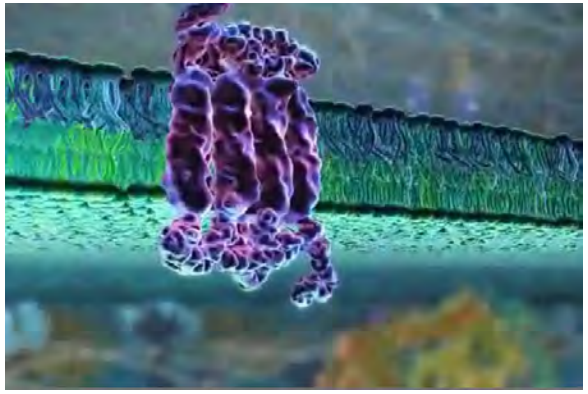
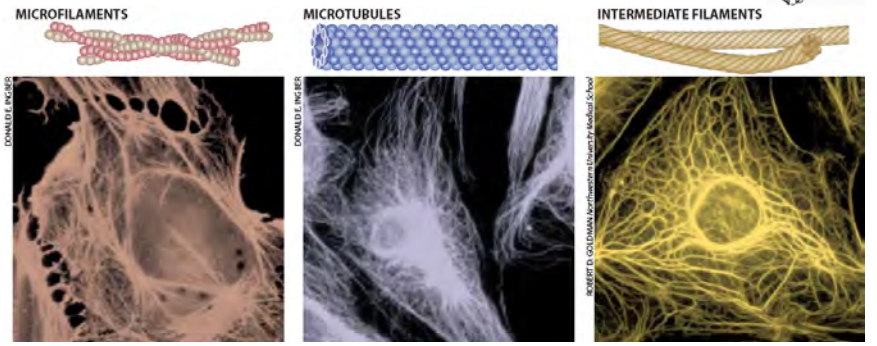
5.1 biomembranes - motivation



the inner life of a cell, viel & lue, harvard [2006]

tensegrity = tension + integrity

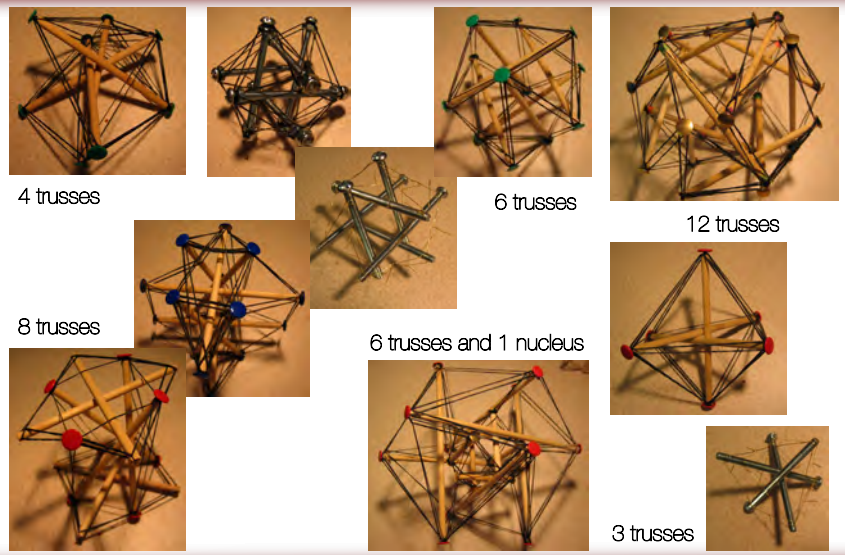


balanced interplay between tension and compression

ingber [1998]

tensegrity = tension + integrity

the term tensegrity was first coined by buckminster fuller to describe a structure in which **continuous tension** in its members forms the **basis for structural integrity**. fuller most famously demonstrated the concept of tensegrity in architecture through the **design of geodesic domes** while his student, the artist kenneth snelson, applied the concept of tensegrity to creating sculptures that appear to defy gravity. snelson's tensegrity sculptures are minimal in components and achieve their stability through dynamic distribution of tension and compression forces amongst their members to create internal balance. it was upon viewing snelson's art that donald ingber became inspired by the sculpture's structural efficiency and dynamic force balance to **adopt tensegrity as a paradigm** upon which to **analyze cell structure** and mechanics. it has been 30 years since the premier appearance of the cellular tensegrity model. although the model is still largely under discussion, empirical evidence suggests that the model may explain a wide variety of phenomena ranging from tumor growth to cell motility.



network kinematics

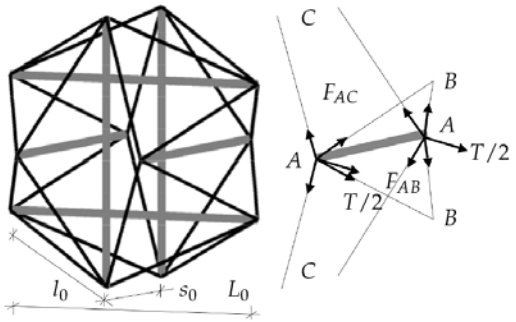
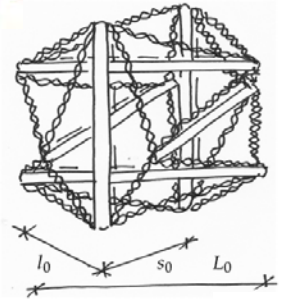


Figure 4.12: Kinematics of simple tensegrity cell model consisting of six compressive trusses (grey) and 24 tensile ropes (black). In the original state, all trusses are of the same length L_0, the rope lengths are $l_0 = \sqrt{3/8}\,L_0$, and the distances between two parallel trusses are $s_0 = 1/2\,L_0$.

tensegrity models for cells



E_0 ... incremental modulus
F_0 ... resting force in actin filaments
L_0 ... length of microtubules
l_0 ... resting length of actin filaments
ε_0 ... strain in actin filaments

$$W^{\text{mac}} \doteq W^{\text{mic}} \qquad W^{\text{mac}} = \frac{1}{2}\,\varepsilon\,E\,\varepsilon \qquad W^{\text{mic}} = \frac{1}{V_0}\int_{s_0}^{s_x} T\,\mathrm{d}x$$

$$E = \frac{2\sqrt{3}}{5\sqrt{2}l_0}\,\frac{T}{s_x - s_0} \qquad \text{small strain} \qquad E_0 = 5.85\,\frac{F_0}{l_0^2}\,\frac{1+4\,\varepsilon_0}{1+12\varepsilon_0}$$

prestress - analytically predicted

- assume prestress is approximately equal in all three directions

$$P \approx \tfrac{1}{3}\,\nu^{\text{actin}}\,\sigma^{\text{actin}}$$

- volume fraction of actin filaments

$$\nu^{\text{actin}} = \frac{V^{\text{actin}}}{V_0} = \frac{24A^{\text{actin}}l_0}{[5\sqrt{2}]/[3\sqrt{3}]l_0^3} = \frac{24A^{\text{actin}}}{1.3608l_0^2}$$

- stress in a typical actin filament

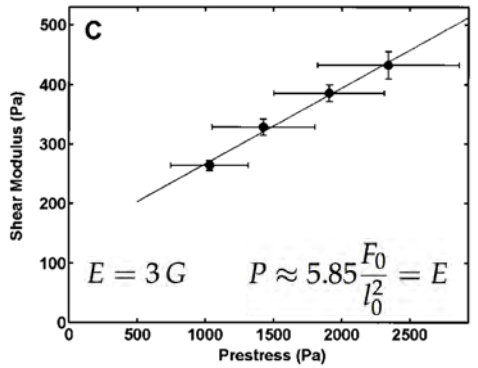
$$\sigma^{\text{actin}} = \frac{F_0}{A^{\text{actin}}}$$

- approximation of prestress

$$P \approx \frac{1}{3}\nu^{\text{actin}}\,\sigma^{\text{actin}} = \frac{1}{3}\,\frac{24\,A^{\text{actin}}}{1.3608l_0^2}\,\frac{F_0}{A^{\text{actin}}} \qquad P \approx 5.85\frac{F_0}{l_0^2} = E$$

prestress is of the same order as young's modulus

prestress - experimentally measured



prestress is of the same order as young's modulus

wang, naruse, stamenovic, fredberg, mijailovich, tolic-norrelykke, polte, mannix, ingber [2001]

the cell membrane

all cellular components are contained within a cell membrane which is **extremely thin**, approximately 4-5nm, and **very flexible**. inside the cell membrane, most cells behave like a liquid as they consist of more than 50% of water. the cell membrane is **semi-permeable** allowing for a controlled exchange between intracellular and extracellular components and information.

mechanisms of transport through the membrane

- passive transport driven by gradients in concentration
- active transport that does require extra energy; it is regulated by ion channels, pumps, transporters, exchangers and receptors

the cell membrane

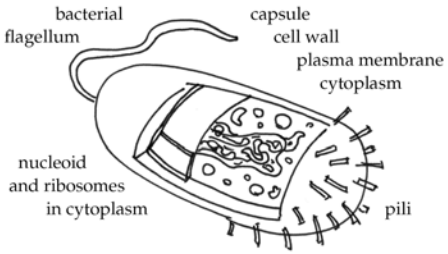
the barrier between the inner and outer cell is the cell membrane, a **bilayer** consisting of **phospholipids** of a characteristic structural arrangement. in aqueous solutions, these phospholipids essentially display two kinds of non-covalent interactions.

non-covalent interactions of phospholipids

- hydrophobic, water avoiding non-polar residues
- hydrophilic, water loving polar head groups

this behavior is similar to fatty acids or **oil in water**, where the hydrophilic polar heads tend to be oriented towards the water phase while the hydrophobic tails are oriented towards the oil phase.

the cell wall



in most cells, the **internal pressure** is much higher than the surrounding pressure. the cell membrane thus has to be strong enough to **prevent the explosion** of the cell. plant cells and most bacteria have found an efficient solution to withstand the internal pressure: their cells have an **external wall** to reinforce their cell membrane and balance the pressure difference across it.

the lipid bilayer

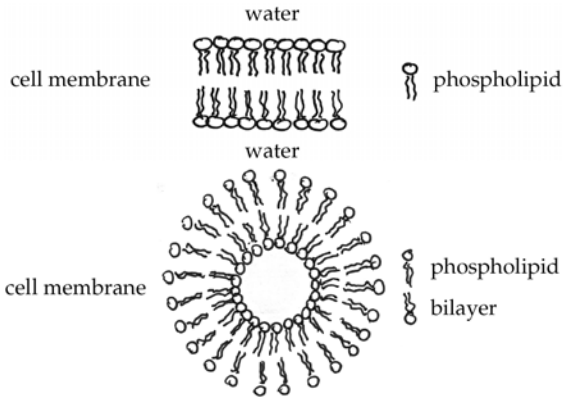


Figure 5.16. Lipid bilayer of the cell membrane. Characteristic arrangement of phospholipid molecules with hydrophilic polar head group being oriented towards the aqueous phase while the hydrophilic tails are oriented towards the non-polar inside.

the lipid bilayer

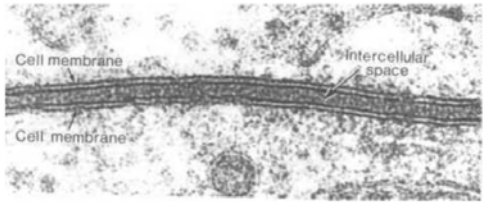


Figure 5.1: Electron microscopy of the cell membrane stained with osmium tetroxide illustrating the polar head groups with a light 2nm space of hydrophobic tails sandwiched between them, adopted from [4]

the cell membrane

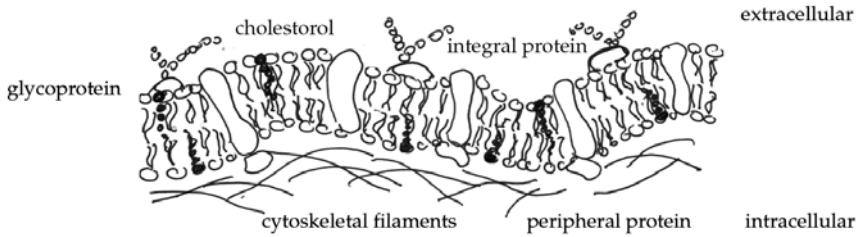


Figure 1.3. Cell membrane. Phospholipic bilayer with hydrophobic water-avoiding tails and hydrophilic water-loving heads.

the lipid bilayer

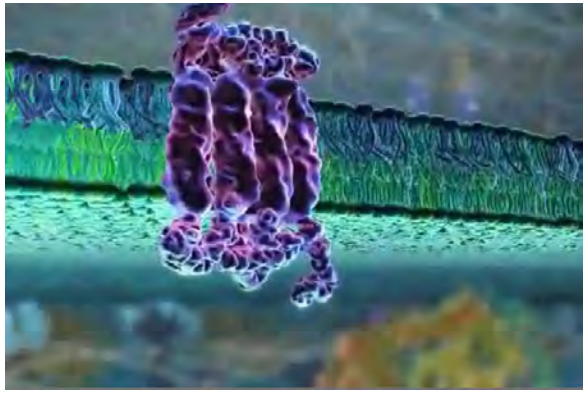


Figure 1.5.1. Lipid bilayer of the cell membrane. Characteristic arrangement of phospholipid molecules with hydrophilic polar head group being oriented towards the aqueous phase while the hydrophilic tails are oriented towards the non-polar inside.

the inner life of a cell, viel & lue, harvard [2006]

the lipid bilayer - lipid rafts

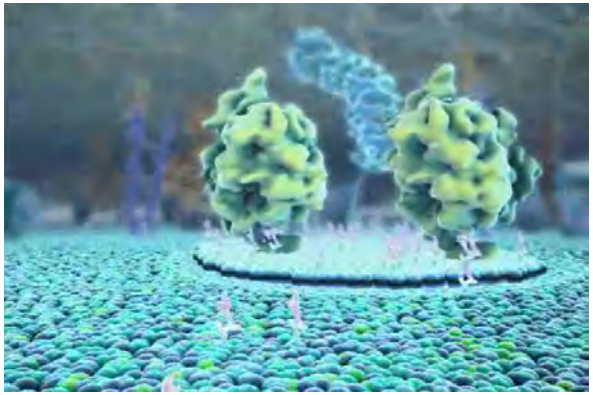


Figure 1.5.2. The lipid bilayer of the cell membrane is by no means static and homogeneous. Lipids are a class of molecules stacking together to form the membrane which can be understood as a sea on which things are floating. The rafts floating on this sea are called lipid rafts.

the inner life of a cell, viel & lue, harvard [2006]

micropipette aspiration

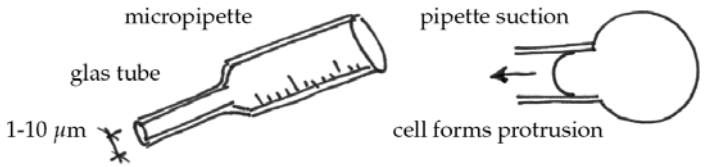


Figure 5.2: During micropipette aspiration, a cell is aspired into a thin glass tube. Knowing the applied suction pressure, we can determine the surface tension of the cell based on changes in cell geometry.

micropipette aspiration

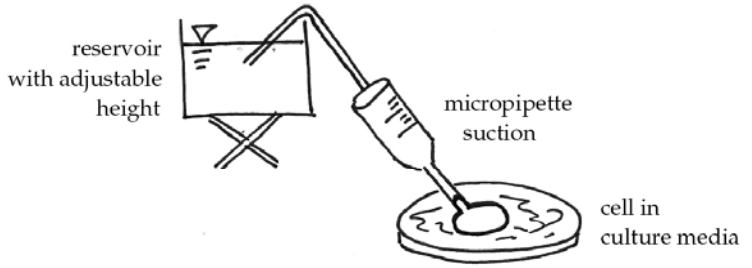


Figure 5.3: Experimental setup of micropipette aspiration. The applied suction pressure can be varied by adjusting the height of a fluid filled reservoir. Cell deformation is measured optically.

micropipette aspiration

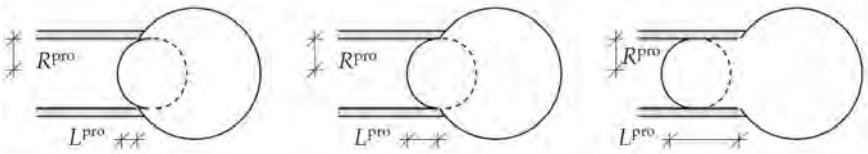


Figure 5.4: The three stages during mircopipette aspiration. The initial state with $L^{pro}/R^{pro} < 1$, left, the critical state with $L^{pro}/R^{pro} = 1$, middle, and the final state with $L^{pro}/R^{pro} > 1$, right.

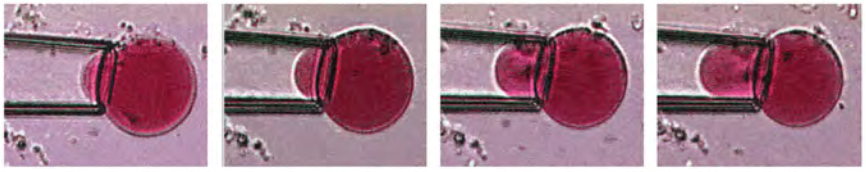


Figure 5.5: Experimental observation of different stages during micropipette aspriation adopted from http://newton.ex.ac.uk/research/biomedical/membranes.

surface tension

$$n = \sigma\, h \qquad \text{with} \qquad [\,n\,] = [\,\text{force / length}\,]$$

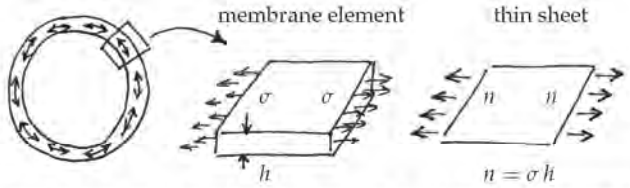
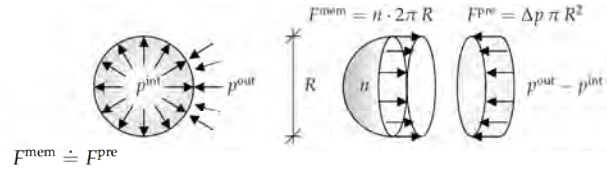


Figure 5.6: Liquid drop model. The internal fluid pressure is balanced by a thin elastic shell. The membrane element of thickness h is subjected to membrane stresses σ. Equivalently, the membrane can be represented as a thin sheet subjected to the surface tension n which results from the integration of the membrane stress over the thickness as $n = \sigma h$.

law of laplace



$F^{mem} \doteq F^{pre}$

where

$F^{mem} = n\,C \qquad \text{with} \qquad C = 2\,\pi\,R$

are the forces of the cell membrane acting along the circumference C and

$F^{pre} = [\,p^{int} - p^{out}\,]\,A \qquad \text{with} \qquad A = \pi\,R^2$

are the forces generated by the pressure difference across the cell wall acting on the surface area A. When combining these three equations, we obtain the law of Laplace

$$p^{int} - p^{out} = 2\,\frac{n}{R} \qquad \ldots \text{ Law of Laplace}$$

law of laplace

$$p^{int} - p^{out} = 2\,\frac{n}{R} \qquad \ldots \text{ Law of Laplace}$$

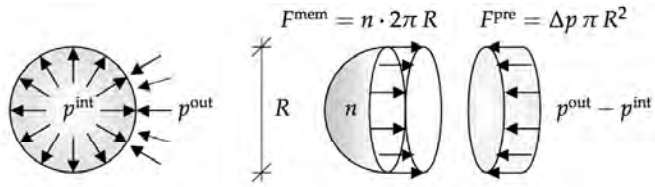


Figure 5.7: Law of Laplace. The membrane force $F^{mem} = n \cdot 2\pi R$ is the result of the surface tension n acting on the cell membrane along the circumference $C = 2\,\pi\,R$. It is in equilibrium with the forces F^{pre} resulting from the pressure difference Δp acting on the cell area $A = \pi\,R^2$.

law of laplace

$$\Delta p = 2\,n\left[\frac{1}{R^{cell}} - \frac{1}{R^{pro}}\right] \qquad \text{with} \qquad \Delta p = p^{pip} - p^{out}$$

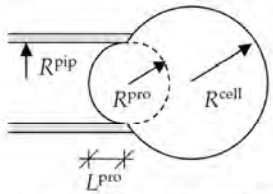


Figure 5.8: Kinematics of micropipette aspiration. For the limit state, at $L^{pro}/R^{pro} = 1$, the Law of Laplace can be used to determine the surface tension n.

law of laplace

$$p^{pip} + p^{int} - p^{out} = 2\,n\,\frac{1}{R^{pip}} \qquad \ldots \text{ law of Laplace for the protrusion}$$

$$p^{int} - p^{out} = 2\,n\,\frac{1}{R^{cell}} \qquad \ldots \text{ law of Laplace for the cell}$$

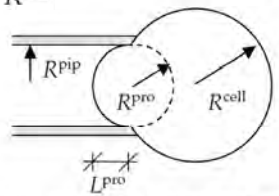


Figure 5.8: Kinematics of micropipette aspiration. For the limit state, at $L^{pro}/R^{pro} = 1$, the Law of Laplace can be used to determine the surface tension n.

$$p^{pip} = 2\,n\left[\frac{1}{R^{pip}} - \frac{1}{R^{cell}}\right]$$

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Review

Micropipette aspiration of living cells

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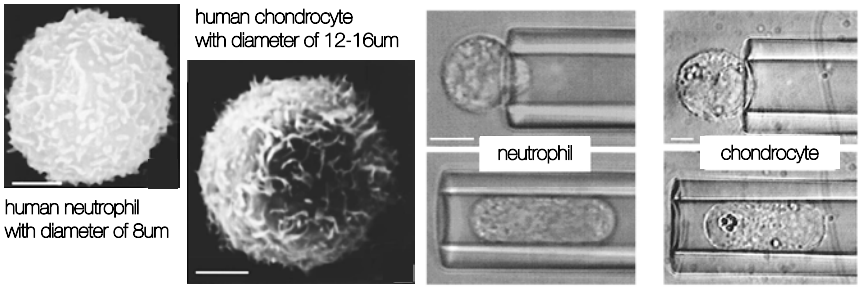
Abstract

The mechanical behavior of living cells is studied with micropipette suction in which the surface of a cell is aspirated into a small glass tube while tracking the leading edge of its surface. Such edges can be tracked in a light microscope to an accuracy of ± 25 nm and suction pressures as small as 0.1–0.2 pN/μm² can be imposed on the cell. Both soft cells, such as neutrophils and red cells, and more rigid cells, such as chondrocytes and endothelial cells, are studied with this technique. Interpretation of the measurements with basic continuum models leads to values for a cell's elastic and viscous properties. In particular, neutrophils are found to behave as a liquid drop with a cortical (surface) tension of about 30 pN/μm and a viscosity on the order of 100 Pa s. On the other hand, chondrocytes and endothelial cells behave as solids with an elastic modulus of the order of 500 pN/μm² (0.5 kPa).

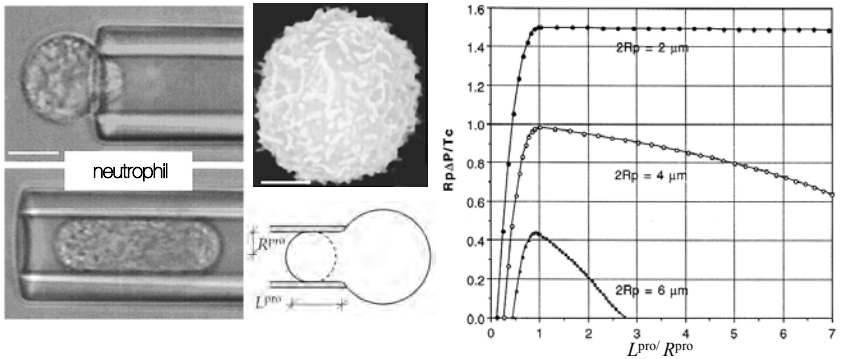
micropipette aspiration



the figure on the left shows a human neutrophil with a diameter of ~8um and a human chondrocyte with a diameter of ~12-16um. scale bars indicate 2um.the figure on the right shows a neutrophil and a chondrocyte each being aspired into a micropipette. scale bars indicate 5um.

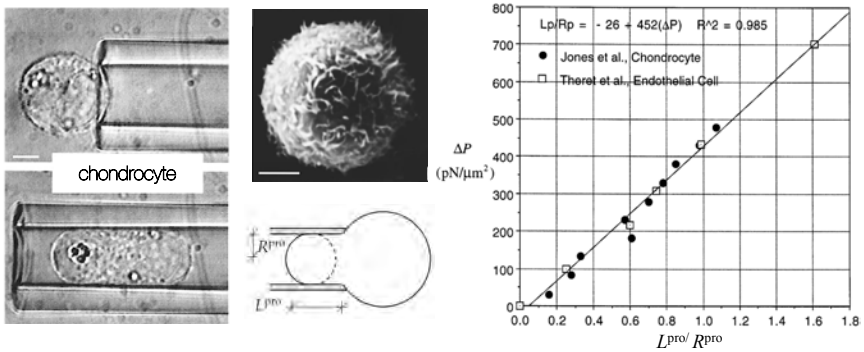
hochmuth [2000]

micropipette aspiration - neutrophil



micropipette aspiration of a liquid drop with a constant cortical tension T_c. L^{pro} is the length of the protrusion of the drop into the pipette and R^{pro} is the radius of the protrusion. when L^{pro}/R^{pro} >1, the results are no longer stable to an increase in pressure. the cell flows freely into the pipette when the pressure is increased beyond L^{pro}/R^{pro} =1. cells as neutrophils that flow into the pipette freely at this point behave as liquid drops.

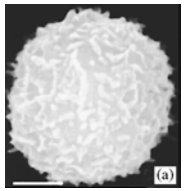
micropipette aspiration - chondrocyte



micropipette aspiration of a chondrocyte and an endothelial cell. chondrocytes and endothelial cells continue to behave as an elastic solid for values L^{pro}/R^{pro} >1 that are significantly larger than one. cells that do not flow into the pipette freely behave as elastic solids.

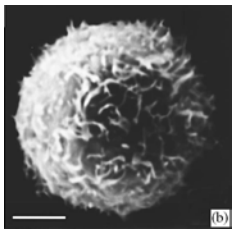
hochmuth [2000]

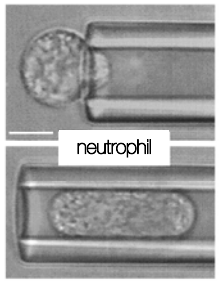
micropipette aspiration

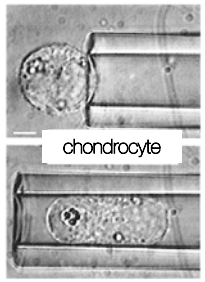


human neutrophil
with diameter of 8um

human chondrocyte
with diameter of 12-16um



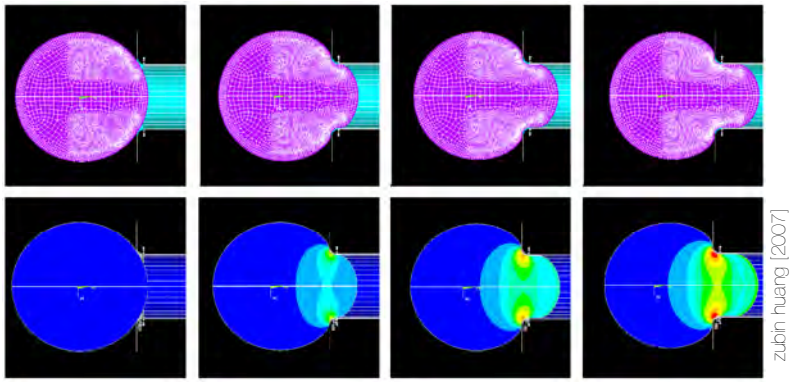




summary neutrophis behave as a liquid drop with a cortical surface tension of about 30pN/um and a viscosity of the order of 100Pa. chondrocytes and endothelial cells behave as solids with an elastic modulus of the order of 500pN/um=0.5kPa.

hochmuth [2000]

finite element simulation of micropipette aspiration



zubin huang [2007]

Figure 5.10: Finite element simulation of micropipette aspiration of a chondrocyte modeled as an elastic solid. In contrast to analytical results, finite element simulations can account for large deformations, heterogeneous stress distributions, and a more realistic representation of the boundary conditions [21].

zubin huang [2007]

finite element simulation of micropipette aspiration