Dynamical Control of the Shape and Size of Stereocilia and Microvilli

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Hair cells, stereocilia; microvilli

Kachar's law

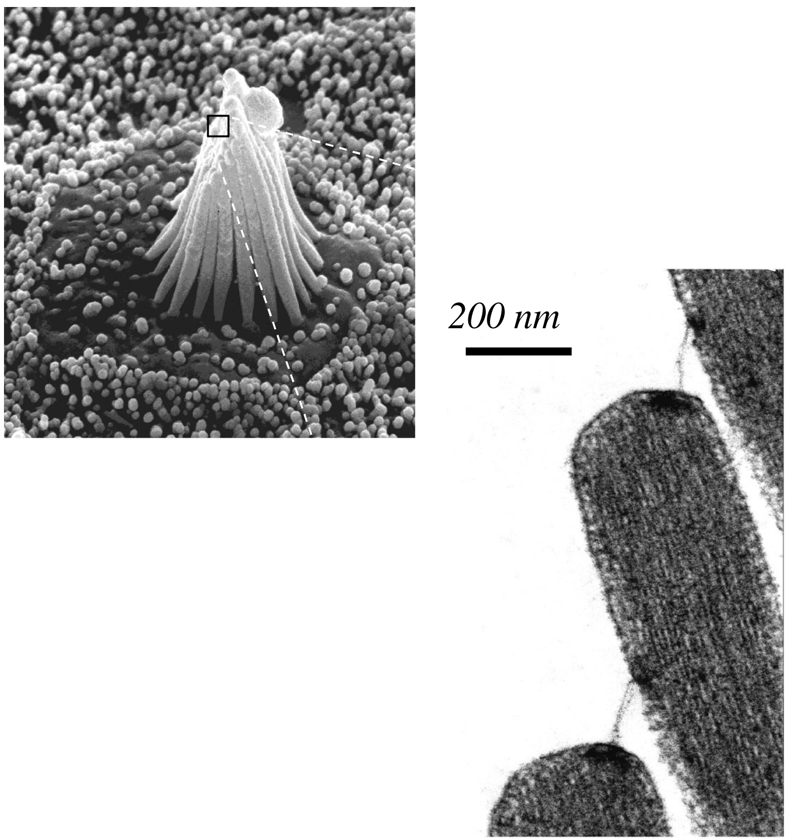
Tip and Membrane dynamics

Stereocilia shape: *depolymerization*
membrane shape

Penetration in the cortical layer

Lamellipodium motion

Hair cells



Ciliated cells of the inner ear

Bundle of actin cilia

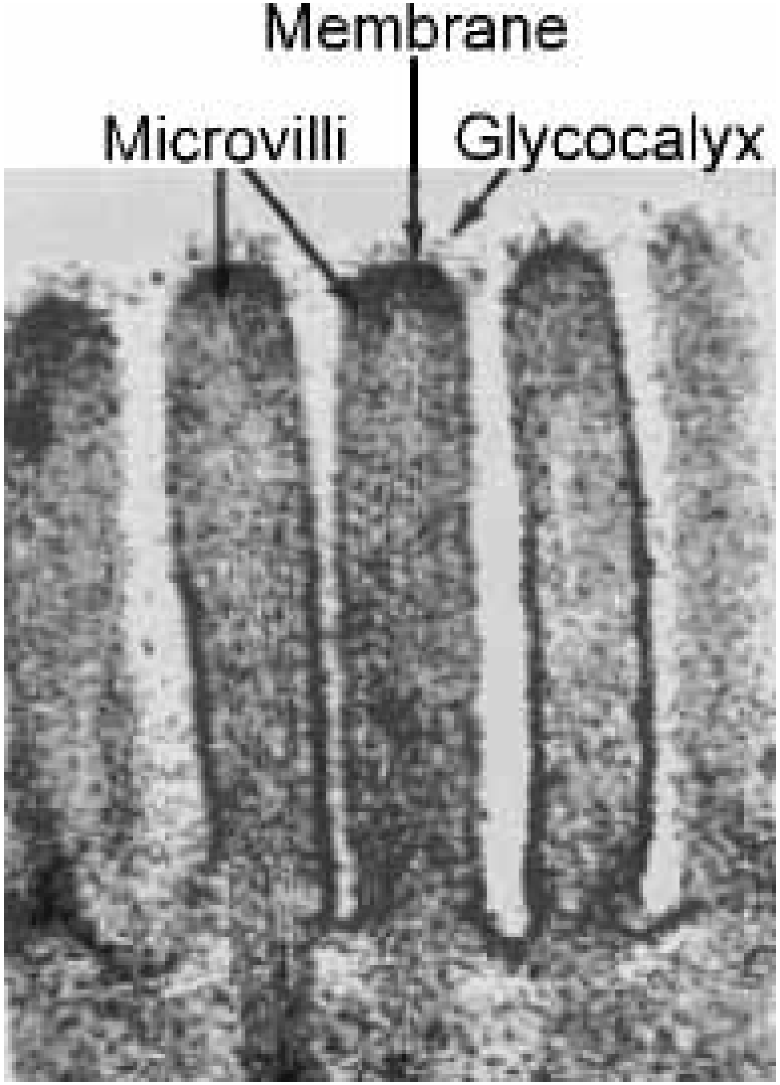
Graded sizes in a bundle

Connections via tip-links

Bundles of varying sizes

Shape and size regulation?

Other ciliated cells



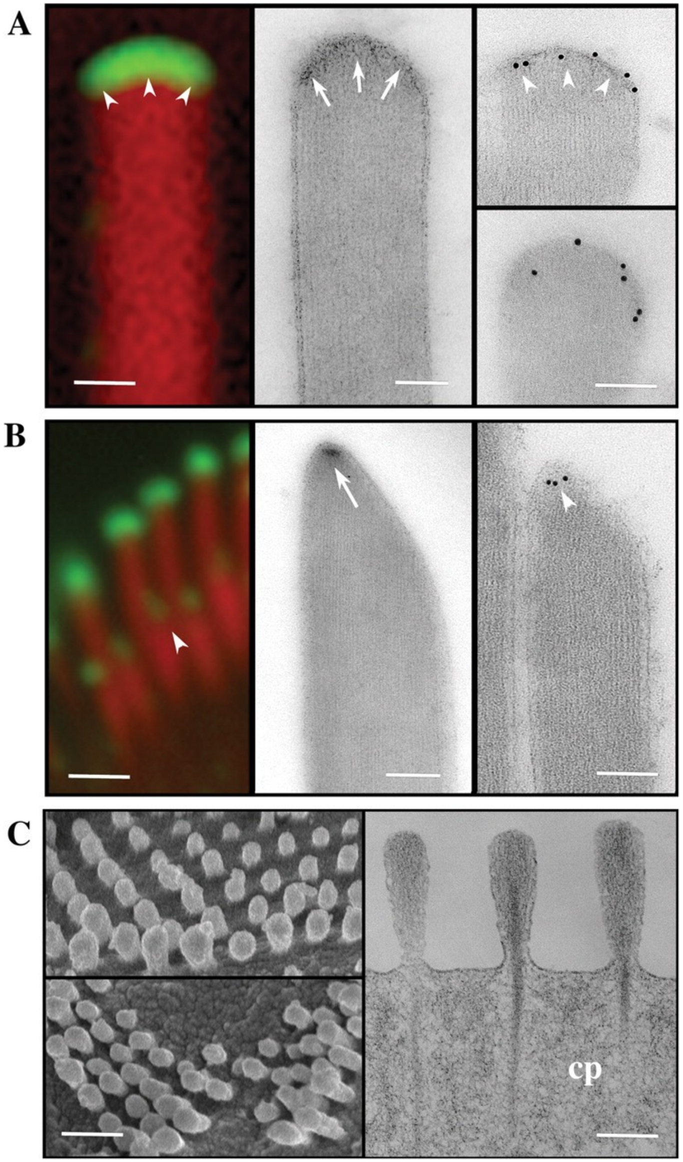
Intestinal epithelial brush border cells

Microvilli (actin structures)

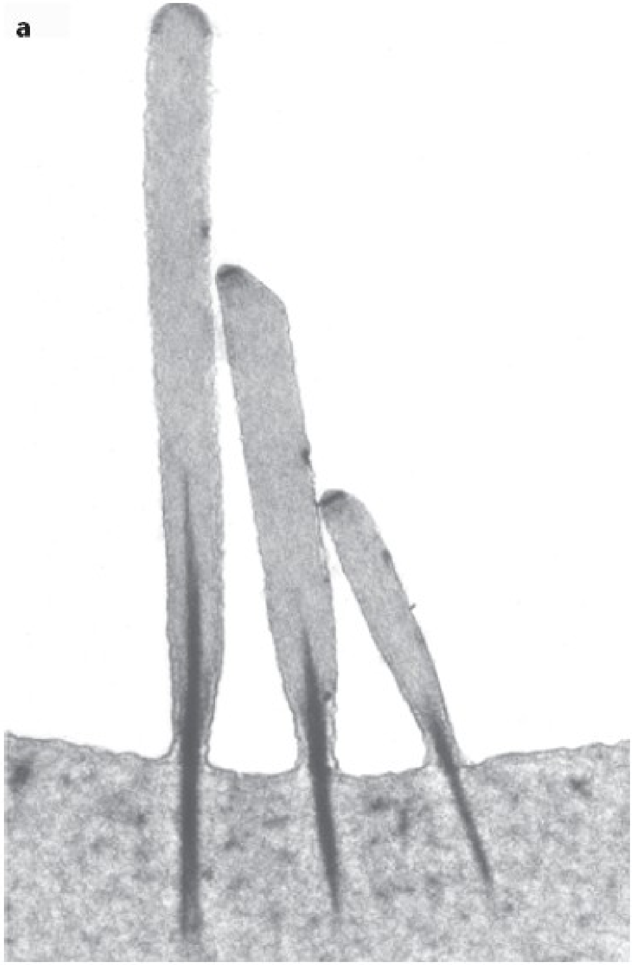
Spines and boutons in neurons

Filipodia-lamellipodia

Stereocilia shape in hairbundle

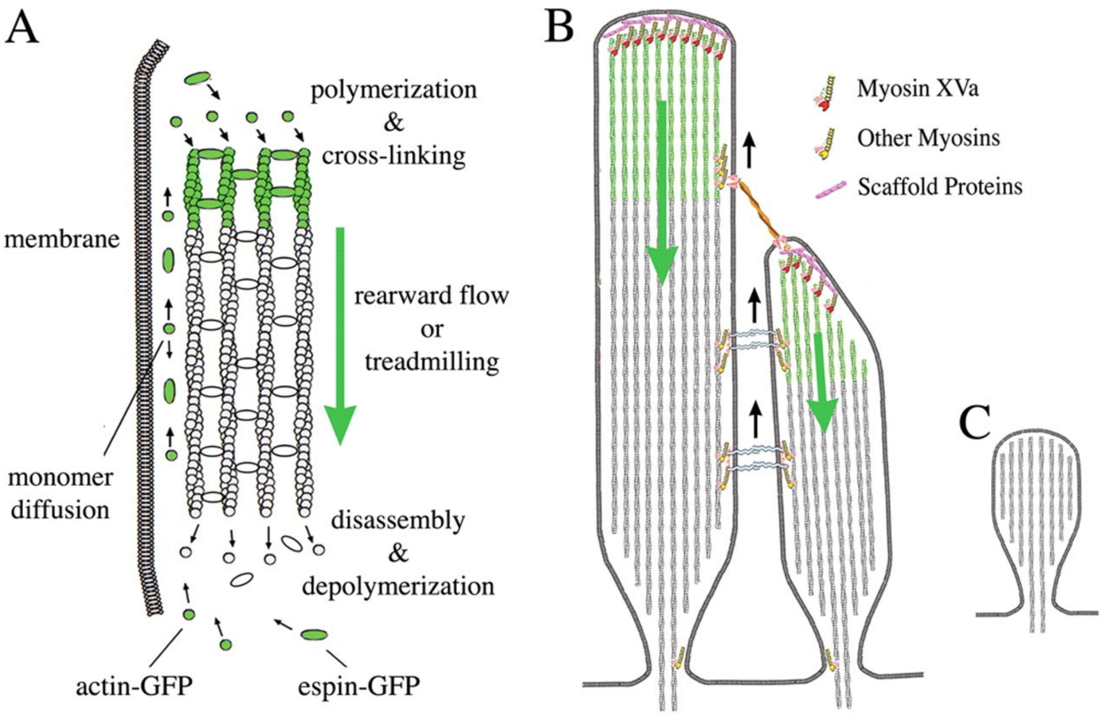


Radzinska et al

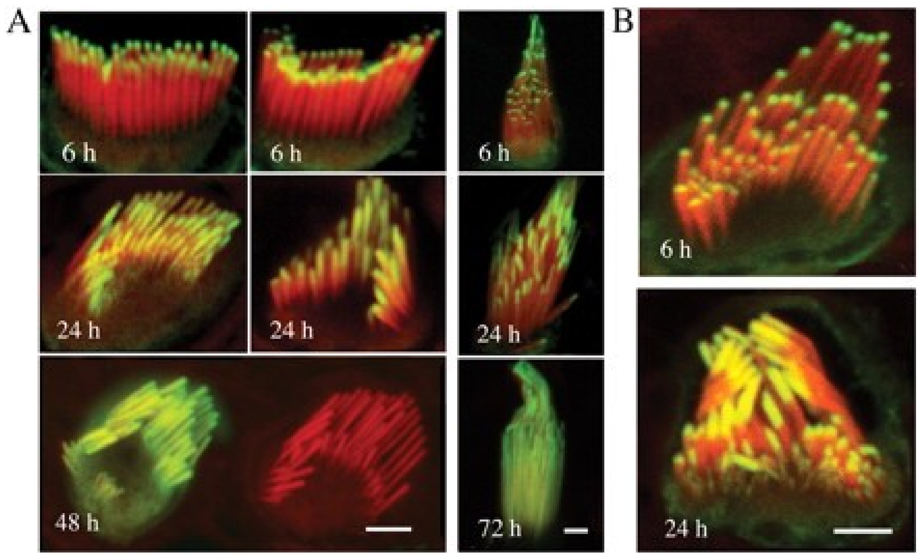


Fettiplace and Hackney

Actin and espin in stereocilia Radzinska et al.



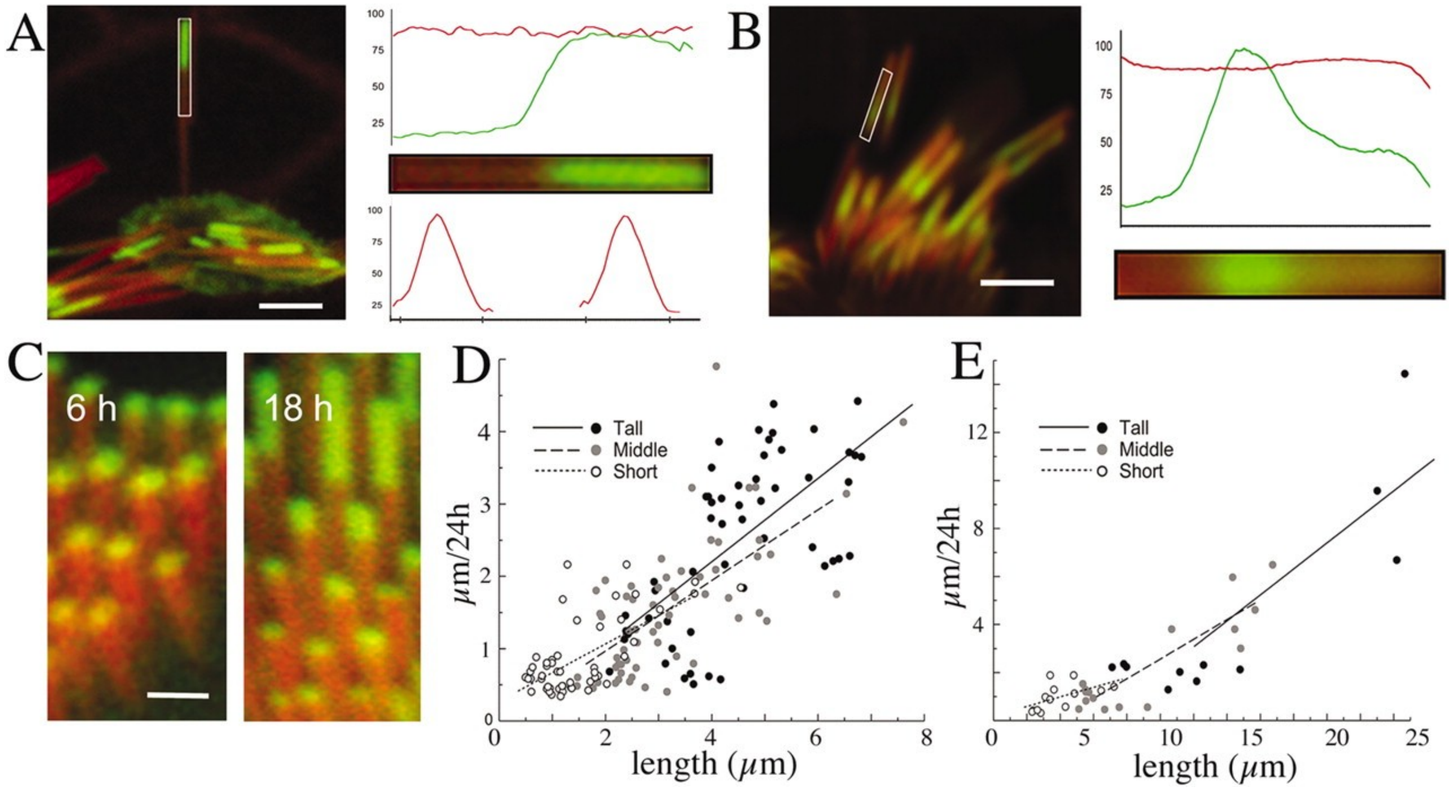
Stereocilium structure



Actin and espin incorporation

organ of corti and vestibule

Kachar's treadmilling laws *Radzinska et al.*

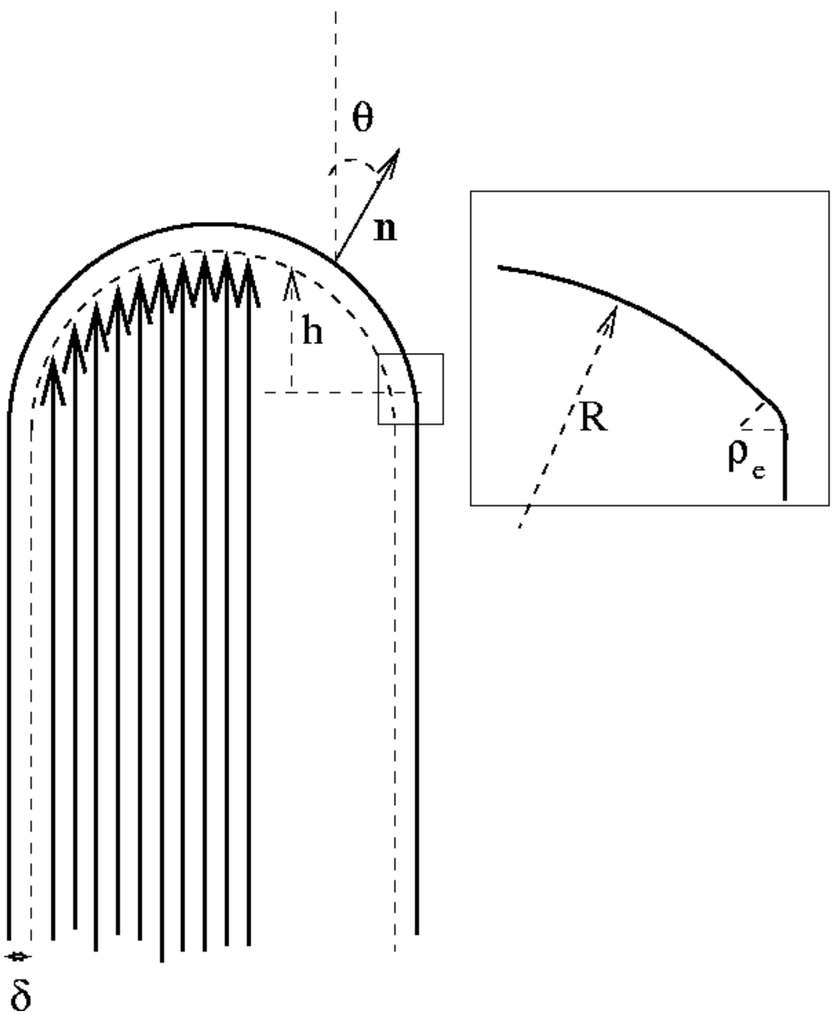


Treadmilling velocity proportional to stereocilum length

constant treadmilling time

Thicker stereocilia have a larger treadmilling velocity

Membrane dynamics and polymerization front



Free energy

$$F_m = \int ds_m \left\{ \sigma + \frac{1}{2} \kappa H^2 \right\} - \int P \, dv$$

$$F_i = \int ds_m \frac{1}{2} k (\delta - \delta_0)^2$$

Ignore orientation dependence of δ_0 and σ

Linear dynamic equation

$$v_n = -\lambda_m \frac{\delta F}{\delta r_n}$$

$$\frac{\partial h}{\partial t} + v_T = -\lambda_a \frac{\delta F}{\delta h} + v_p^0$$

Steady state treadmilling

Membrane shape equation

$$\frac{\delta F_m}{\delta \mathbf{r}_n} = \frac{v_p^0 - v_T}{\lambda_a} + \frac{1}{2}\frac{H(v_T - v_p^0)^2}{k\lambda_a^2}$$

Effective tension

$$\sigma_{eff} = \sigma + \frac{1}{2}\frac{(v_T - v_p^0)^2}{k\lambda_a^2}$$

Effective pressure

$$P_{eff} = P + \frac{v_p^0 - v_T}{\lambda_a}$$

P_{eff}~3 10^3 Pa, Total force 100 pN, Force per filament 3 10^{-1} pN

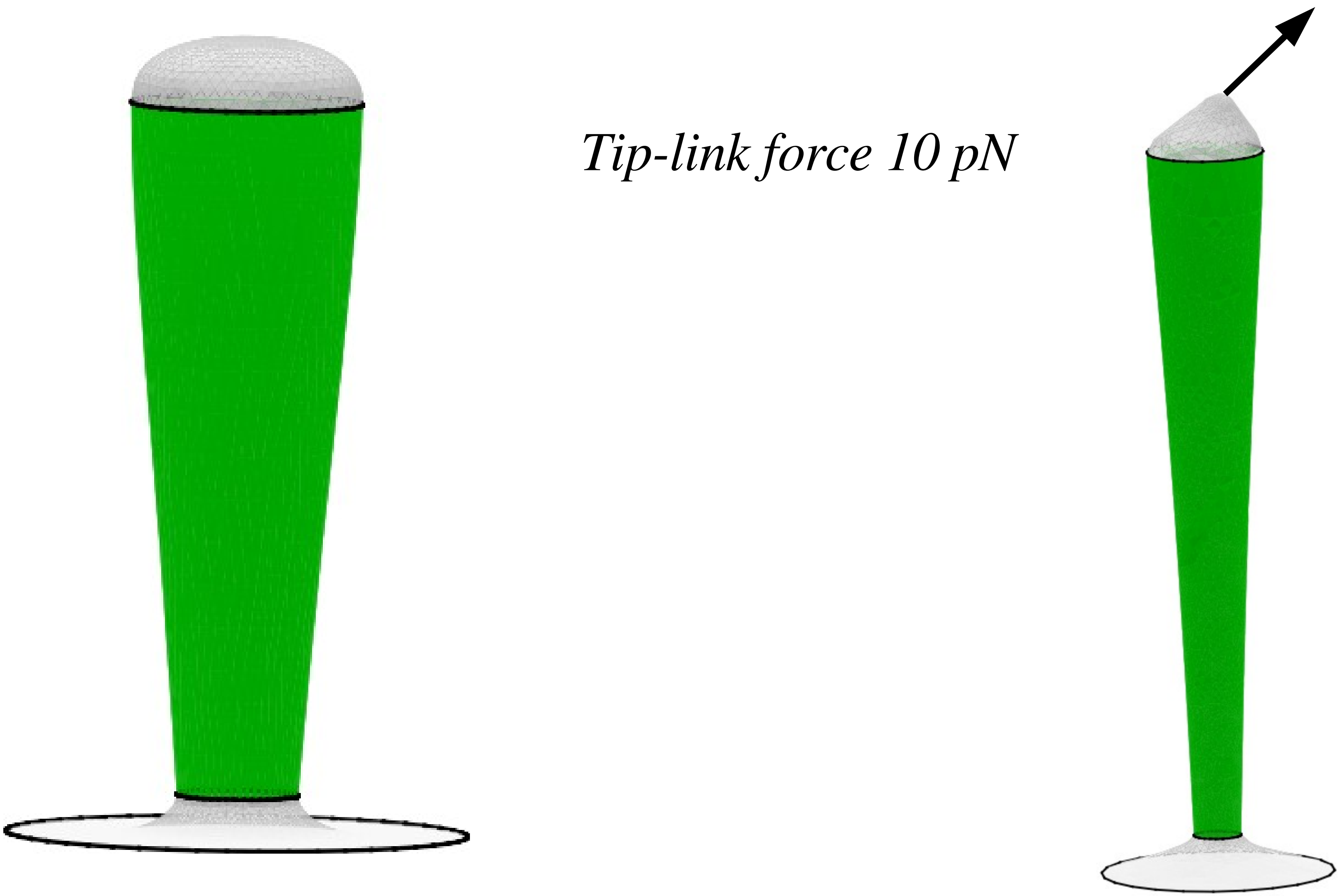
Treadmilling velocity

$$v_T = v_p^0 - \lambda_a\left(\frac{2\sigma_{eff}}{\mathbf{r}_0} + \frac{\kappa}{\mathbf{r}_0^3}\right)$$

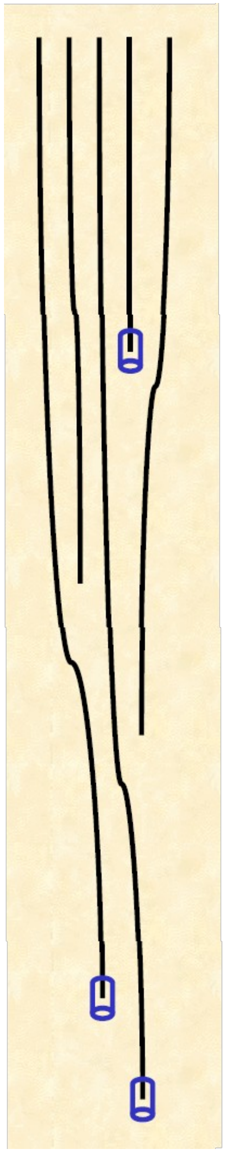
Thicker cilia have a large treadmilling velocity Gale et al.

Mean field theory, ignores non-linear effects

Tip-link force *C.Barbotta*



Shape of the stem: depolymerization



Polymerization at the barbed end

At the tip z=0 with a rate k_p

Capping protein of the pointed end (espin)

prevents depolymerization
uncaps with a rate k_u

Depolymerization at the pointed end

only uncapped filaments
rate k_d

Depolymerization kinetics

Rate equations

$$\frac{\partial p^c(n)}{\partial t} = -k_u p^c(n) + k_p p^c(n-1) - k_p p^c(n)$$

$$\frac{\partial p^u(n)}{\partial t} = k_u p^c(n) + k_p p^u(n-1) - k_p p^u(n) + k_d p^u(n+1) - k_d p^u(n)$$

Stereocilium shape

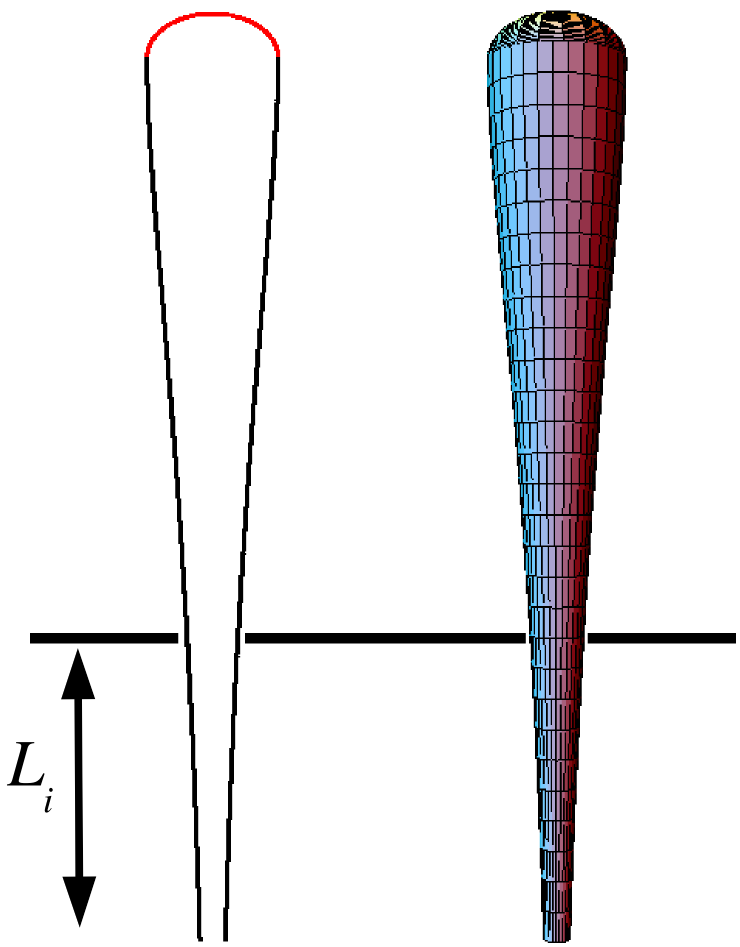
Constant inplane density

$$r(z) = r_0 \left[\frac{k_d - k_p}{k_d - k_u - k_p} \left(\frac{k_p}{k_p + k_u} \right)^{z/a} - \frac{k_u}{k_d - k_u - k_p} \left(\frac{k_p}{k_d} \right)^{z/a} \right]^{1/2}$$

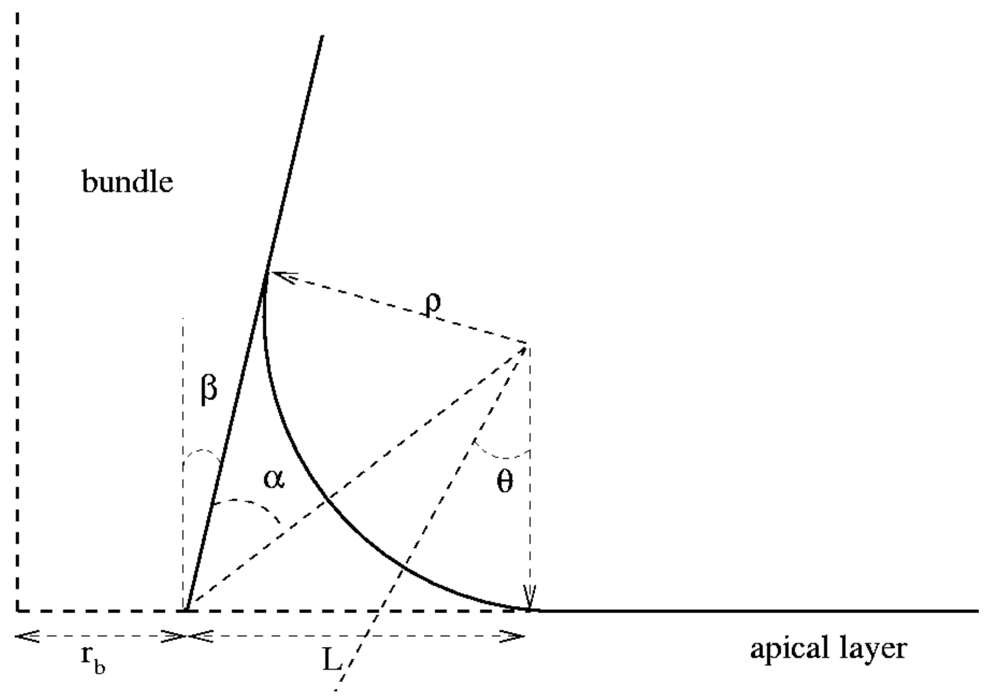
exponential decay over $\lambda = v_T k_u^{-1}$

Kachar's law $L_T = 2 v_T k_u^{-1} \log \frac{r_0}{a} \left(\frac{k_d - k_p}{k_d - k_p - k_u} \right)^{1/2}$ *time scale fixed by uncapping*

Shape of stereocilia



Membrane shape



Curvature radius $\rho \sim (\kappa / 2\,\tilde{\sigma})^{1/2}$

Emerging part of stereocilia

Force balance between

Membrane force $f_m = 2\pi r_b \sigma$

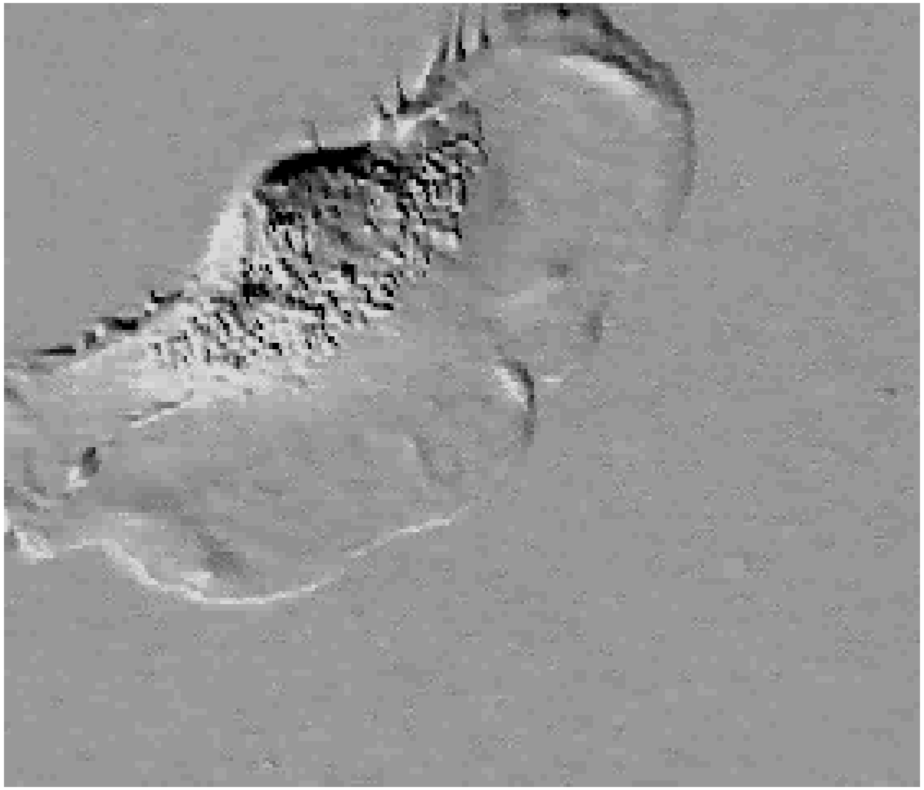
Viscous friction between actin fascicle and cortical layer $f_f = \alpha \eta L_i v_T$

Immersed length $$\frac{L_i}{2\lambda} \exp - \left(\frac{L_i}{2\lambda}\right) = \frac{a\sigma}{(\alpha/\pi)\lambda v_T \eta} = \epsilon$$

large ε *totally immersed fascicle*
small ε *finite immersed length smaller than* 2λ

Maximum immersed length $L_i < L_T/3$

Keratocyte motion



Flat region

Lamellipodium at the front

only actin

fast retrograde flow

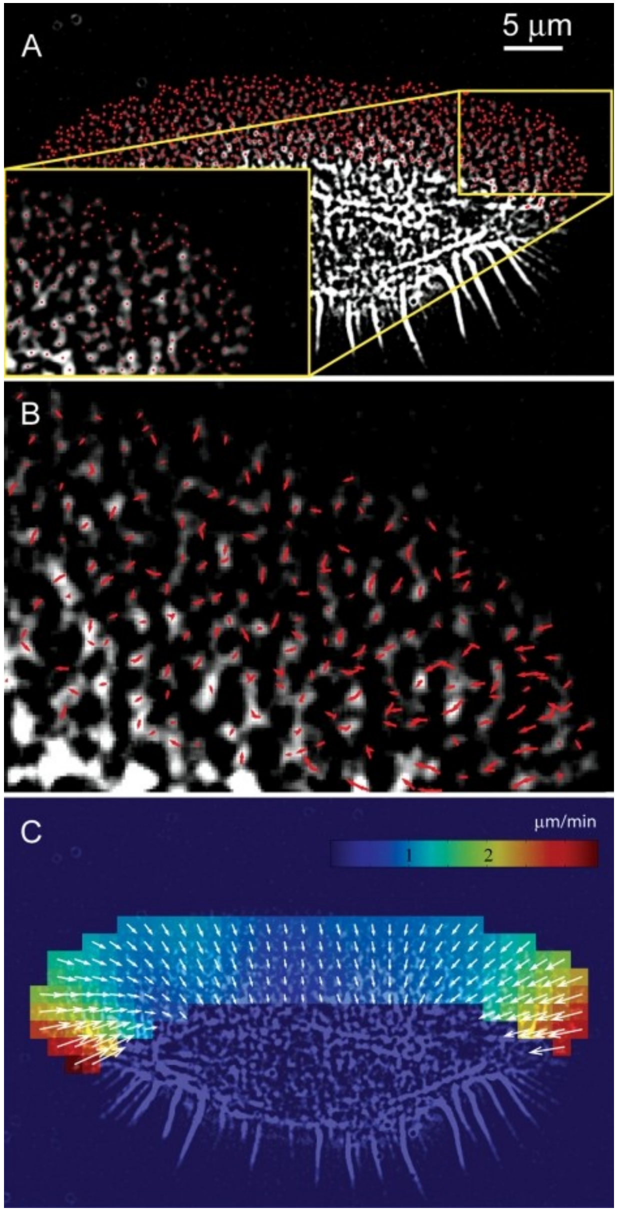
Lamella at the back

actin and myosin

slow retrograde flow

Advancing velocity 10 μm/min.

Keratocyte motion



Velocity field obtained by speckle microscopy Vallotton et al.

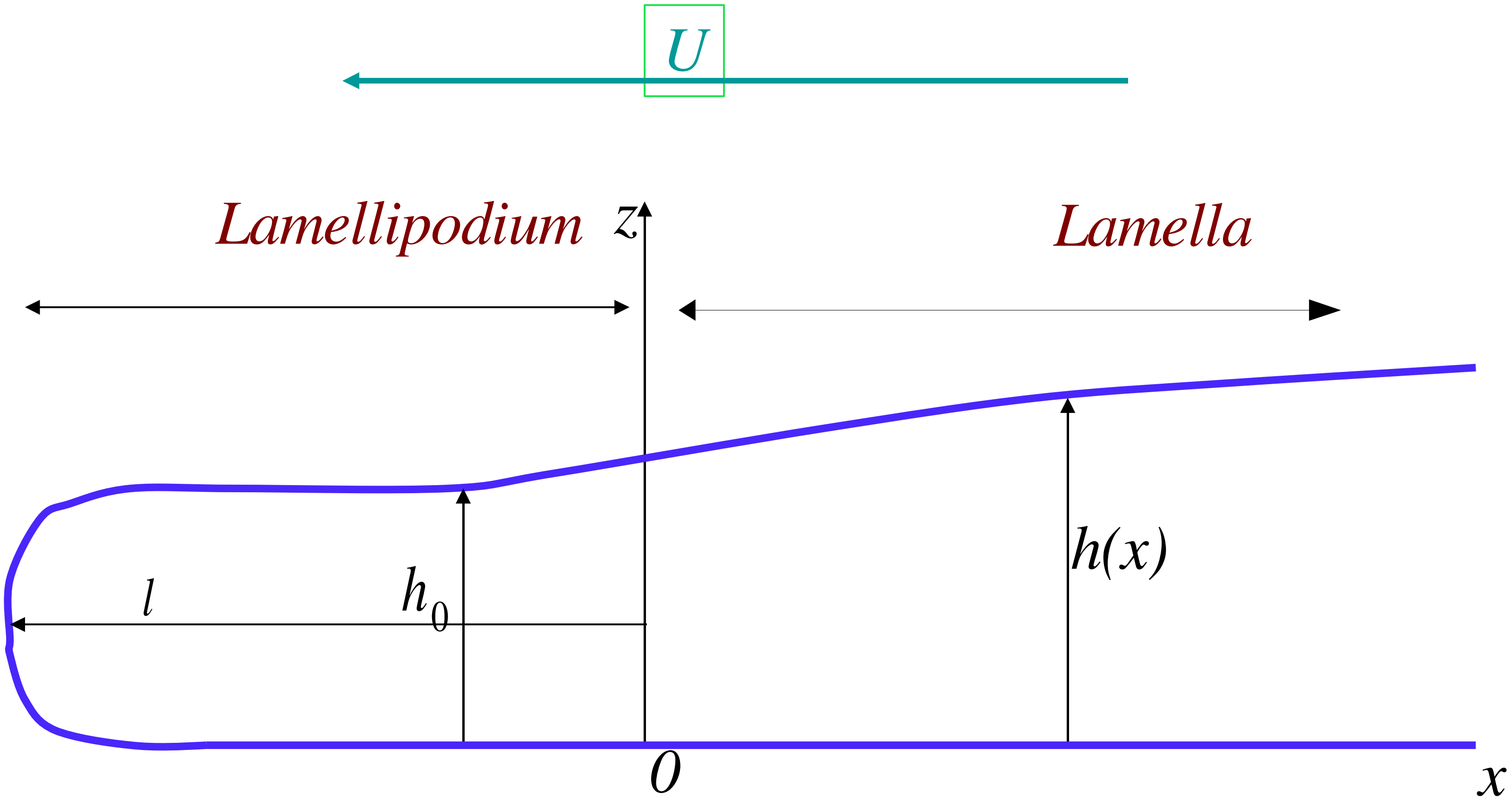
Advancing velocity 10 µm/min

Retrograde flow 1 µm/min

Surface stress distribution $\sigma_{xz} = 4.10^2$ N/m^2 *Oliver et al.*

Actin viscosity $\eta = E\tau \sim 10^5 Pa.s$ *Käs et al.*

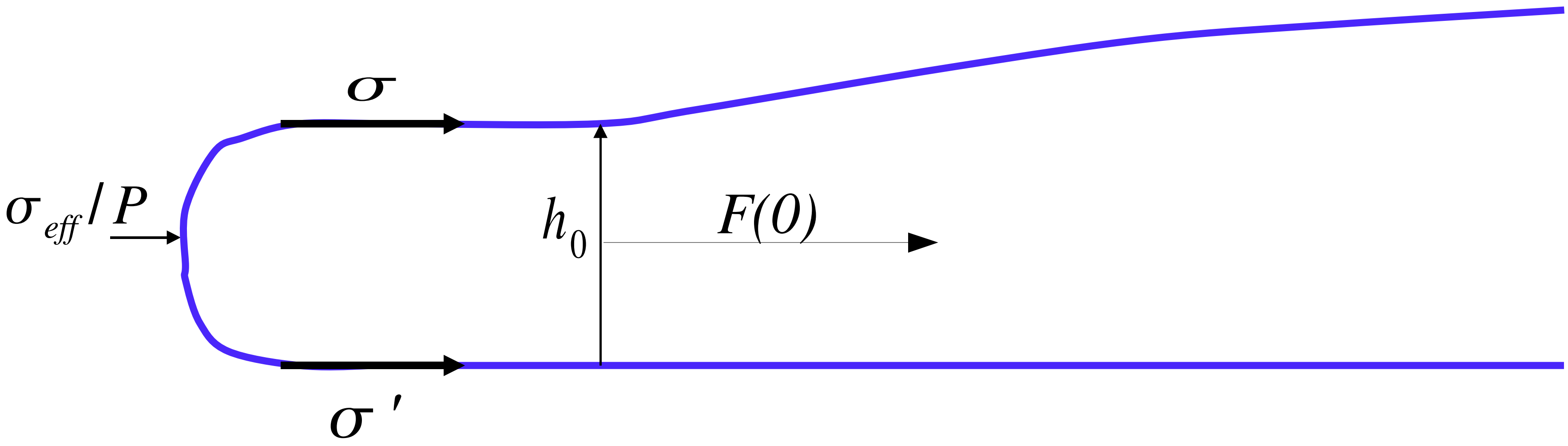
Lamellipodium motion



Actin viscoelasticity: *solid-like region at the front (lamellipodium)*
liquid-like region at the back (lamella)

Size of lamellipodium $l=(U+v(0))\,\tau$

Solid like motion of lamellipodium



Force balance on the tip (moving frame)

Effective polymerization pressure

$$P_{eff} = \frac{v_p^0 - (U + v(0))}{\lambda_a}$$

Force balance on the lamellipodium

$$F(0) = \sigma + \sigma' + F_{ext} - \xi v(0) l$$

Force balance on the membrane

$$P_{eff} h_0 = \sigma + \sigma' + F_{ext}$$

Liquid like motion of the lamella

Active gel theory

Constitutive equation $$2\eta \frac{\partial v}{\partial x} = \sigma_{xx} + \zeta \Delta \mu$$

Viscous friction on the substrate $$\sigma_{xz}(z=0) = \xi v$$

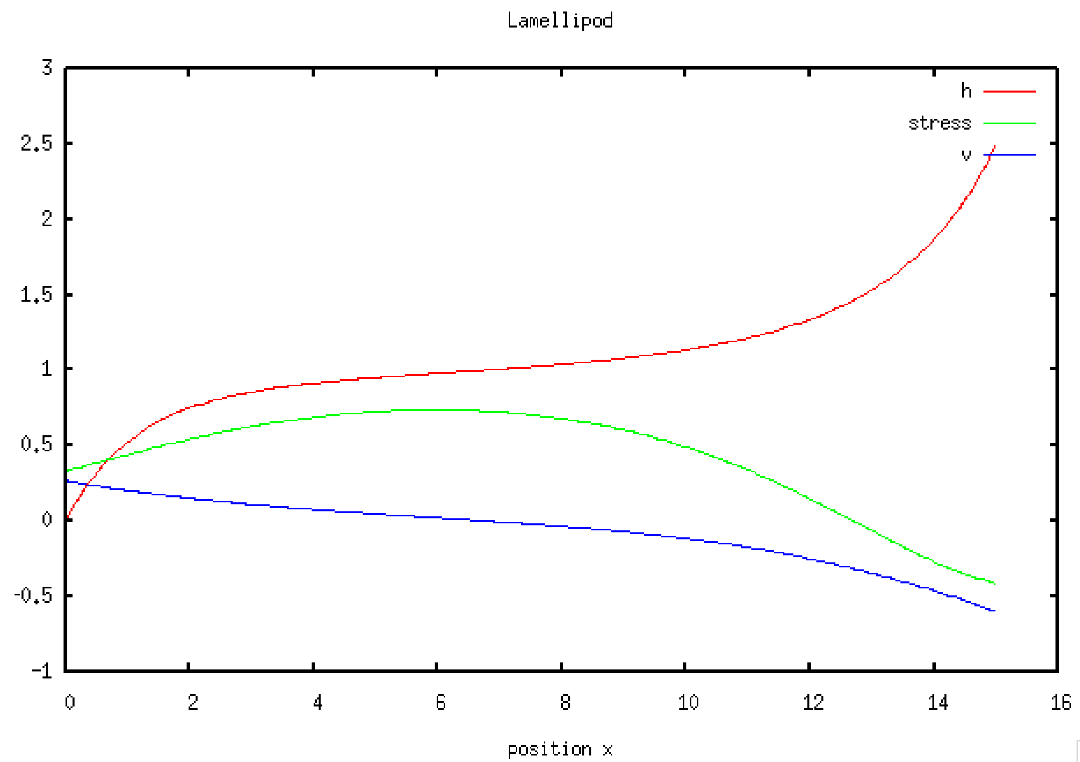
Force balance $$\frac{\partial(\sigma_{xx} h)}{\partial x} = \frac{\partial F}{\partial x} = \xi v$$

Mass conservation $$h(x)(U + v(x)) = cst$$

Matching with the solid region

h_0, $v(0)$, $-F(0) = \sigma_{xx} h_0$

Lamellipodium profile



Lamellipodium thickness $\mathbf{h} = \mathbf{h}_0 \frac{\mathbf{v}_d}{\mathbf{u}}$

Advancing velocity $\mathbf{u} = \mathbf{v}_d - \left(\frac{\mathbf{h}_0}{4\eta\xi}\right)^{1/2} \zeta \Delta \mu$ *active effects 10%*

Force dipole due to active stresses $Q = \zeta \Delta\mu \; L_x L_y h \sim -6\ 10^{-13}\ J$

Concluding remarks

Kachar's law under the assumption that depolymerization is controlled by a capping protein

Qualitative shape of the stereocilium reproduced

Immersed length of the stereocilium

> *One parameter undetermined: radius of stereocilium*
> *Mean field theory: polymerization fluctuations at the tip*
> *Role of molecular motors: myosin XV*
> *myosin VI*

Application to lamellipodium motion