# Molecular, Cellular & Tissue Biomechanics

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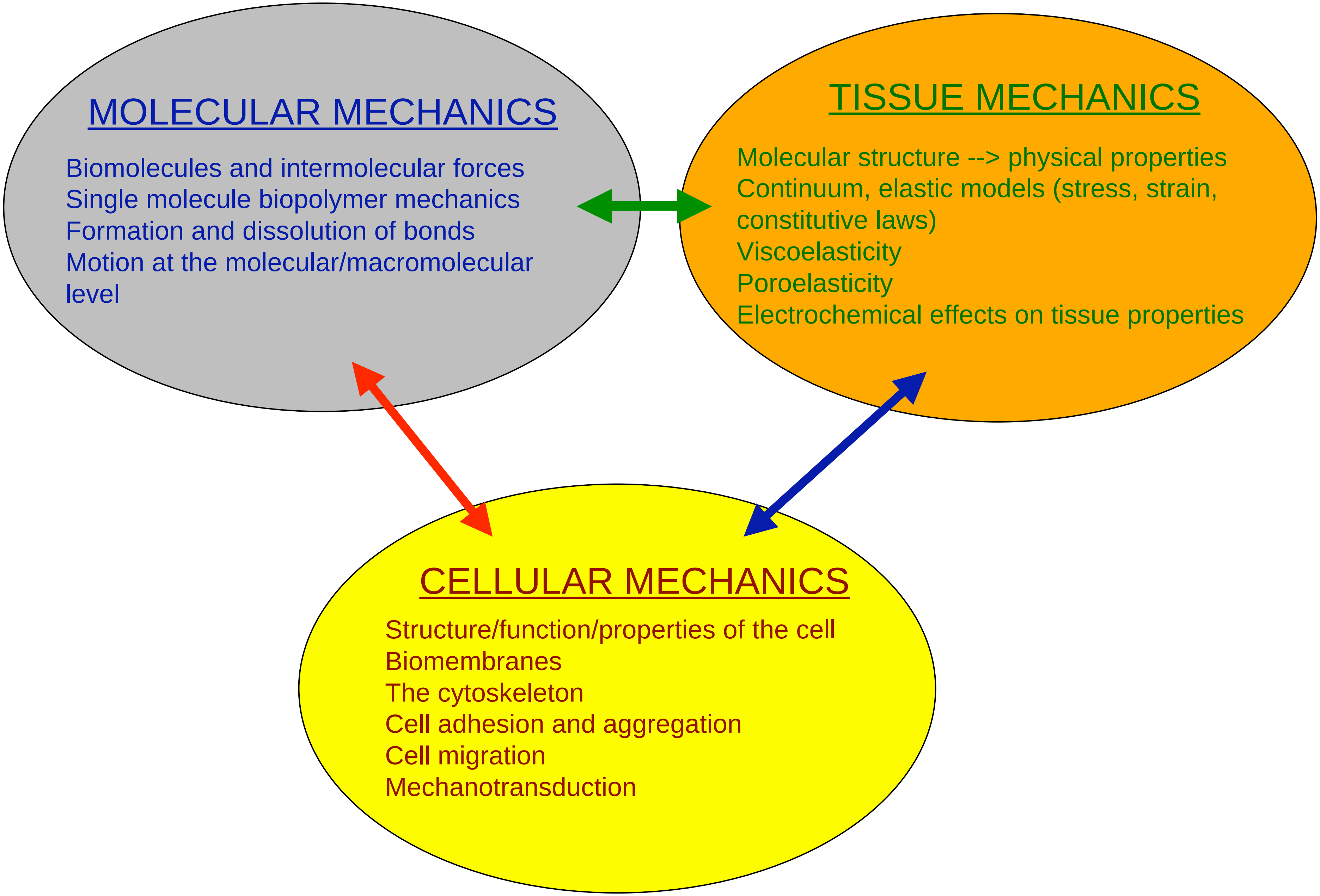
**Goal**: Develop a *fundamental* understanding of biomechanics over a wide range of length scales.



## MOLECULAR MECHANICS

Biomolecules and intermolecular forces
Single molecule biopolymer mechanics
Formation and dissolution of bonds
Motion at the molecular/macromolecular level

## TISSUE MECHANICS

Molecular structure --> physical properties
Continuum, elastic models (stress, strain, constitutive laws)
Viscoelasticity
Poroelasticity
Electrochemical effects on tissue properties

## CELLULAR MECHANICS

Structure/function/properties of the cell
Biomembranes
The cytoskeleton
Cell adhesion and aggregation
Cell migration
Mechanotransduction

# Some Learning Objectives

1. To understand the fundamental concepts of mechanics and be able to apply them to simple problems in the deformation of continuous media
2. To understand the underlying basis for the mechanical properties of molecules, cells and tissues
3. To be able to model biological materials using methods appropriate over diverse length scales
4. To be familiar with the wide spectrum of measurement techniques that are currently used to determine mechanical properties
5. To appreciate the close interconnections between mechanics and biology/chemistry of living systems

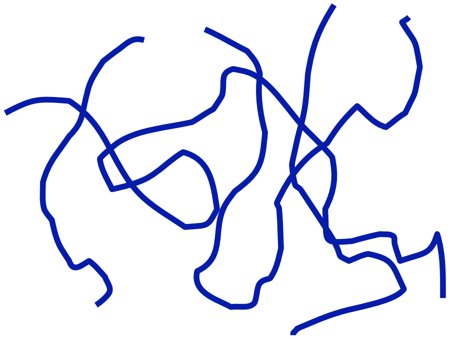
# Modeling Complex Material Properties

## Continuum

## Microstructural

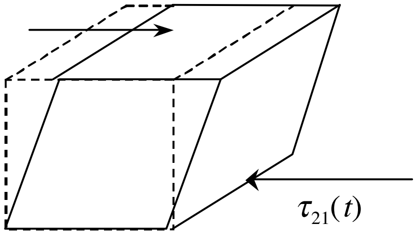
*bending plate*

*entangled polymer*



Constitutive relations and force balance

*Viscoelastic or poroelastic solid*



*strut model*

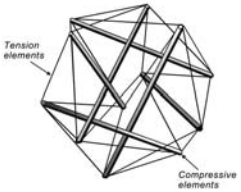
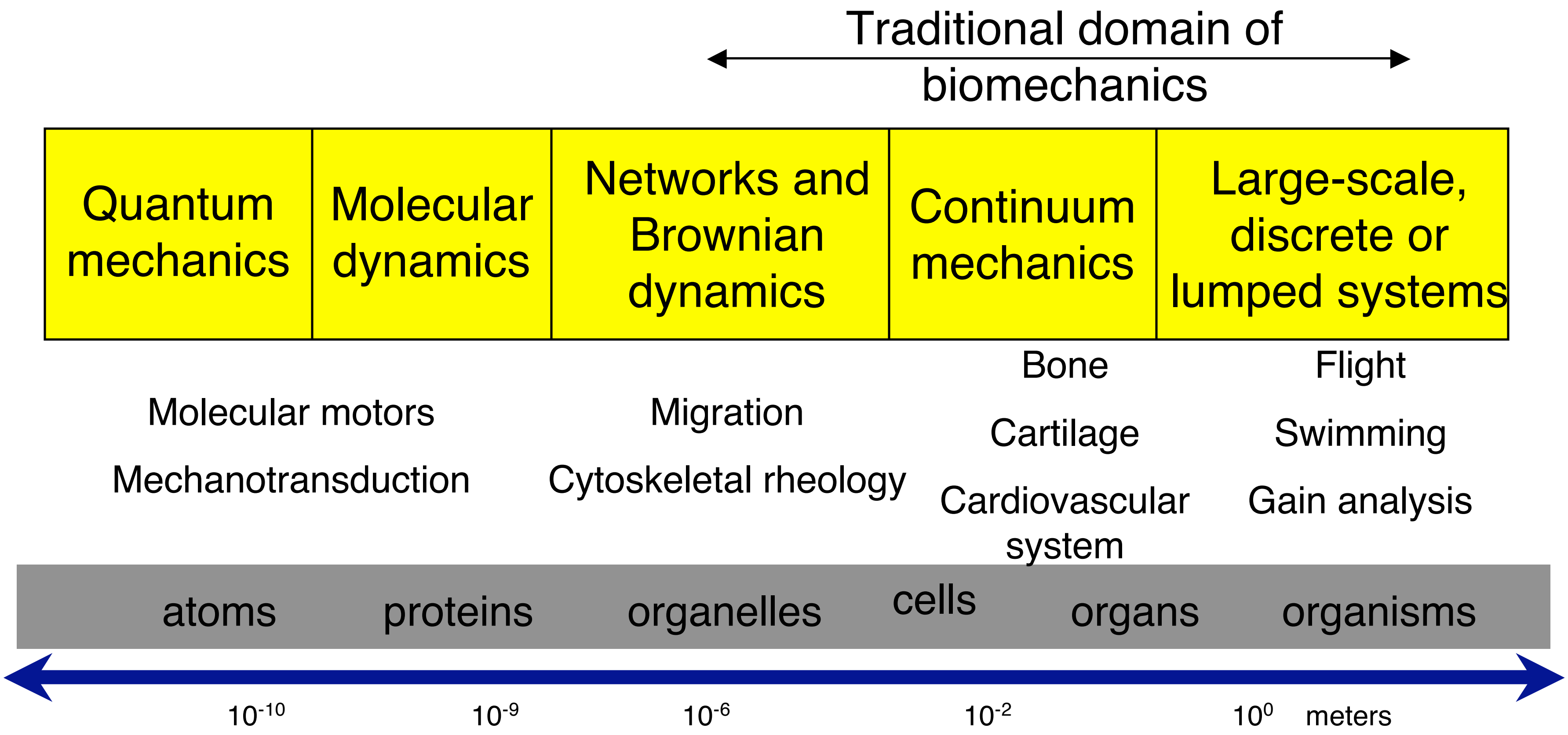


Figure by MIT OCW.

# Biomechanics at all length scales



Traditional domain of biomechanics

Quantum mechanics

Molecular dynamics

Networks and Brownian dynamics

Continuum mechanics

Large-scale, discrete or lumped systems

Molecular motors

Mechanotransduction

Migration

Cytoskeletal rheology

Bone

Cartilage

Cardiovascular system

Flight

Swimming

Gain analysis

atoms

proteins

organelles

cells

organs

organisms

$10^{-10}$

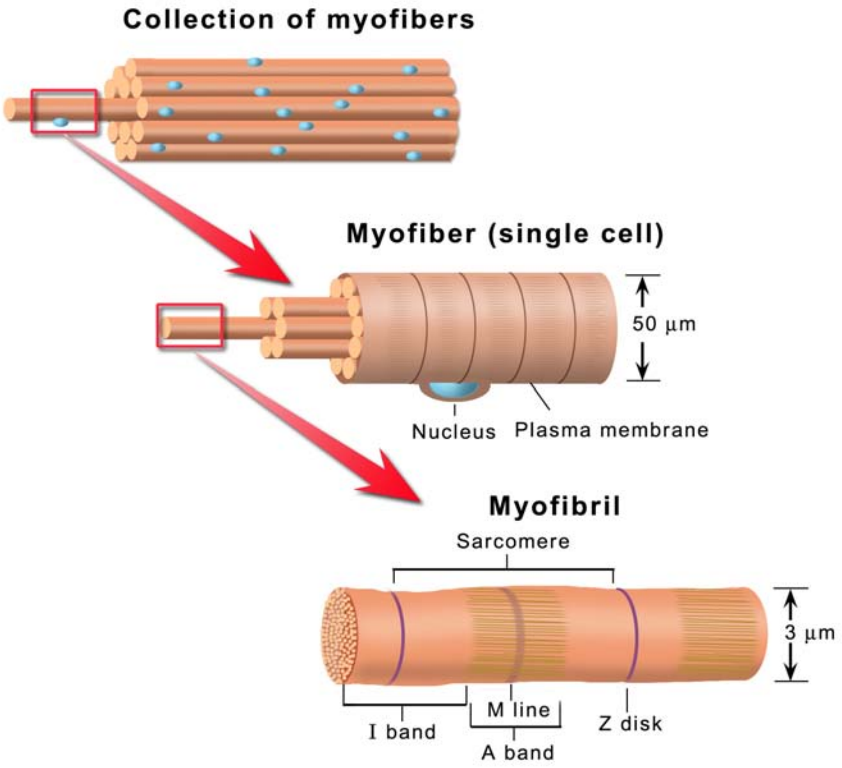
$10^{-9}$

$10^{-6}$

$10^{-2}$

$10^{0}$ meters

# Muscles: Spanning from Macro to Nano



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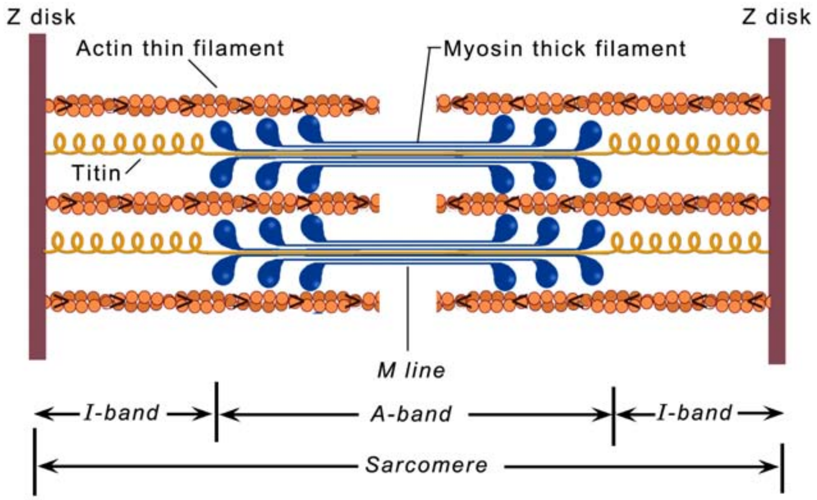

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# Typical Eukaryotic Cell

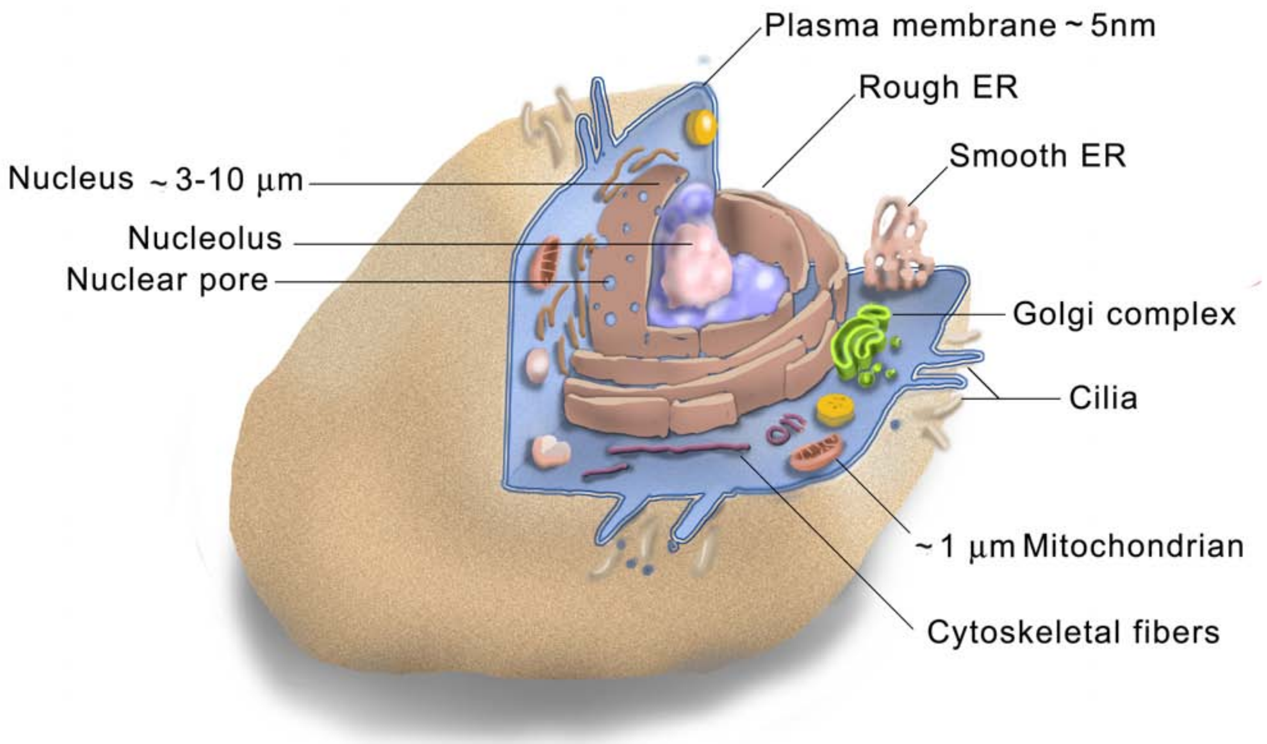


Figure by MIT OCW.

1 $\mu$m = $10^{-6}$ m
1 nm = $10^{-9}$ m
1 Å = $10^{-10}$m

# Plasma Membrane

Plasma Membrane

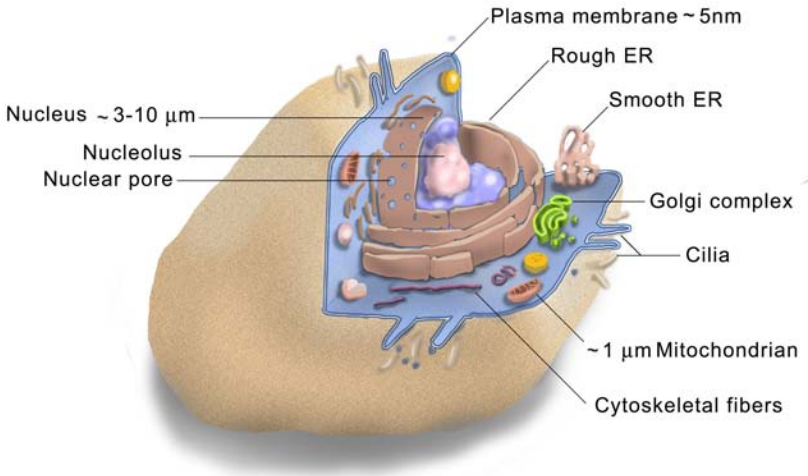
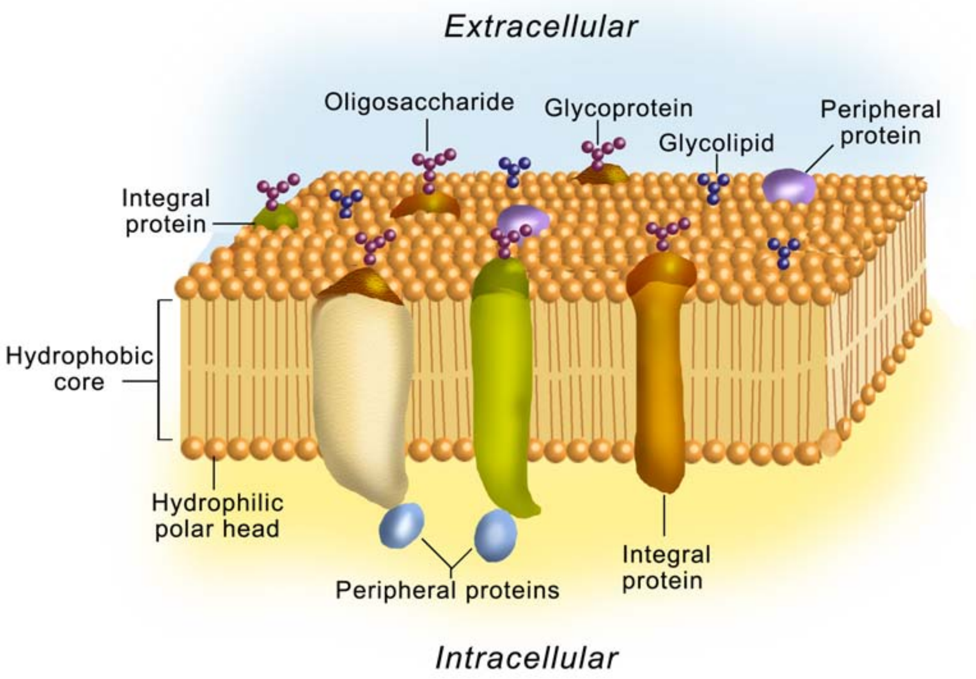


Figure by MIT OCW.

## *2-D Elastic Plate*



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# Cytoskeleton

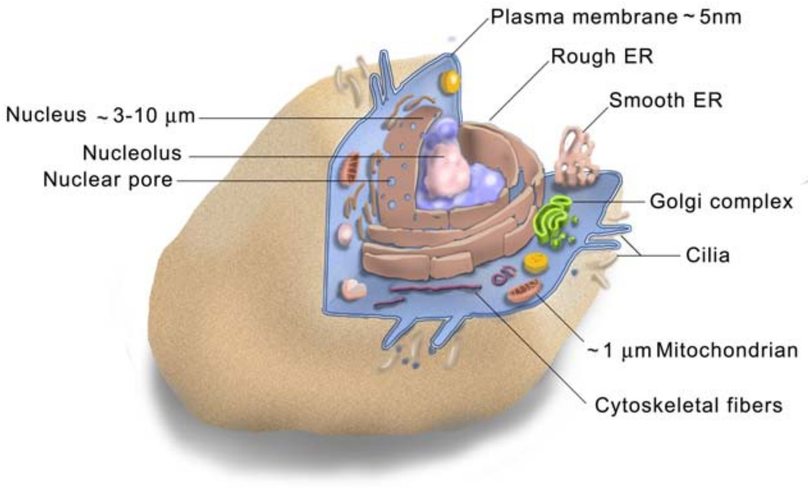

Figure by MIT OCW.

TEM image of a cytoskeleton removed due to copyright restrictions.

*"rigidity"*

| | Diameter (nm) | Persistence Length (µm) |
|---|---|---|
| actin | 6-8 | 15 |
| microtubule | 10 | 60,000 |
| intermediate filament | 20-25 | 1-3 |

TEM image of a cytoskeleton removed due to copyright restrictions.

When stressed, cells form stress fibers, mediated by a variety of **actin-binding proteins**.

TEM of cytoskeleton, Hartwick, http://expmed.bwh.harvard.edu

Actin filament: a force of 10 pN supported by a single actin filament (E~$10^9$ Pa) stretches by only 0.02%!!

Diagram showing the structure of actin removed due to copyright restrictions.

# Measuring Complex Material Properties

Aspiration

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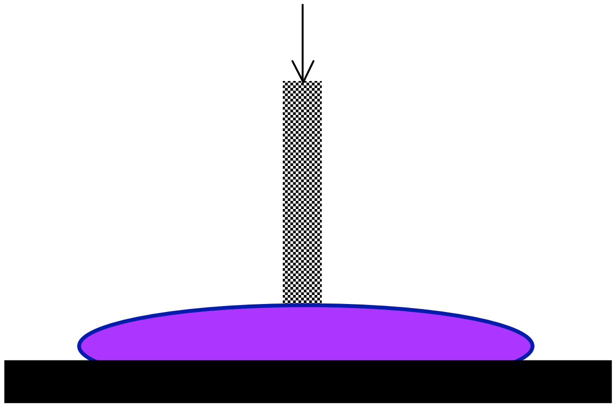
Cell Poking



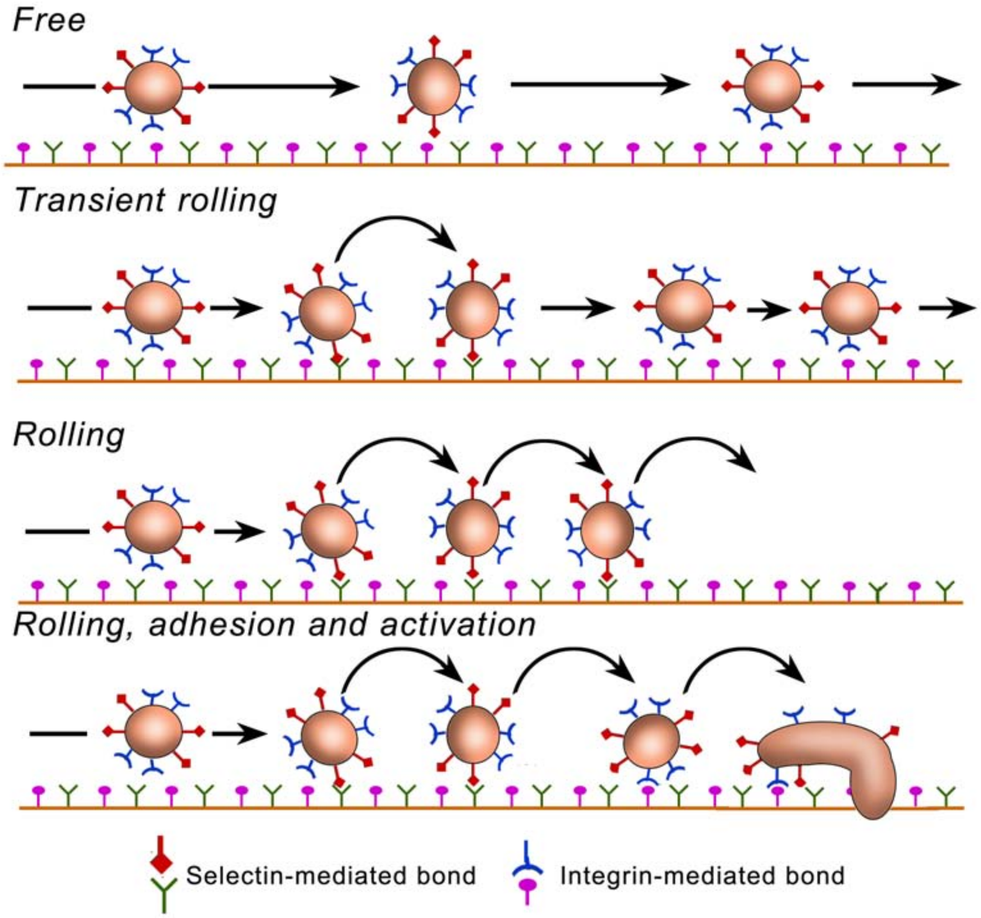
T. Savin, MIT

# Cell Adhesion

310 **Review** *TRENDS in Biotechnology* Vol.19 No.8 August 2001

**Molecular properties in cell adhesion: a physical and engineering perspective**

**Chase E. Orsello, Douglas A. Lauffenburger and Daniel A. Hammer**



Physical forces effect bond association/dissociation

Finite contact times

Cell deformation

Figure by MIT OCW.

# Dynamic Processes: Cell Migration

Cell Motility

Fluorescently
marked actin

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- Actin is a polymer that contributes to the stiffness of the cytoskeleton
- The cytoskeleton is active
- Coordinated processes: adhesion, (de-) polymerization

# Active Cell Contraction

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Cardiac myocyte (Jan Lammerding)

# Cytoskeletal Mechanics Probed by External Force

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Fibroblast with fluorescent mitochondria forced by a magnetic bead

D. Ingber, P. LeDuc

# Mechanotransduction:
# Hair cell stimulation

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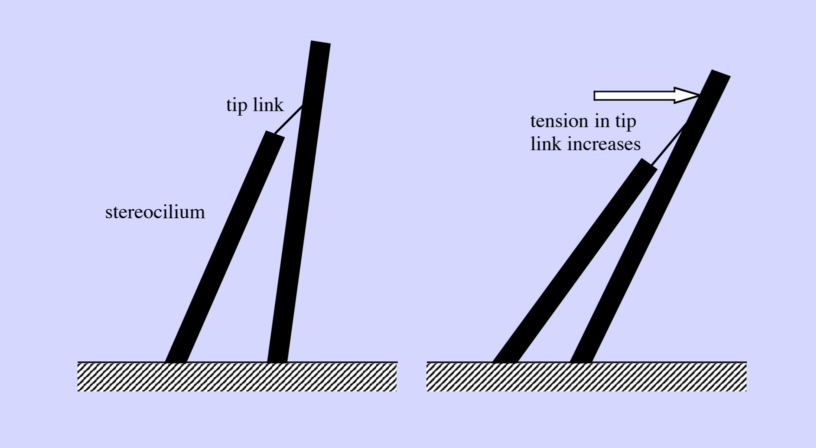

SEM of the stereocilia on the surface of a single hair cell (Hudspeth)

Tension in the tip link activates a stretch-activated ion channel, leading to intracellular calcium ion fluctuations.

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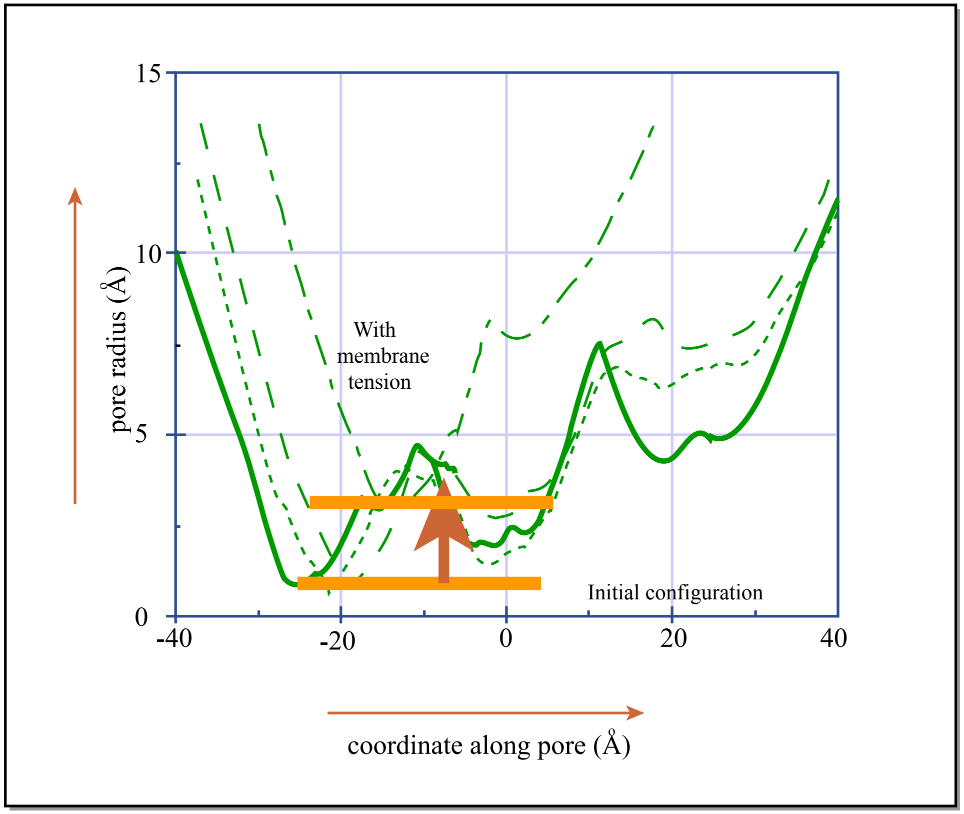
# Molecular dynamics simulation of channel regulation by membrane tension

(Gullingsgrud, et al., Biophys J, 2001)



*But other evidence suggests that the pore increases to >20 angstroms!*

Figure by MIT OCW.

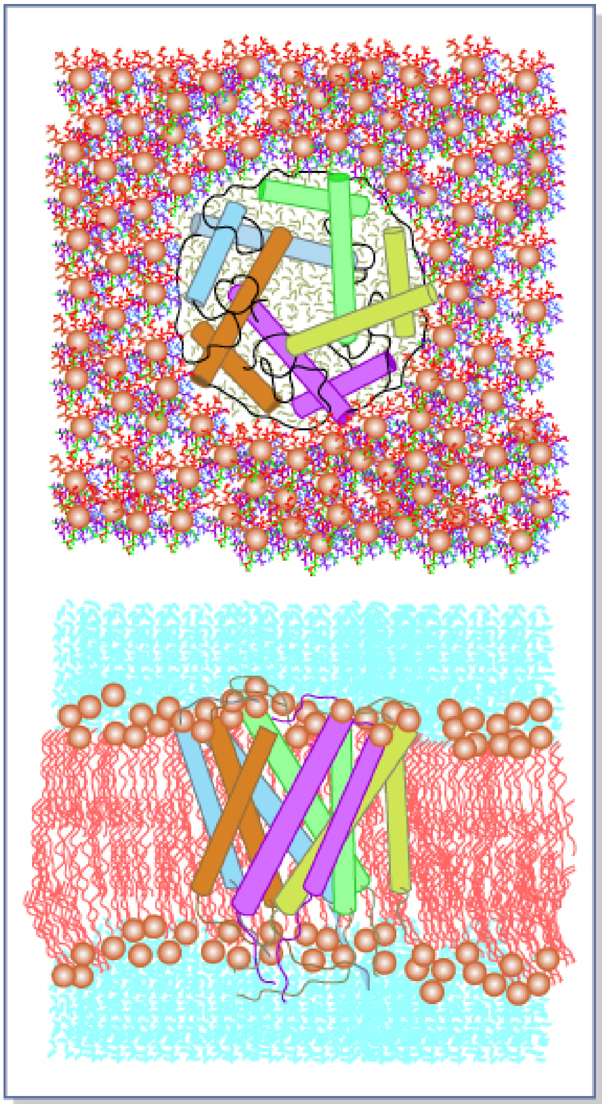


Figure by MIT OCW.

# Molecular, Cellular & Tissue Biomechanics

*Biology is soft, wet & dynamic*

## Using Engineering/Physics to Unravel & Manipulate Biology

- Scaling arguments
- Mechanical models
- Experimental techniques
- Importance of the stochastic nature of biology

# Further Information

Suggested Readings:

(a) Y. C. Fung, **Biomechanics: Mechanical Properties of Living Tissues**, 2nd Edition, Springer - Verlag, 1993

(b) D. Boal, **Mechanics of the Cell**, 2001.

(c) H. Lodish, D. Baltimore, L. Zipurksy, P. Matsudaira, **Molecular Cell Biology**, 2002.

(d) K. Dill and S. Bromberg, **Molecular Driving Forces**, 2003

(e) J. Howard, **Mechanics of Motor Proteins and the Cytoskeleton**, 2001

(f) M. Mofrad and R. Kamm, **Cytoskeletal Mechanics: Models and Measurements**, 2006.

(g) J. Humphrey, **Introduction to Biomechanics**, 2004.