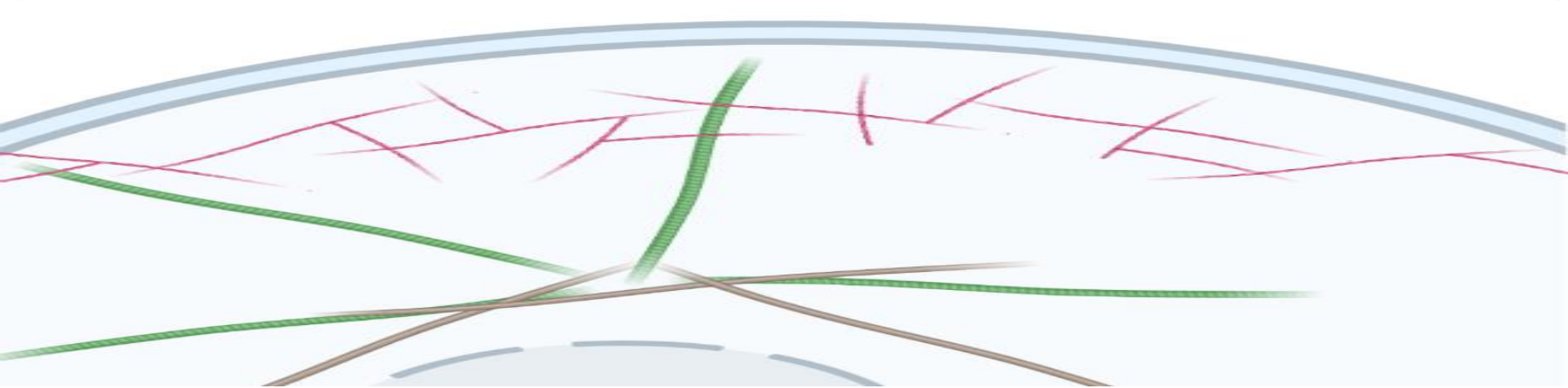




Cell and tissue mechanics

Motivation ...

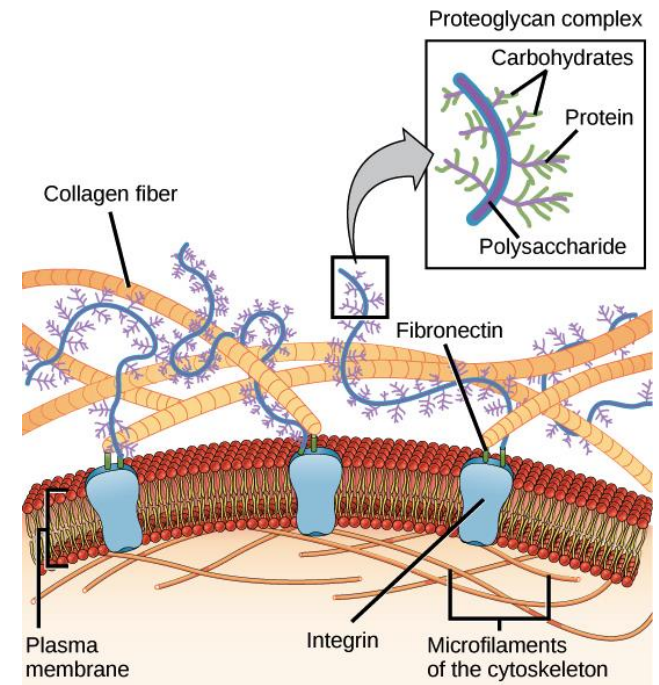
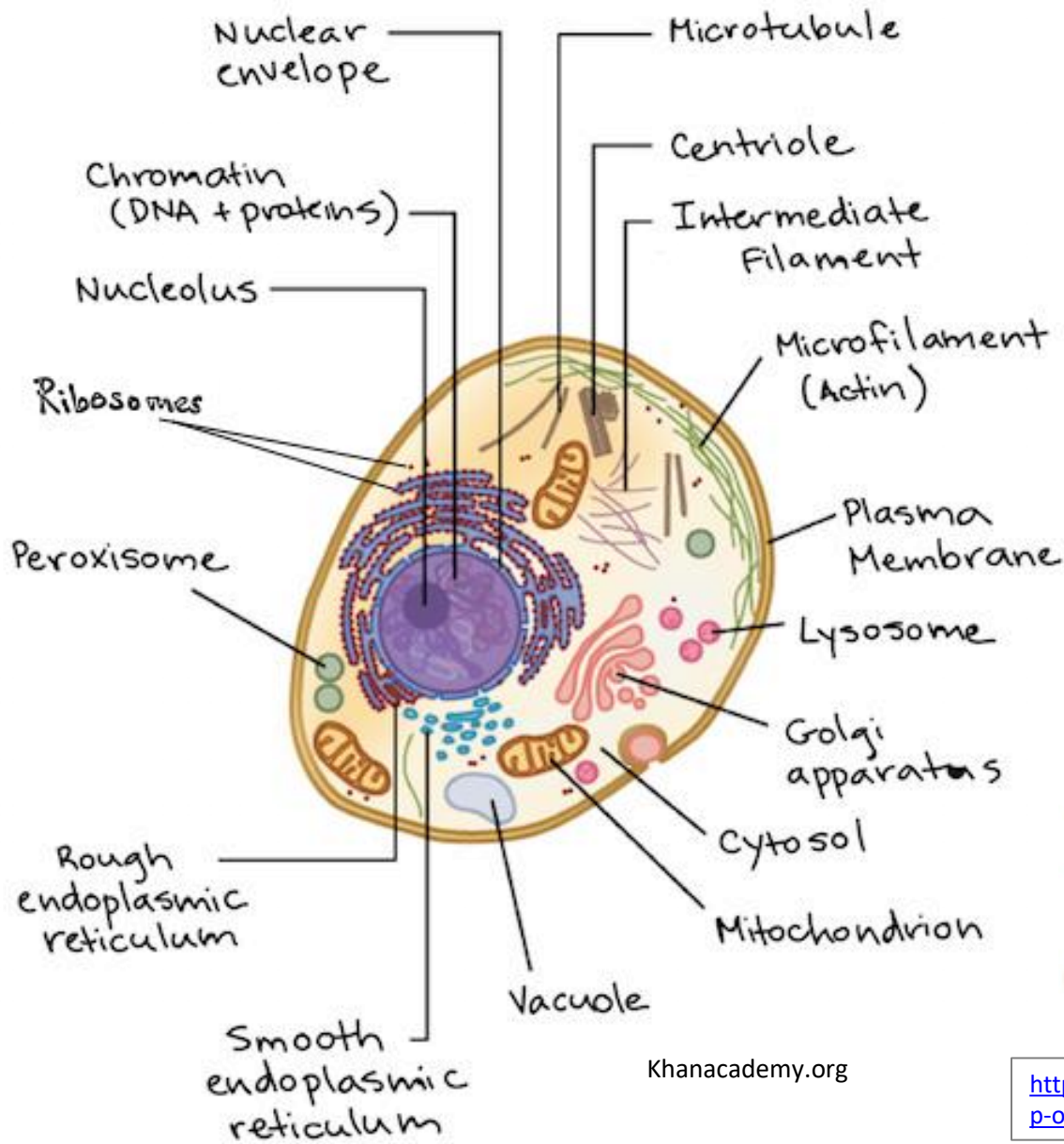


- What is cell mechanics?
- Why is it important?
- Why should we study it?
- How can we study it?
 - └→ methods?
- What kind of applications are there in this field?

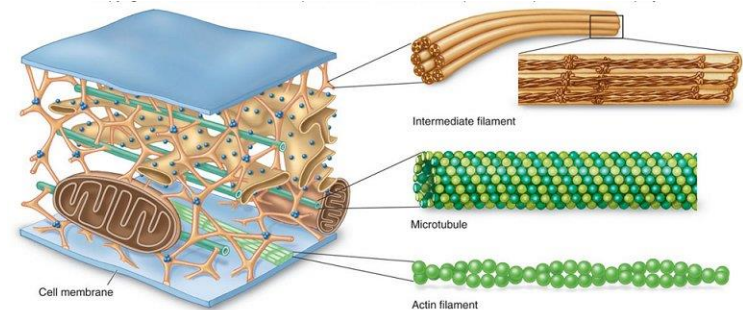
Outline



- Cell basics
- Molecular and structural basis of cell mechanics
- Presentation of some papers and research topics



Khanacademy.org



<https://thebuildingblocksofbiology.wordpress.com/category/friendship-of-animal-and-plant-cell-what-we-have-in-common/cytoskeleton/>

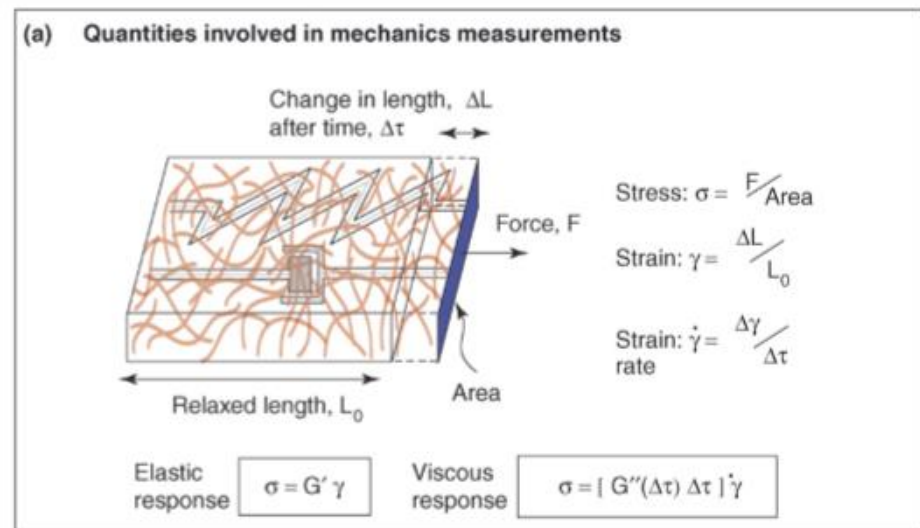
The cells in our body ...

- have a very dynamic nature
- Are extraordinarily amenable to adapting to changes, which
- Induce a physical and/or biochemical response

└→ cellular events (stiffening, maturation, morphological changes) or disease states (cancer, osteoporosis, asthma, glaucoma...)

The cell as a material

- Cells have both elastic and viscous properties
- The elasticity makes them resist deformation like a simple spring – the energy of deformation is stored in the material
- The viscosity allows them to flow as a fluid – the energy put into the deformation is dissipated



Weitz et al 2007

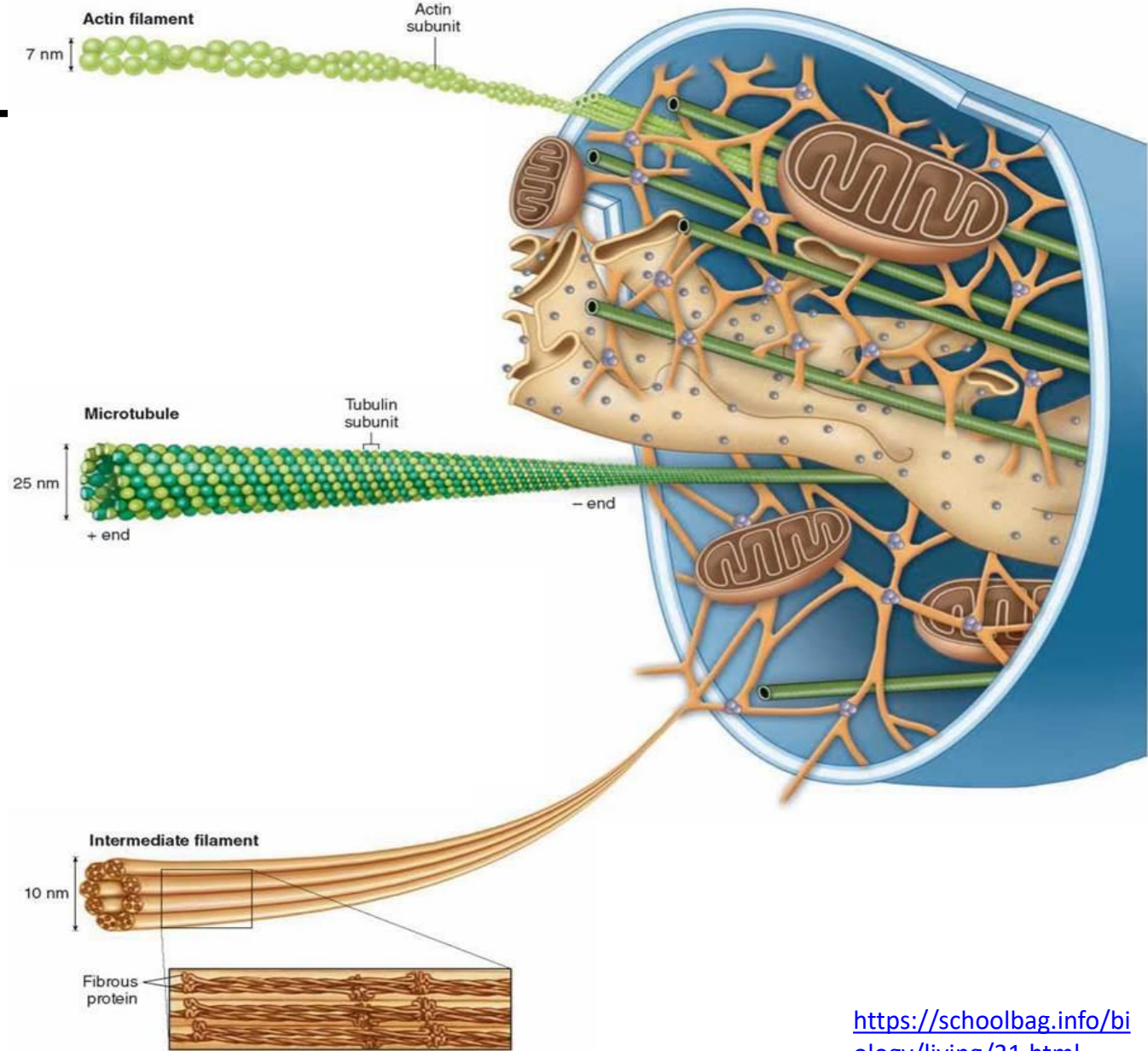
○ A biopolymer network - consisting of three major components

- Actin filaments
- Intermediate filaments
- Microtubules

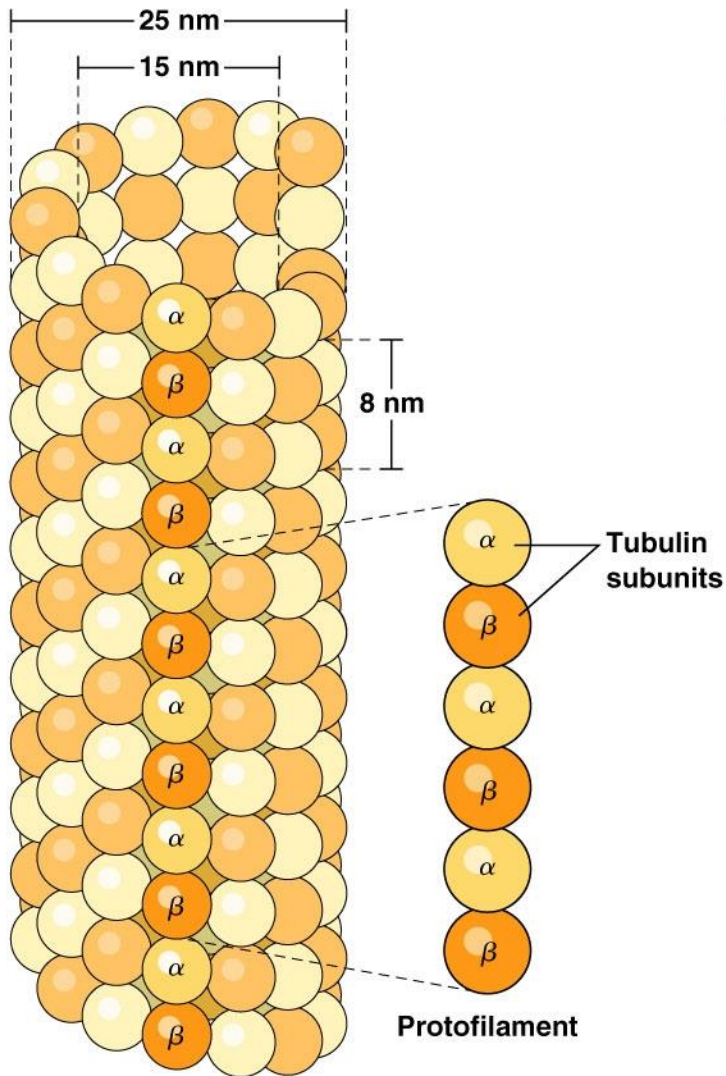
○ Lego like structures



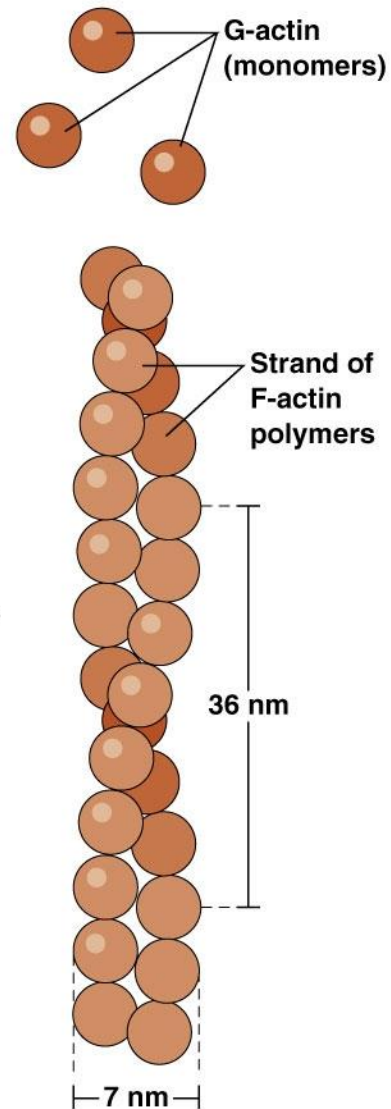
○ A dynamic network that can resist deformation



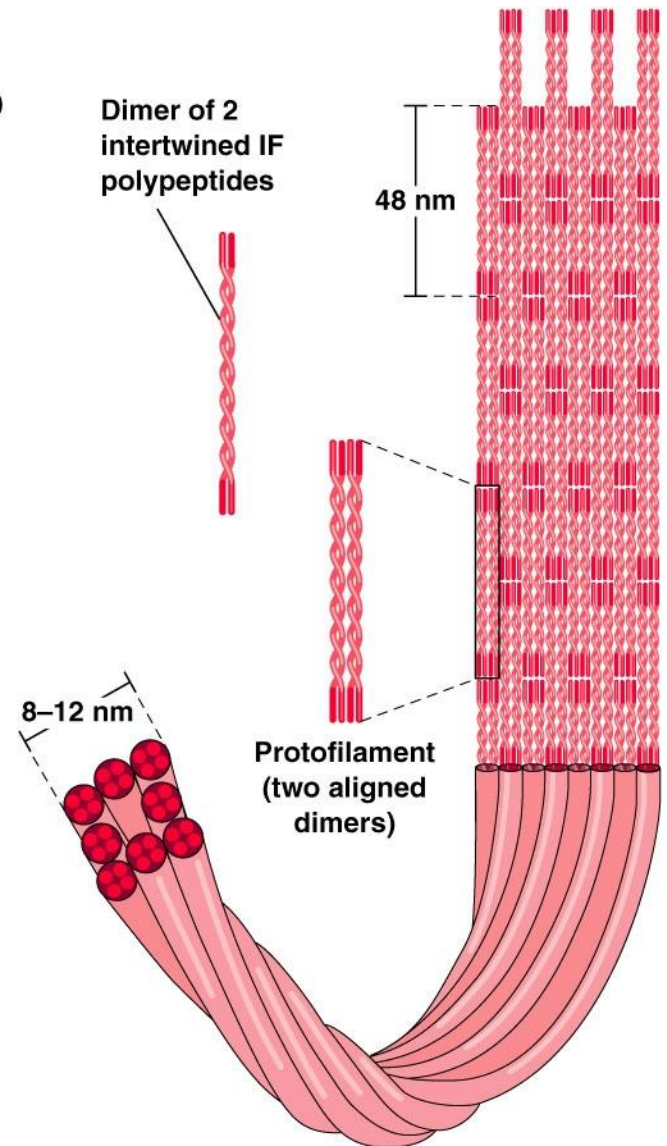
<https://schoolbag.info/biology/living/31.html>



(a) Microtubule



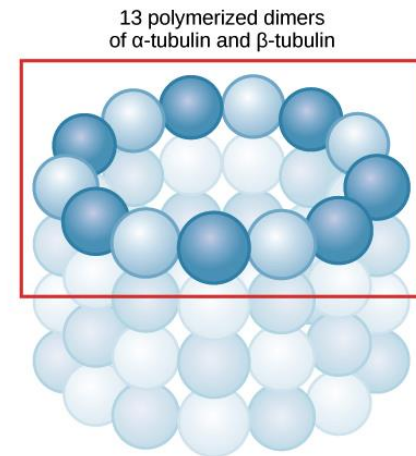
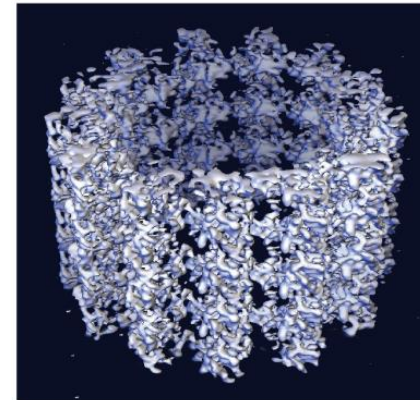
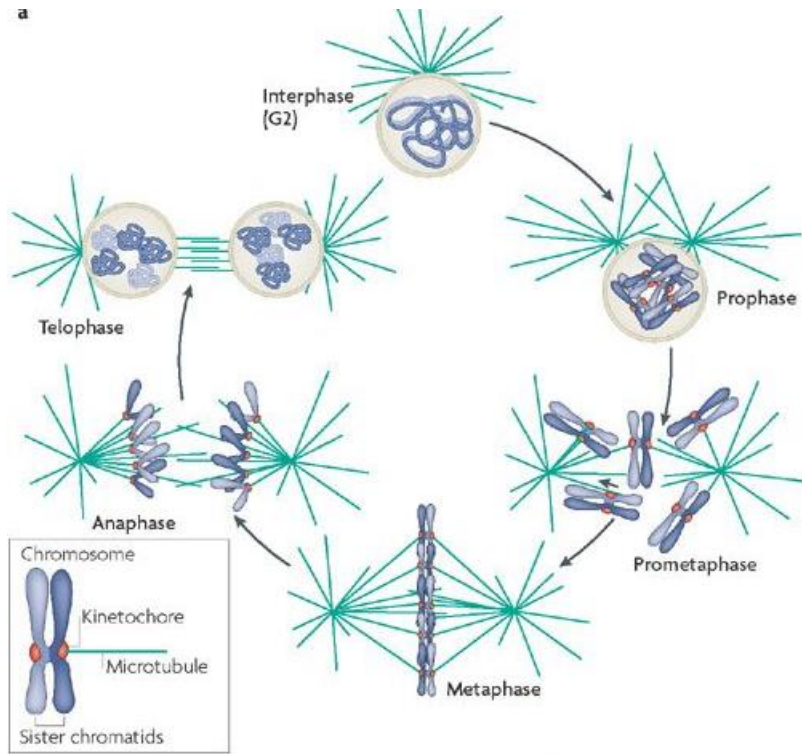
(b) Microfilament



(c) Intermediate filament

The cytoskeleton

Microtubules – $P \sim 5\mu\text{m}$, form linear tracks that span the length of a cell

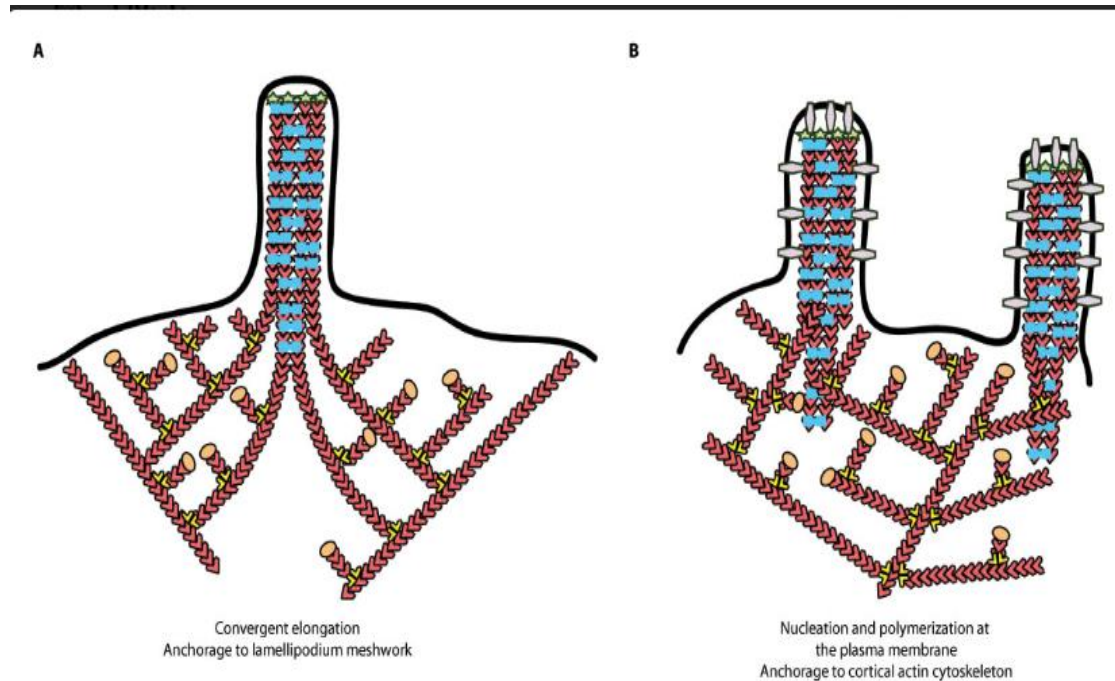


<https://www.quora.com/How-do-microtubules-attach-to-chromosomes-during-mitosis>

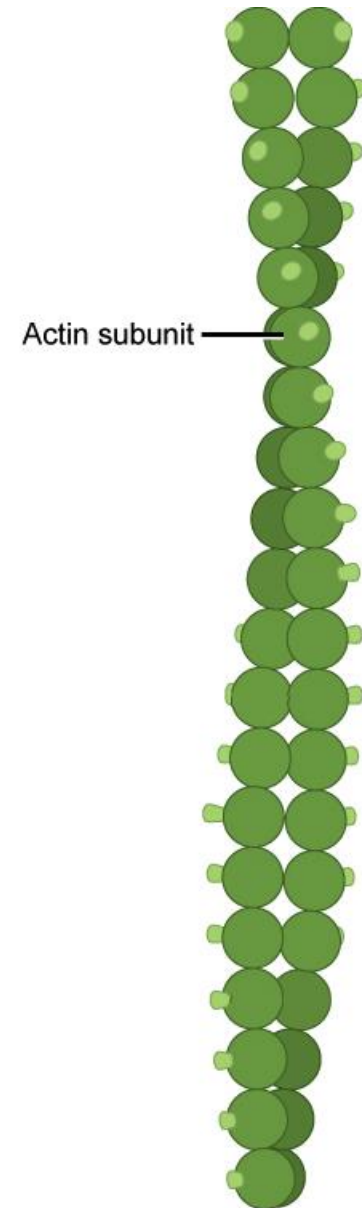
Molecular and structural basis of cell mechanics

The cytoskeleton

Actin filaments – less rigid than microtubules, but highly organized, stiff structures due to high C of cross-linkers

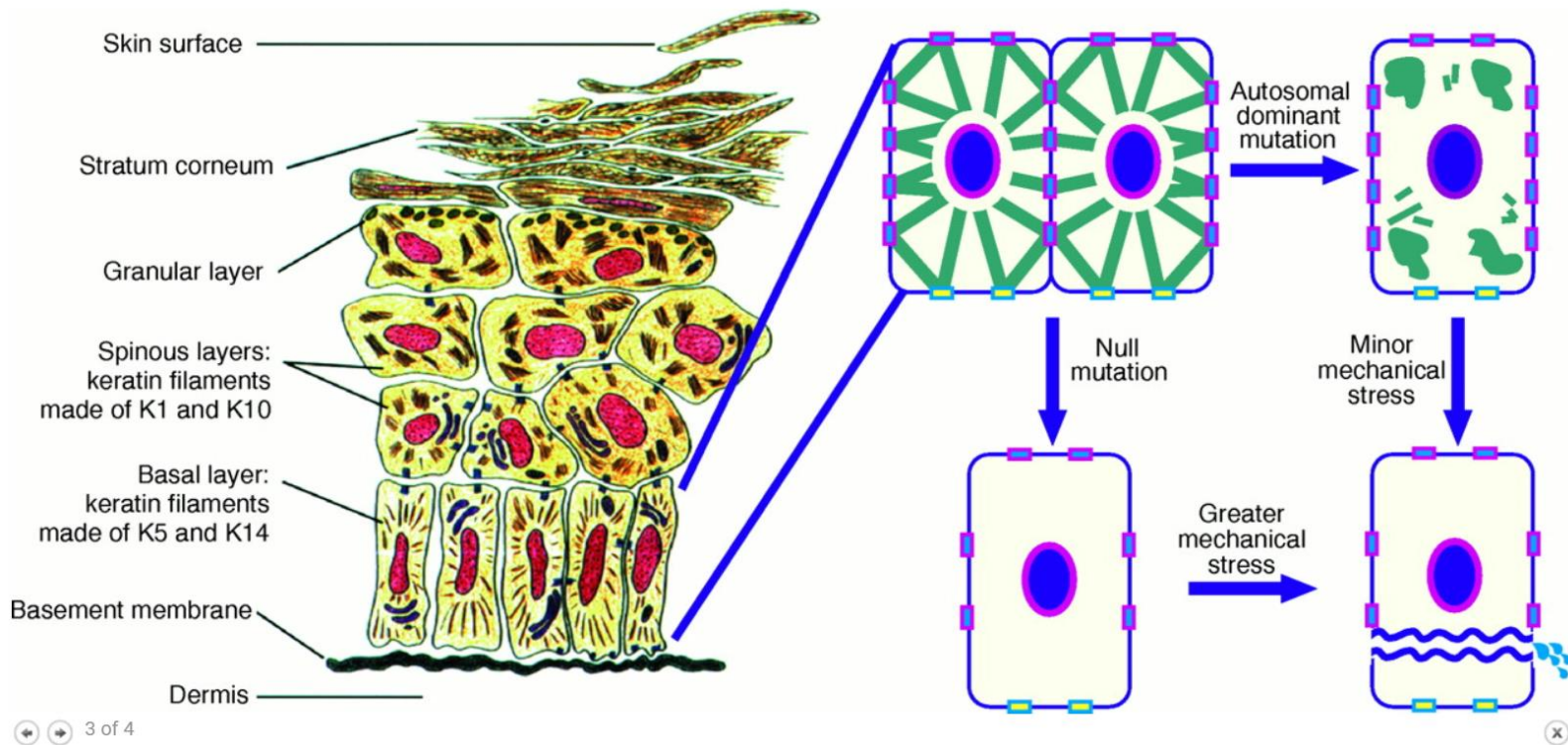


Gupton et al, 2007



The cytoskeleton

Intermediate filament – least stiff of all three. Cross-linked to each other forming networks

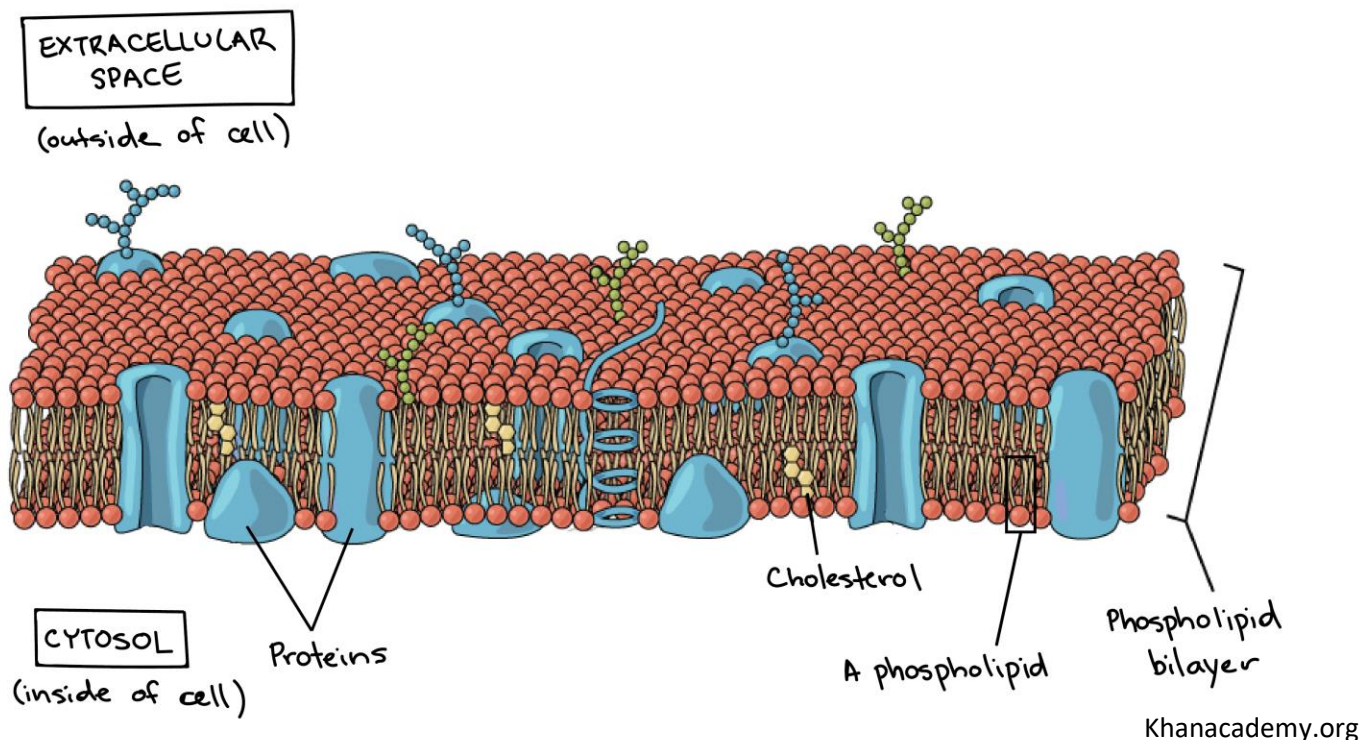


<https://science.sciencemag.org/content/279/5350/514/tab-figures-data>

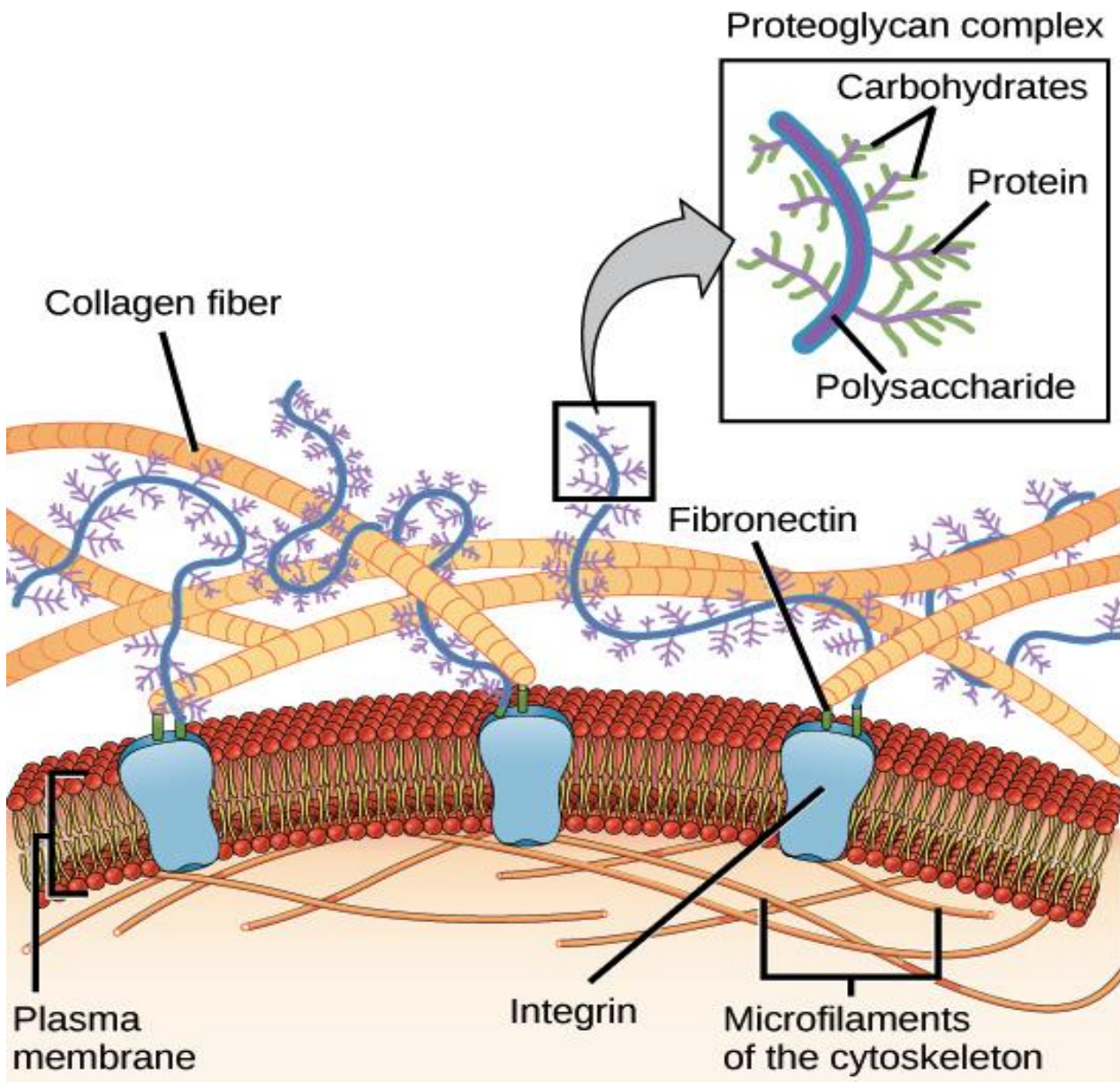
The cytoskeleton

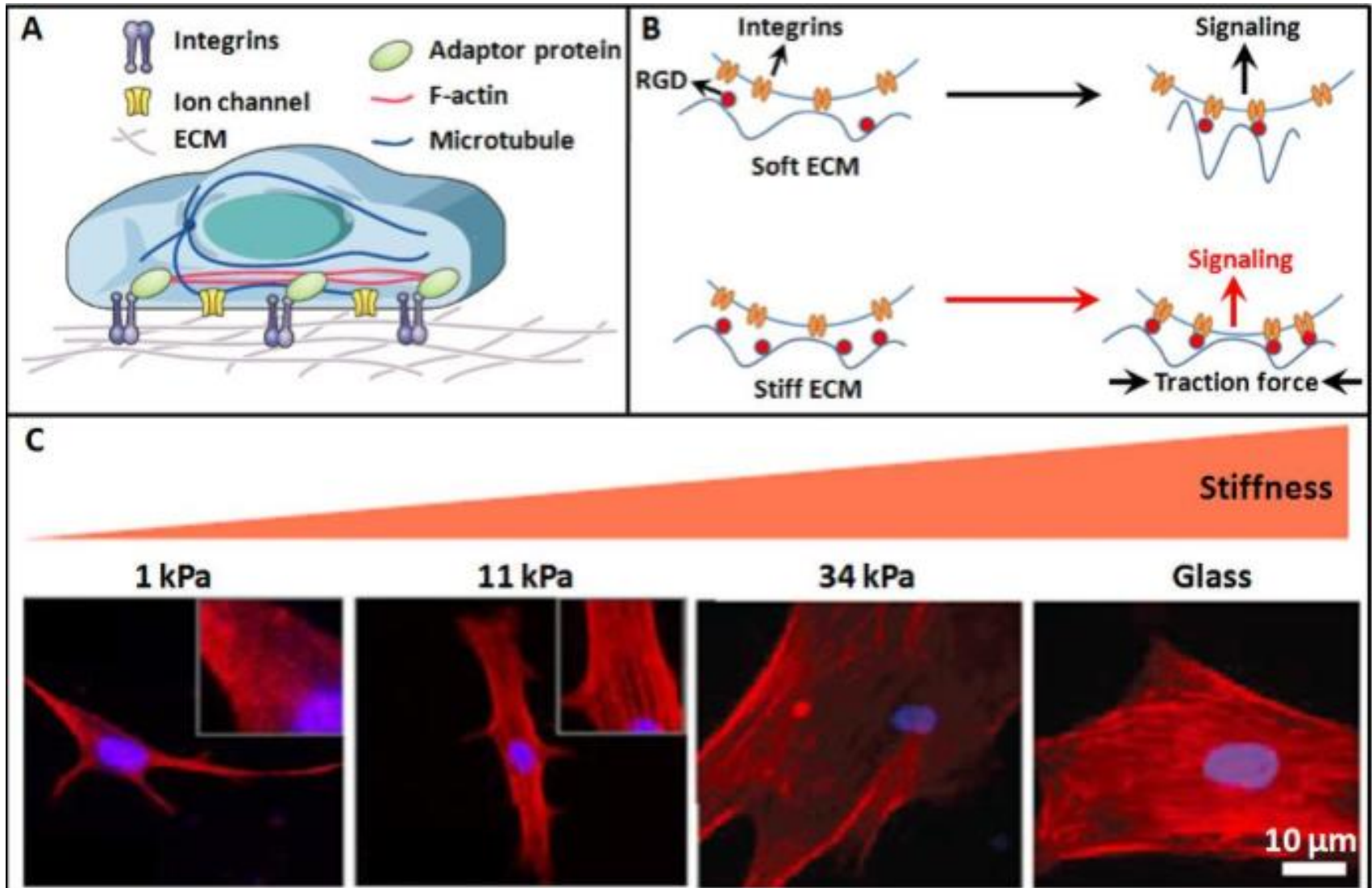
- ✓ Establishes order in the cytoplasm
 - ✓ Turns seemingly chaotic collection of molecules into highly organized living cells
 - ✓ Determines the cell stiffness
- Stiffness of diseased cells can be dramatically different (e.g. cancer cells or sickle red blood cells)

- Adhesion of the cell to the ECM results in structural organization of the cell itself
- Cell – matrix and cell – cell interactions are important in maintaining structural and functional integrity
- Sensing and assessing of the microenvironment



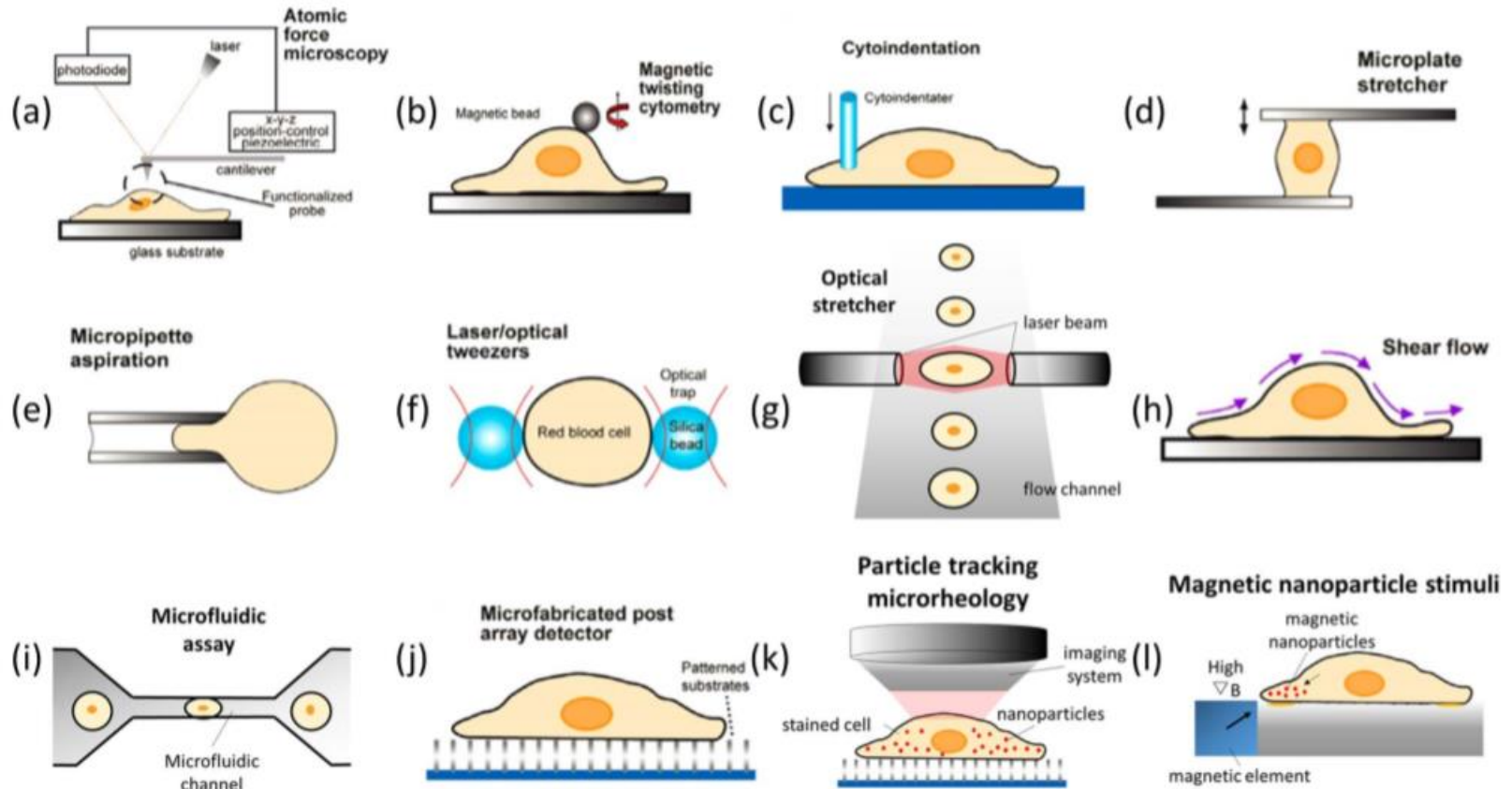
- Complex network of mechanotransduction influences the chemical properties and biological functions of cells
- Force propagation from ECM to the nucleus might take up to 1ms
- Different behaviors result in altered cellular responses





Li et al., 2017

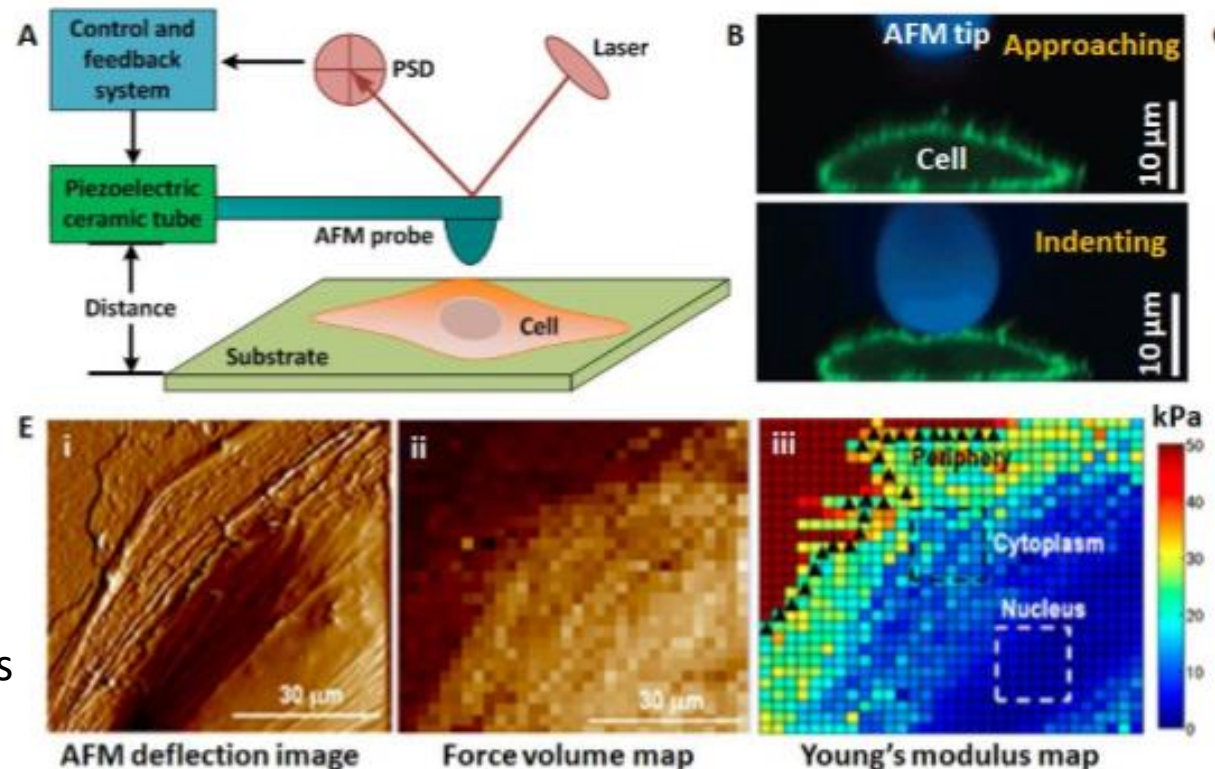
Conventional analysis and imaging methods for studying cell mechanics



Unal et al., 2014

Atomic force microscopy - AFM

- AFM is a powerful tool for simultaneously obtaining structural and mechanical information of a single cell
- Force volume mode vs. peak force tapping mode
- Real-time analysis yields multiple parameters that reflect the physical properties

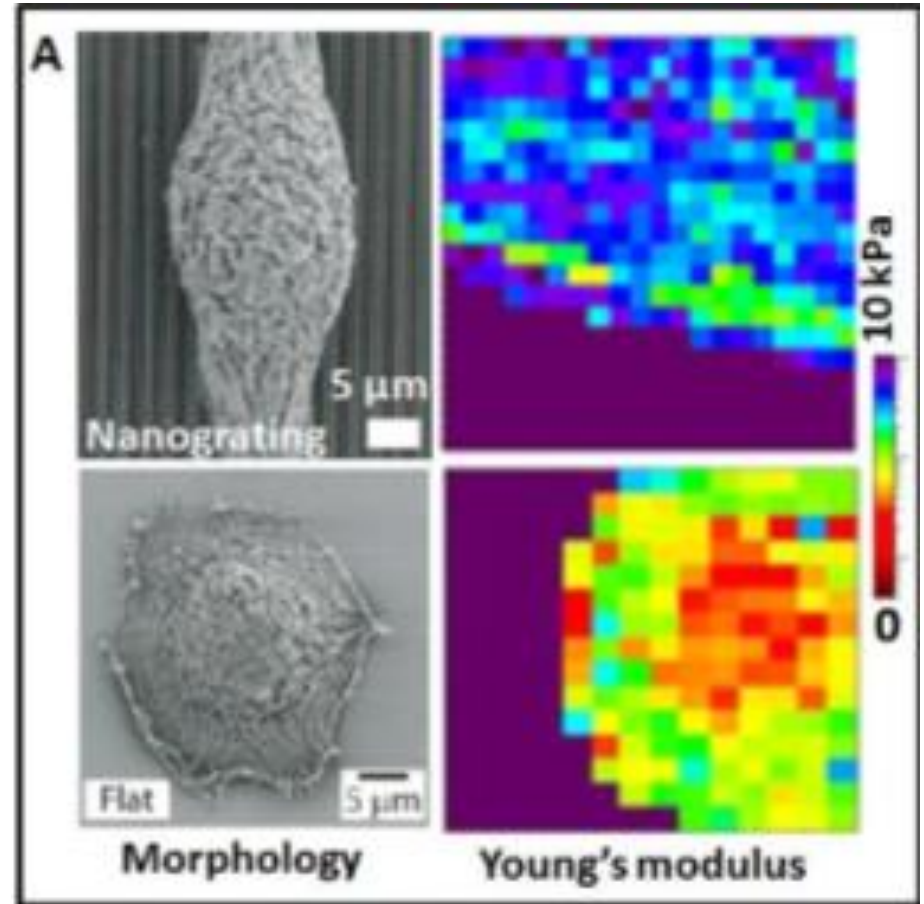


Unal et al., 2014

Mechanical changes of cells in response to external stimuli

A. Substrate topography

- Cellular, morphological changes are often accompanied with cellular mechanical changes
- Nano-topography of the substrate influences diverse cell behavior
- Important for the field of regenerative medicine

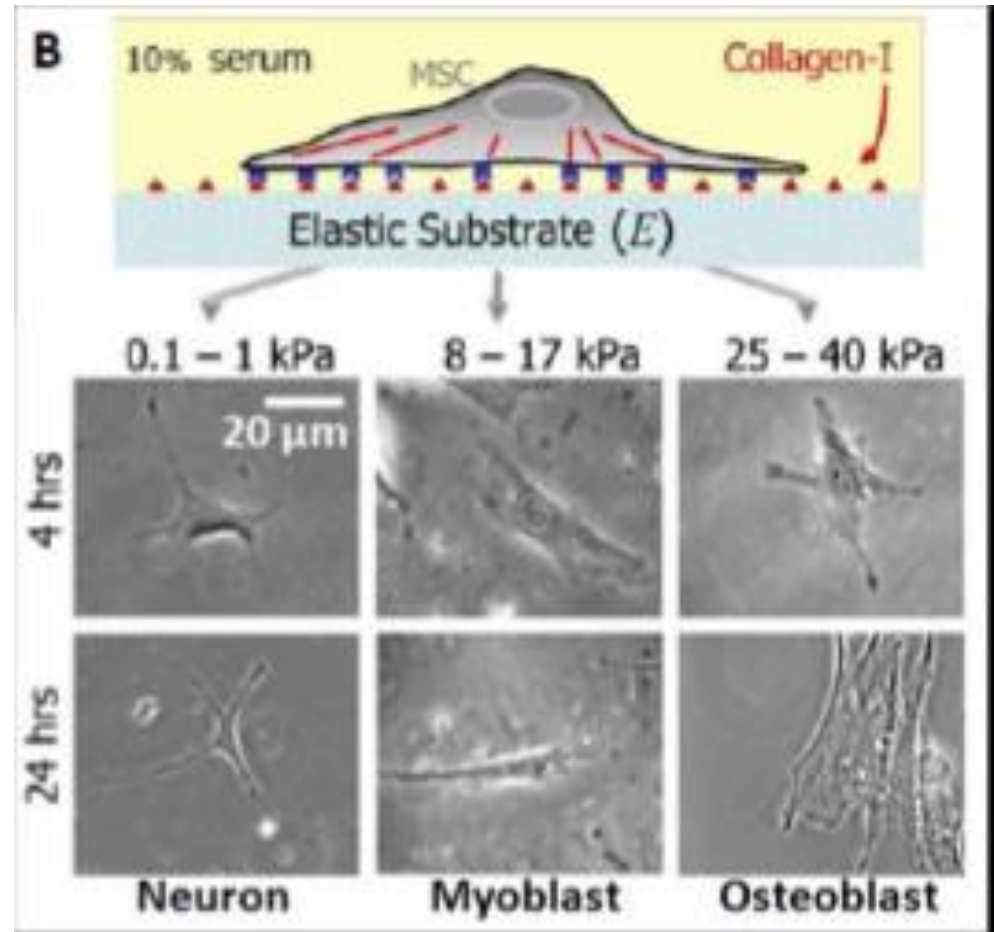


Rianna et al., 2015

Mechanical changes of cells in response to external stimuli

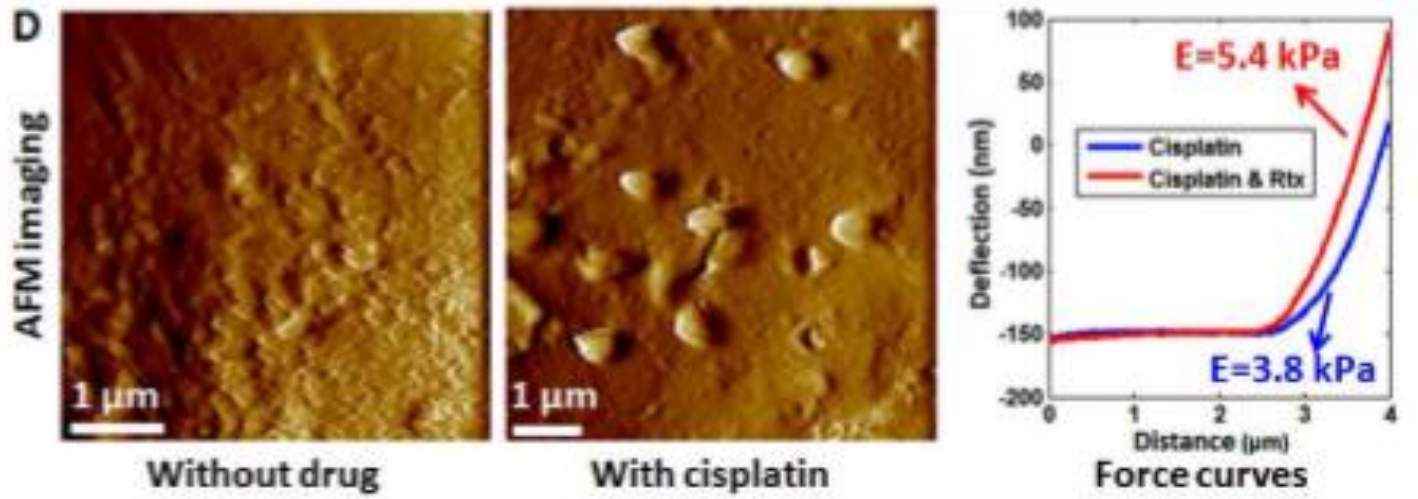
B. Substrate stiffness

- The stiffness of the substrate has an important effect on cell behaviour
- Combination of substrate stiffness and specific ECM guides the stem cell lineage specification
- A landmark study by Engler et al



Engler et al., 2006

Mechanical changes of cells in response to external stimuli



Wang et al., 2007

C. Drug stimulation

- Mechanical changes of cells after stimulation of drugs
- Lymphoma cells after treatment with two chemotherapy drugs and one targeted drug
- Significant morphological changes

Literature

1. Weitz et al: Current Opinion in Cell Biology 2007, 19:101–107
2. Daniel A. Fletcher & R. Dyche Mullins: Cell mechanics and the cytoskeleton 2010, Vol 463/28
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6. Unal et al: Micro and Nano-scale technologies for cell mechanics, DOI: 10.5772/59379
7. Wang et al: Atomic Force Microscopy in Characterizing Cell Mechanics for Biomedical Applications: A Review 2017, DOI 10.1109/TNB.2017.2714462