LECTURE 7: SINGLE CELL MECHANICS

Outline :

Objectives: To understand the fundamentals of single cell mechanics, in particular the structural components and how they are typically modeled

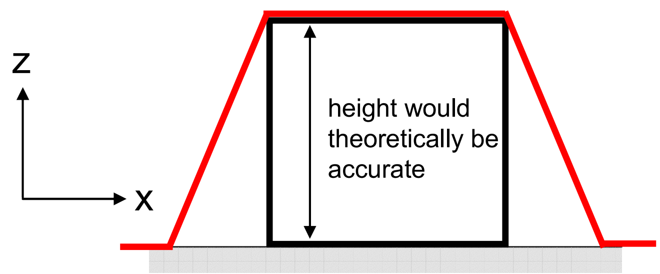
Readings: Dao, et al. J. Mech. Phys. Solids 51 (2003) 2259-2280 (a "Supplementary Resource"-not in course reader).

Multimedia : Listen to "Malaria" Podcast corresponding to journal article : Suresh, et al. *Acta Biomaterialia* **2005** 1, 15, 2)

ATOMIC FORCE MICROSCOPY : ARTIFACTS AND APPLICATIONS

●**Factors affecting spatial resolution**; piezo amplifier, sensor, and control electronics, mechanical parameters; specimen deformation and thermal fluctuations, adhesion force, cantilever thermal noise, probe tip sharpness; tip deconvolution

2D Height Profile



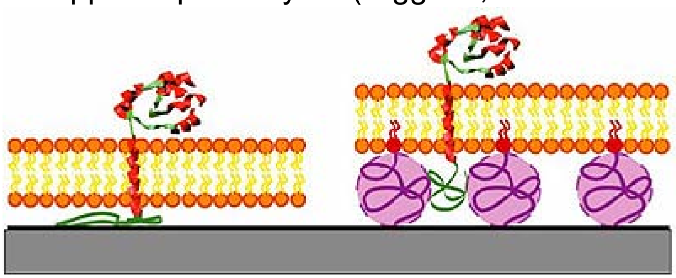
$$\tan(\theta) = \frac{x}{w} \rightarrow x = w\tan(\theta)$$

$$r^* = \frac{w}{2} + w\tan(\theta)$$

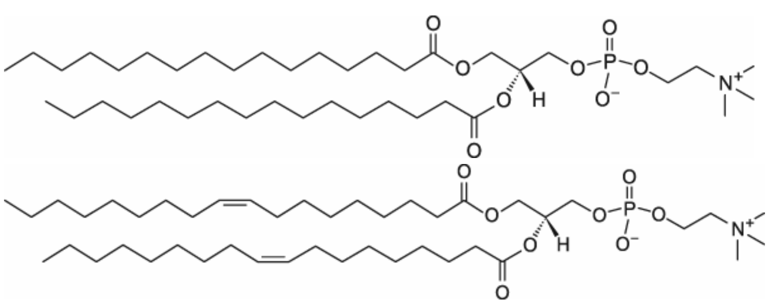
$$\frac{r^*}{w} = \frac{1}{2} + \tan(\theta)$$

3 Applications :

- AFM Imaging of Biological Macromolecules (DNA)
- Bone Implant Materials : AFM combined with HRFS : Spatially Specific Measurements
- Support Lipid Bilayers (Higgens, et al. Structured Water Podcast)



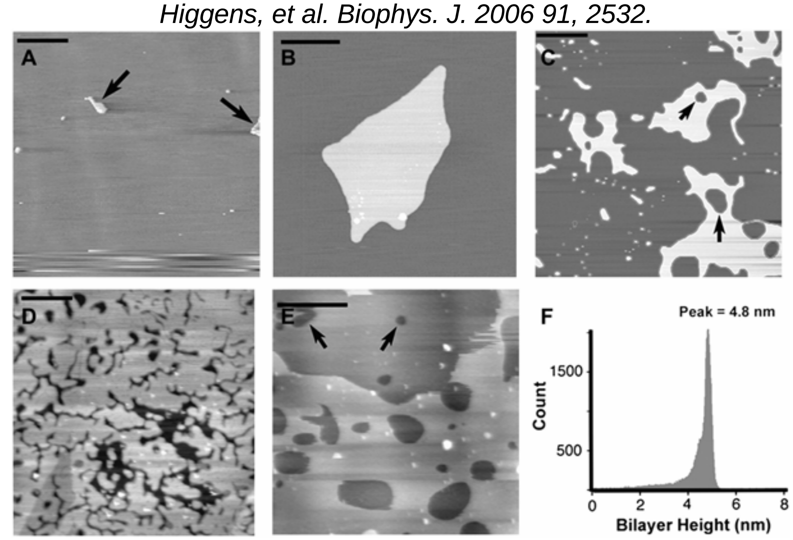
Courtesy of Lukas K. Tamm and the Biophysical Society. Used with permission.
See Wagner, M., and L. K. Tamm. *Biophysical Journal* 79 (2000): 1400-1414.



DPPC

DOPC

Higgens, et al. Biophys. J. 2006 91, 2532.



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THE NANOMANIPULATOR (UNC Chapel Hill)

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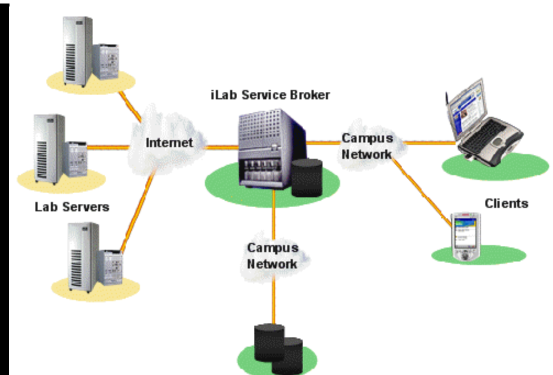
See http://www.cs.unc.edu/Research/nano/cismm/come.html.

A **3D virtual reality visual interface** is provided to the microscope that is similar to looking at a real human-scale physical surface (essentially magnifying the object under study up to a million times) with a **"haptic" display** (a Phantom forcefeedback device) or "touch" interface similar to operating on a human-scale materials with a hand-tool such as a pencil, scalpel, or broom.

The scientist can **guide the tip directly in order to feel the surface** and can increase the force used in order to **modify the sample**. Haptic feedback guides the progress of an experiment. This system allows the scientist to see, touch, and manipulate it directly.

- More **intuitive** data interpretation (**sense of touch**) to allow scientists to more readily understand data, better control over nanomanipulation.

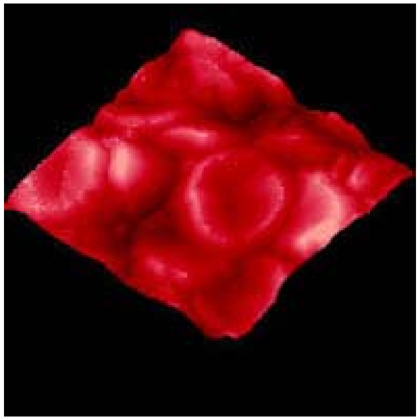
Remote experimentation - MIT iLabs: Internet access to real labs - anywhere, anytime (*http://icampus.mit.edu/ilabs/*) :



SINGLE CELL AFM IMAGING

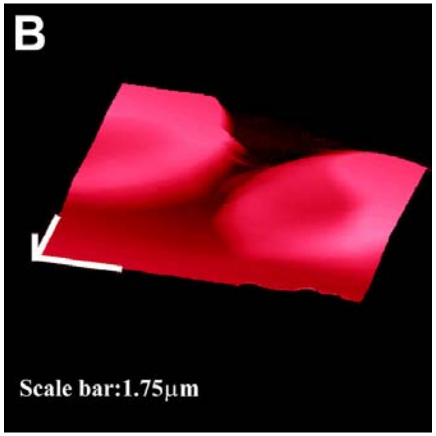
Contact mode image of **human red blood cells** - note cytoskeleton is visible. blood obtained from Johathan Ashmore, Professor of Physiology University College, London. A false color table has been used here, as professorial blood is in fact blue.

Courtesy of Mervyn J. Miles. Used with permission.

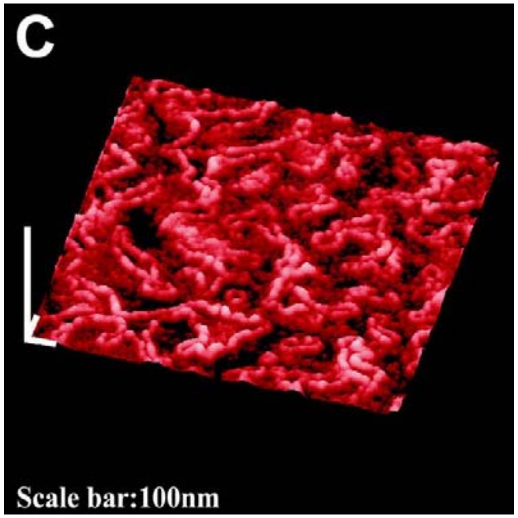


Red Blood Cells

Shao, et al., : http://people.virginia.edu/~zs9q/zsfig/random.html



Courtesy of Zhifeng Shao. Used with permission.



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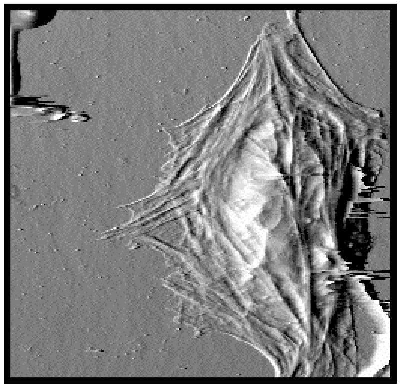
Courtesy of Manfred Radmacher. Used with permission.



Radmacher, et al., **Cardiac Cells**
http://www.physik3.gwdg.de/~radmacher/

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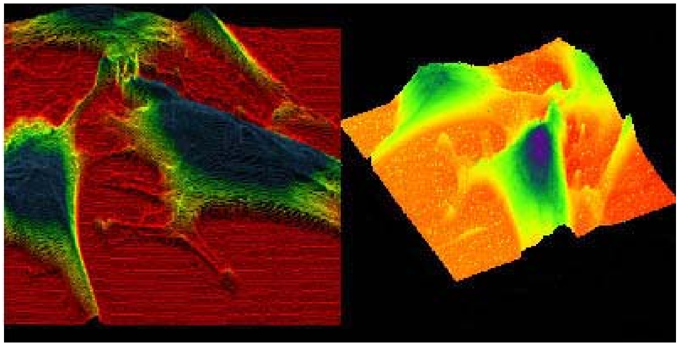
Rat Embryo Fibroblast *(*M. Stolz,C. Schoenenberger, M.E. Müller Institute, Biozentrum, Basel Switzerland)*



Height image of **endothelial cells** taking in fluid using Contact Mode AFM. 65 μm scan courtesy J. Struckmeier, S. Hohlbauch, P. Fowler, Digital Intruments/Veeco Metrology, Santa Barbara, USA.

Courtesy of Veeco Instruments. Used with permission.

SINGLE CELL MECHANICS : MOTIVATION *(Bao, et al 2003 Nature Materials.)*

Mechanical forces are essential to living cells!

Examples **:**

-**Musculoskeletal Tissues** : Cells in our tissues (e.g. cartilage, bone) are subjected to physiological stresses/strains which are a critical determinant of remodeling. Nonphysiological stress states result in cellular dysfunction producing diseased states (i.e. ACL tear→osteoarthritis).

-**Circulatory System** : Human red blood cell (RBC's) (diameter ~ 8 μm) experience 100% elastic deformation as blood flows through narrow capillaries, must deform repeatedly reversibly ~half million times- deformability is critical to RBC circulation!! 120 day lifetime; aged and defective RBCs with decreased deformability are detected and removed from circulation by the spleen.

See http://www.denniskunkel.com/product_info.php?products_id=712

D. Kunkel Microscopy, Inc.

Biomechanics Fung, 1993.

See http://nmhm.washingtondc.museum/news/imgs/red_blood_cells_lg.jpg.

-**Brain** : Large fast strains of the axon of neuronal cells for example as a result of traumatic brain injury causes cell death while slow stretching of the axon promotes neural cell growth.

EXPERIMENTAL METHODS FOR SINGLE CELL MECHANICS *(Bao, et al 2003 Nature Materials.)*

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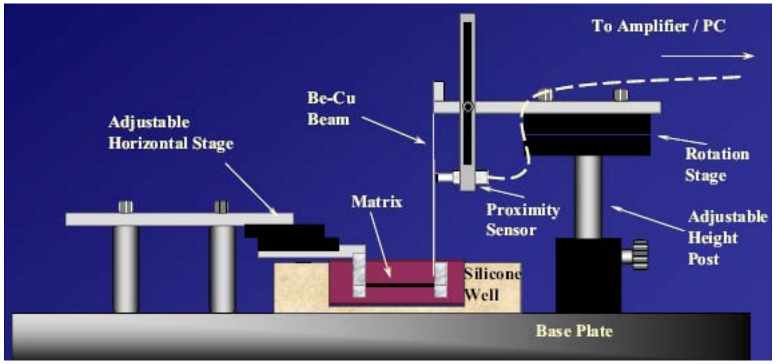
See Figure 2 in Bao and Suresh, *Nature Materials* 2, 715 - 725 (2003).

A, B a localized area of the cell is deformed

C,D mechanical loading of an entire cell

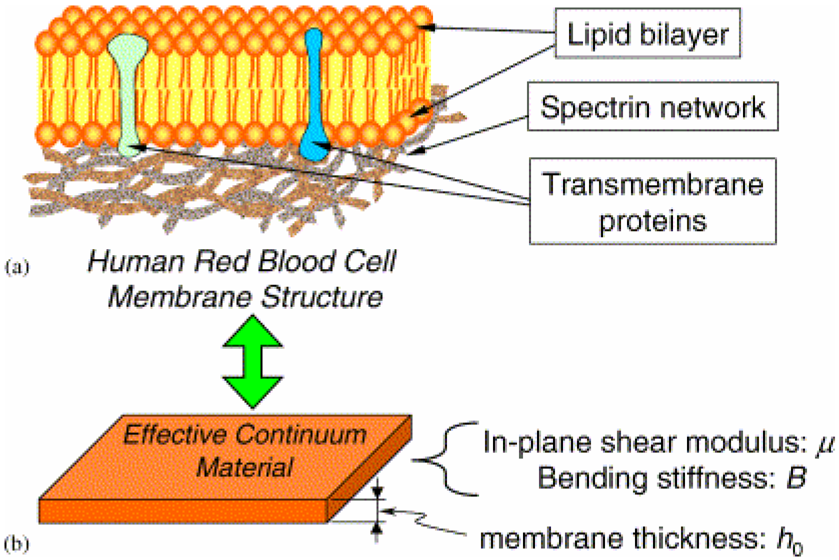
E, F, G simultaneous mechanical loading of a population of cells

G



Cell force monitor : *(B. Harley, L.J. Gibson, After Freyman 2001)*

MECHANICS OF SINGLE CELLS *(Bao, et al 2003 Nature Materials, Dao, et al 2003 J. Mech. Phys. Solids.)*

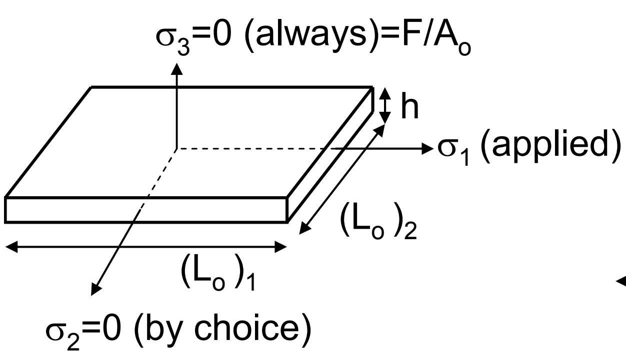


See Figure 1c in Bao and Suresh, *Nature Materials* 2, 715 - 725 (2003).

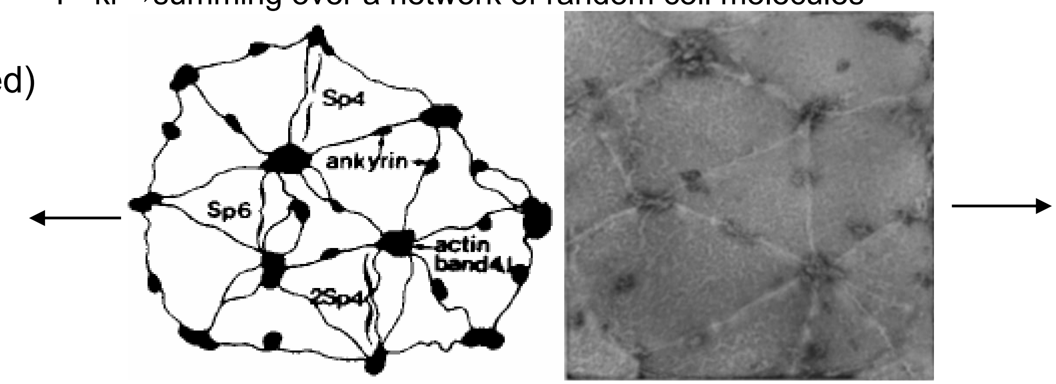
- The cell is surrounded by a lipid bilayer that provides little mechanical strength.
- The cell stiffness is largely determined by the cytoskeleton.
- The composite is modeled as an isotropic, elastic, continuum, incompressible (constant volume), constant surface area

MECHANICS OF SINGLE CELLS *(Dao, et al 2003 J. Mech. Phys. Solids.)*

Constitutive Law : stress vs. strain relationship that describes a particular material



Single macromolecule Gaussian linear elastic Hookean spring
F=kr→summing over a network of random coil molecules



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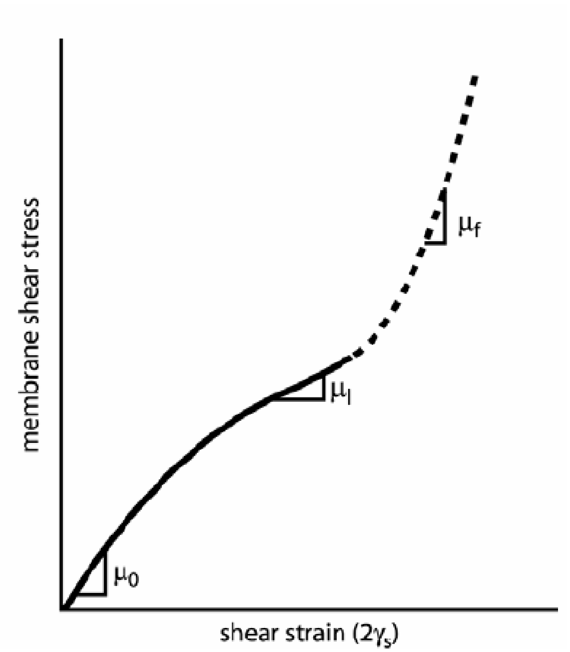
[1]Mohandas, Narla; Evans, Evan: Mechanical properties of the red cell membrane in relation to molecular structures and genetic defects. Annu. Rec. Biophys. Struct. 1994. 23:787-818



$$\underbrace{U}_{\text{Strain energy of a 3D rubber elastic network}} = \underbrace{\frac{G_o}{2}\left(\lambda_1^{\,2}+\lambda_2^{\,3}+\lambda_3^{\,2}-3\right)}_{\text{Neo-Hookean Rubber Elasticitry}} + \underbrace{C_3\left(\lambda_1^{\,2}+\lambda_2^{\,3}+\lambda_3^{\,2}-3\right)^3}_{\text{nonGaussian Nonlinear Strain Hardening Term}}$$

λ = extension or stretch ratio, $\lambda_1 = \dfrac{(L_f)_1}{(L_o)_1}, \lambda_2 = \dfrac{(L_f)_2}{(L_o)_2}, \lambda_3 = \dfrac{(L_f)_3}{(L_o)_3}$

G_o = shear modulus

uniaxial normal stress, $\sigma_n(\text{N/m}^2) = \dfrac{\partial U}{\partial \lambda_1}$

by definition

constant volume constraint = $\lambda_1\lambda_2\lambda_3$ $\rangle$ from definition of extension ratio & geometry