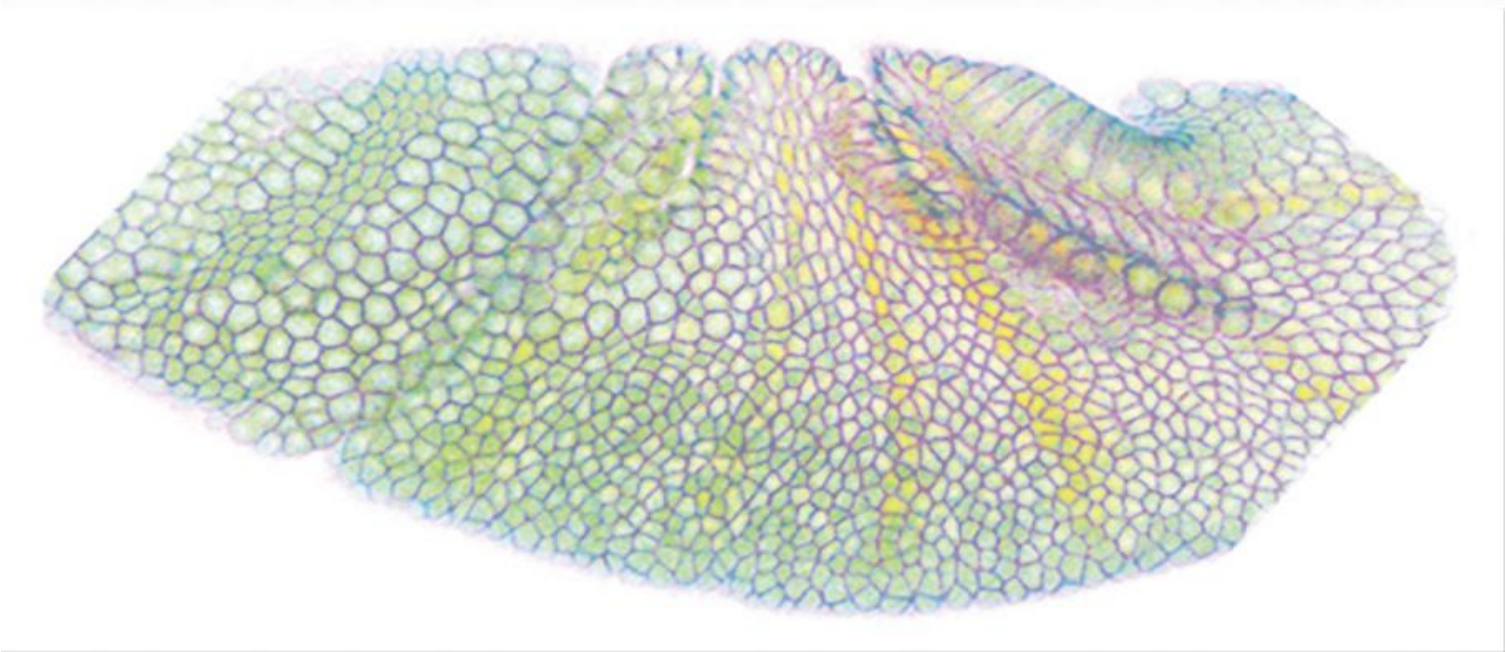
Mechanics of Morphogenesis



Lecture 5: Cellular tension - membrane tension

Thomas Lecuit
chaire: Dynamiques du vivant

COLLÈGE DE FRANCE
1530

Summary- tissue organisation and plasticity

- *Organisation:*
  - Cells adopt morphologies and configurations that tend to approach minimal surface energy
  - Reflects balance between:
    -hydrostatic/turgor pressure + protrusive forces
    -cortical tension
    -cell walls/cortex stiffness
    - cell-cell adhesion
- *Dynamics:*
  - Cell connectedness varies so tissues can be modelled as gaz, viscoelastic fluids or elastic solids.
  - Reflects differences in *cell-cell adhesion.*
  - Cell shape changes and cell movements are driven by *active contractile systems* in animals.
  - Cell-cell adhesion resists active remodelling and maintains tissue cohesion under stress.
  - But Adhesion molecules also transmit sub cellular contractile tension. Adhesion and Cortical tension are interdependent

Summary: Adhesion as an active, dissipative process

- Cadherin based adhesion is an out-of-equilibrium system whereby active processes control the dynamic organisation in clusters.

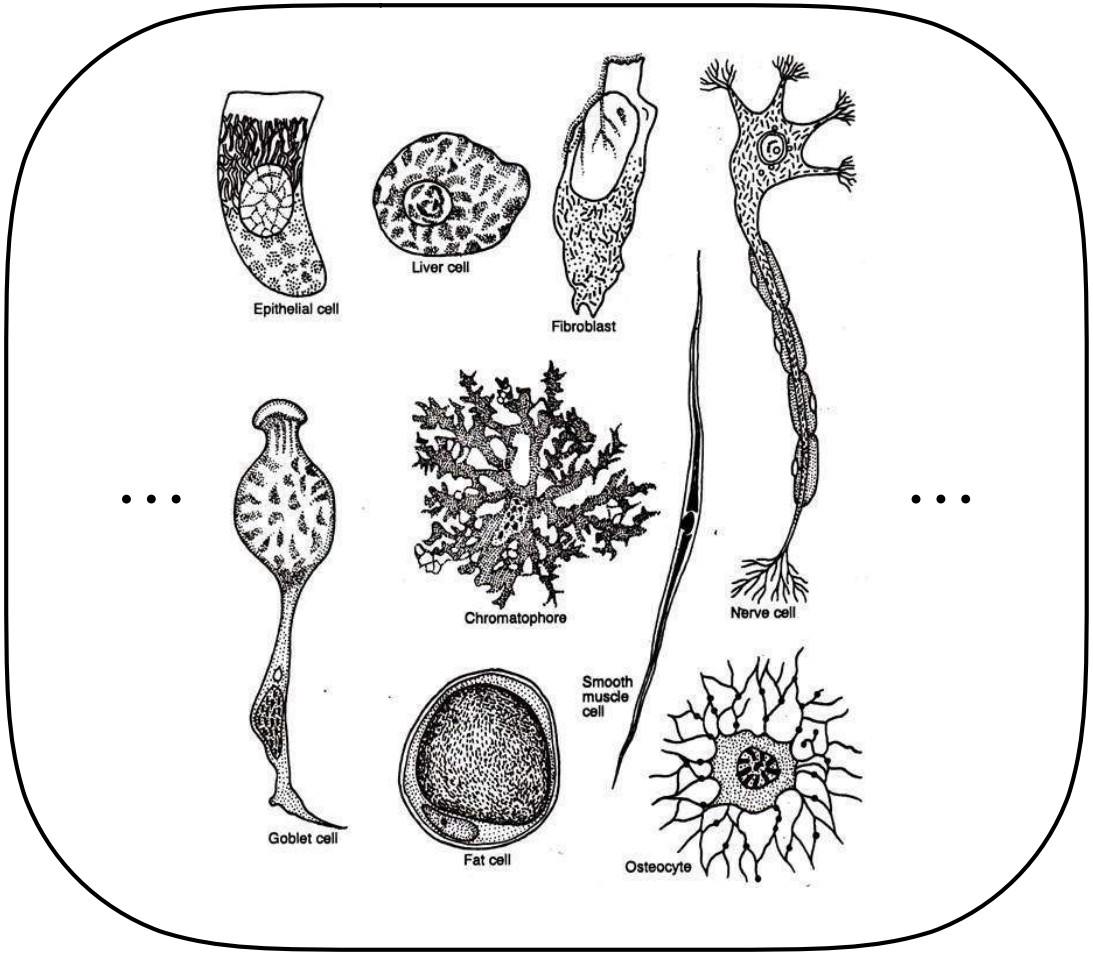
- Cadherin clusters transmit cortical tension and response to force:
  -cluster organisation: turnover, density
  -molecular coupling: catch bond , strain dependent reinforcement etc

- Energy is constantly dissipated at adhesion sites:
  -turnover of all molecular components (~10 seconds)
  -many weak bonds (low affinity interactions) concentrated locally

- Viscoelastic properties of adhesion sites underlie organisation/plasticity paradox of tissue dynamics.

Mechanics of Cell shape - Geometry & Dynamics

- Cells « morpho-space » is a huge multidimensional space
- Dimensionality reduction and unifying model of cell shape?
- How many parameters for description of and control over cell shape



Physical parameters

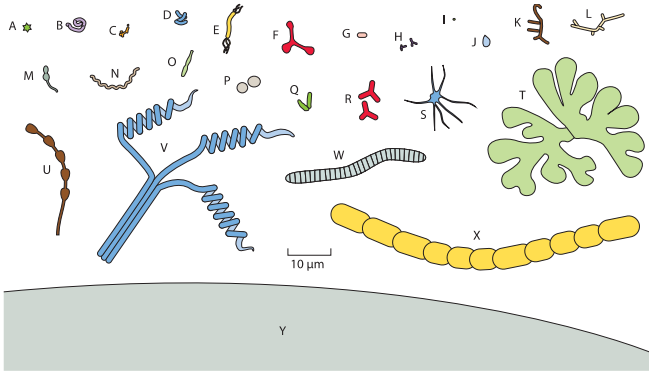
↑ ↓

Biological parameters

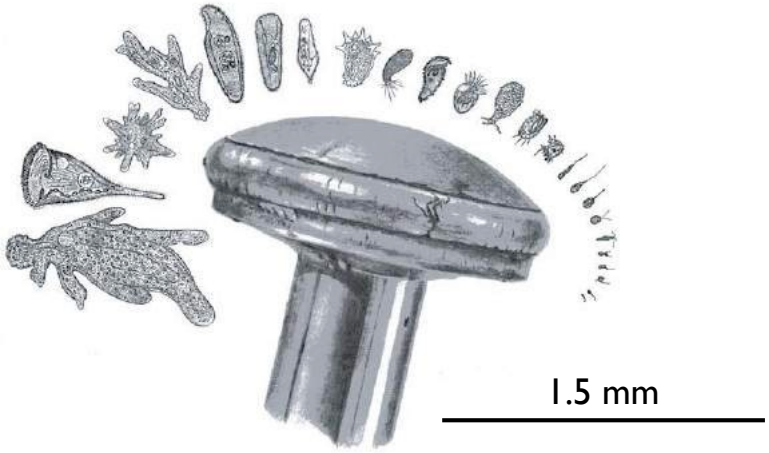
Mechanics of Cell shape - Geometry and Size variation

cell type	average volume (μm^3)	BNID
sperm cell	30	109891, 109892
red blood cell	100	107600
lymphocyte	130	111439
neutrophil	300	108241
beta cell	1,000	109227
enterocyte	1,400	111216
fibroblast	2,000	108244
HeLa, cervix	3,000	103725, 105879
hair cell (ear)	4,000	108242
osteoblast	4,000	108088
alveolar macrophage	5,000	103566
cardiomyocyte	15,000	108243
megakaryocyte	30,000	110129
fat cell	600,000	107668
oocyte	4,000,000	101664

Mammalian cells



Microbial cell shape and size



Protists

Cell Biology by the numbers. Ron Milo, Rob Phillips, *illustrated* by Nigel Orme. *Garland Science* 2012

Cell Shape and Cell Tension

Surface Tension

Membrane Tension

Cortex Tension

Cell shape and Surface Tension: Statics

J. Plateau, *Statique expérimentale et théorique des liquides…*, 1870

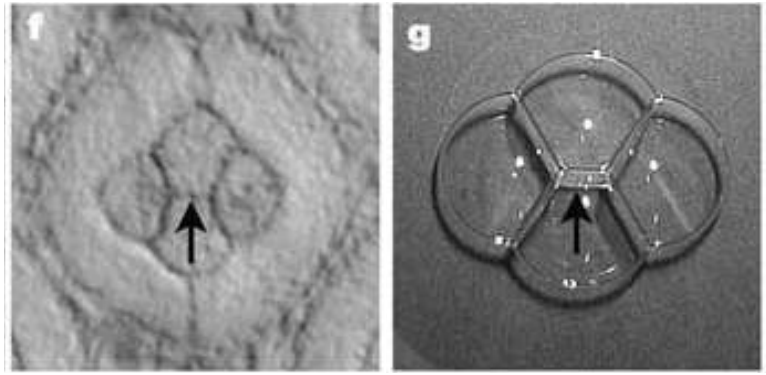
d'Arcy W Thompson, *On Growth and Form*, chapter V, 1917

- Thermodynamic description: near equilibrium/quasi-static

  > « Justified » by separation of time scales between molecular and cellular processes?

- Minimisation of surface energy E
- Minimisation of surface S
- *Surface tension* $E = \lambda . S$ *Biological significance?*

  λ: amount of work done per unit of surface change



Hayashi T & Carthew R, *Nature*, 431:647 (2004)

Cell Surface Tension: historical evidence

THE COALESCENCE OF LIVING CELLS WITH OIL DROPS

II. ARBACIA EGGS IMMERSED IN ACID OR ALKALINE CALCIUM SOLUTIONS

M. J. KOPAC AND ROBERT CHAMBERS

Eli Lilly Research Division, Woods Hole, Massachusetts and Washington Square College, New York University

JOURNAL OF CELLULAR AND COMPARATIVE PHYSIOLOGY, VOL. 9, NO. 3

1937

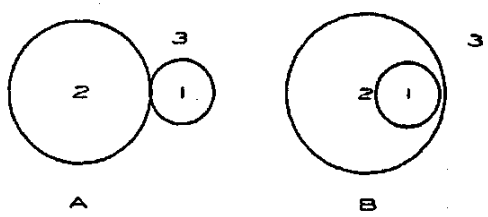
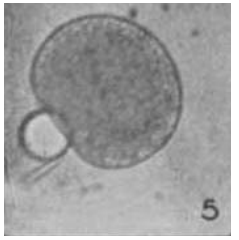
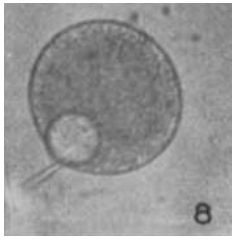


Fig. 1 A, oil drop in contact with egg's surface before coalescence and B, oil drop inside egg following coalescence. 1, oil drop; 2, egg, and 3, aqueous phase.





$T_{1/2}$: 0.6 dyn/cm (=0.6. 10^{-3} N/m)
$T_{2/3}$: 0.2 dyn/cm
$T_{1/3}$: measured for oleic oil/acid

If 2 drops have similar surface S before coalescence, and the engulfing drop has surface S_1 after coalescence

Energy change $$E = S\,(T_{1/3} + T_{2/3}) - (S\,T_{1/2} + S_1\,T_{2/3})$$

and $T_{1/3} > T_{2/3}$ and $T_{1/3} - T_{1/2} > T_{2/3}$

$$E_A = \pi\,[d_1^2\,T_{1/3} + d_2^2\,T_{2/3}]$$

$$E_B = \pi\,[d_2^2\,T_{1/2} + (d_1^3 + d_2^3)^{\frac{2}{3}}\,T_{2/3}]$$

Fusion if $E_A/E_B > 1$

	SEA WATER								
	pH 6.0			pH 6.8			pH 8.2		
	d_1	dE	$E_{A/B}$	d_1	dE	$E_{A/B}$	d_1	dE	$E_{A/B}$
1 a	50	930	11.2	..	..	..	0	..	..
2 b	29	230	5.5	..	..	..	..	..	..
3 b	53	780	9.1	..	..	..	..	..	..
4 a	18	115	3.8	45	560	8.3	0	..	..
5 a	10	36	2.1	23	147	4.2	0	..	..
6 b	..	..	..	..	..	..	28	130	3.6
7 b	..	..	..	..	..	..	14	53	1.9
8 b	0	..	..	..	..	..	50	417	5.7

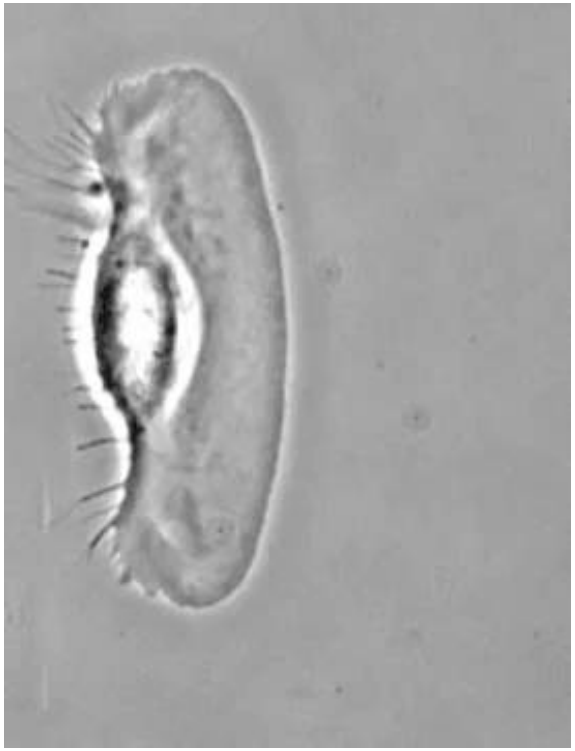
This behavior immediately suggested that the tension at the oil/aqueous-phase interface is an important factor which determines whether or not an oil drop will penetrate a naked Arbacia egg. It is well known that the

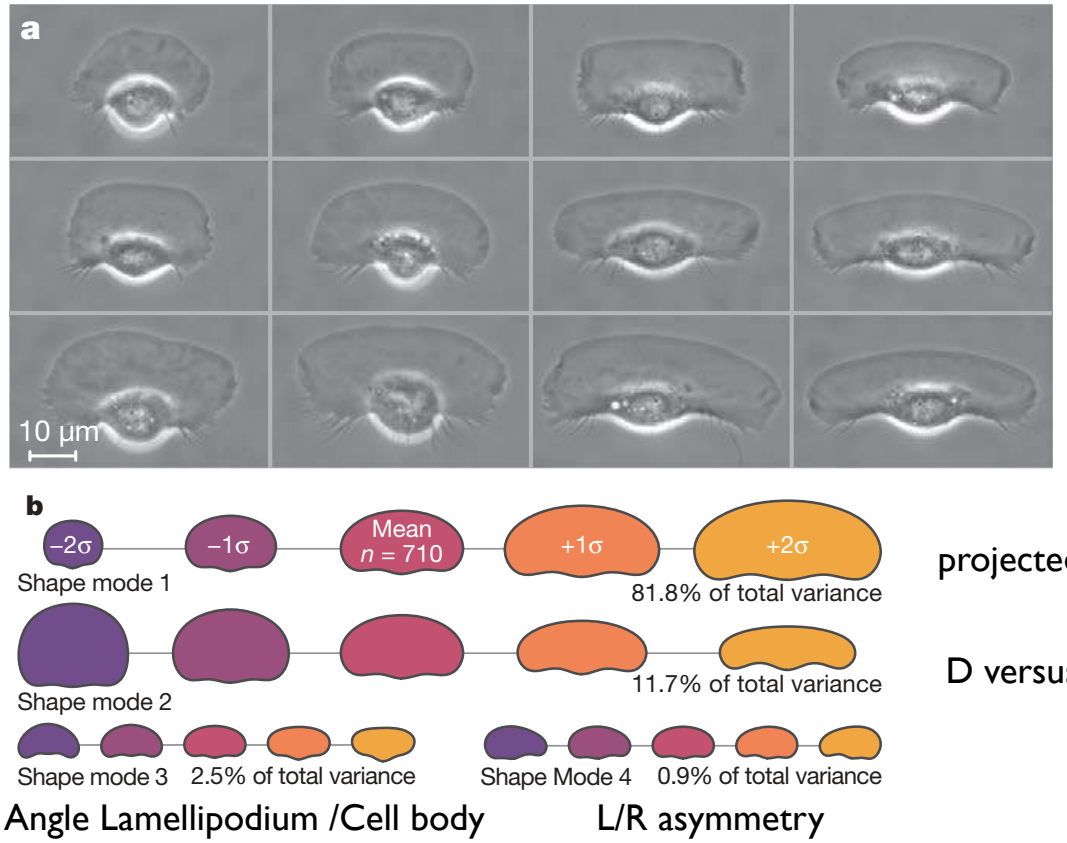
An oil drop applied to the egg's surface gives a system of 2 drops in contact which are immersed in an aqueous phase but immiscible with it. The potential energy of this system is higher than when the oil drop is within the egg. This results from the reduction in the tension at the surface of the oil drop when in contact with cytoplasm. Therefore, the oil drop enters spontaneously.

Arbacia

However: Cell shape is dynamically determined

- Low dimensionality of cell shape: 4 modes.
- « Morpho-space » of cells (*ie*. occupied by functional states) is a small fraction of theoretical shape-space.





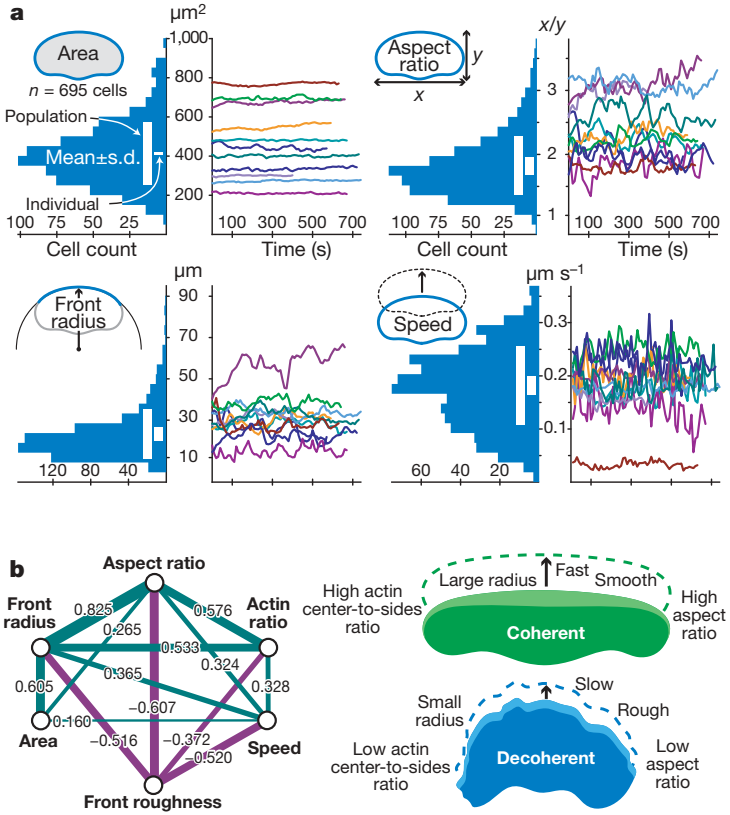
projected surface

D versus Canoe

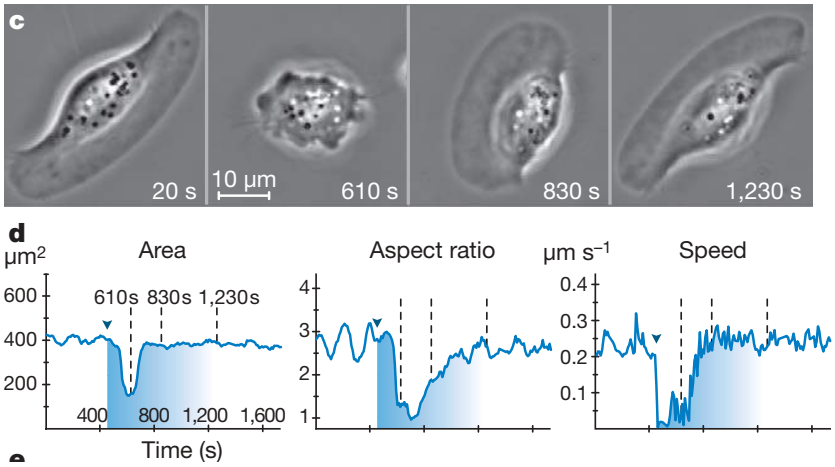
Keren K. et al, Mogilner A. and Theriot J., *Nature*, 453:475 (2008)

Cell shape is dynamically determined

- Cells exhibit low variability of shape over time (despite high cell-cell variability in population)
- Cells evolve along single phenotypic continuum: decoherent — coherent states
- Cell shape is independent of cell history: reflects a self-organized dynamics and the invariant value of a few cell parameters: e.g. available membrane, concentration of actin network components.



Single Phenotypic continuum



Transient DMSO treatment: lamellipodium collapse

Keren K. et al, Mogilner A. and Theriot J., *Nature*, 453:475 (2008)

Cell shape is dynamically determined

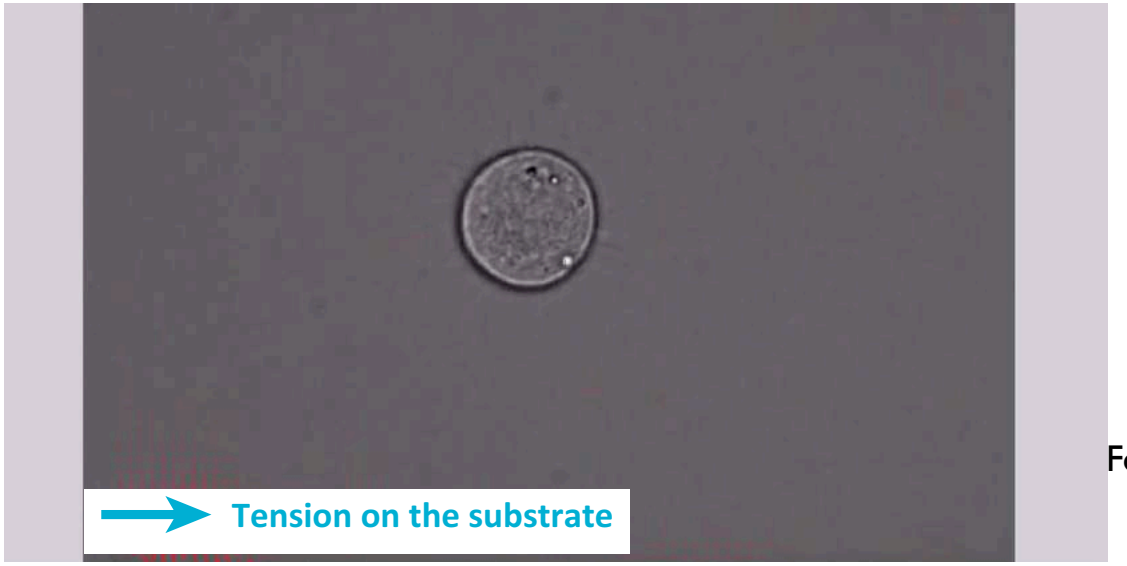
- Cell shape seems to emerge from intermolecular dynamics as a steady state solution: dynamic stability of shape

- What is the underlying mechanical model?
- It depends on:
  - Properties of the membrane
  - Properties of the underlying actin cytoskeleton
  - Interactions between the membrane and the actin cortex

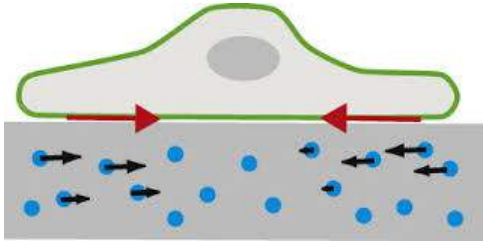
Keren K. et al, Mogilner A. and Theriot J., *Nature*, 453:475 (2008)

Single Cell Tension

- Cell shape changes are associated with changes in tension on substrate
  > cell division

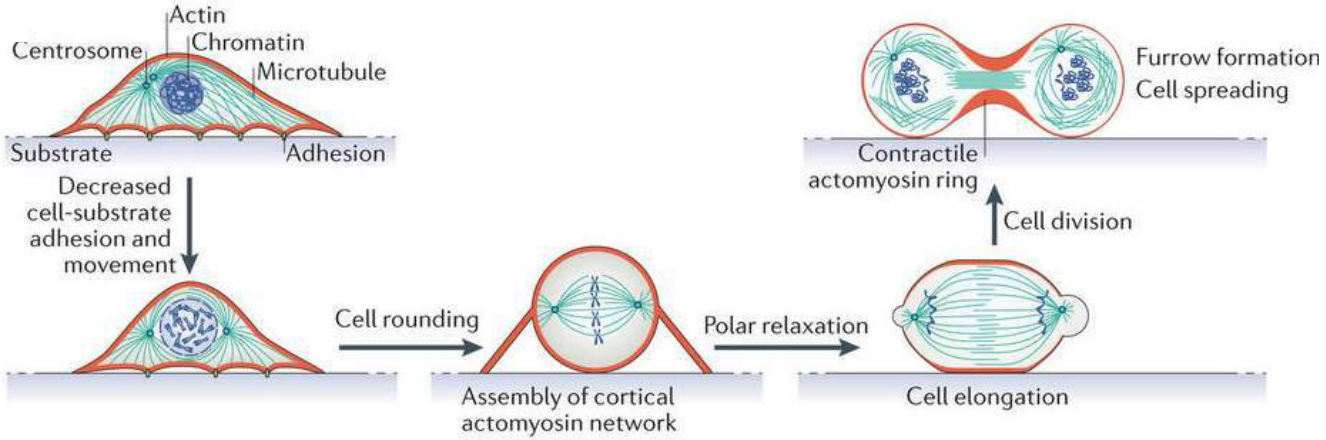


Traction Force Microscopy



Traction Force Microscopy

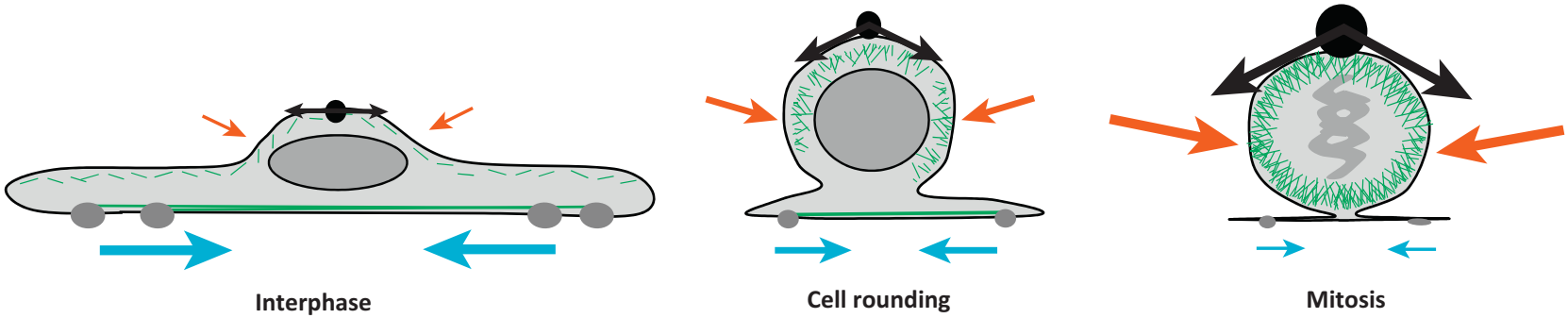
Forces derived from displacement of beads in viscoelastic gel



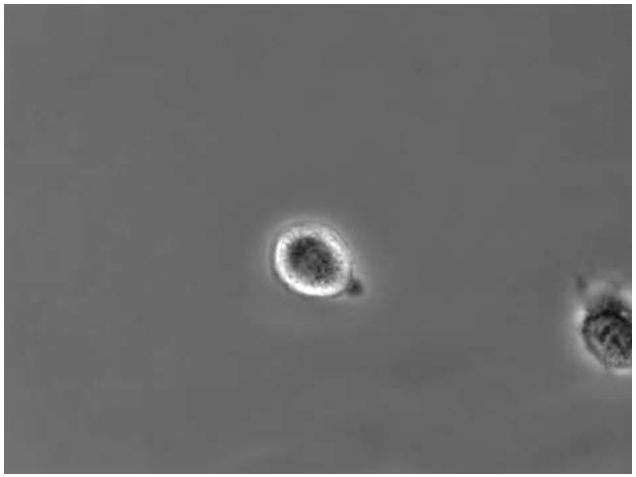
Ramkumar N. and Baum B. *Nature Rev. Mol. Cell Biol*, 2016

Single Cell Tension

- Cells experience different kinds of tension



TRENDS in Cell Biology



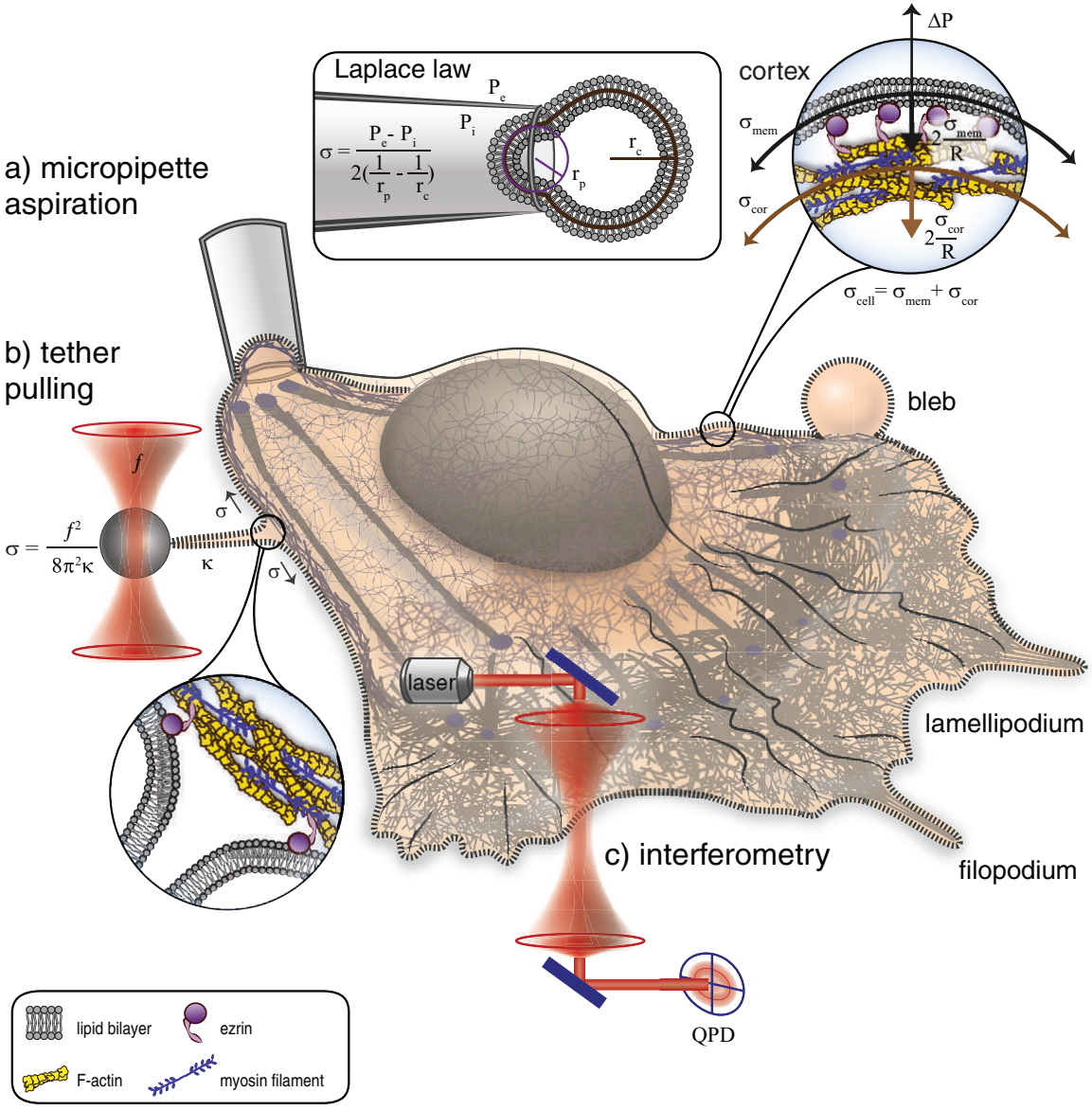
Gauthier N., Masters T. and Sheetz M. *Trends in Cell Biol*, 22:527. 2012

Membrane vs Cortical Tension

- Micropipette aspiration:
  -measures chiefly cortical tension

  Fibroblasts in suspension:
  ~400pN/µm in intact cells
  ~40pN/µm with actin depolymerisation

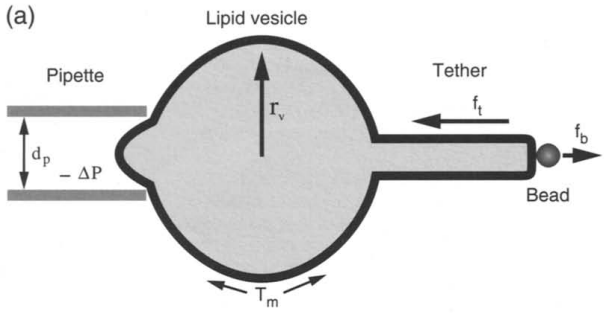
- Tether pulling:
  -measures membrane tension:
  can extract in-plane tension when no actin (bleb, drug)

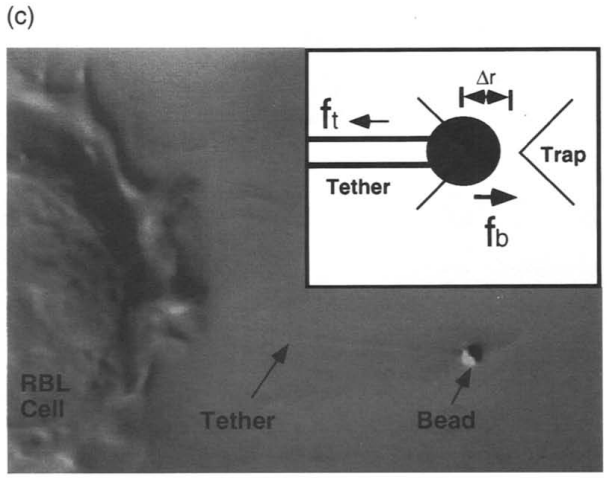


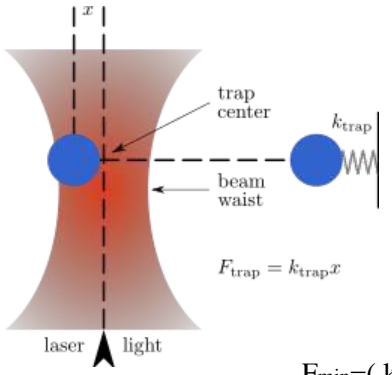
Sens P and Plastino J. *J. Phys.: Condens. Matter.* 27:273103. 2015

Membrane tension

Membrane tension measurements: tether forces







$F_{min}=(k_{trap} k_B T)^{½}$

Sheetz M. and Dad J. *Trends Cell Biol*. 6:85. 1996

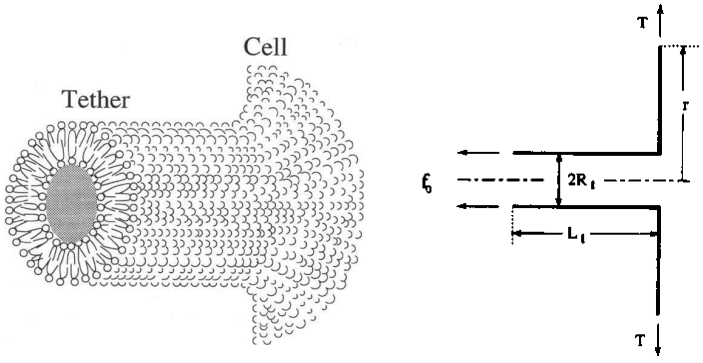
Mechanics of the plasma membrane

- in-plane tension vs membrane/cytoskeleton adhesion

Deformation and Flow of Membrane into Tethers Extracted from Neuronal Growth Cones

Robert M. Hochmuth,* Jin-Yu Shao,* Jianwu Dai,‡ and Michael P. Sheetz‡
*Department of Mechanical Engineering and Materials Science and ‡Department of Cell Biology, Duke University, Durham, North Carolina 27708 USA

Biophysical Journal Volume 70 January 1996 358–369



Mechanics of membrane flows and origin of viscosities

- Apparent/Effective Membrane Tension Tm = in-plane membrane tension T + Adhesion between membrane and cortex γ
  =Surface tension (due to inelasticity of mb)) (generates a tension in mb)

$$f_0 = 2\pi R_t(T + \gamma) + \frac{\pi B}{R_t}$$

Tether force — Membrane tension Tm — Bending

B: bending modulus

- Contributions of in-plane membrane tension and membrane/cortex adhesion hard to disentangle
- Equal contribution of apparent membrane tension and bending implies: $f_0 = \frac{2\pi B}{R_t}$ and $f_0 = 2\pi\sqrt{2B(T+\gamma)}$

$$T + \gamma = \frac{B}{2R_t^2}$$

> Can calculate B *from* R_t and f_o, and T_m from B and f_o

> Can compare relative membrane tension from tether force measurements:

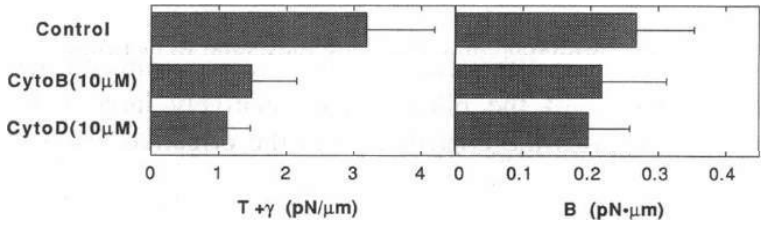
$$T_{m1}/T_{m2} = (f_{o1}/f_{o2})^2$$

Hochmuth RM et al Sheetz M. *Biophysical J*. 70:358. 1996

Mechanics of the plasma membrane

- in-plane tension vs membrane/cytoskeleton adhesion

- Effective membrane tension requires cortical actin



$T + \gamma = f_o^2 / 8B\pi^2$ $\quad B = f_o R_t / 2\pi$ $(\approx 10^{-19}$ Nm $\approx 20\ k_B T)$

> very low

- Disentangling the contribution of in-plane membrane tension and cortex/membrane adhesion.

-Tension T: the lipid bilayer is an inelastic fluid (stress equilibrates within ms):

-at low tension: entropic contribution due to membrane fluctuations

-at high tension: purely elastic contribution (elastic modulus $k \approx 0.1$mN/m) ($T = k\,\Delta A/A$, A is area)

- T can be measured in actin free conditions: cell blebs or actin depolymerization

$$T = f_{bleb}^2 / 8B\pi^2$$

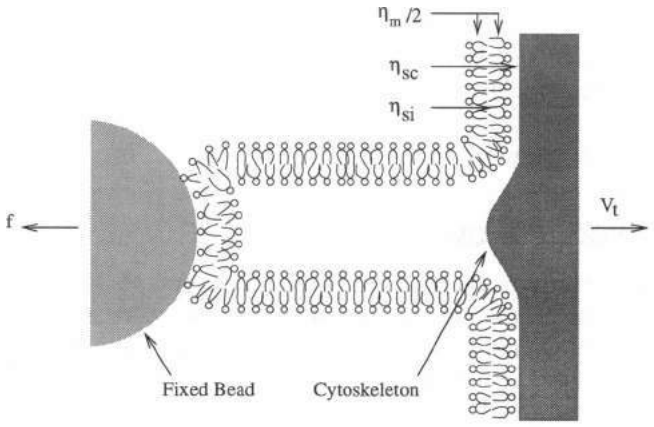
-Cortex/membrane adhesion γ $\quad \gamma = (f_o^2 - f_{bleb}^2)/ 8B\pi^2$

in general $f_{bleb} < 0.5\, f_o$ so γ accounts for over 75% of effective membrane tension

Hochmuth RM et al Sheetz M. *Biophysical J*. 70:358. 1996
Reviewed in Diz-Muñoz A., Fletcher DA. and Weiner O. *Trends in Cell Biol*, 23:47. 2013

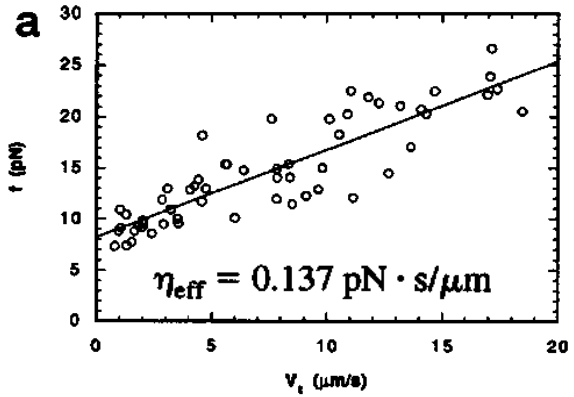
Mechanics of the plasma membrane

- in-plane tension vs membrane/cytoskeleton adhesion



$$f = 2\pi R_t(T + \gamma) + \pi B/R_t + \pi h(T_e - T_i) - \pi h\gamma$$
$$+ 2\pi V_t[2\eta_m + \eta_{si}h^2\ln(R_o/R_t) + \eta_{sc}R_t^2\ln(R_o/R_t)].$$

membrane bulk viscosity — inter-bilayer slip — **cytoskeletal slip**



$$\eta_{eff} = \frac{f - f_0}{2\pi V_t}.$$

$2\eta_m = 0.002$ pN · s/μm

$\eta_{sc}R_t^2\ln(R_o/R_t) = 0.129$ pN · s/μm

$\eta_{sc} = 1.0$ pN · s/μm^3

Equivalent to viscous resistance created by a layer of water 1nm thick

>Cytoskeletal slip viscosity dominates
(amplification due to large tether radius)

Hochmuth RM et al Sheetz M. *Biophysical J*. 70:358. 1996

Mechanics of the plasma membrane

- in-plane tension vs membrane/cytoskeleton adhesion

Membrane tension varies 3-276 pN/µm

Membrane tension rupture far greater:
3000-10000 pN/µm

Contribution of membrane in-plane tension only

Membrane adhesion to actin cortex is often the chief contributor of measured membrane tension

	Tether force (pN)	Membrane tension (pN μm^{-1})*	Reference
***C. elegans* sperm cell**			
—isotonic conditions**	35	150	[29]
—hyperosmotic shock**	15	30	
Keratocyte			
—no treatment	54	276	[27]
	~40	Not calculated	[36]
—on blebs	~33	~100	[27]
—actin cytoskeleton disruption (cytochalasin)	20	35	[36]
Melanoma cells			
—on blebs	15	11	[25]
—on attached membranes	26	32	
—actin cytoskeleton disruption (cytochalasin)	Not applicable (tension measured by interferometry)	18	[35]
Epithelial cells			
—on blebs	8	3	[25]
—on apical membranes	22	22	
Neutrophils			
—resting	8.5	Not calculated	[17]
—activated (chemoattractant addition)	16.6		
—inhibit myosin	~14		
Fibroblasts	7	Not calculated	[37]
Endothelial cells, epithelial-like cells and brain tumor cells	~30	Not calculated	[38]
—All three cell types, actin cytoskeleton disruption (latrunculin)	~15		
Mitotic HeLa cells			
—on glass**	~20	Not calculated	[30]
—on fibronectin**	~30		

*κ used to calculate the membrane tension from the tether force ranged from 1–3 × 10^{-19} N m.
**Tubes pulled in different regions of the cell with different cytoskeleton organizations give identical values, so contribution of cytoskeleton attachment to tether force is considered negligible.

Sens P and Plastino J. *J. Phys.: Condens. Matter.* 27:273103. 2015

Is membrane tension uniform?

Principle:

- The membrane is a fluid, so lipids would flow if there were a gradient of tension within a cell.
- Flow could, in principle be maintained if the system were brought out of equilibrium by gradient of e.g. rapid/polarised exo/ endocytosis over sufficiently large distance.

Evidence:

- Lipids are stationary and do not flow (in most cases)
- Cortical actin does flow
- Surface proteins can flow when coupled to actin

Conclusion: Tension is, in general uniform

Lipids in the membrane do not flow

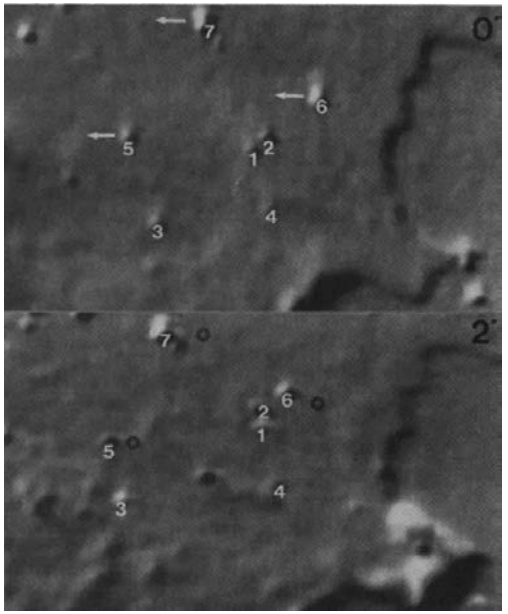
Nanometre-level analysis demonstrates that lipid flow does not drive membrane glycoprotein movements

Michael P. Sheetz*, Stephen Turney*, Hong Qian† & Elliot L. Elson†

* Department of Cell Biology and † Department of Biochemistry and Molecular Biophysics, Washington University School of Medicine, 660 S. Euclid Avenue, St Louis, Missouri 63110, USA

Nanometre-level analyses of the movements of membrane glycoproteins tagged with gold particles demonstrate that diffusing particles are not under the influence of a lipid flow, although a subset of particles which appear attached to the cytoskeleton are moving rearward.

NATURE · VOL 340 · 27 JULY 1989



40nm Gold-Concanavalin A particles (bind glycoproteins).

30Hz acquisition: detects diffusion within range of 10^{-10} — 10^{-13} $cm^2.s^{-1}$

Mean square displacement: $\rho(\tau) = \langle (r - r_0)^2 \rangle$

$$\rho(\tau) = 4D\tau + (V\tau)^2$$

Diffusion Flow

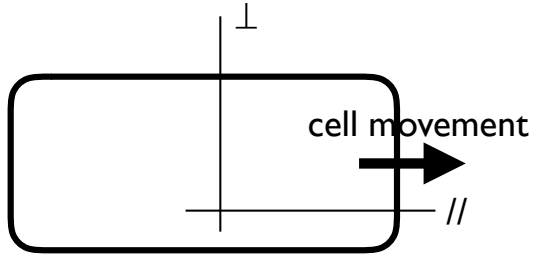
D: diffusion coefficient

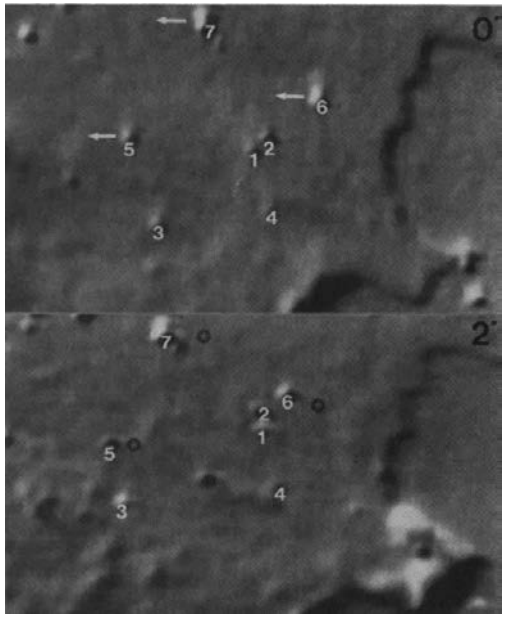
V: velocity of directed movement

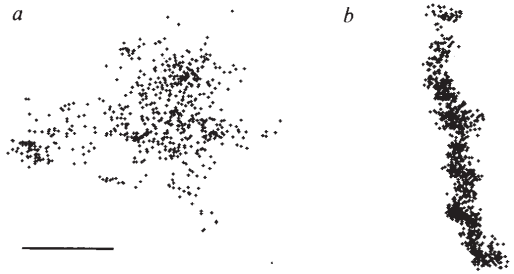
Sheetz M., Turney S. Qian H. and Elson E. *Nature* 340:284. 1989

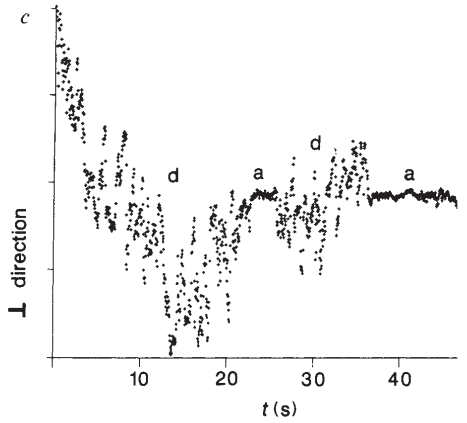
Lipids in the membrane do not flow

- Particles exhibit diffusive and directed motility at the cell surface

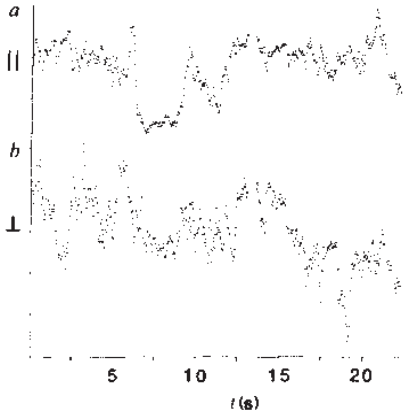




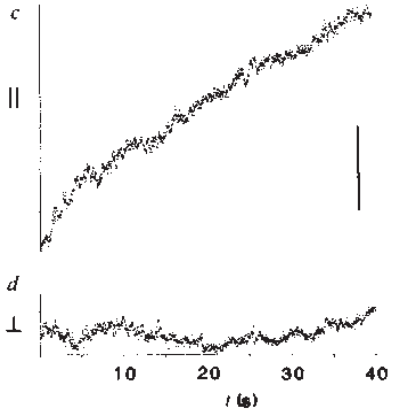




Position in direction perpendicular to active cell movement



Diffusive behaviour



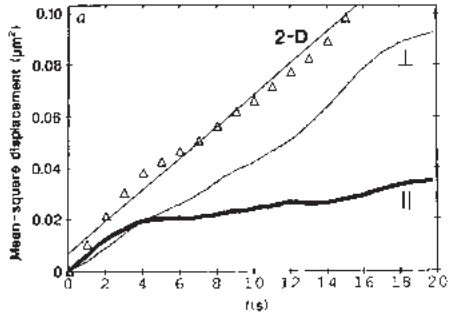
Directed movement

Sheetz M., Turney S. Qian H. and Elson E. *Nature* 340:284. 1989

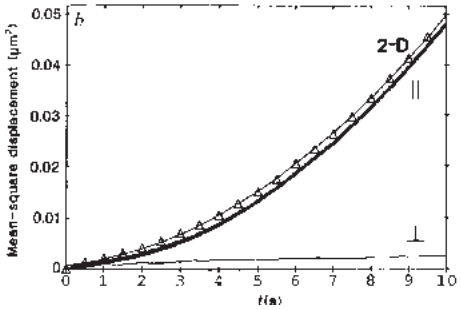
Lipids in the membrane do not flow

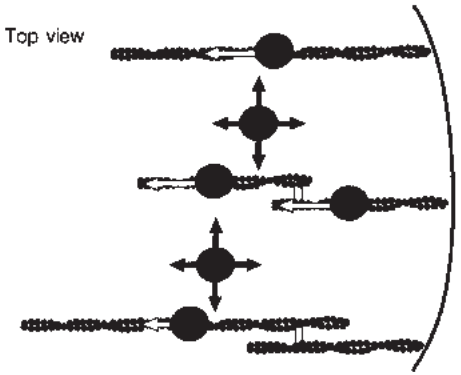
- Rapid switching between diffusive and directed movement
- F-actin coupling responsible for directed movement.

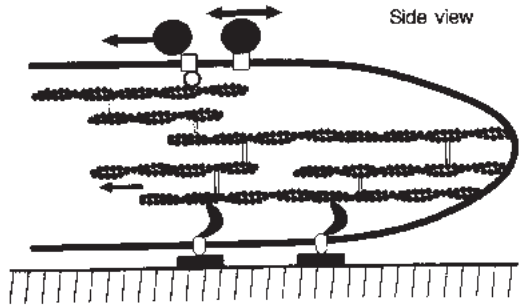
Diffusing particle



Directed movement







Using a popular analogy of biological membranes as oceans with protein logs floating in them, these results indicate that directed movement of a subset of logs does not need to produce a current in the ocean which would carry other logs along (Fig. 6). Certainly the fluidity of the lipid phase is sufficient to allow independent movement of membrane glycoproteins. □

TABLE 1 Diffusion behaviour of con A-gold

	Parallel		Perpendicular		Two-dimensional	
Particle type	$V^2 \times 10^{+12}$ (cm s^{-1})^2	D (cm^2 s^{-1})	$V^2 \times 10^{+12}$ (cm s^{-1})^2	D (cm^2 s^{-1})	$V^2 \times 10^{12}$ (cm s^{-1})^2	D (cm^2 s^{-1})
Diffusing	−4.1 ± 3.0	$4.0 \pm 2.1 \times 10^{-11}$	+0.8 ± 3.3	$3.2 \pm 1.4 \times 10^{-11}$	0	3.6×10^{-11}
Directed	+2.3 ± 0.5	$1.8 \pm 0.6 \times 10^{-12}$	−0.5 ± 0.9	$1.4 \pm 1.1 \times 10^{-12}$	1.3	1.6×10^{-12}
Stationary	−1.3	4.1×10^{-14}	−0.0006	4.8×10^{-14}	0	4.5×10^{-14}

Sheetz M., Turney S. Qian H. and Elson E. *Nature* 340:284. 1989
see arguments with Mark Bretscher in *Nature*

As in the case of the fabled unicorn, there may be somewhere where lipid flow can be found, but we have not seen evidence for it in motile cells.

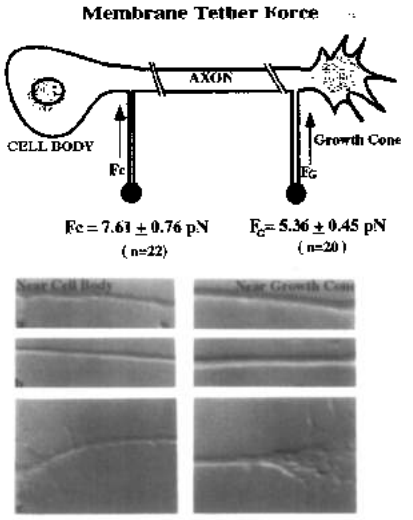
Membrane flows in very large cells

Membrane tethers and tension gradients reveal the existence of lipid flows (in axons)

Axon Membrane Flows from the Growth Cone to the Cell Body

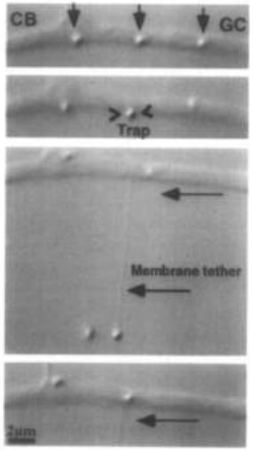
Jianwu Dai and Michael P. Sheetz
Department of Cell Biology
Duke University Medical Center
Durham, North Carolina 27710

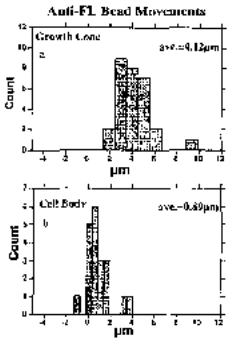
Cell, Vol. 83, 693–701, December 1, 1995

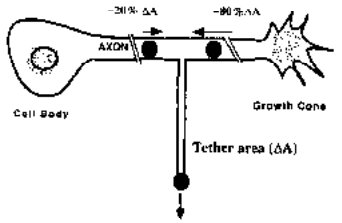


- Membrane flow observed
- Can be accounted for by gradient of tension (given known viscous resistance)

- Tethered induced flow







Mechanics of the plasma membrane

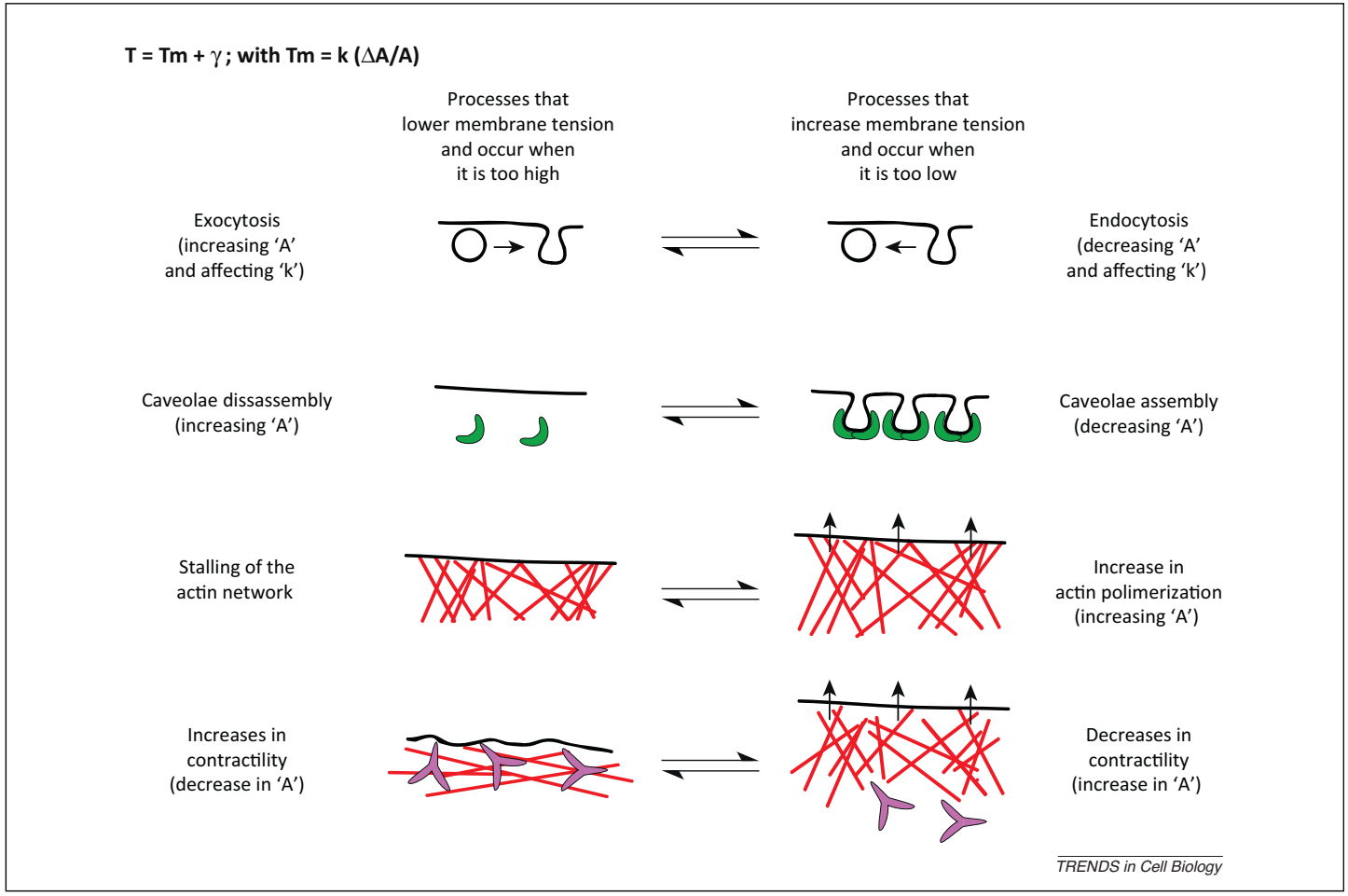
- Membrane is an inelastic fluid.
- Membrane lipids (in general) do not flow
- Membrane tension comprises a contribution of

in-plane tension and membrane/cytoskeleton *adhesion*

- Implications:
  - ◇ membrane tension is uniform across the cell and can, in principle, propagate instantly across a cell.
  - ◇ can be potentially tuned by actin dynamics and membrane availability.
  - ◇ can integrate cell mechanics via feedback control.

Integration of Membrane Tension and Cell Mechanics

- Feedbacks between membrane tension and cellular processes



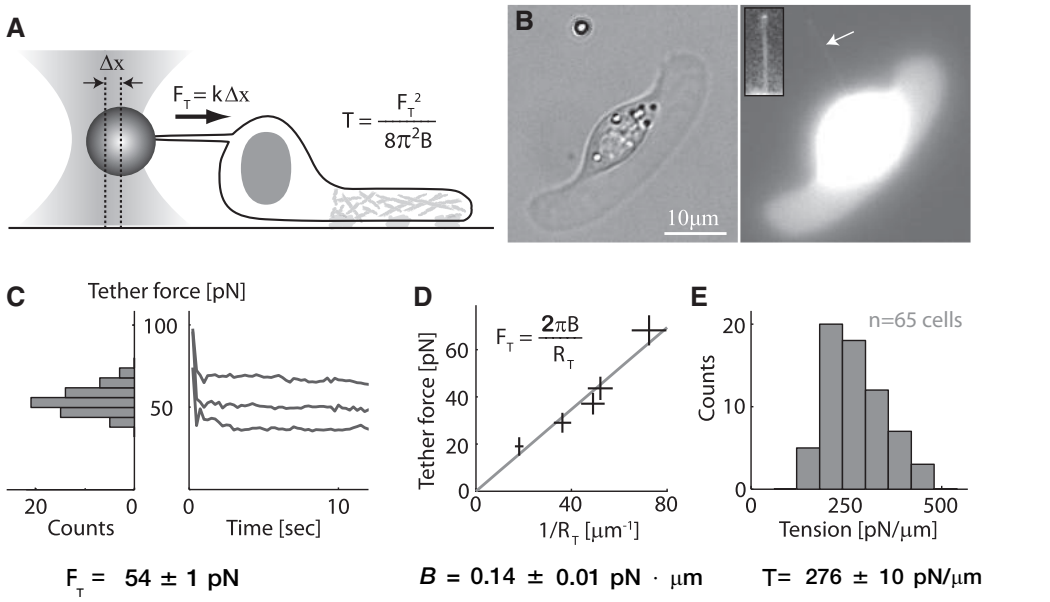
Lung endothelial cells
(Sinha et al 2011)

Keratocytes
(Lieber et al 2013
Keren et al 2008)

Review: Diz-Muñoz A., Fletcher DA. and Weiner O. *Trends in Cell Biol*, 23:47. 2013

Membrane tension and cytoskeletal forces

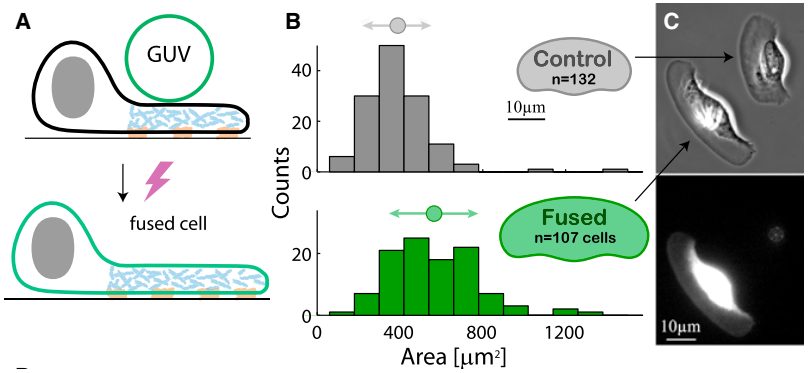
- What are the respective contributions of available membrane area and membrane/cytoskeletal adhesion to membrane tension?

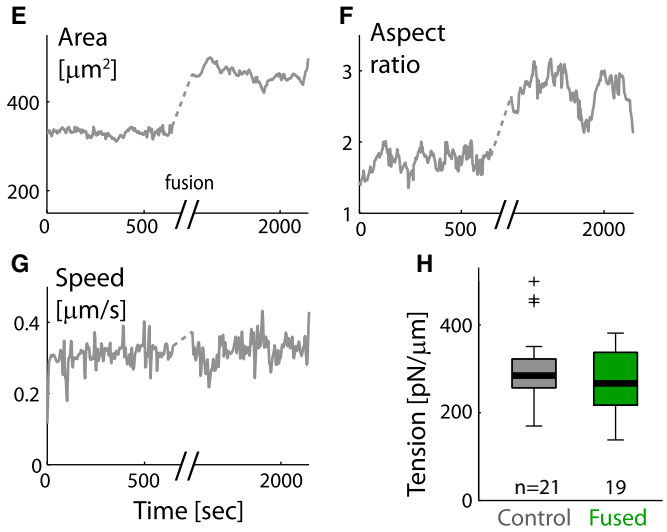


Lieber AD. et al, Theriot J, and Keren K. *Current Biol*. 23:1409. 2013

Membrane tension and cytoskeletal forces

- Increasing surface area does not affect membrane tension

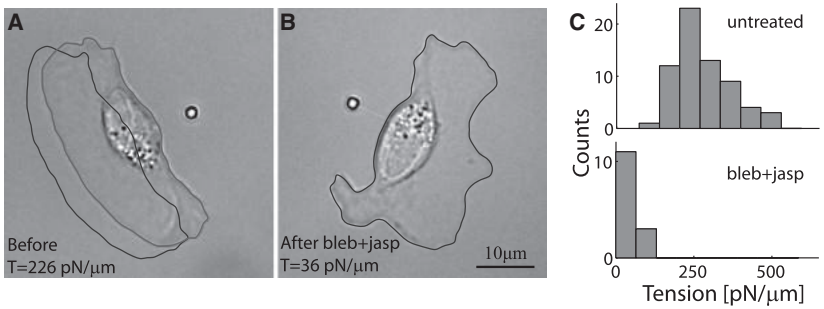




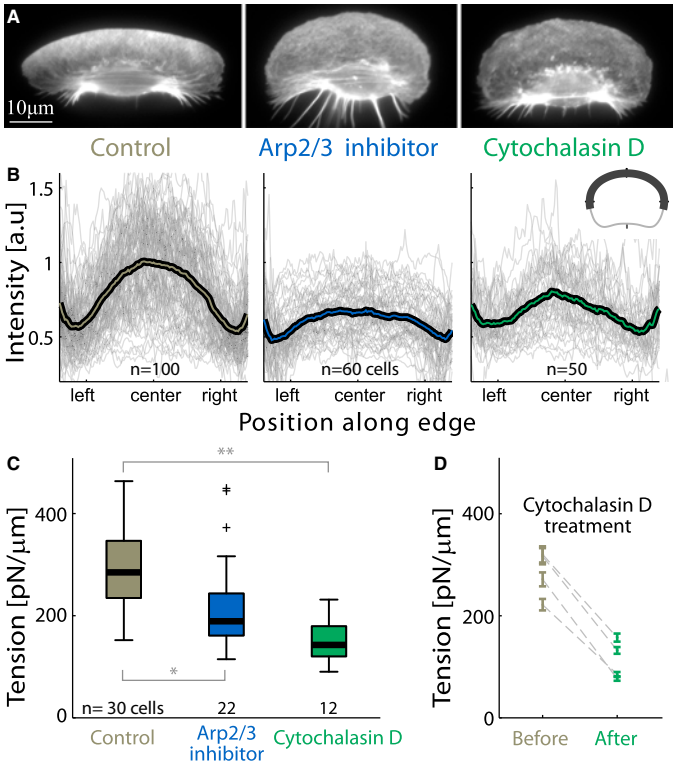
Lieber AD. et al, Theriot J, and Keren K. *Current Biol*. 23:1409. 2013

Membrane tension and cytoskeletal forces

- Tension requires an « active » cytoskeleton (turnover and contraction)



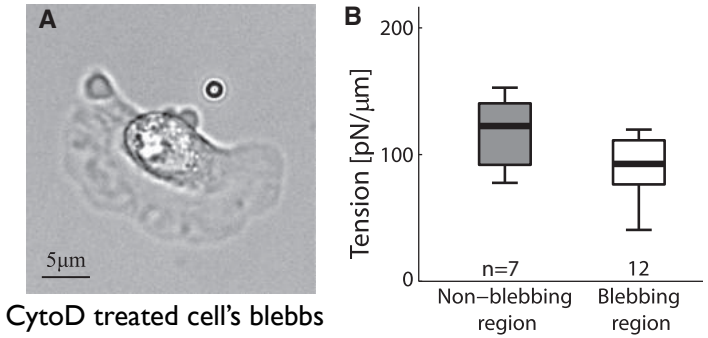
- Tension is enhanced by actin based protrusive forces at cell front



Lieber AD. et al, Theriot J, and Keren K. *Current Biol*. 23:1409. 2013

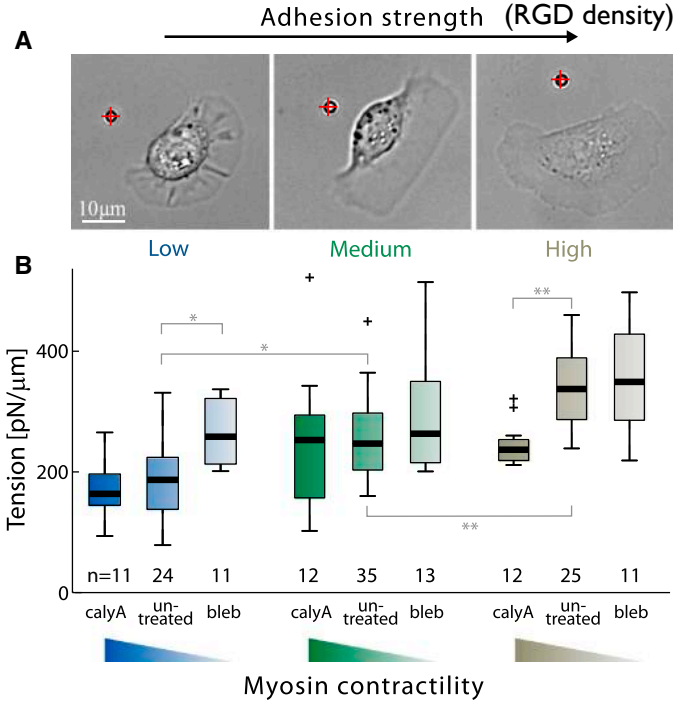
Membrane tension and cytoskeletal forces

- In-plane tension is the main contributor of tension in keratocytes (tension in blebs similar to non-bleb regions)



CytoD treated cell's blebbs

- Tension is enhanced by cell-substrate adhesion and low contractility

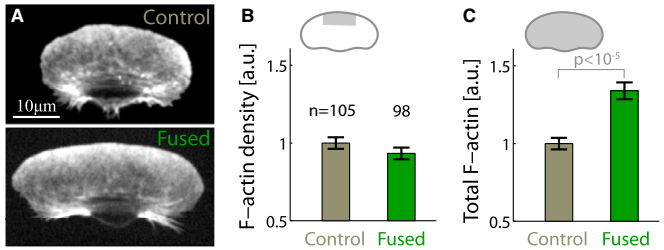


Lieber AD. et al, Theriot J, and Keren K. *Current Biol*. 23:1409. 2013

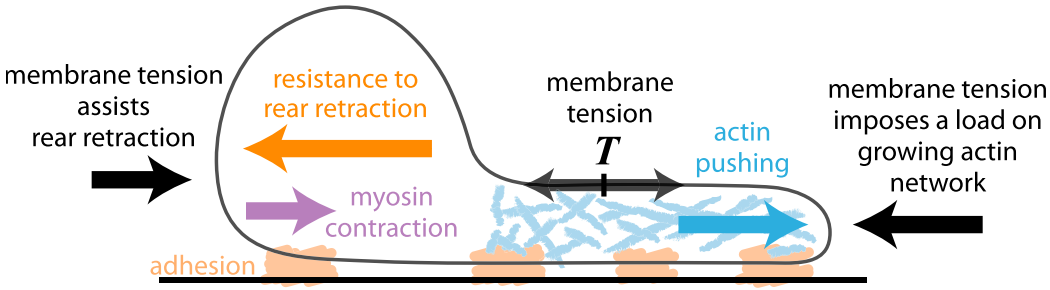
Membrane tension and cytoskeletal forces

- Cells adjust actin polymerisation to membrane surface area so as to maintain membrane tension:

  >Feedback of tension on actin polymerization?



- Membrane tension determined by mechanical force balance between actin pushing forces, load exerted by membrane tension, myosin contraction and adhesion to substrate.



Lieber AD. et al, Theriot J, and Keren K. *Current Biol*. 23:1409. 2013

Membrane tension and cytoskeletal forces determine shape

- Mechanical model of cell shape in motile keratocytes

  - Geometry:

    > rectangle approximation (area A, aspect ratio S, leading edge L)

    $$A = xy,\ S = x/y,\ L = x + 2y$$

  - Biology:

    > inelastic membrane (constraints on area)
    > graded actin density at leading edge (parabolic distribution)

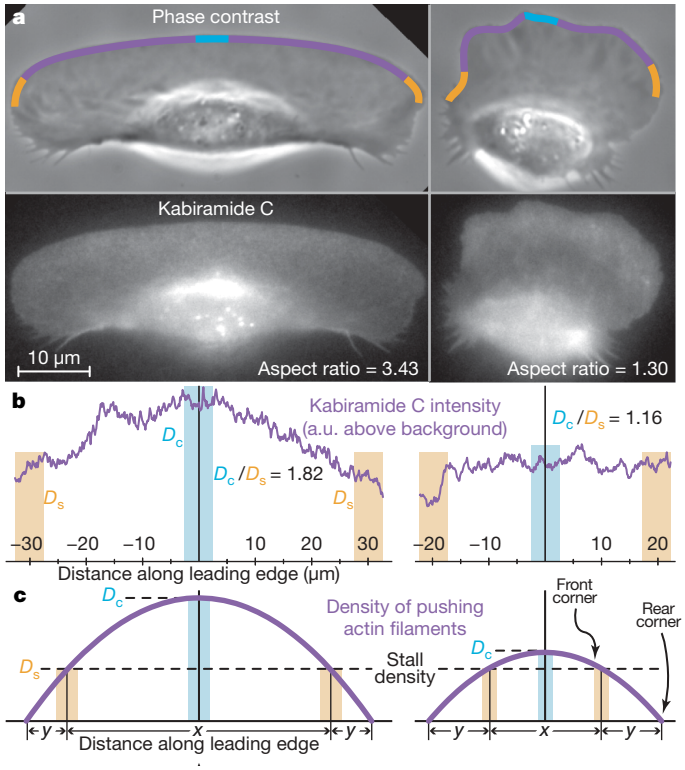
    $$D(l) = \frac{\beta}{L\gamma}\left(1 - \left(\frac{l}{L/2}\right)^2\right)$$

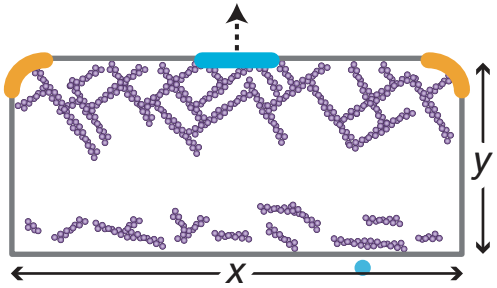
    β : # actin filaments that branch off /cell/s

    γ : rate of actin capping

  - Mechanics:

    >Actin polymerisation is stalled by membrane tension T
    T is uniform: assumtion, at sides, actin density $D_s = \frac{T}{f_{stall}}$





Keren K. et al, Mogilner A. and Theriot J., *Nature*, 453:475 (2008)

Membrane tension and cytoskeletal forces determine shape

- Predicted link between Actin density distribution and cell shape $\left[D(l)=\frac{\beta}{L\gamma}\left(1-\left(\frac{l}{L/2}\right)^2\right)\right]$

$$D_{cs}=\frac{D_c}{D_s}=\frac{(S+2)^2}{4(S+1)}$$

e.g. Cells with more actin at center have higher aspect ration S

- All mechanical and biological parameters can be collapsed into 1 single parameter related to actin tread milling

$$z=\frac{T\gamma}{f_{stall}\beta}$$

e.g. ~ratio of tension to force needed to stall actin at centre

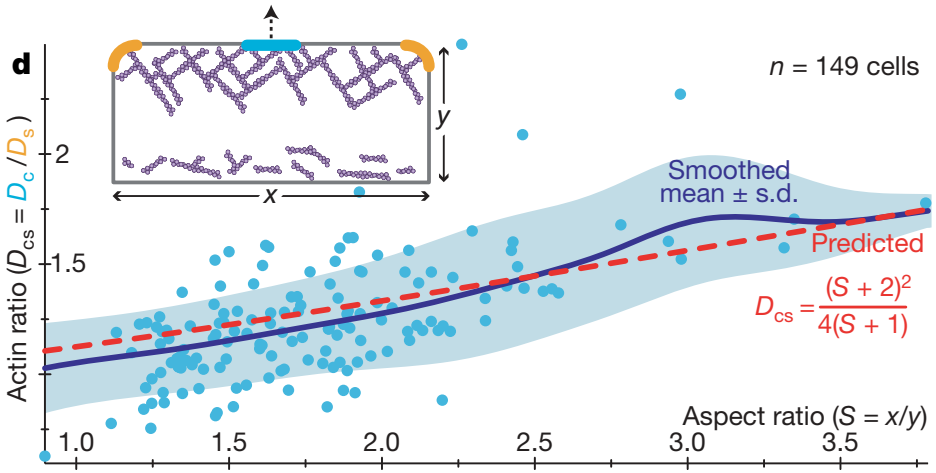
β : # actin filaments that branch off /cell/s

γ : rate of actin capping

$$z\equiv\frac{T\gamma}{f_{stall}\beta}=\frac{1}{L}\left(1-\left(\frac{x}{L}\right)^2\right)=\frac{1}{L\cdot D_{cs}}$$

biology +mechanics — shape — biology

- Area A and z fulling describe/predict shape



Keren K. et al, Mogilner A. and Theriot J., *Nature*, 453:475 (2008)

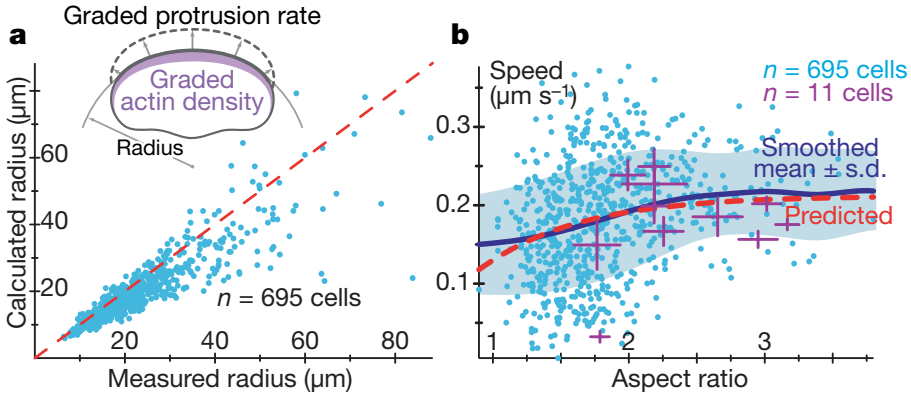
Membrane tension and cytoskeletal forces determine shape

- Connecting cell shape and cell speed:
  - Need force-velocity relationship

    Principle:

    > Uniform membrane tension, graded actin density implies graded resistive force per filament and hence graded actin protrusion rate.

    > Predicts cell curvature at leading edge (radius R).



Force-velocity (to match well data)

$$V = V_0\left(1-\left(\frac{f}{f_{stall}}\right)^{w}\right), \text{ where } w = 8$$

f : force per actin filament

f_{stall} : stall force per actin filament

Prediction of radius $R \approx \frac{L}{8}\sqrt{(zL)^{-8}-1}$

Prediction of velocity: $f = T/D_c$ and $f_{stall} = T/D_s$ so $f/f_{stall} = D_s/D_c$

$$V_{cell} = V_0\left(1-\left(\frac{4(S+1)}{(S+2)^2}\right)^{8}\right)$$

Keren K. et al, Mogilner A. and Theriot J., *Nature*, 453:475 (2008)

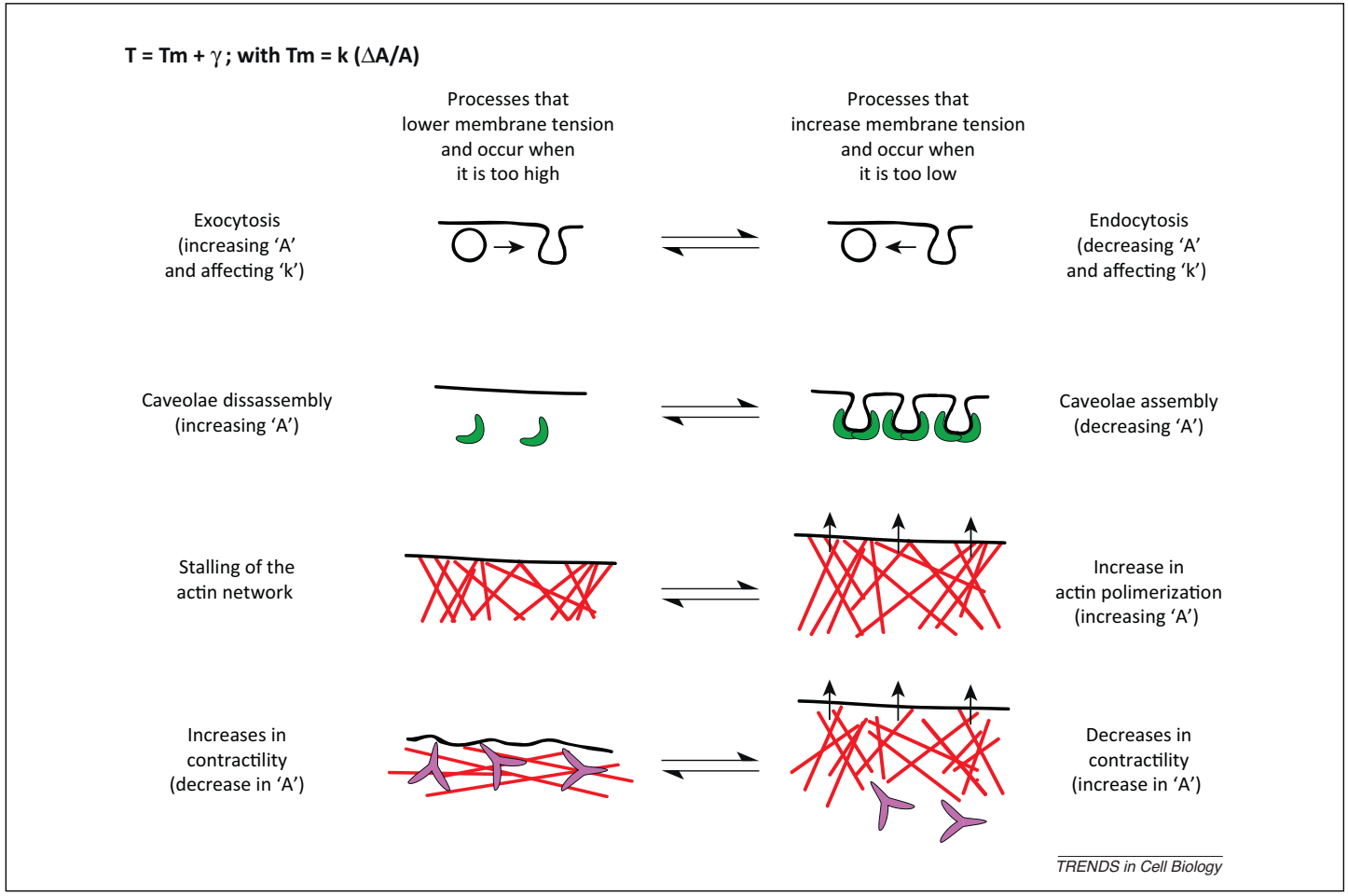
Membrane tension and cytoskeletal forces determine shape

- Explain cell shape and dynamics on the basis of coupling between membrane tension and actin tread-milling

- Essential regulatory role of membrane tension:
  - impacts on actin assembly rate
  - couples protrusion and retraction in distinct regions of cells
  - Estimate of $T = 100\text{pN}/\mu\text{m}$

Integration of Membrane Tension and Cell Mechanics

- Feedbacks between membrane tension and cellular processes



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(Lieber et al 2013
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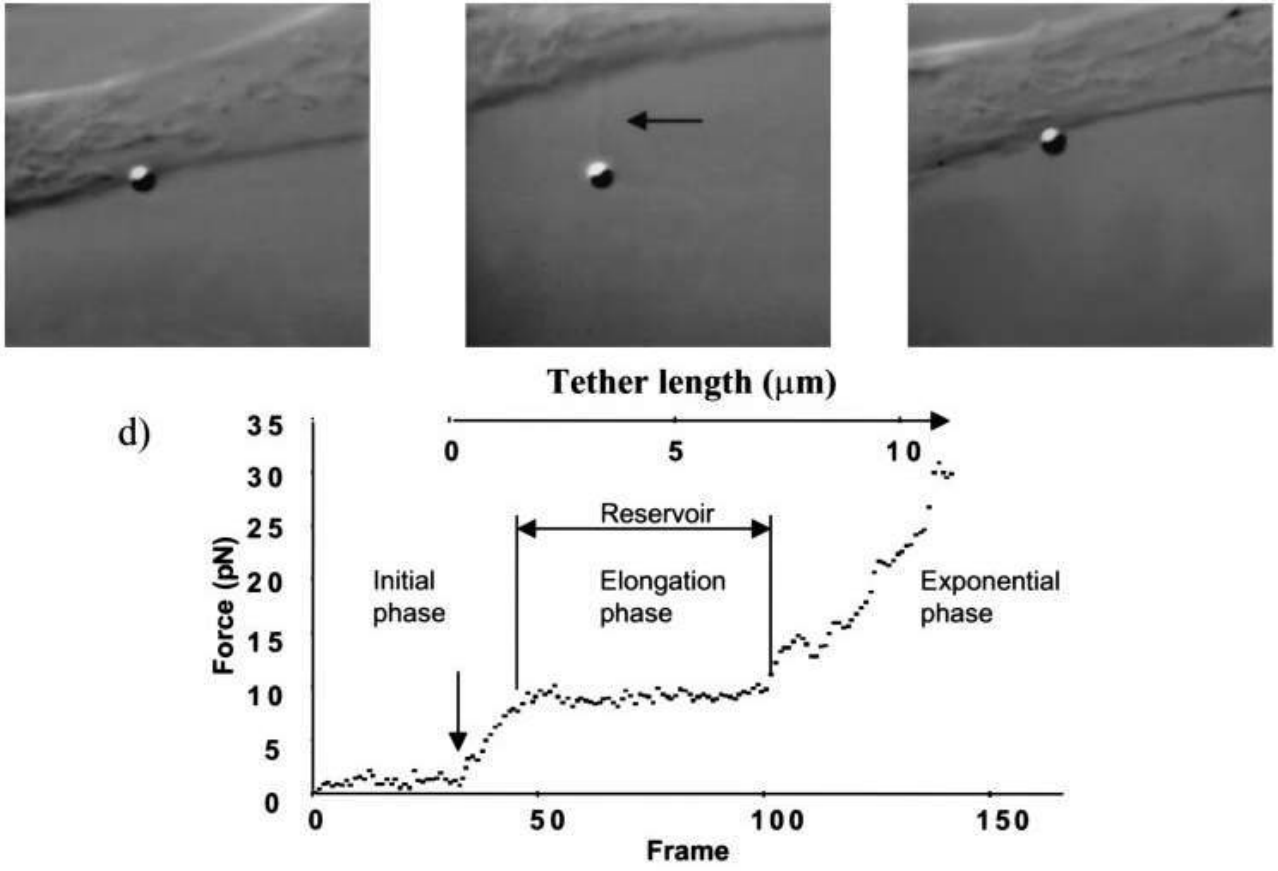
Review: Diz-Muñoz A., Fletcher DA. and Weiner O. *Trends in Cell Biol*, 23:47. 2013

Membrane tension and membrane reservoir

- A plasma membrane reservoir buffers membrane tension: experimental evidence

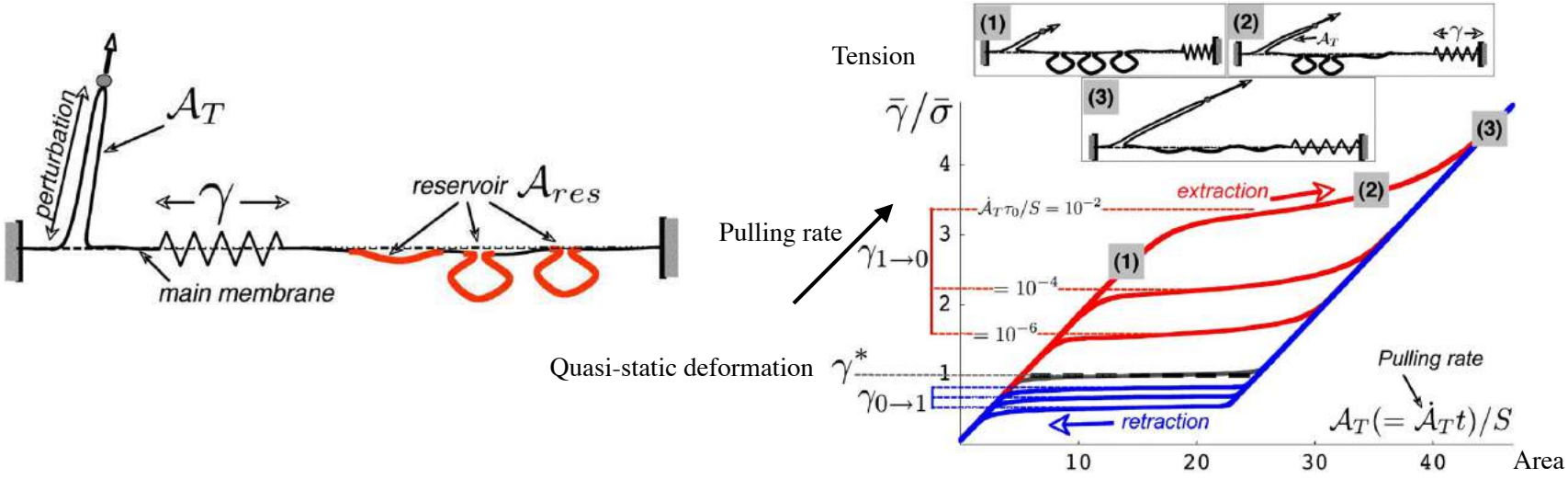
Drazen Raucher and Michael P. Sheetz
Department of Cell Biology, Duke University Medical Center, Durham, North Carolina 27710 USA

Biophysical Journal Volume 77 October 1999 1992–2002



Membrane tension and membrane reservoir

- Budded membrane micro domains as reservoirs that buffer membrane tension: theoretical study



- At low strains, membrane tension increases linearly (i.e. elastically) with membrane area.
- At high strain, all invaginations are open and tension increases also linearly.

- At intermediate strains, as tension increases, membrane invaginations unfold, which reduces tension. So there is a regime where tension remains quasi-constant.

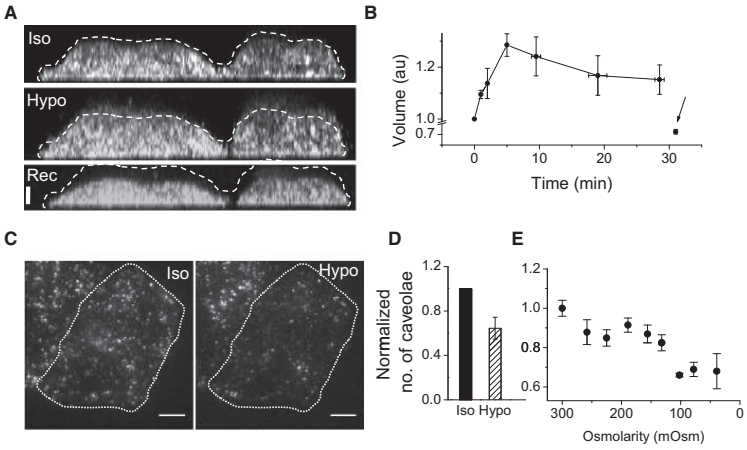
- Quasi-static deformations are reversible.
- Rapid deformations gives rise to hysteresis (stems from kinetic asymmetry in budded domain formation vs flattening)

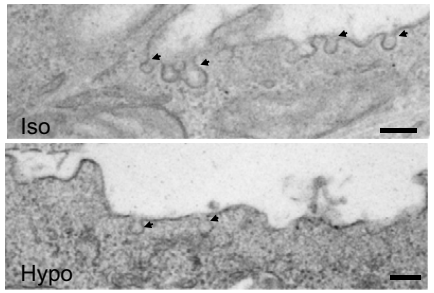
Sens P. and Turner M. *Physical Review E*. 73:031918. 2006

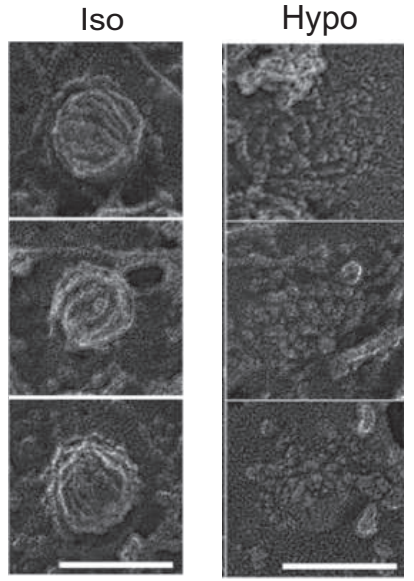
Membrane tension and membrane reservoir

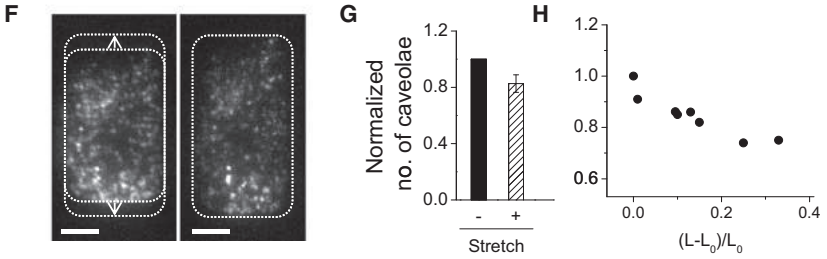
- A plasma membrane reservoir buffers membrane tension: a mechanism
- Cell response to mechanical stress: membrane availability tuned by caveolae

- Cell hypotonic swelling and stretching reduce caveolae at the plasma membrane
- Flattening of caveolae







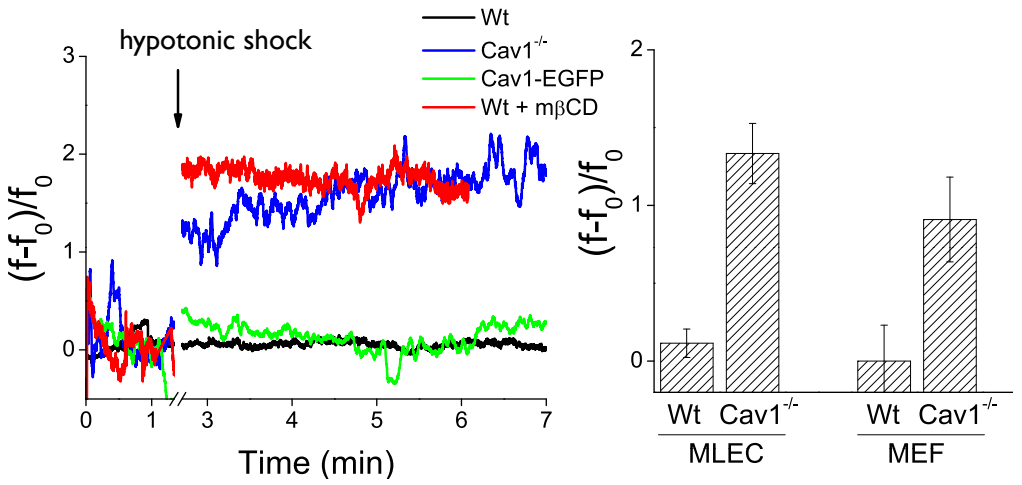


Sinha B., Körster D. et al, Sens P., Lamaze C. and Nassoy P. *Cell*. 144:402. 2011

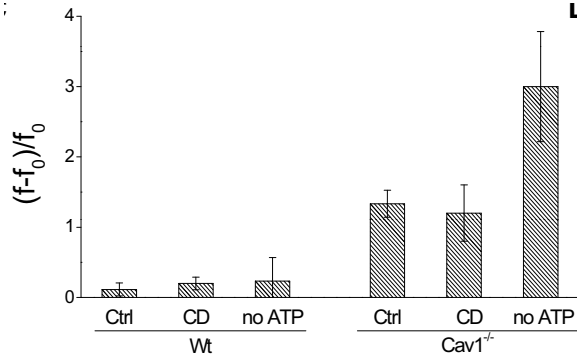
Membrane tension and membrane reservoir

- Cell response to mechanical stress: membrane availability tuned by caveolae

- Use of membrane tethers to measure membrane tension
- Homeostasis of membrane tension requires caveolae
- Independent of Actin and ATP



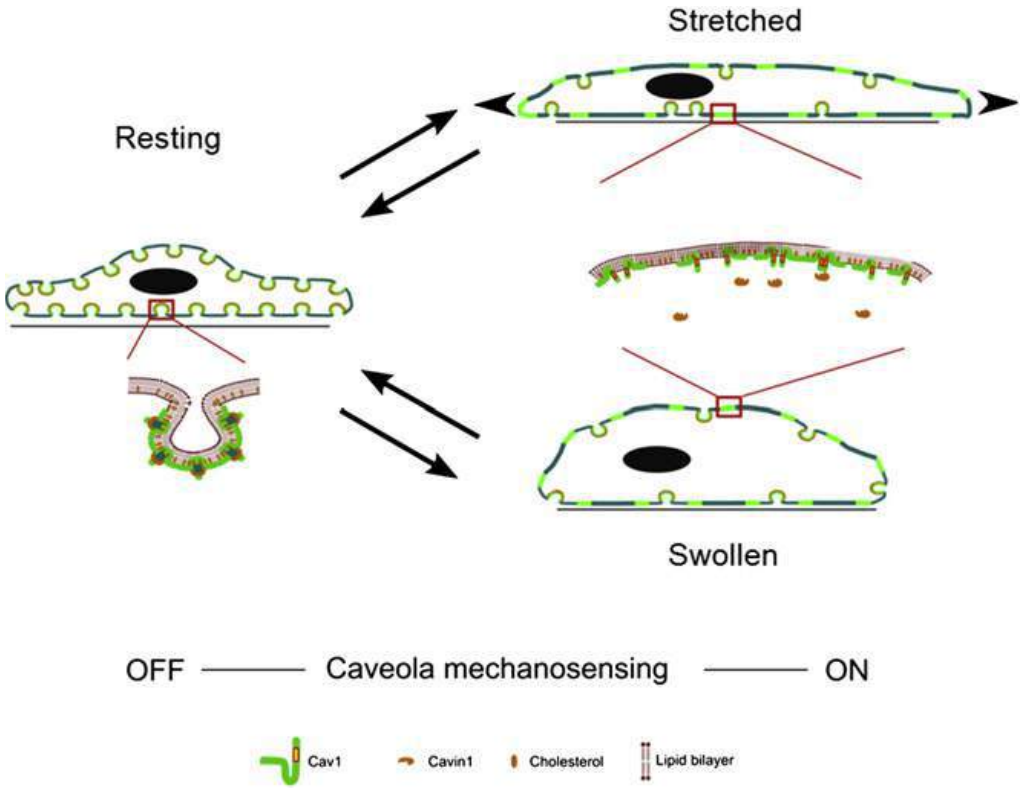
mßCD: cholesterol depletion and caveolae disassembly



Sinha B., Körster D. et al, Sens P., Lamaze C. and Nassoy P. *Cell*. 144:402. 2011

Membrane tension and membrane reservoir

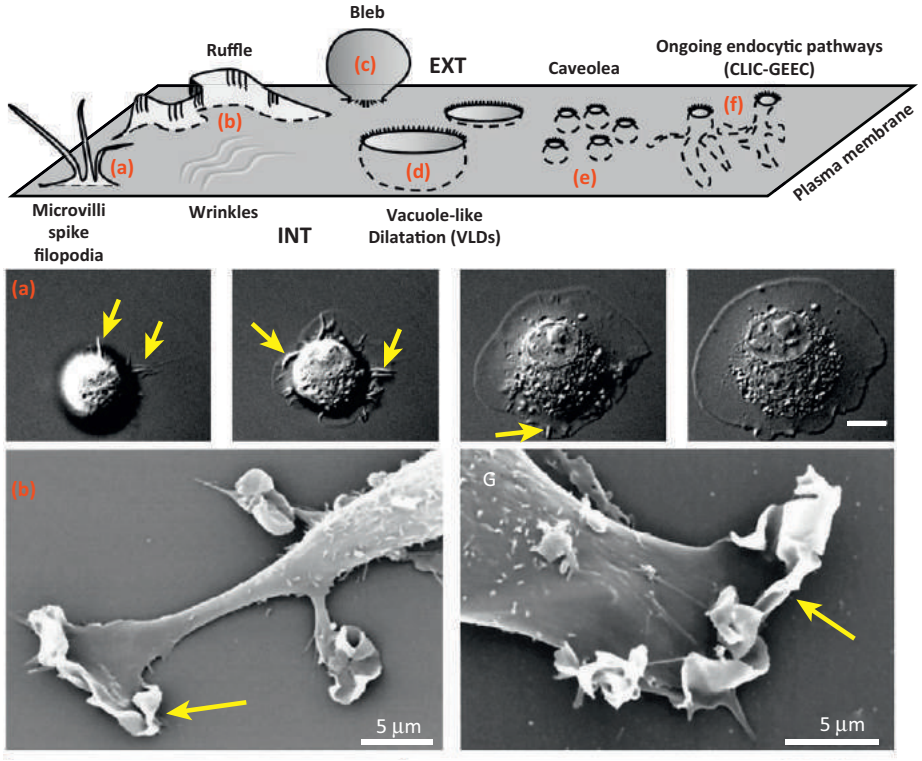
- Cell response to mechanical stress: membrane availability tuned by caveolae

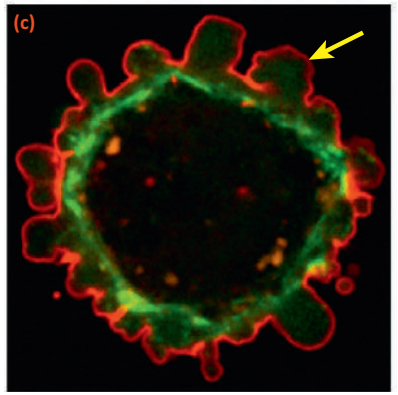


Sinha B., Körster D. et al, Sens P., Lamaze C. and Nassoy P. *Cell*. 144:402. 2011

Membrane tension and membrane reservoir

- A diversity of membrane reservoirs

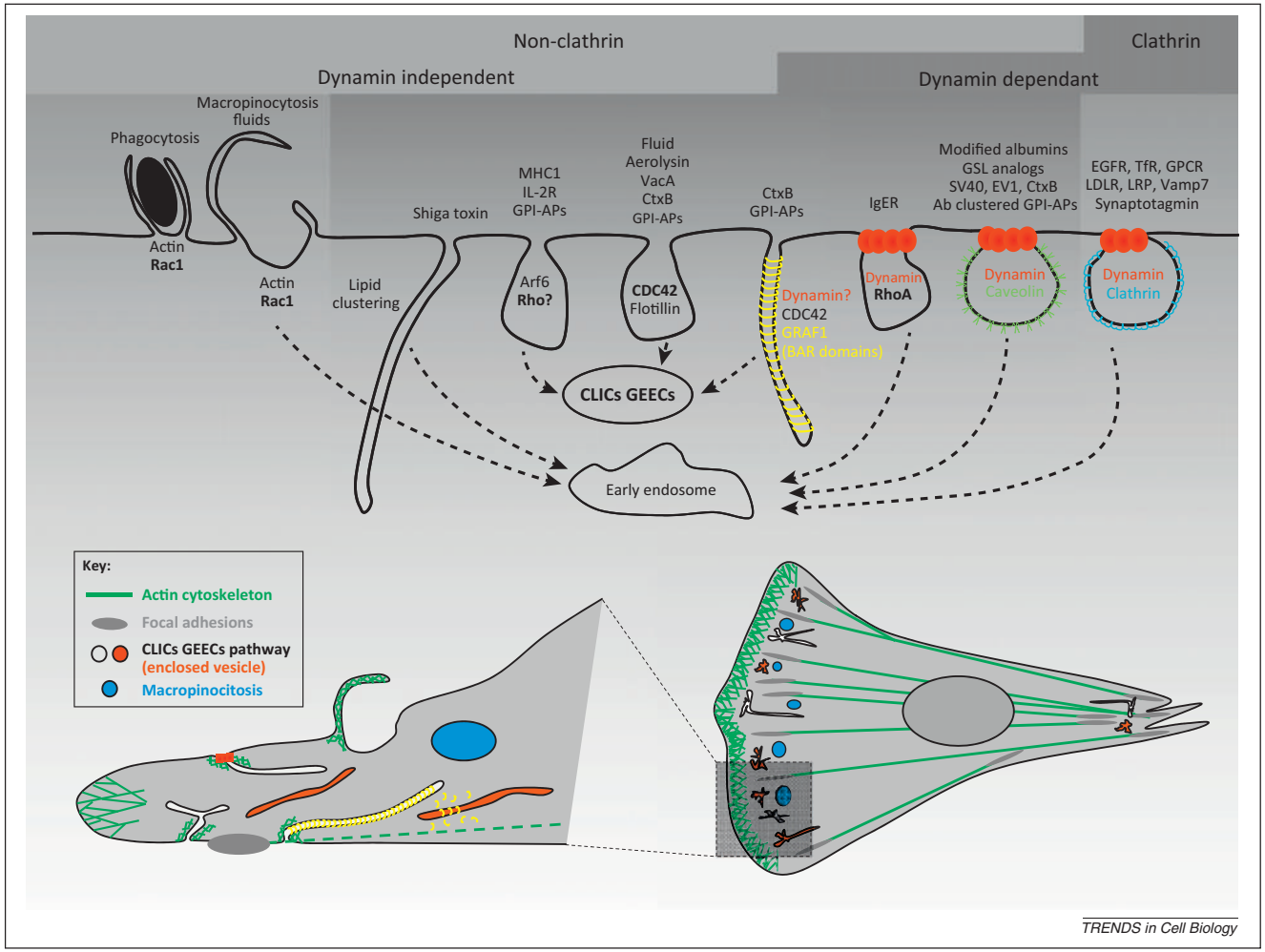




Gauthier N., Masters T. and Sheetz M. *Trends in Cell Biol*, 22:527. 2012

Membrane tension and membrane reservoir

- A diversity of membrane reservoirs

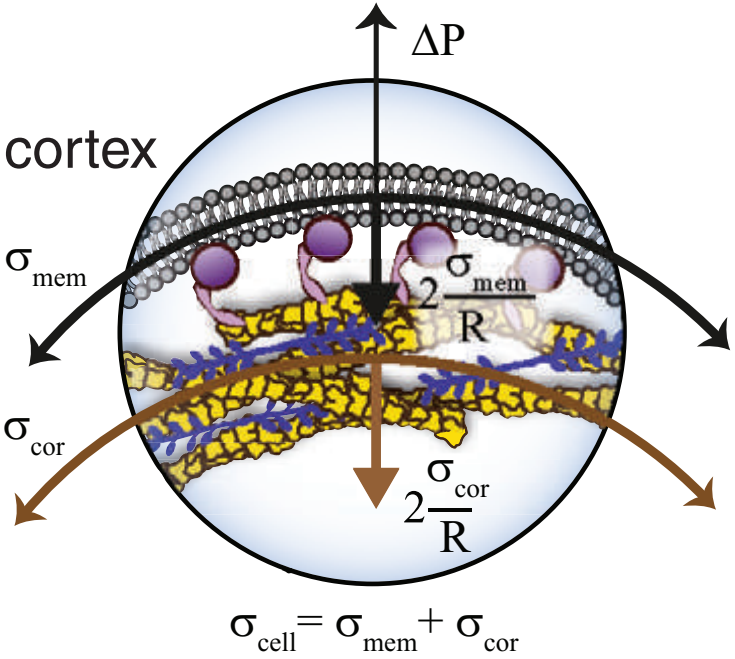


Gauthier N., Masters T. and Sheetz M. *Trends in Cell Biol*, 22:527. 2012

Membrane Tension: Conclusions

- Membrane is a composite material comprising a lipid bilayer coupled dynamically to an actin rich cortex.
- The effective membrane tension reflects contributions of in-plane tension and adhesion between the cortex and the membrane
- The membrane is an inelastic fluid so membrane tension can, in some conditions, propagate mechanical information nearly instantly across a cell
- Coupling between membrane tension and actin turnover can determine cell shape and cell motility (keratocytes).
- Membrane availability and possibility to change surface can tune membrane tension: but this is a slow process
- In general coupling between the membrane and actin cortex is the main contributor of effective membrane tension (but not always: keratocytes…)
- Dynamic coupling between actin and membrane tunes effective viscosity associated with membrane flows.

Membrane vs Cortical Tension



- Membrane is not permeable and bears most of pressure difference

$$\Delta P = \sigma_{\mathrm{mem}} C + f_{\mathrm{link}} \rho_{\mathrm{link}}$$

ρ_{link} : density of linkers

f_{link} : force per membrane/cortex linker

- Linkers are under tension due to cortical tension

$$f_{\mathrm{link}} \rho_{\mathrm{link}} = \sigma_{\mathrm{cor}} C$$

>> Cell tension contributed by both membrane and cortex tension

$$\Delta P = (\sigma_{\mathrm{mem}} + \sigma_{\mathrm{cor}}) C$$

- Cell tension = Membrane tension + Cortical tension

Sens P and Plastino J. *J. Phys.: Condens. Matter.* 27:273103. 2015

Cell tension - Cortical tension

28 Novembre 2017