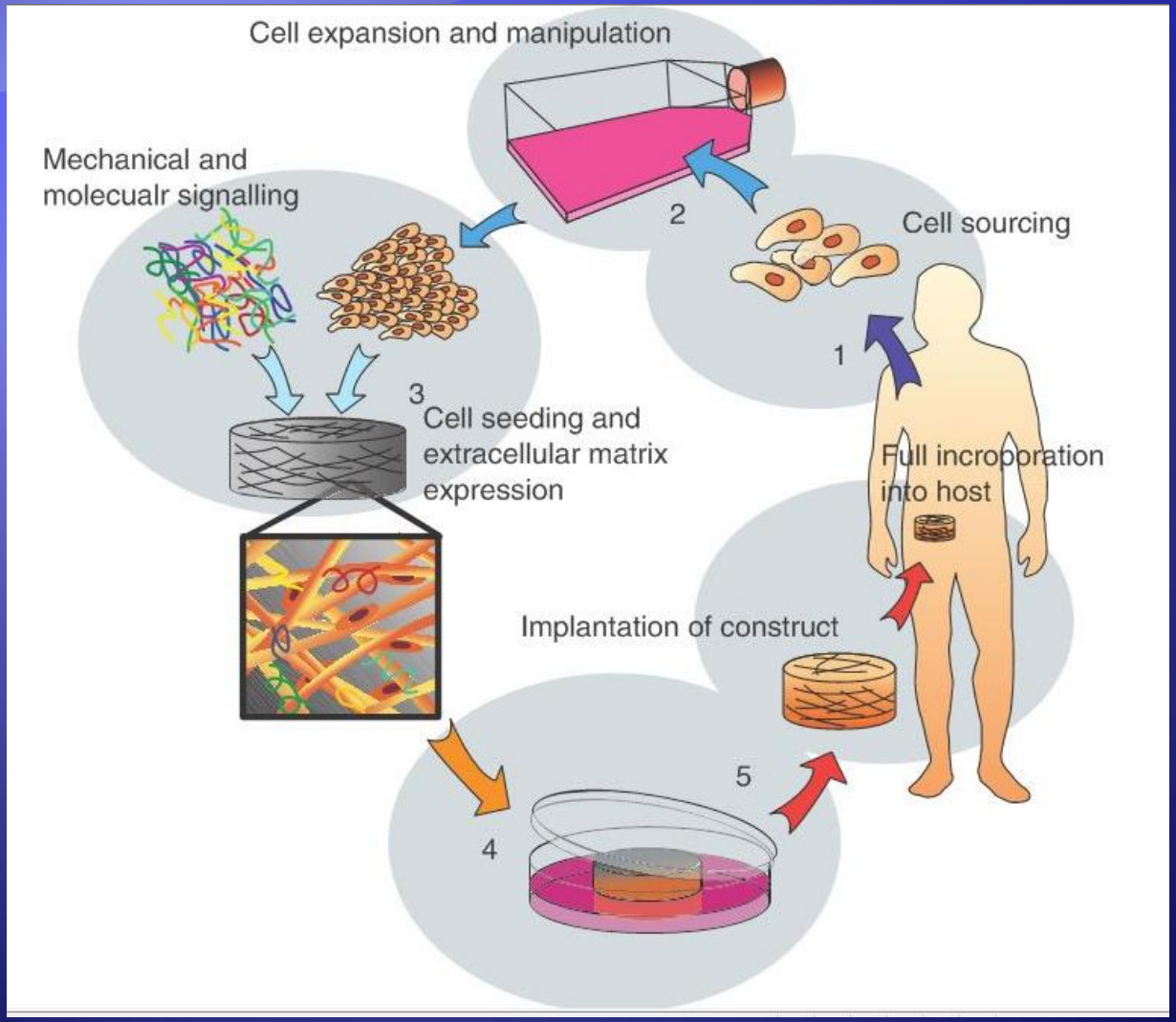


Active Cell Contraction



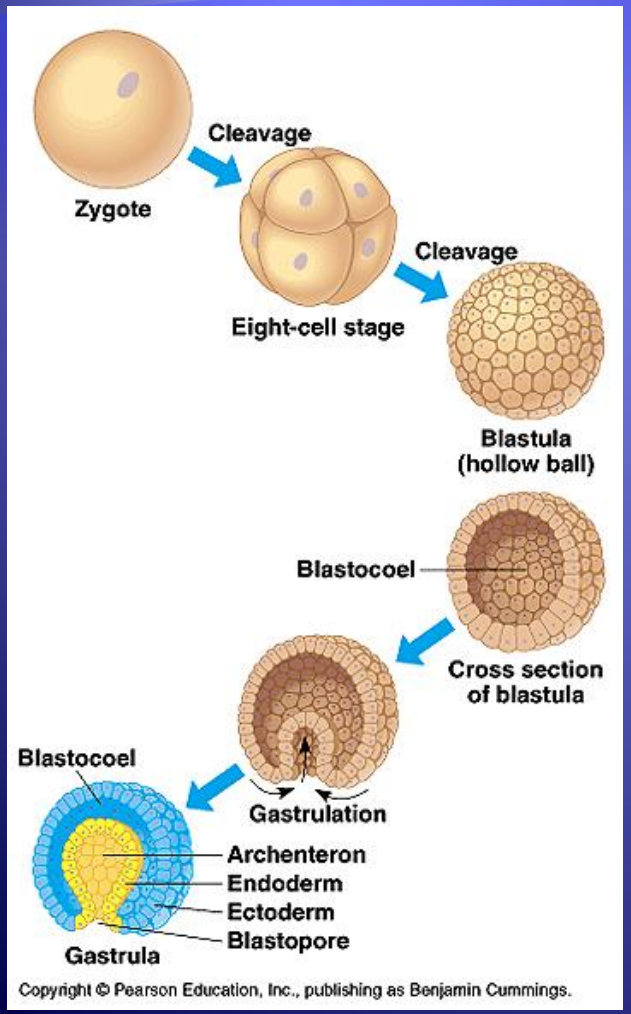
http://www.youtube.com/watch?v=ren_IQPOhJc

Tissue Engineering



Morphogenesis

- Cell Shape & Migration



	Protrusiveness	Contractility	Cell-cell	Cell-matrix
Cuboidal	–	++	++	++
Border cells	+++	+++	+++	–
Squamous	+/–	+/–	+/–	+++
Columnar	–	++	++	+