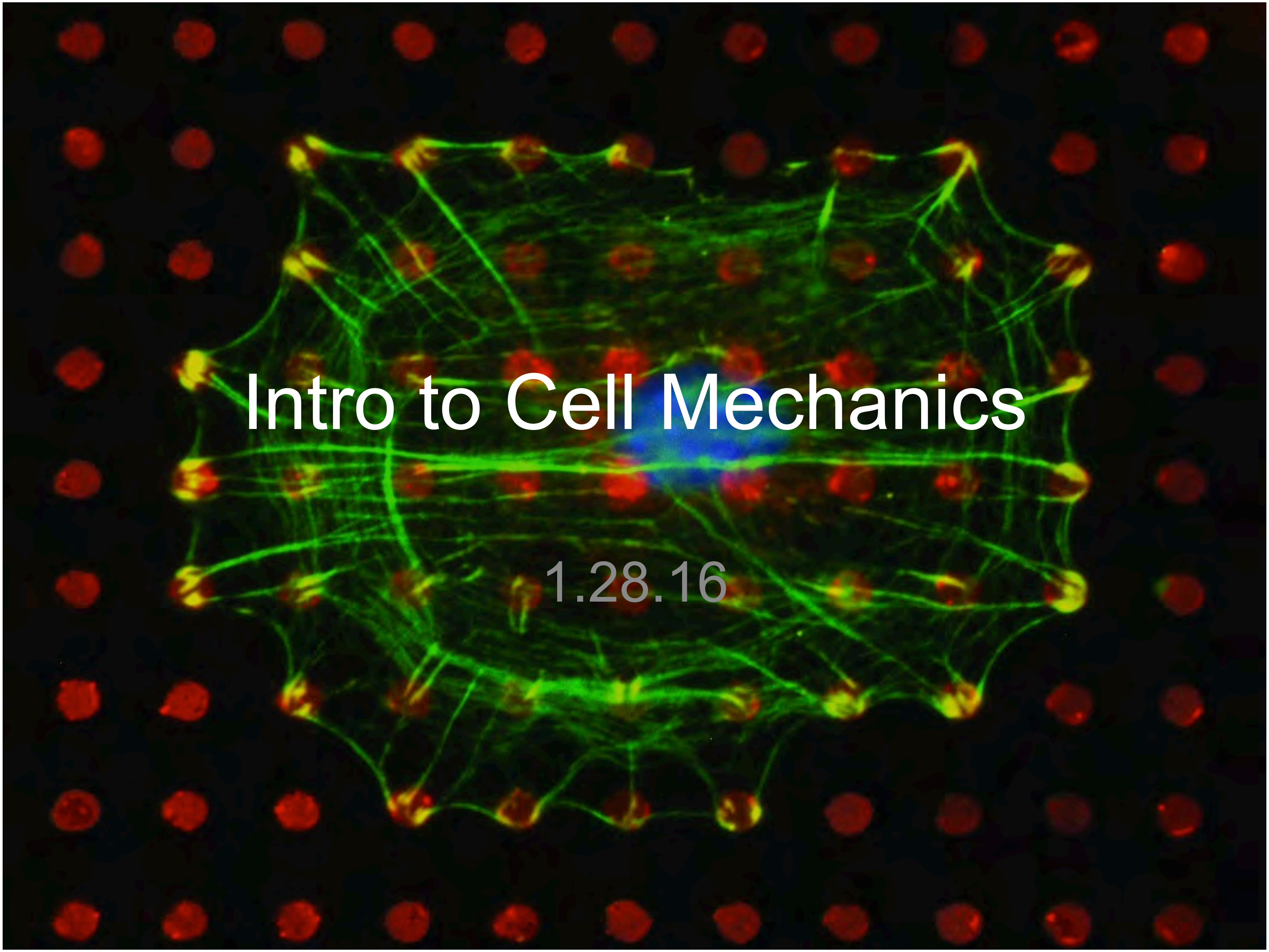
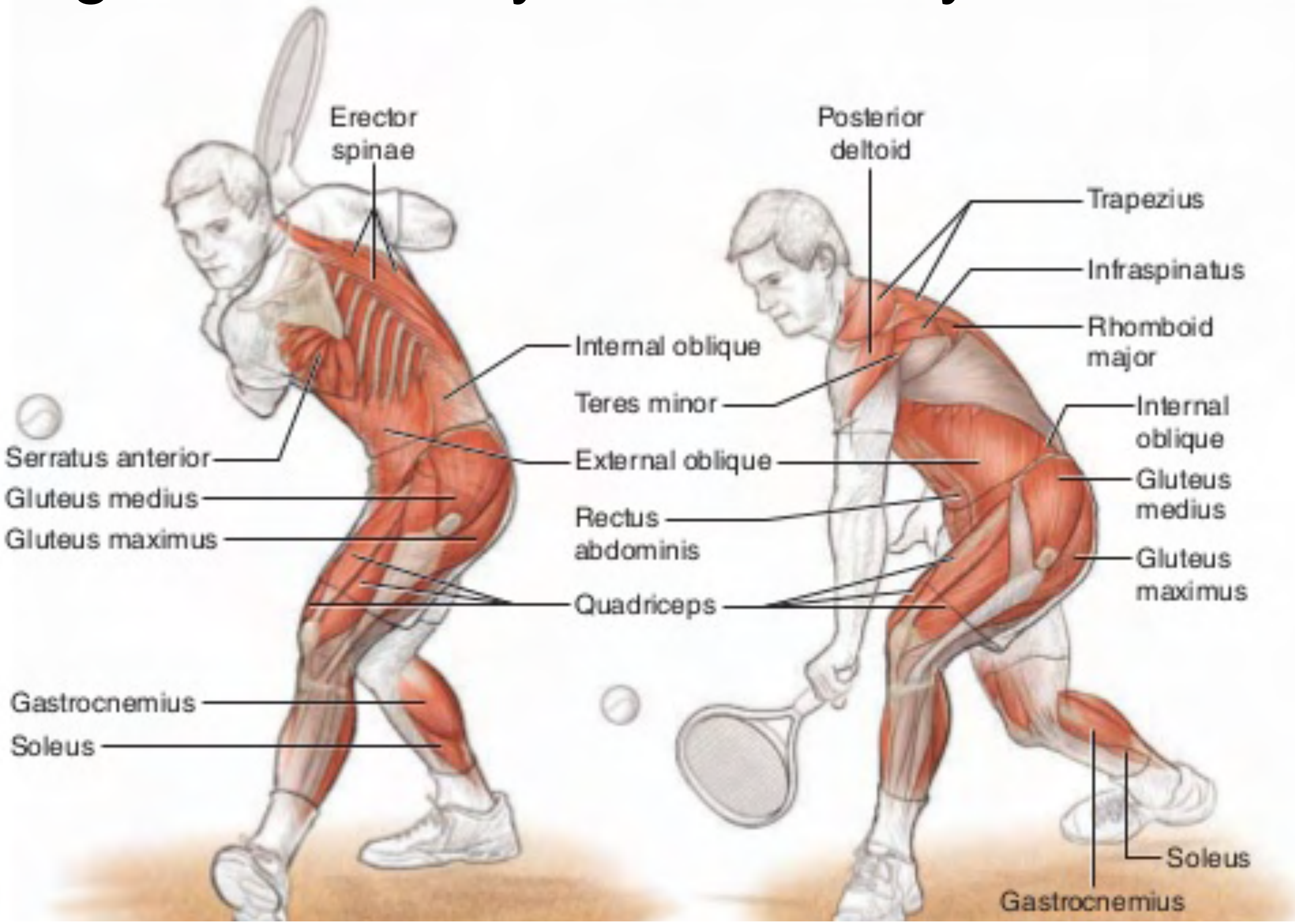


Intro to Cell Mechanics

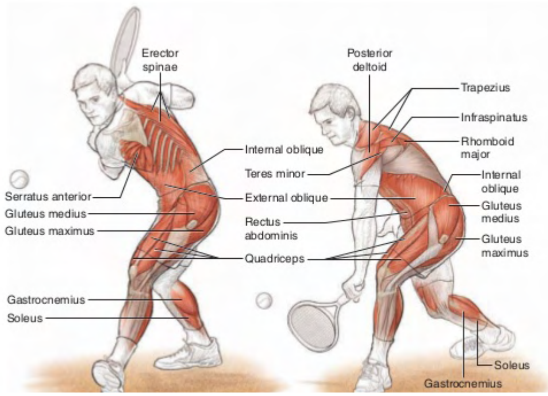
1.28.16

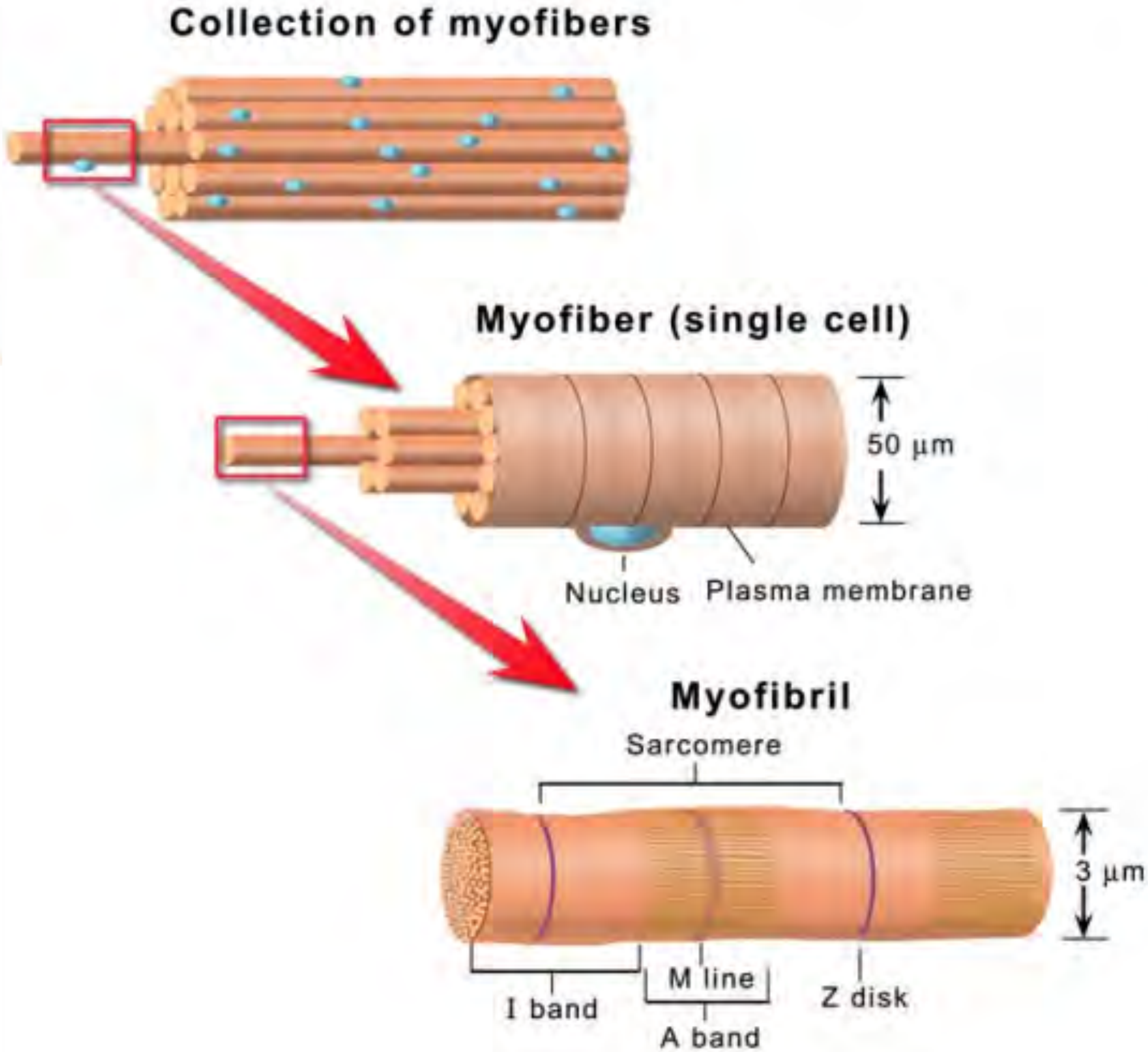
Biological Hierarchy- Whole Body



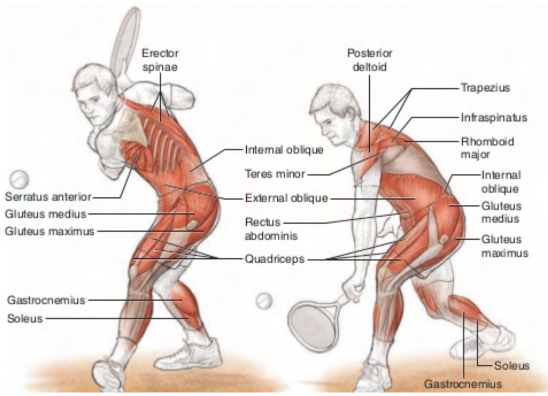
Tennis Anatomy (2011)

Biological Hierarchy – Muscles to Cells

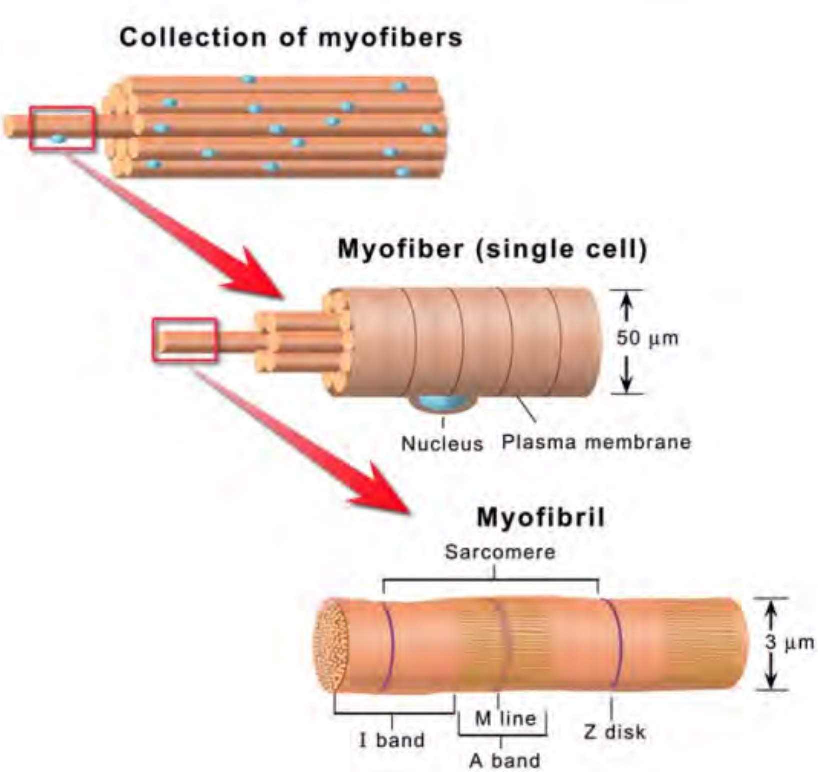


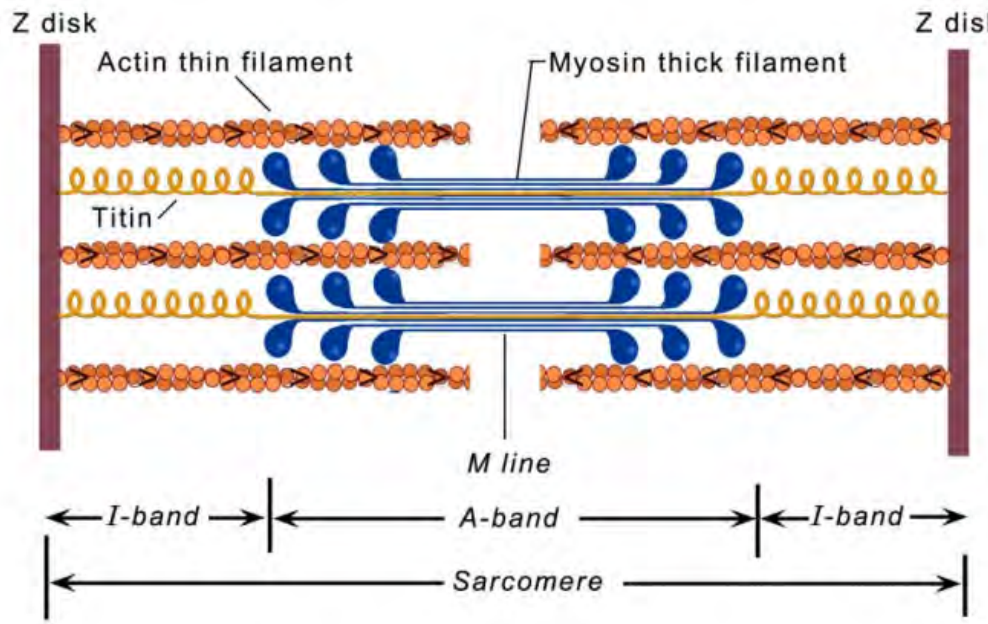


Biological Hierarchy – Cells to Proteins



Muscles contract via sliding the myosin and actin filaments along each other.





Actin: semiflexible polymer
Myosin: molecular motor
Titin: resting elasticity

Fermi Problem: Number of cells

The Human Body ~ 70% water, ρ =1000 kg/m^3
Let's say the average mass of a human is 85 kg.

Fermi Problem: Number of cells

The Human Body ~ 70% water, $\rho = 1000\ kg/m^3$

Let's say the average weight of a human is 85 kg.

$\rho = m/V$

$\rightarrow 1000\ kg/m^3 = (0.7)(85\ kg)(1/V_{human})$

$V_{human} \sim 0.0595\ m^3$

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What is the volume of a cell? Pretend a cell is a cube.

$V_{cell} = (20\ \mu m)^3 = 8 \times 10^{-15}\ m^3$

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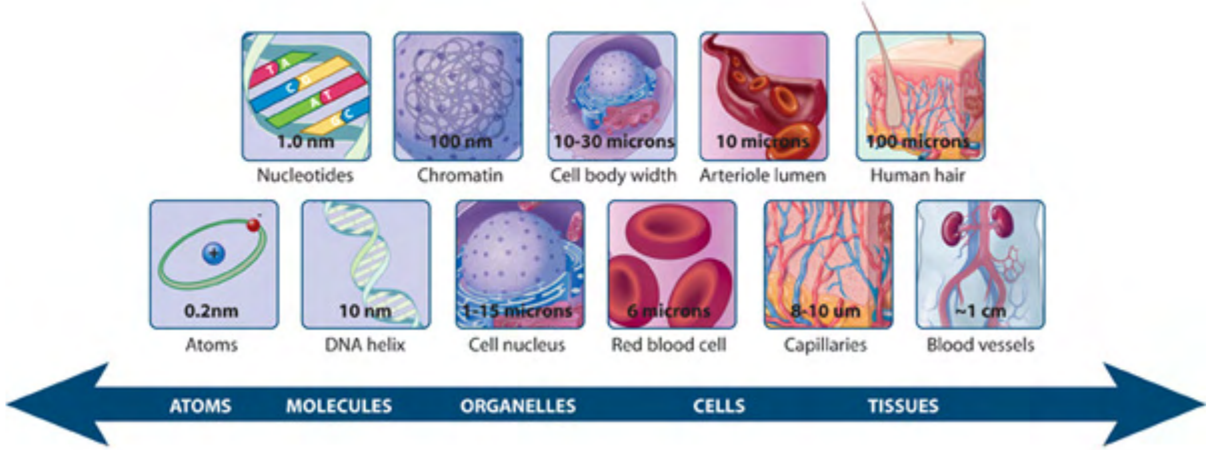
$V_{cell} = (20\ \mu m)^3 = 8 \times 10^{-15}\ m^3$

$N_{cell} = V_{human}/V_{cell} \sim$ 10 trillion

The Numbers



Current data estimation ~ 3.72×10^{13}

Types of cells ~ 210

Typical mass ~ 1 ng

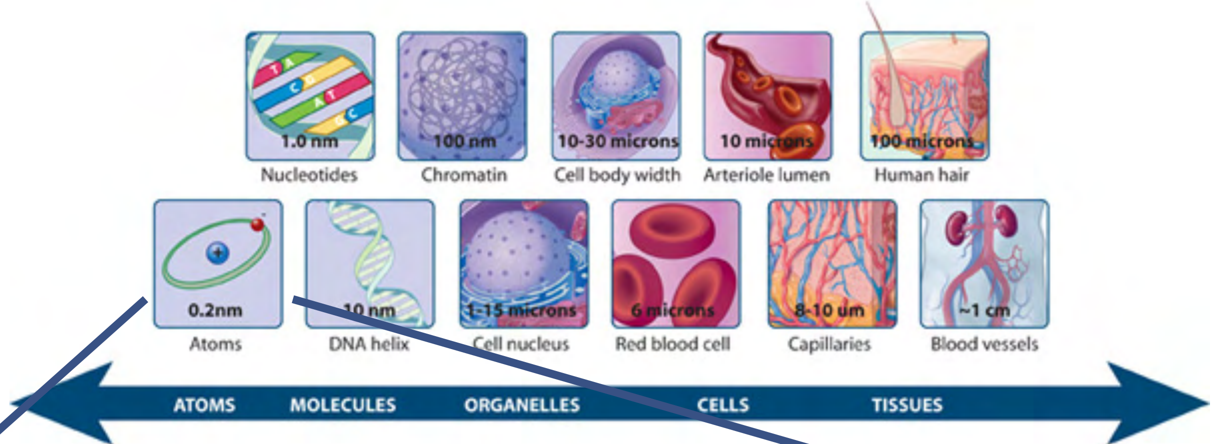
Distance – microns

Force – pN to nN

Stress – 1 Pa to 1 kPa

Nature Education

The Numbers



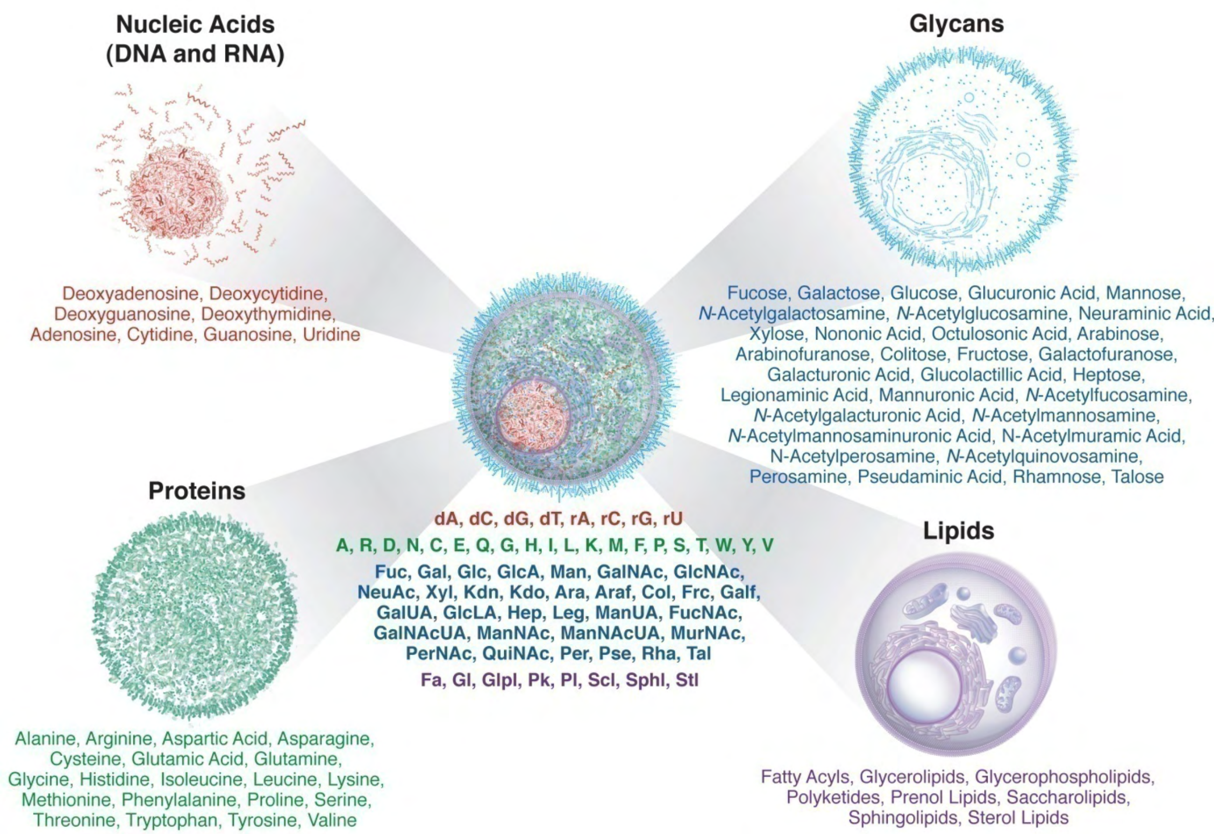
"If an apple is magnified to the size of the earth, then the atoms in the apple are approx. the size of the original apple."
~ Richard Feynman

Nature Education

68 Molecular Building Blocks

<u>Nucleic Acids</u>
8 nucleosides

<u>Glycans</u>
32+ sugars



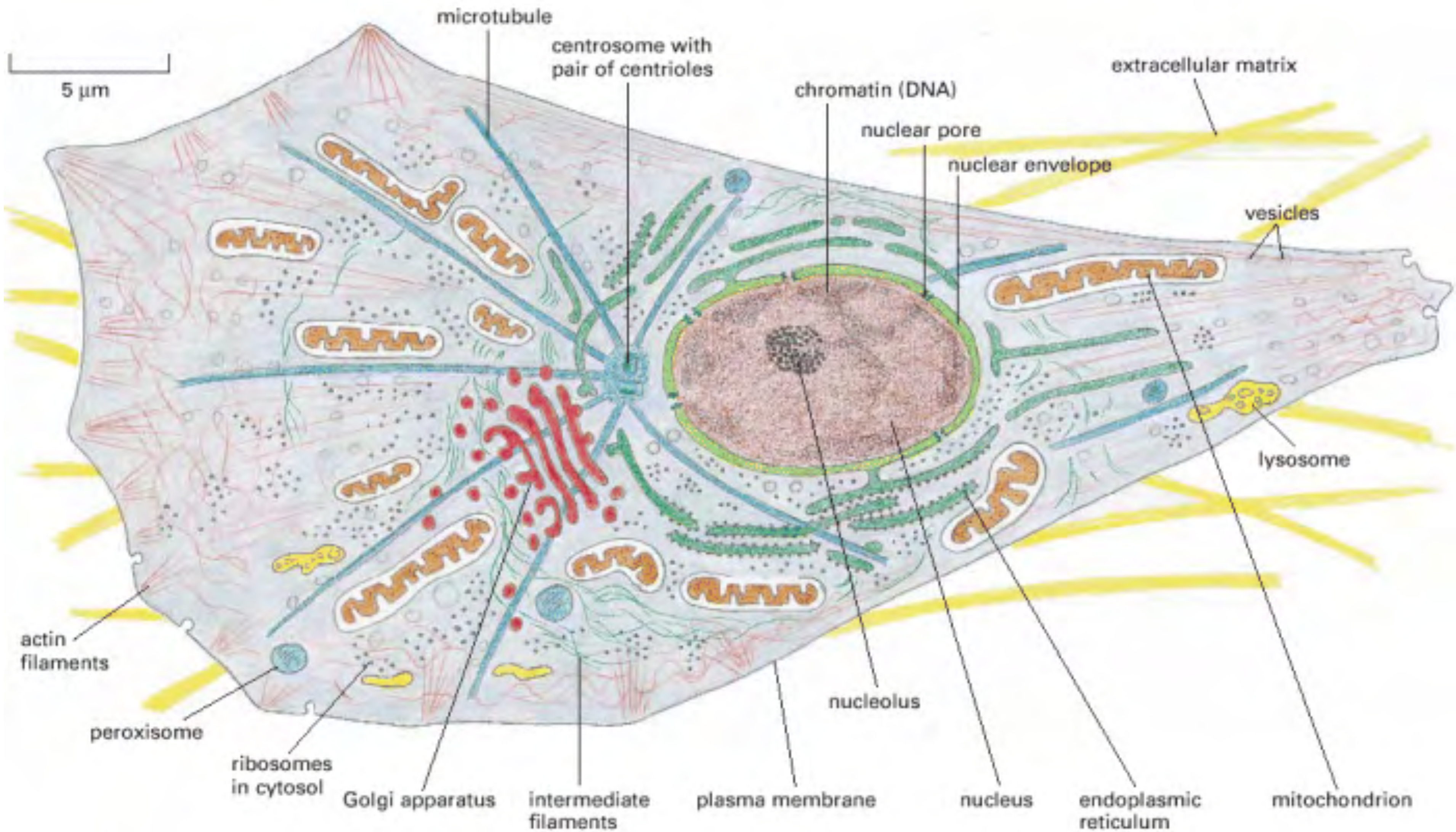
<u>Proteins</u>
20 amino acids

<u>Lipids</u>
8 types

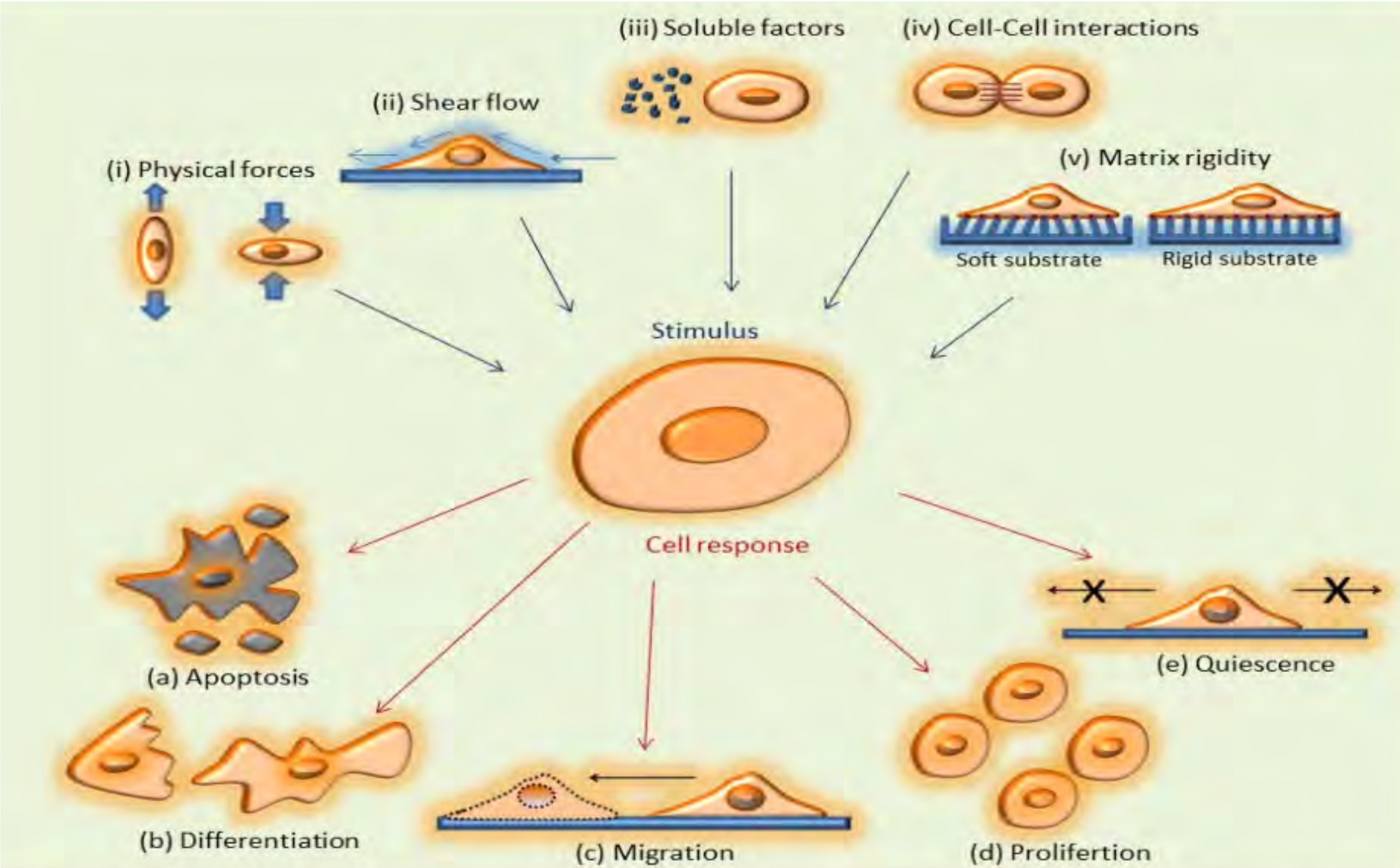
"From the construction, modification, and interaction of these components, the cell develops and functions." –Jamey Marth

J. Marth "A Unified Vision of the Building Blocks of Life" *Nature Cell Biology*, 2008,10(9):1015-16

The Subsystems (Organelles)



From Stimulus to Cell Response

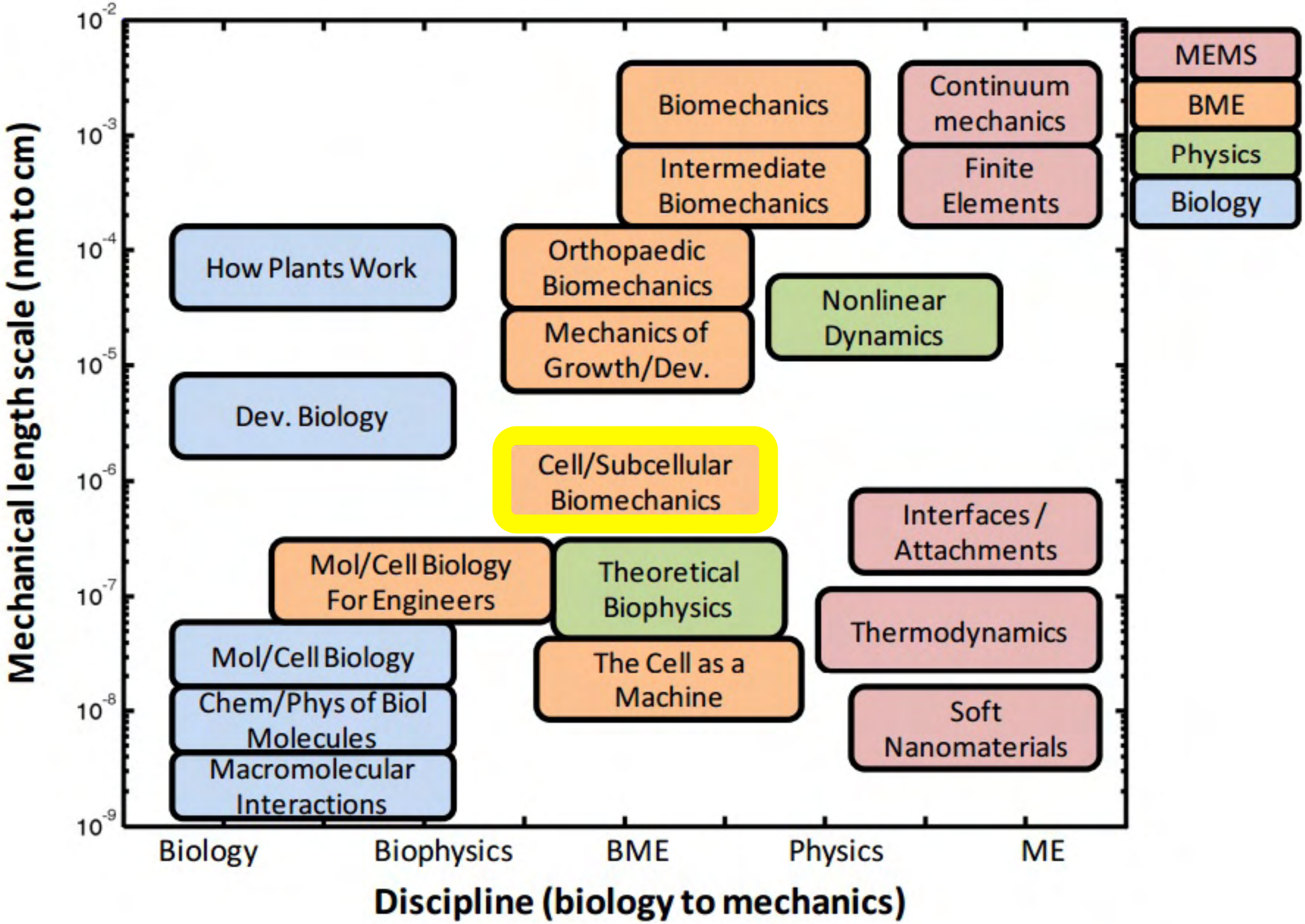


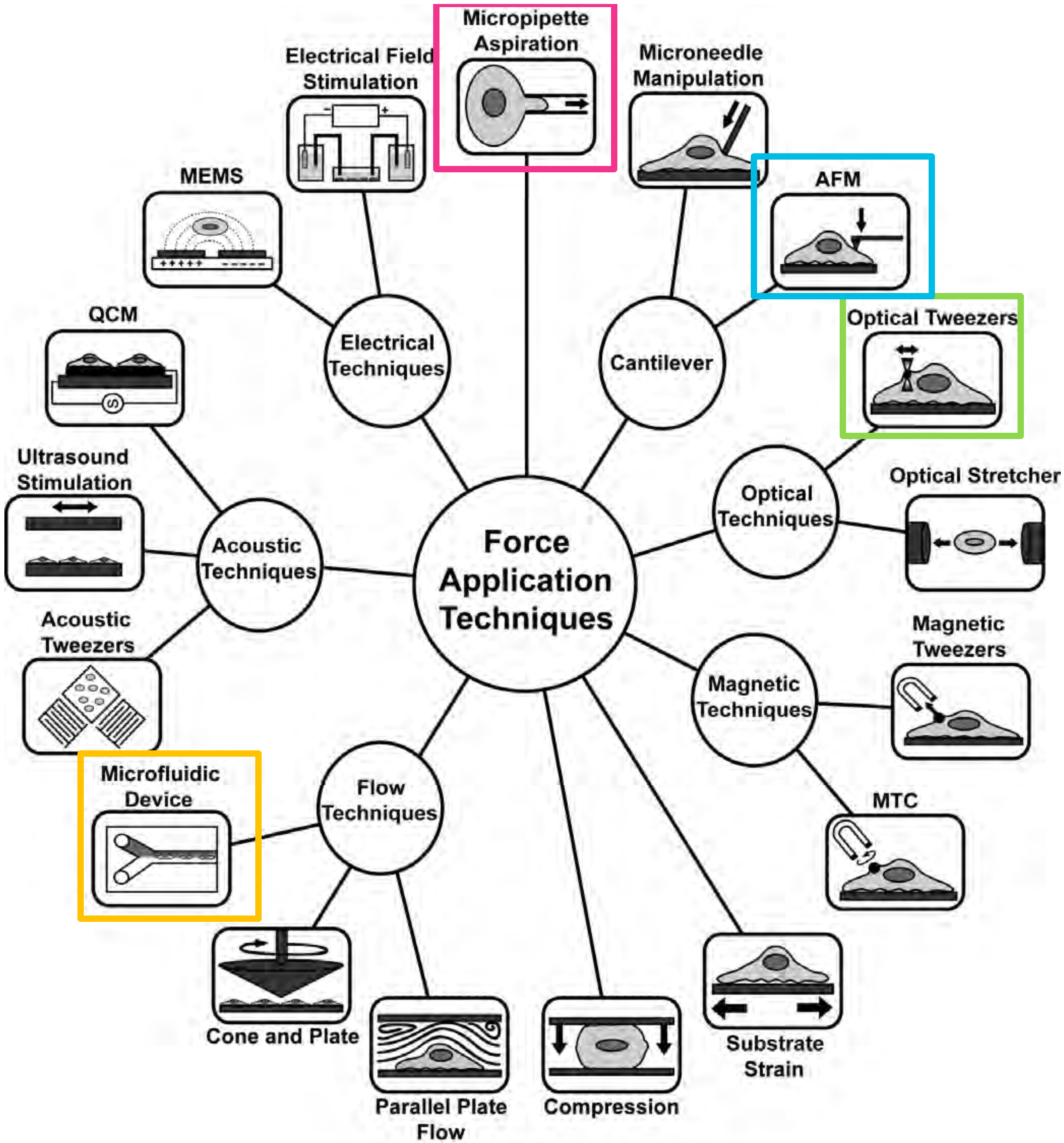
Nanobiomedicine, 2014, 1:5 | doi: 10.5772/59379

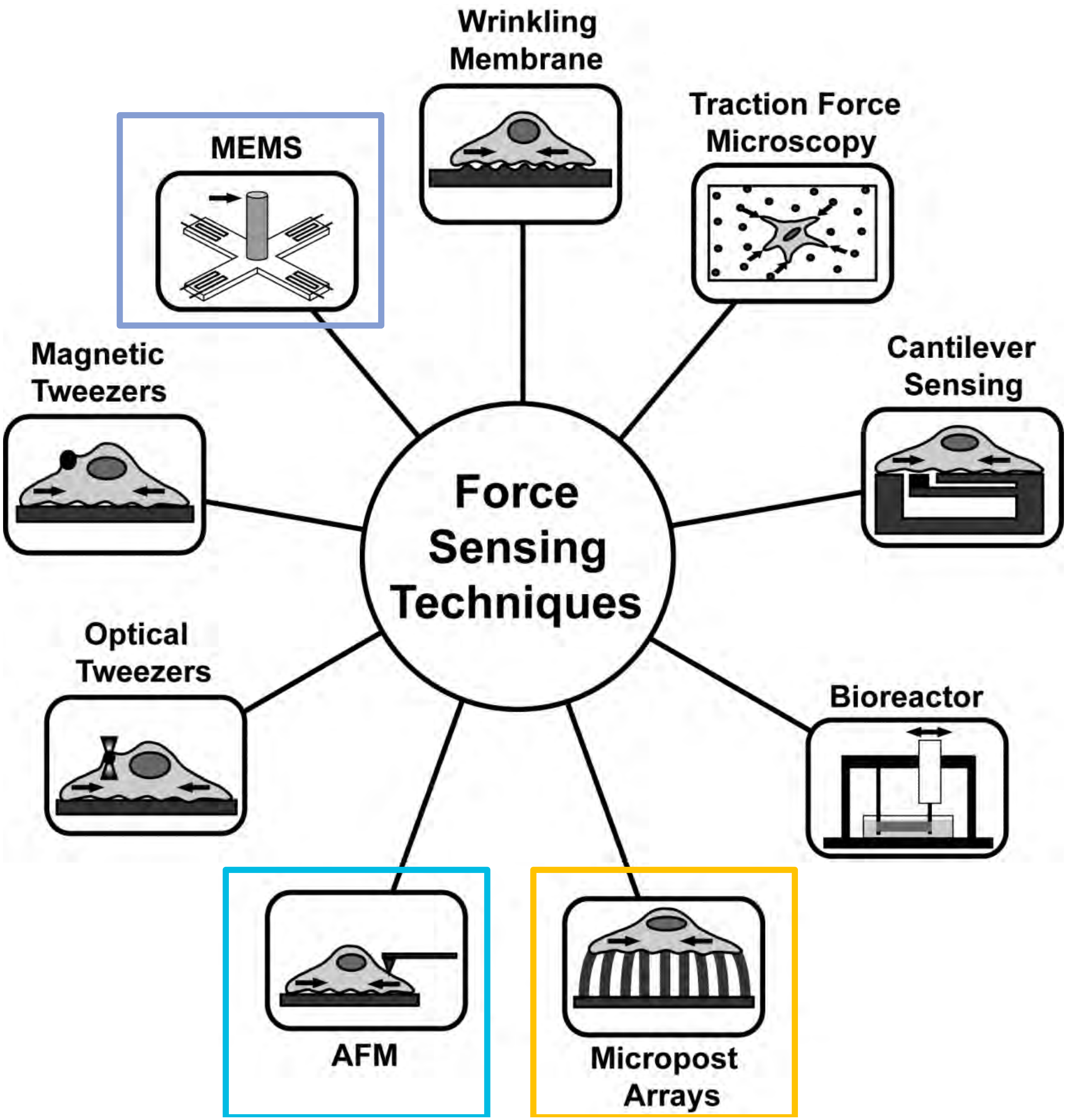
What is Cell Mechanics?

"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

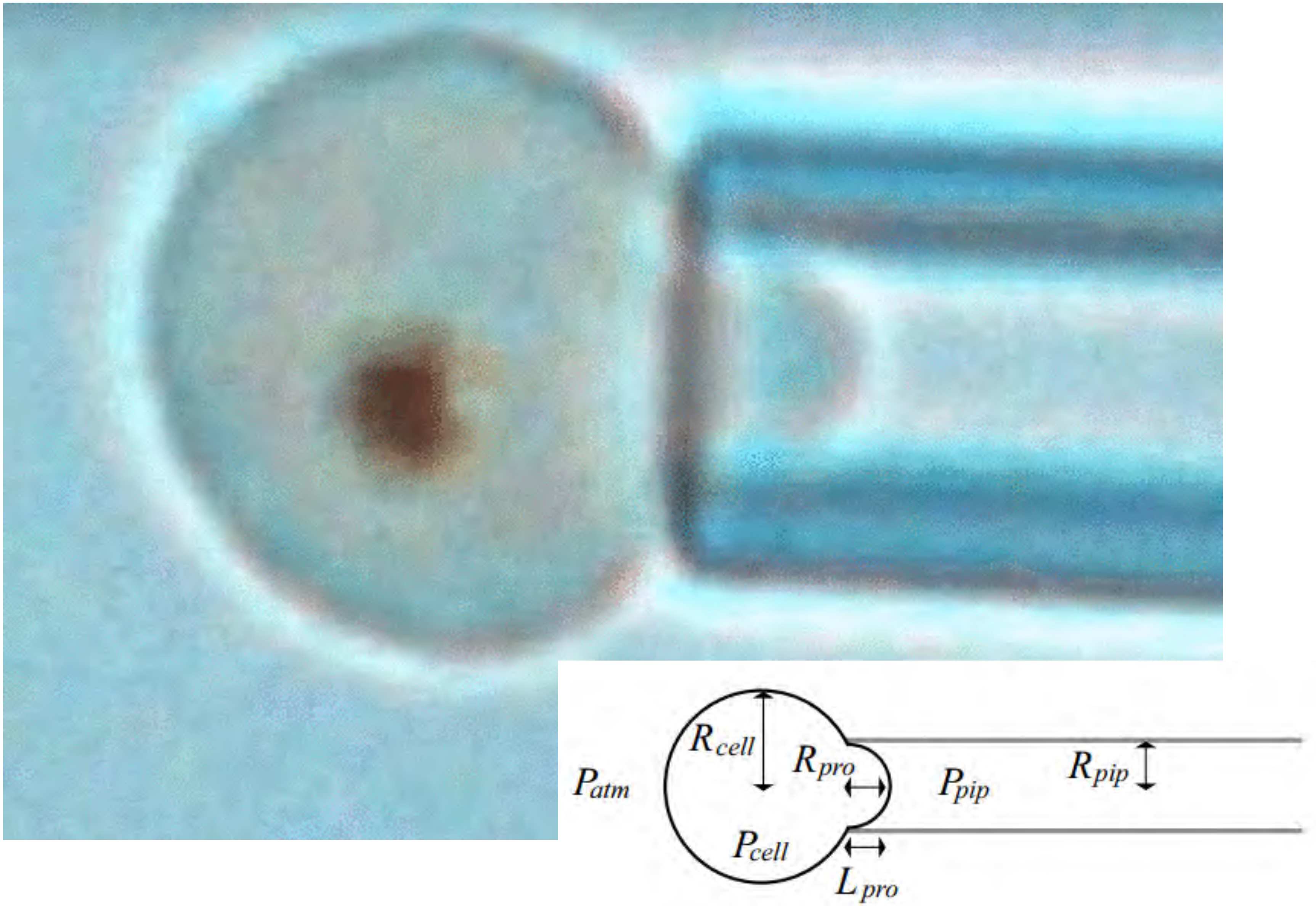

Mechanical length scale (nm to cm)
10-2
10-3
10-4
10-5
10-6
10-7
10-8
10-9
Biomechanics
Intermediate Biomechanics
Continuum mechanics
Finite Elements
How Plants Work
Orthopaedic Biomechanics
Mechanics of Growth/Dev.
Nonlinear Dynamics
Dev. Biology
Cell/Subcellular Biomechanics
Interfaces / Attachments
Mol/Cell Biology For Engineers
Theoretical Biophysics
Thermodynamics
Mol/Cell Biology
Chem/Phys of Biol Molecules
The Cell as a Machine
Soft Nanomaterials
Macromolecular Interactions
MEMS
BME
Physics
Biology
Biology
Biophysics
BME
Physics
ME
Discipline (biology to mechanics)


Force Application Techniques
Electrical Techniques
Cantilever
Optical Techniques
Magnetic Techniques
Flow Techniques
Acoustic Techniques
Micropipette Aspiration
Electrical Field Stimulation
Microneedle Manipulation
AFM
Optical Tweezers
Optical Stretcher
MEMS
QCM
Ultrasound Stimulation
Acoustic Tweezers
Microfluidic Device
Magnetic Tweezers
MTC
Cone and Plate
Parallel Plate Flow
Compression
Substrate Strain



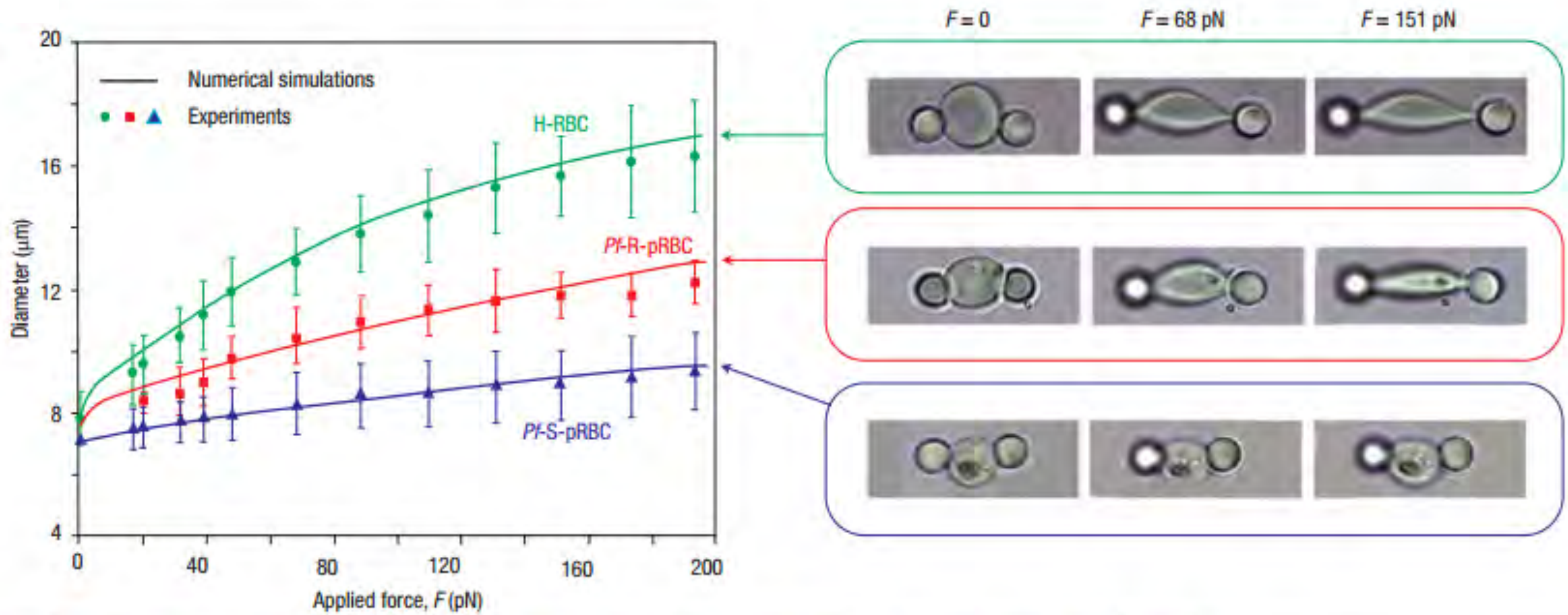
Force Sensing Techniques
Wrinkling Membrane
Traction Force Microscopy
Cantilever Sensing
Bioreactor
Micropost Arrays
AFM
Optical Tweezers
Magnetic Tweezers
MEMS

Micropipette Aspiration (Application)



Optical Tweezers (Application)

Biomechanics of RBC infected by the malaria-inducing parasite *P. falciparum*. Normal RBCs (H-RBC, *n* = 7) and RBC infected by *P. falciparum* at the ring stage (*Pf*-R-pRBC, *n* = 5) and the schizont stage (*Pf*-S-pRBC, *n* = 23).



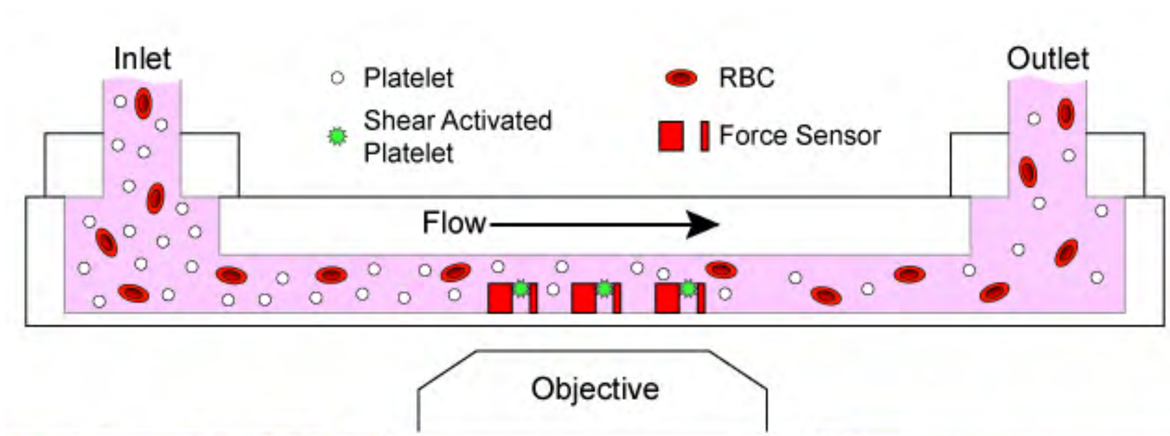
The solid lines are from three-dimensional finite-element simulations of an optical tweezers stretching experiment of RBC with an effective shear modulus of the cell membrane = 5.3 N m^{-1} (H-RBC), 16 N m^{-1} (*Pf*-R-pRBC) and 53.3 N m^{-1} (*Pf*-S-pRBC).

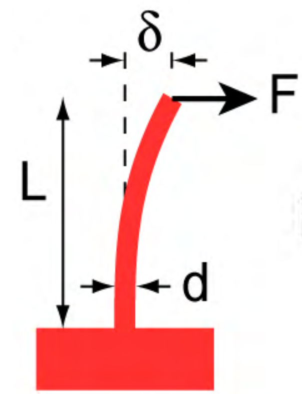
Nature Materials **7**, 15 - 23 (2008)

Laser Tweezers (Application)

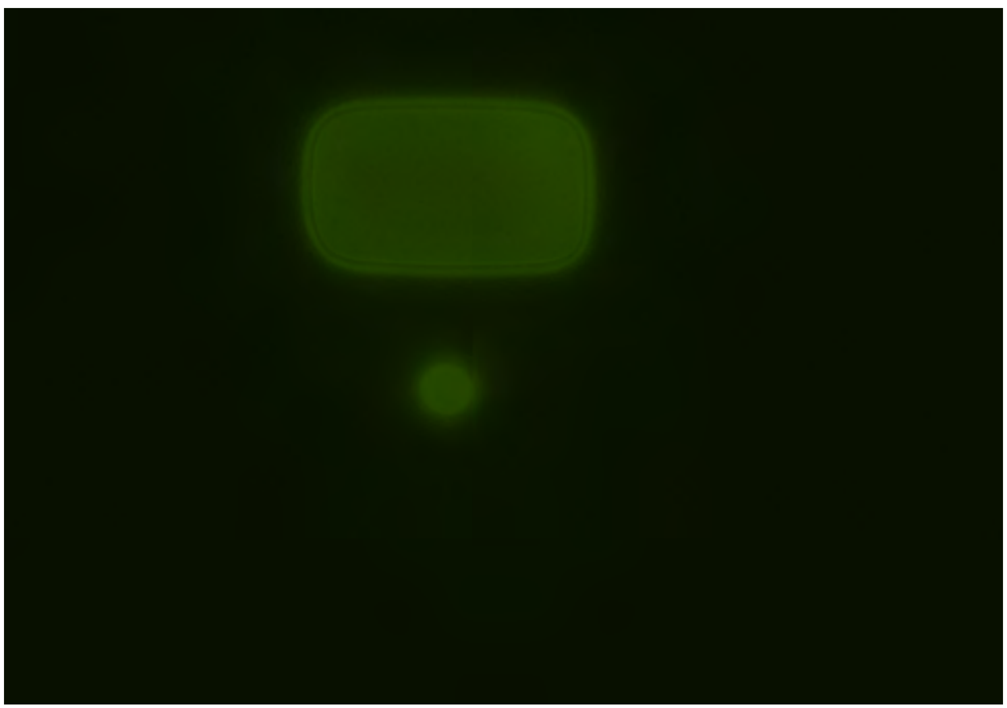
Kapil Bambardekar et al (2015),
Proceedings of the National Academy of Sciences,
DOI: 10.1073/pnas.1418732112

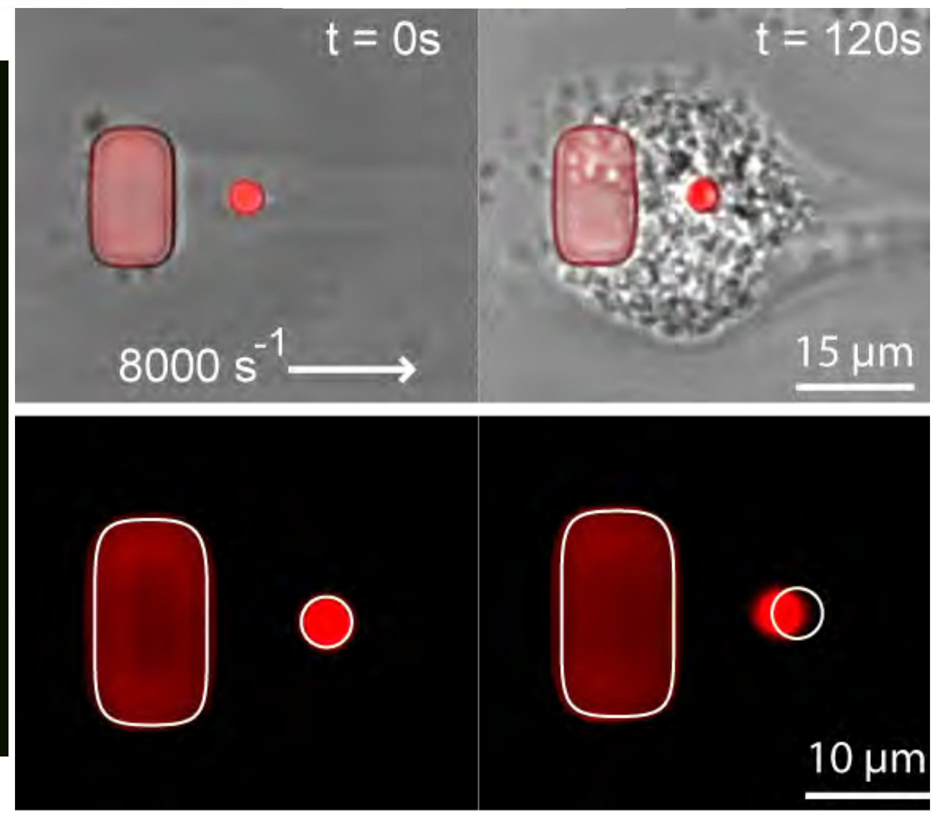
Microfluidic Device (Application/Sensing)



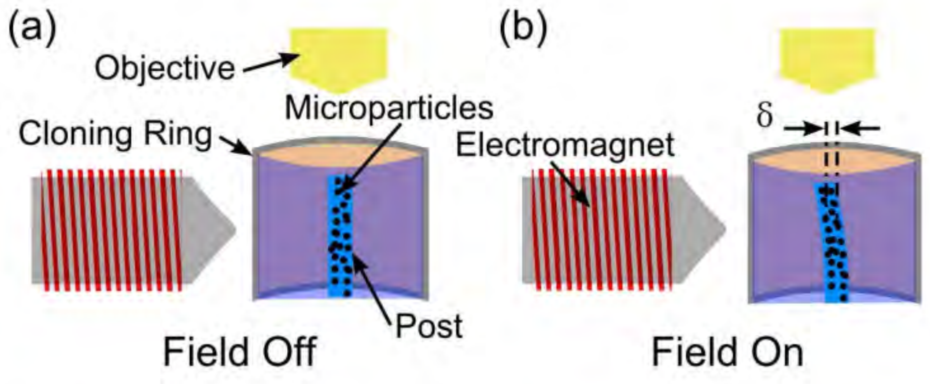


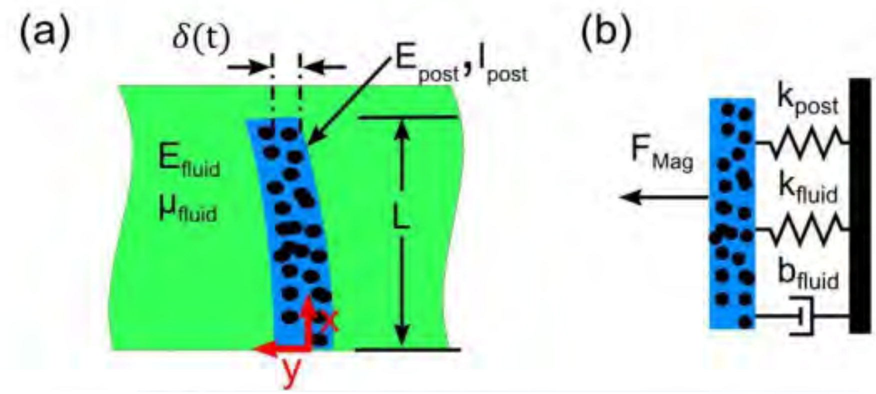
$$F = \frac{3\pi E d^4}{64 L^3}\delta$$

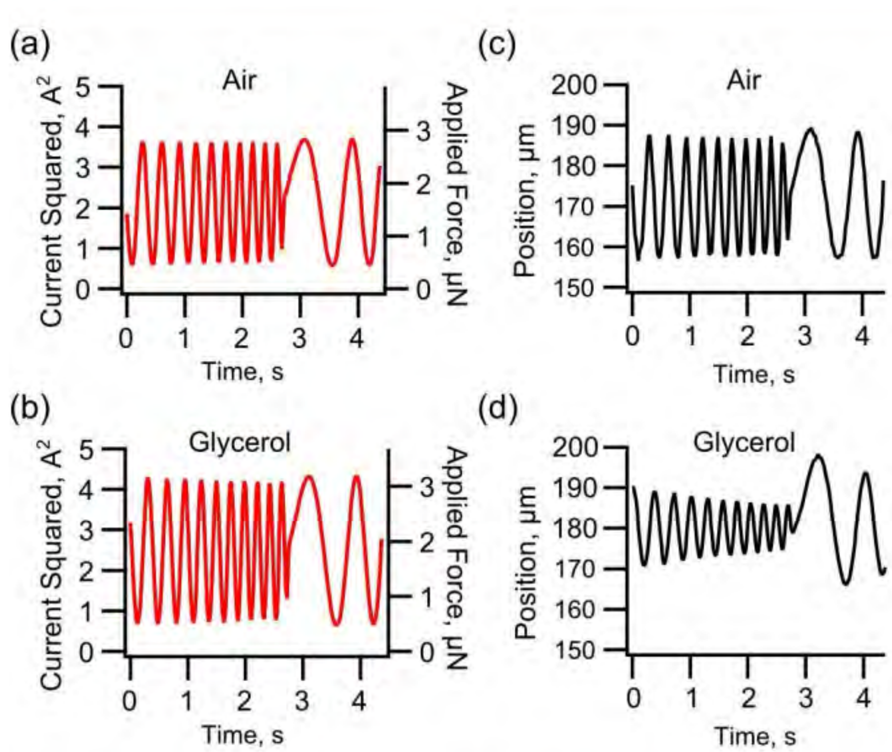


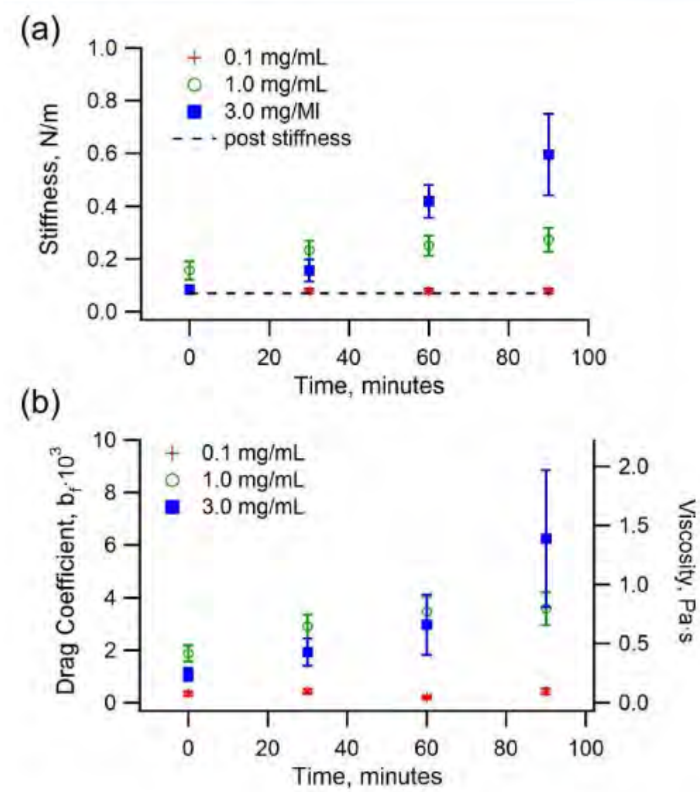


Magnetic Cantilever (Actuation)



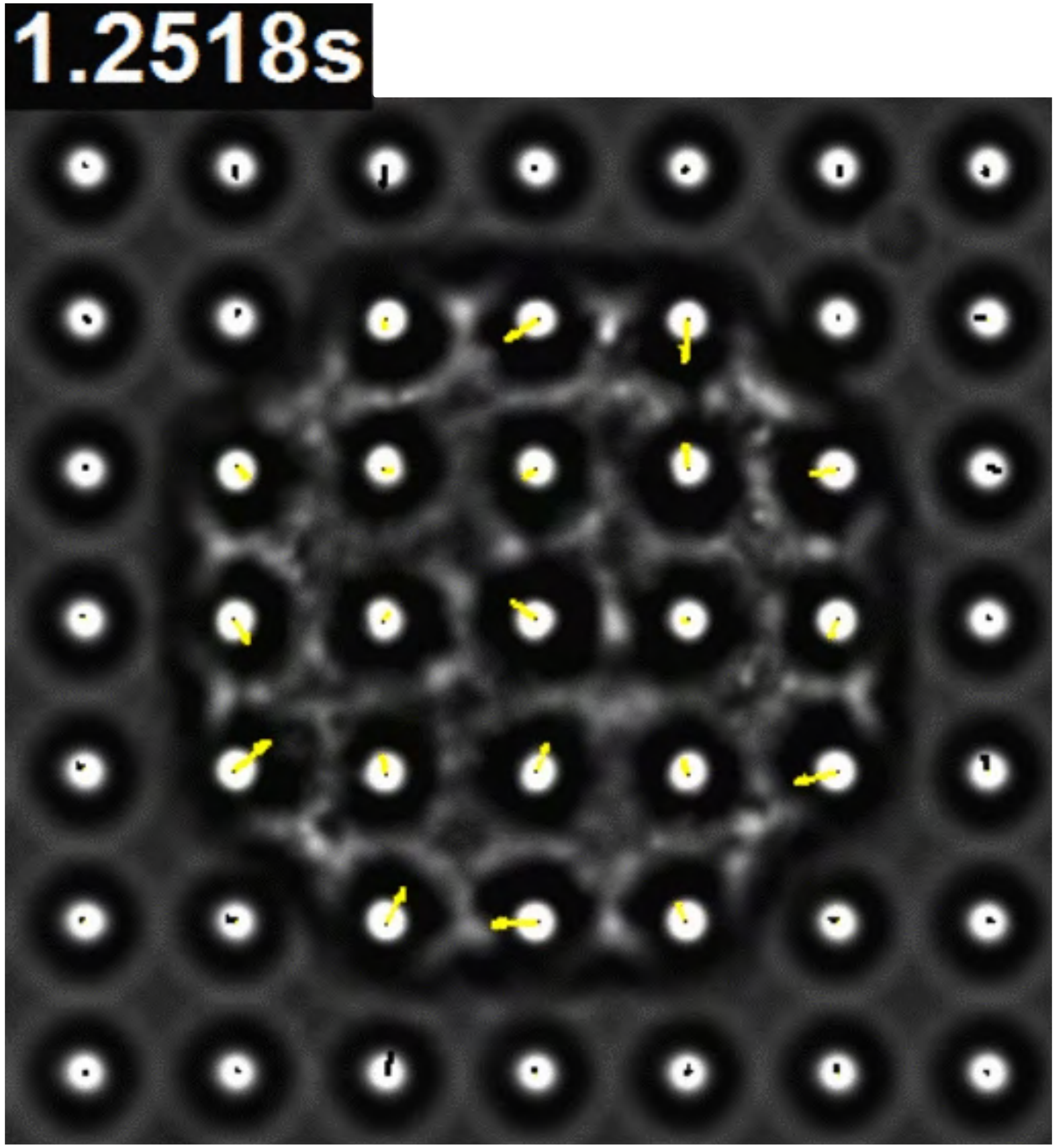






Bielawski, K.S., Sniadecki, N.J., J Microelectromechanical Systems. (2015)

Micropost Technology (Sensing)



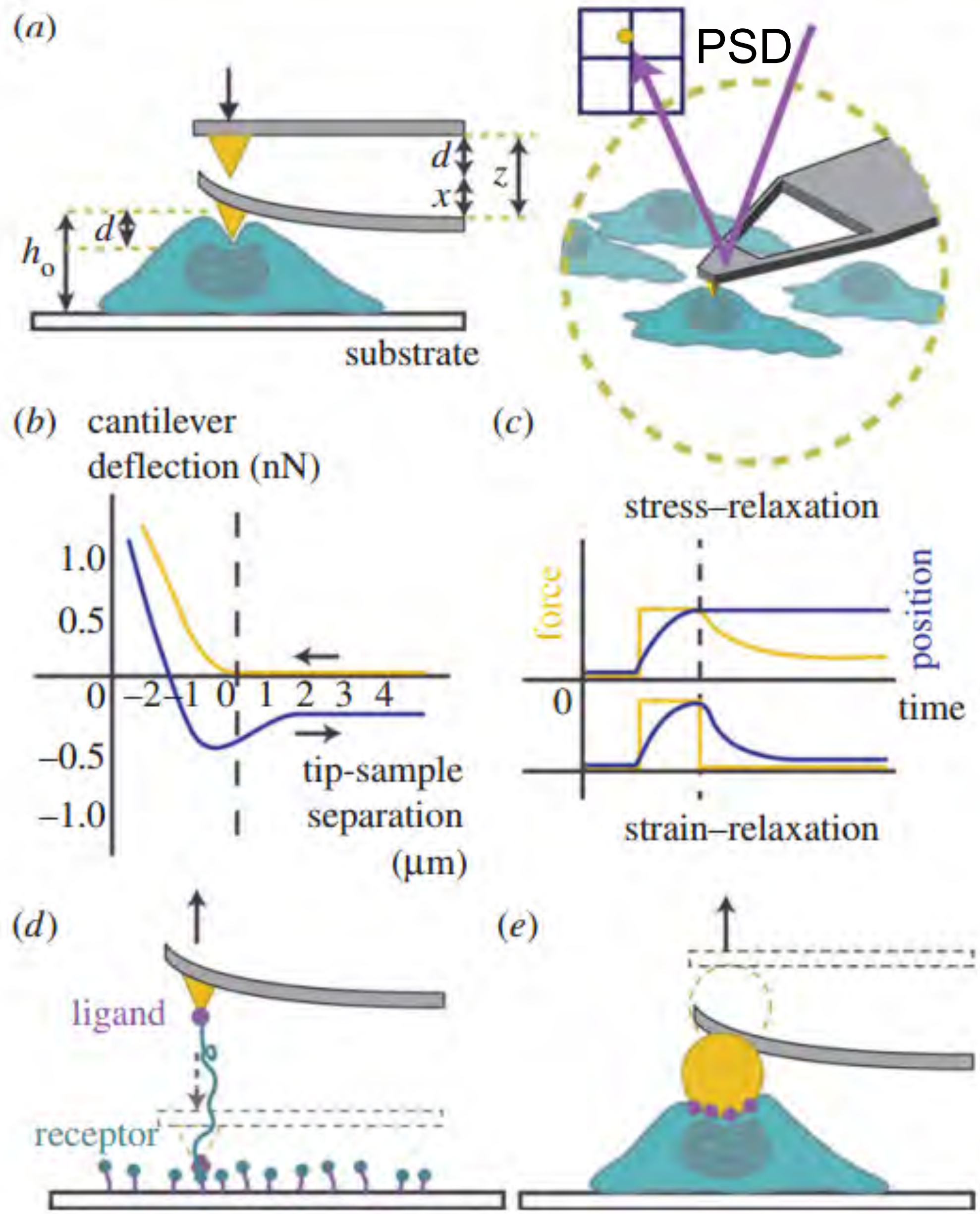
Rodriguez, M.L., et al (2014) *J Biomechanical Engineering*, 136(5), 051005

AFM (Application and Sensing)

Apply compressive strains

AFM force - indentation curve used to measure elasticity

Single molecule interaction experiments

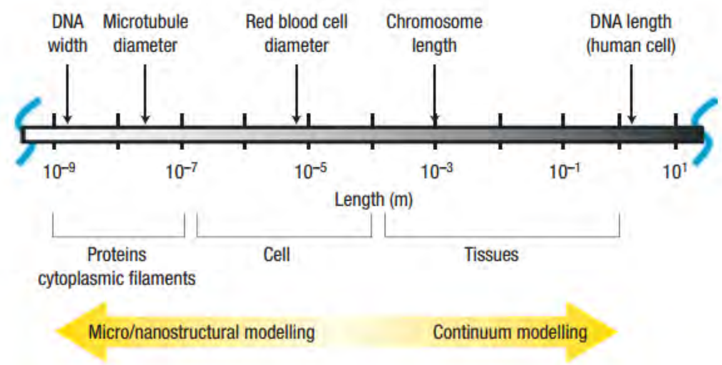


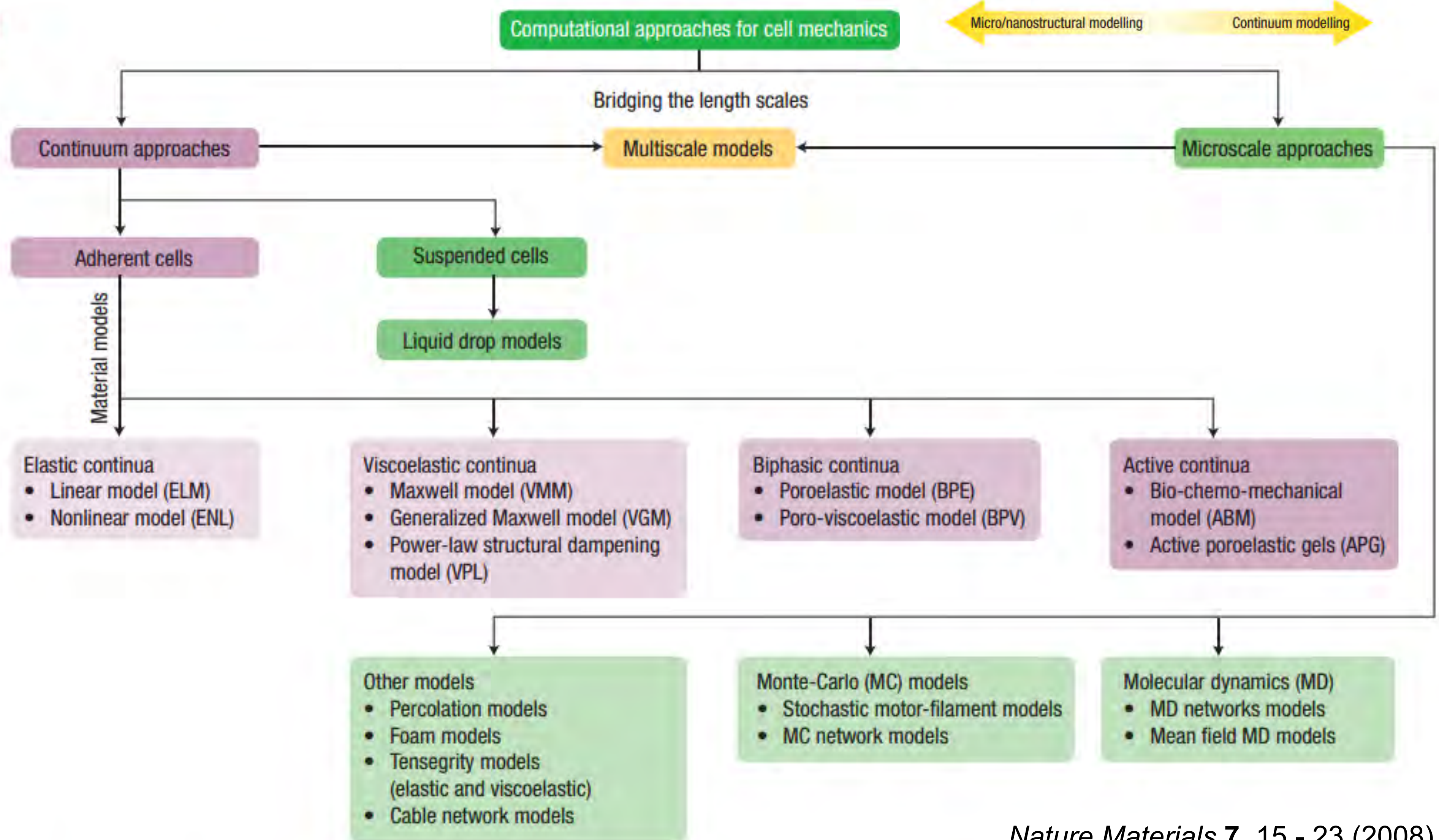
Stress and strain relaxation curves to measure time dependent cellular behaviors

Spherical tip used to measure distributed forces

Haase K, Pelling AE. (2015) J. R. Soc. Interface 12: 20140970.

Modeling Approaches





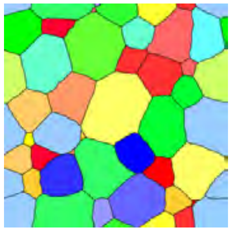
Nature Materials **7**, 15 - 23 (2008)

We study cell mechanics...

- to understand interaction between cells and their environment
- to improve the control/function of cells
- to improve cell growth/cell production
- to manipulate cells for medical applications
- to treatment of certain diseases
- to understand how cells move and change cell motion
- to build/engineer tissues with desired mechanical properties
- to understand how cell growth is affected by stress and mechanical properties of the substrate the cells are in
- to understand how cells are affected by their environment
- to understand how mechanical factors alter cell behavior and gene expression
- to understand how different cells interact with each other
- to understand how mechanical loading affects cells, e.g. stem cell differentiation or cell morphology
- to understand how mechanically gated ion channels work
- to understand how the loading of cells could aid developing structures to grow cells or organize existing cells more efficiently
- to understand macrostructural behavior
- to build machines/sensors similar to cells
- to be able to study the impact of different parts of a cell on its overall behavior
- to provide scientific guidance for targeted cell manipulation

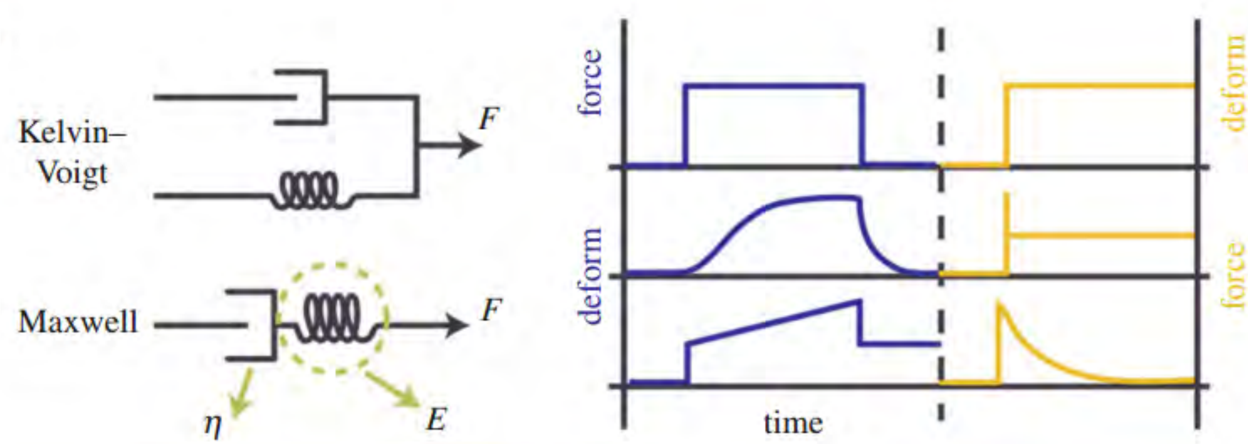
Back Up

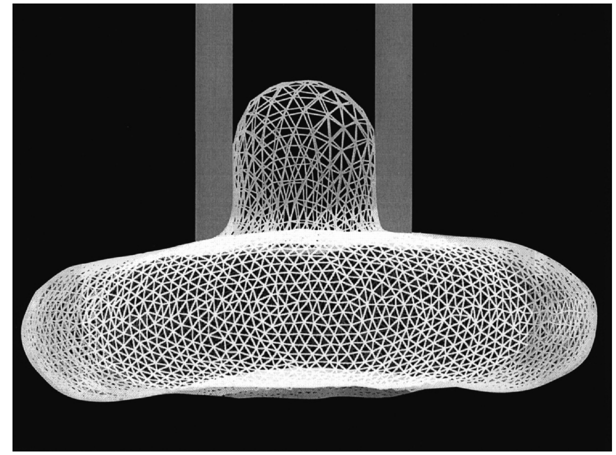
Cells in Context

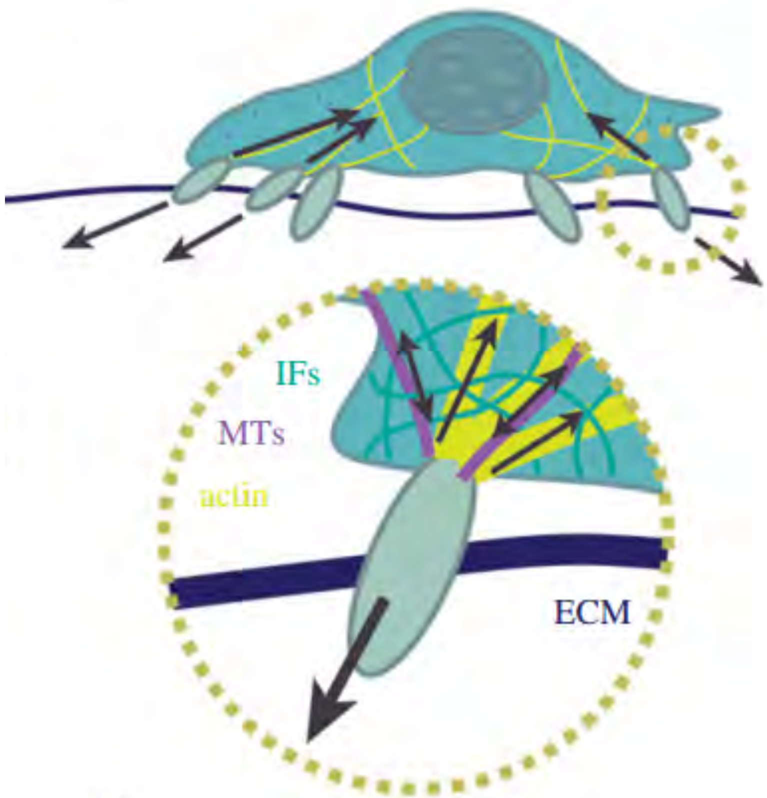


Cells/Tissue	Grains/Material
Animate	Inanimate
Basic Unit of Living	Basic Unit of Metal/Ceramics
Composed of Proteins	Composed of Atoms
Defines structure/function of tissue	Defines structure strength of material
Sensitive to temperature, radiation, water, pH, nutrients, pressure, ionic strength, osmolarity,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

Modeling Approaches







Haase K, Pelling AE. (2015) J. R. Soc. Interface 12: 20140970.

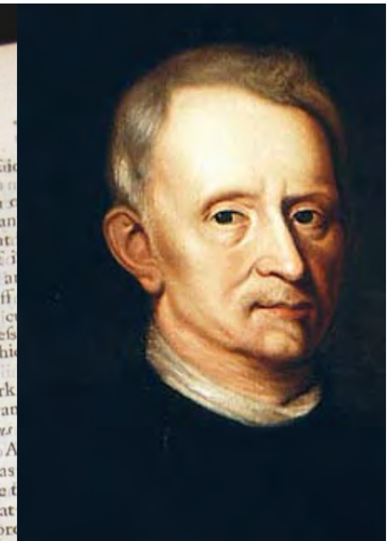
Table 2 Material constants used for cells

Cell type	Young's modulus (kPa)	Poisson's ratio	Technique	Reference(s)
Adipocyte				
Human joint	0.61		AFM	[82]
Cancer cells				
Bladder carcinoma	0.4–1.4		AFM	[129]
Chondrosarcomas	1–2.5	0.4	AFM/C	[83,275]
Melanoma	0.3–2		MTC	[84]
Human osteosarcoma	0.92–1.09	0.37	MN	[79]
Chondrocyte				
Bovine articular	0.69–8	0.26	MN/C	[106,287]
Bovine cartilage	2.55–2.7		C	[276,288]
Human cartilage	0.36–0.67	0.4	MP	[64,85]
Human femoral	1.1–1.3	0.36–0.38	AFM/MP	[62,82]
Porcine cartilage	0.6–1.2		AFM	[86]
Endothelial				
Bovine aortic	0.32		MP	[87]
Bovine aortic cytoplasm	0.5		C	[289]
Bovine aortic nucleus	5		C	[289]
Human aortic	1.5–5.6		AFM	[88]
Undisclosed Endothelial	0.5		MP	[51]
Epithelial				
A549 human alveolar	0.1–0.2		MTC	[89]
Human bladder	10–13		AFM	[129]
Monkey kidney cortex	0.16		MTC	[90]
Monkey kidney interior	0.04		PT	[90]
Fibroblast				
Avian heart	14.7		C	[285]
Murine L929	4		AFM	[91]
Murine 3T3	0.015–14		AFM/MN/PT/S/C/OT	[92–96,105,179,180]
Muscle cells				
Mouse myoblast C2C12	2		C	[286]
Mouse myogenic C2-7	0.66		S	[97]
Rat aortic smooth muscle	1.5–11		S	[98]
Rat myocyte (cardiac)	35–42		AFM	[99]
Osteoblast				
Human femoral	2.0–5.8		AFM	[82]
Human SaOS2	5.4–7.6		AFM	[100]
Murine MC3T3-E1	1–5		AFM	[136,94]
Murine neonatal long bone	14		AFM	[101]
Rat neonatal long bone	3.175–10	0.2–0.5	AFM	[145,146]
Stem cells				
Human bone marrow	0.56–33		AFM/MP	[82,102,103]
White blood cells				
Lymphocyte	0.2913		MN	[107]
Neutrophil	0.118		MN	[107]
Rat neutrophil	0.38–0.8		AFM	[104]

References cited in the table are [51,62,64,82,107,129,136,145,146,179,180,275,276,285–289].
Note: AFM = atomic force microscopy, C = compression, MN = microneedle, MP = micropipette aspiration, MTC = magnetic twisting cytometry, OT = optical tweezers, PT = particle tracking, and S = stretch.

Aspects of cell mechanics	Cell type	Magnitude	Tool/Technique
Stiffness	Fibroblasts Vascular endothelial cells Vascular smooth muscle cells Rat ASM(airway smooth muscle)cells	0.02 N/m 0.03-0.04 N/m 0.09-0.88 N/m 0.099 N/m	Micropipette Magnetic twisting cytometer
Elastic modulus	Cancer MCF-7 cell Osteoblasts Skeletal muscle cells Cardiocytes Erythrocytes Leukocytes Fibroblasts Endothelial cells Outer hair cells	0.95 - 1.19 kPa 0.3-20 kPa 8-45 kPa 90-110 kPa 14-33 kPa 0.2-1.4 kPa 0.6-12 kPa 0.2-2 kPa 2-4 kPa	Atomic force microscopy
Viscoelasticity	Cytoplasm	210 Pa s 2000 Pa s	Magnetic bead microrheology
Cell adhesion force	Human cervical carcinoma cell Epithelial cells Murine fibroblast cells Rat cardiac fibroblast	19-204 nN 100 nN 300-400 nN 10 nN	Atomic force microscopy High-speed centrifugation technique Manipulation force microscope Traction force microscopy
Cell traction forces	Fibroblasts Fish keratocytes	100 nN 20 nN	Microcantilevers micro pads Flexible substrate
Shear stress	Endothelial cells Bovine aortic endothelial cells Human umbilical vein endothelial cells	1-15 dyn/cm^2 10 dyn/cm^2 1-3 dyn/cm^2	Microfluidics

Table 1. Mechanical properties of cells reported in the literature



Obſerv. XVIII. *Of the* Schematiſme *or* Texture *of* Cork, *and of the Cells and Pores of ſome other ſuch frothy Bodies.*

I Took a good clear piece of Cork, and with a Pen-knife ſharpen'd as keen as a Razor, I cut a piece of it off, and thereby left the ſurface of it exceeding ſmooth, then examining it very diligently with a *Microſcope*, me thought I could perceive it to appear a little porous; but I could not ſo plainly diſtinguiſh them, as to be ſure that they were pores, much leſs what Figure they were of: But judging from the lightneſs and yielding quality of the Cork, that certainly the texture could not be ſo curious,