Soft matter and Biology

Some classical examples and illustrations

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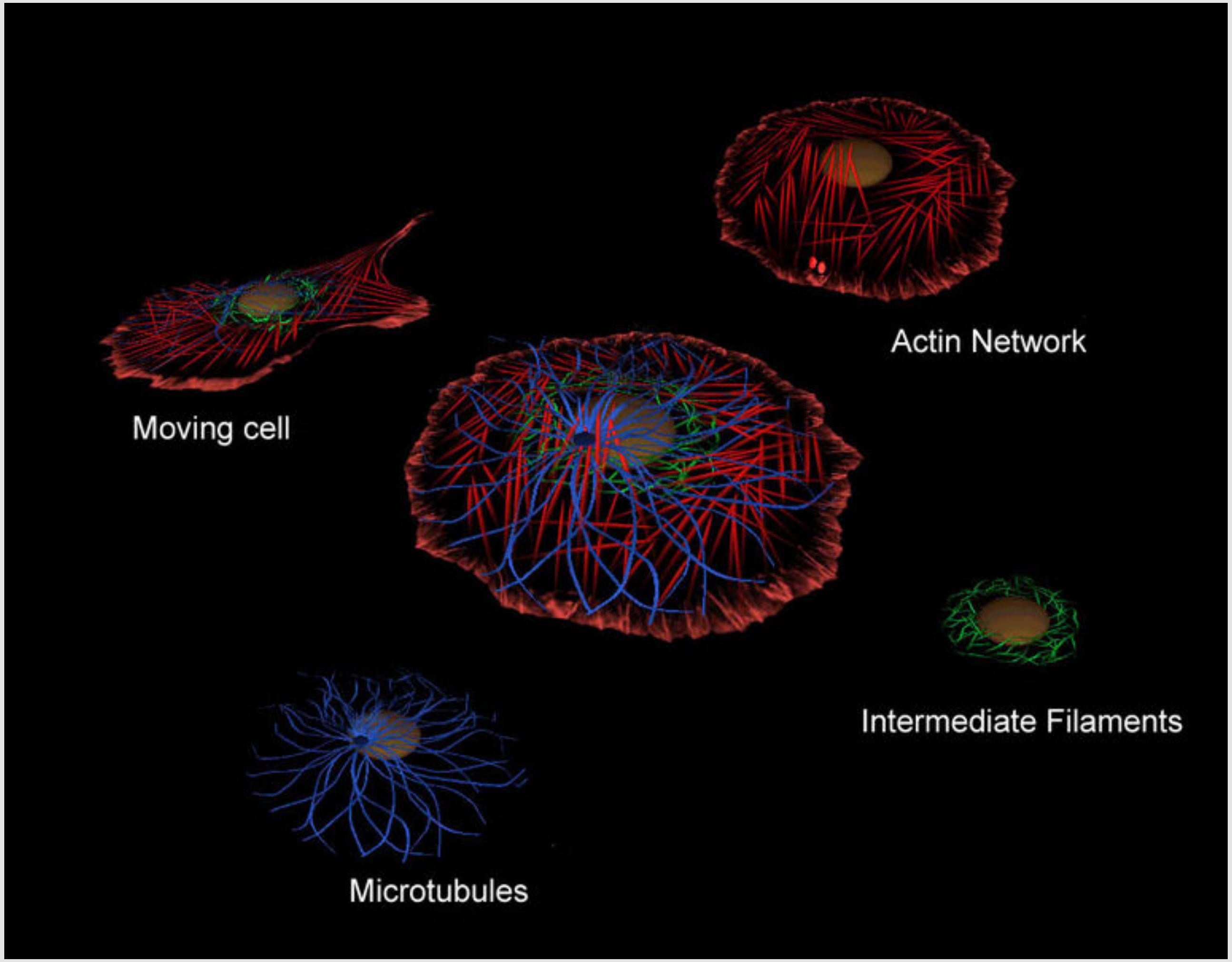
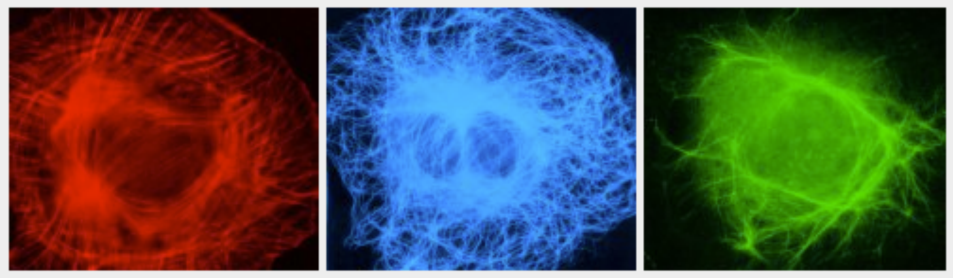
Institut Curie, Paris

The cell cytoskeleton

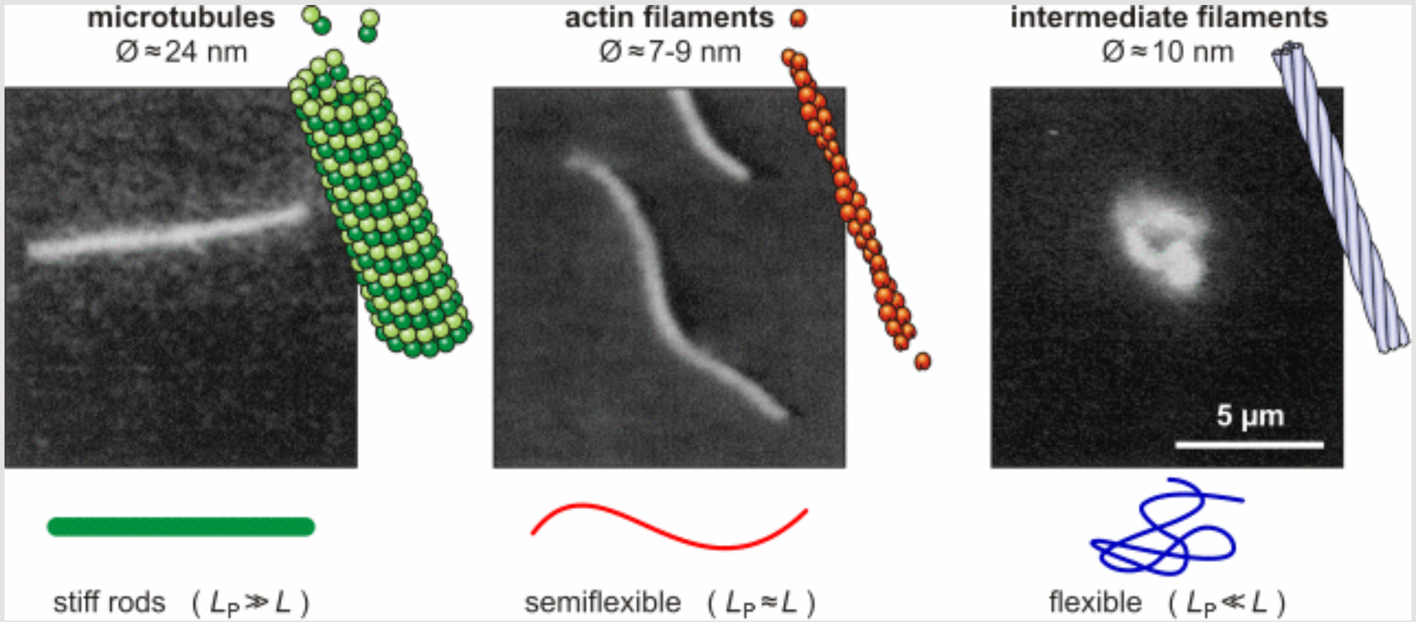


Source: J. V. Small 2013–2014
http://cellix.imba.oeaw.ac.at/cytoskeleton

The cell cytoskeleton



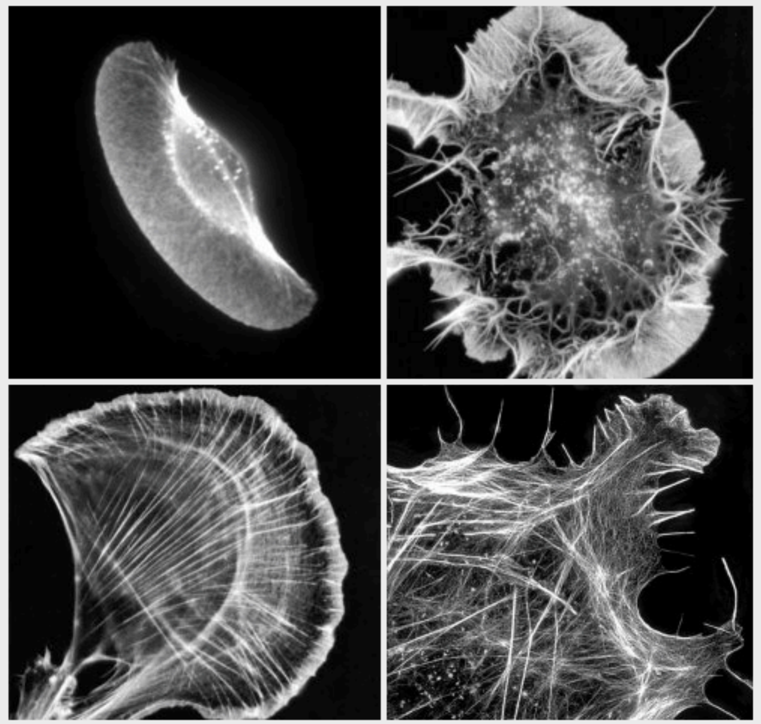
Fibroblast Cytoskeleton
Source: J. V. Small 2013–2014
http://cellix.imba.oeaw.ac.at/cytoskeleton



Source: Josef Käs ; https://www.uni-leipzig.de

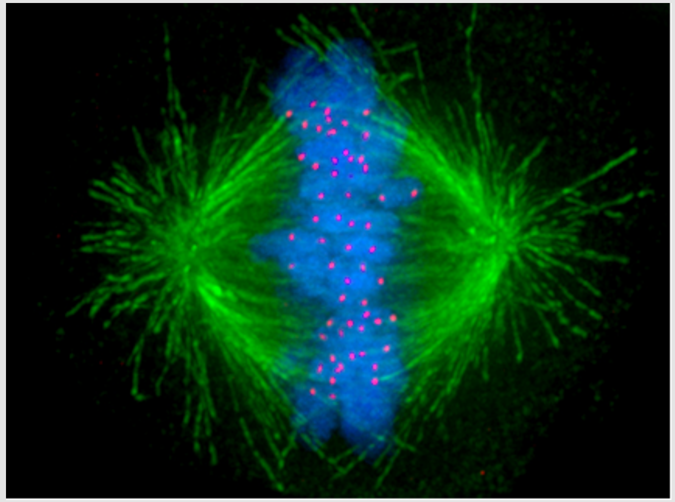
Cytoskeleton and cell motility

Actin



Source: Vic Small
http://cellix.imba.oeaw.ac.at/cytoskeleton

Microtubules

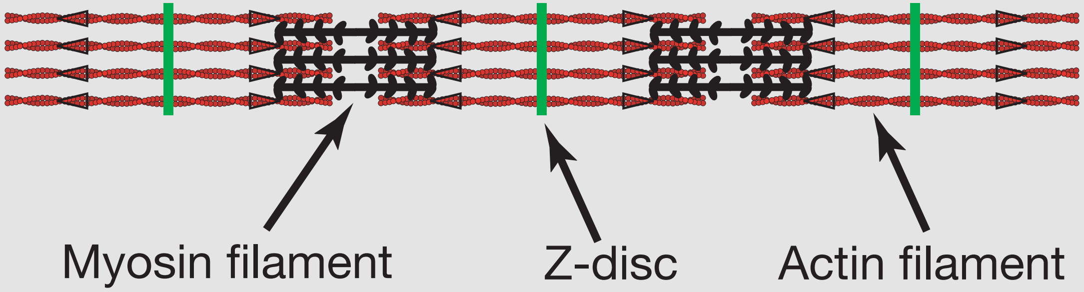


Green: Microtubules ; Blue: Chromosomes ; Pink: Kinetochores.

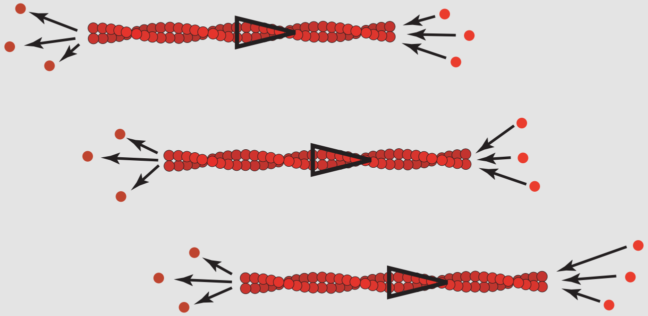
https://fr.wikipedia.org/wiki/Kinétochore

T. Risler, *Cytoskeleton and Cell Motility*,
in **Encyclopedia of Complexity and System Science**, Springer NY (2009)

Sources of activity



Source: K. Kruse
http://www.uni-saarland.de



Source: K. Kruse
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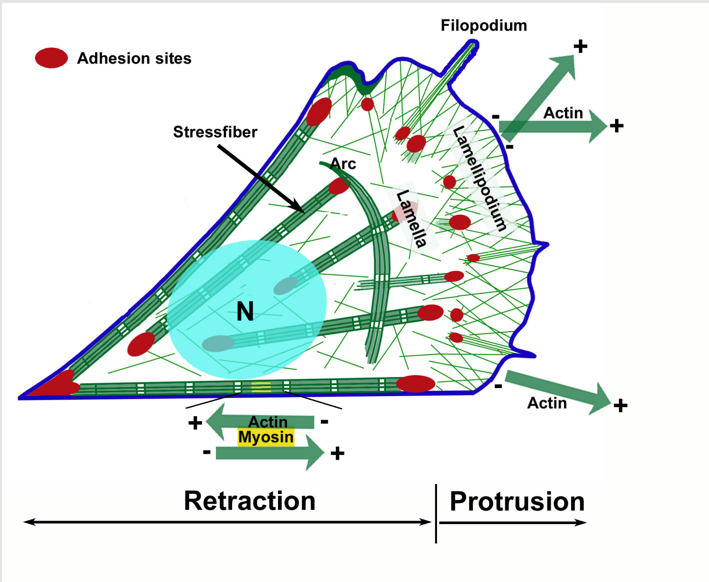
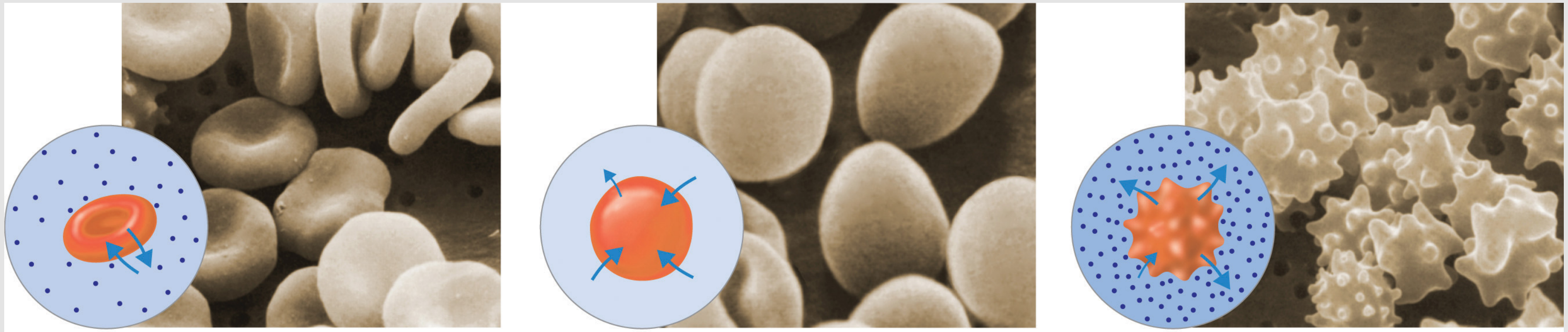


Source:
Vic Small

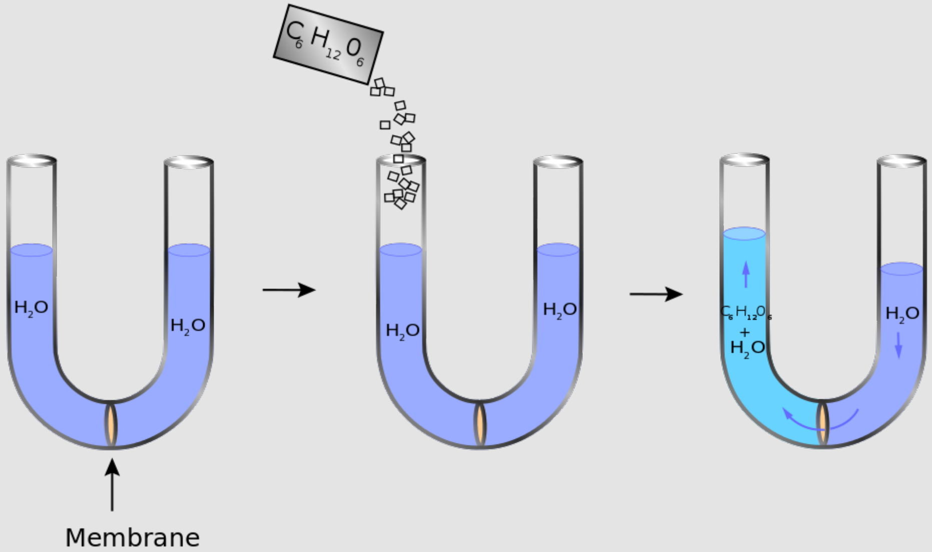
T. Risler, *Cytoskeleton and Cell Motility*,
in **Encyclopedia of Complexity and System Science**, Springer NY (2009)

Osmotic pressure



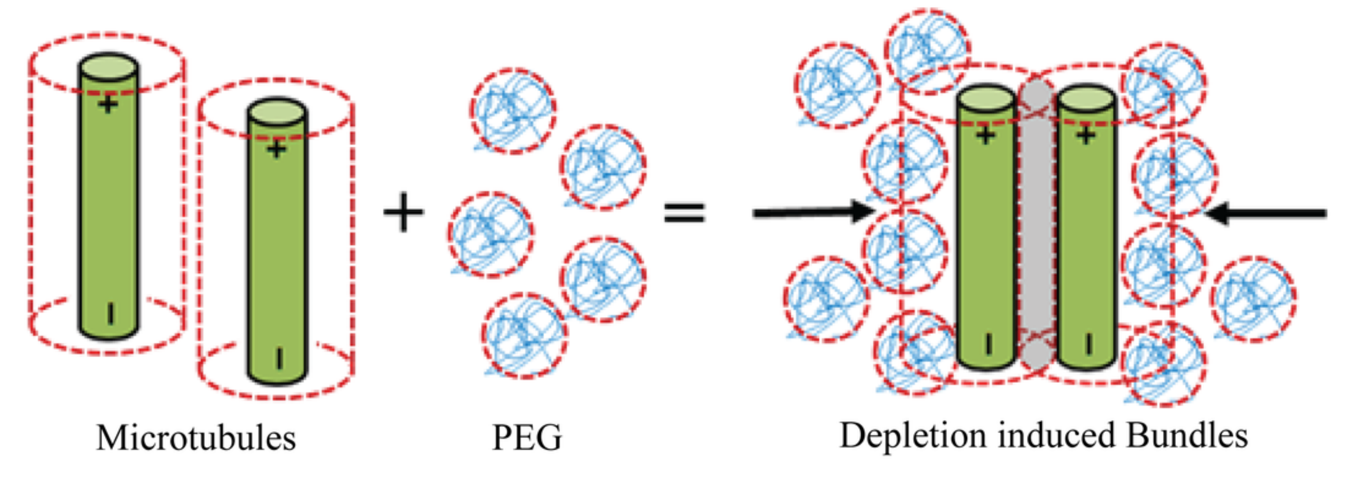
(a) Cells in dilute salt solution (b) Cells in distilled water (c) Cells in concentrated salt solution

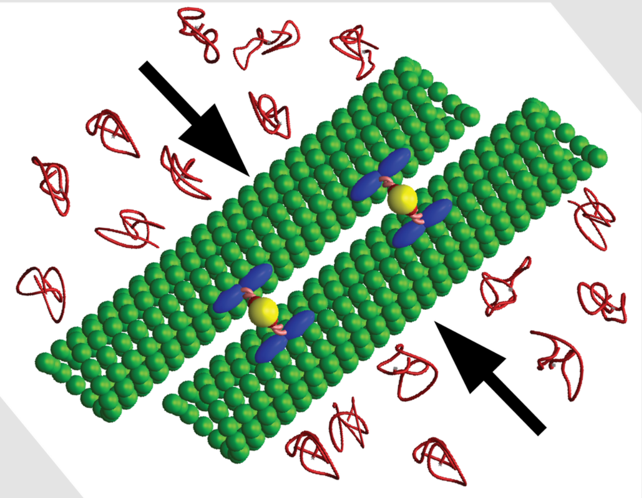
http://chemwiki.ucdavis.edu



Source: Wikipedia

Depletion interaction and microtubule bundles

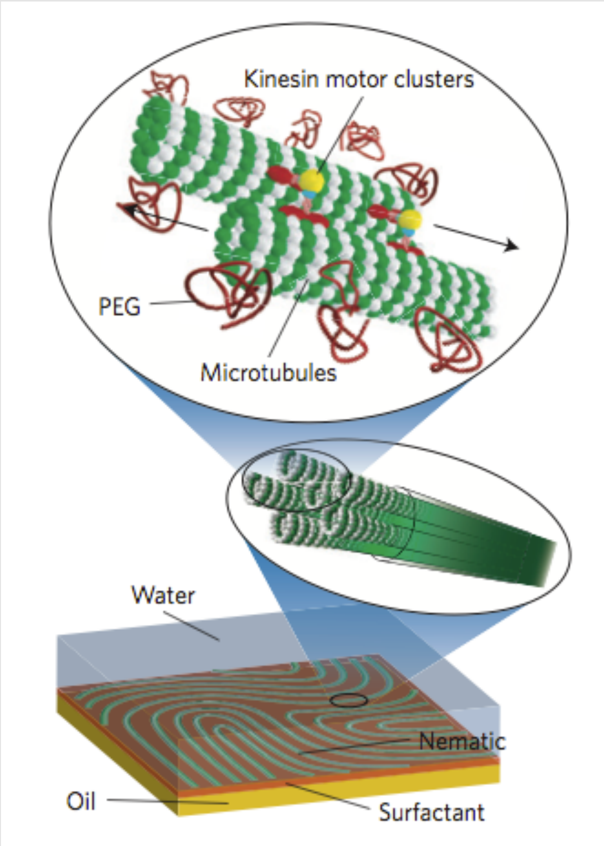


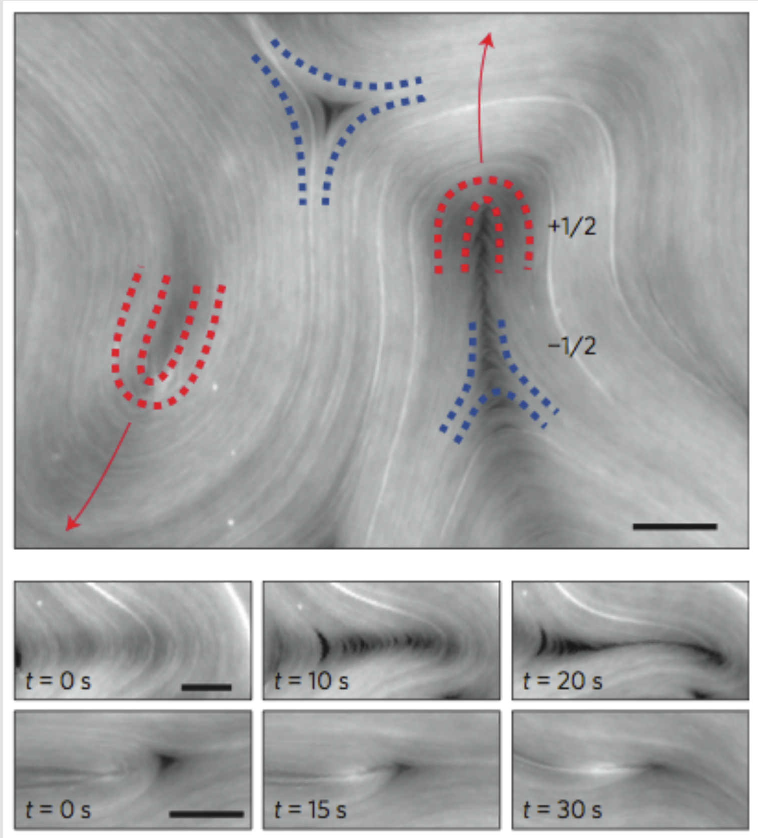


Depletion forces from the polymer PEG
induces spontaneous bundling of Microtubule filaments.

Source: S. DeCamp
http://www.stephenjdecamp.com

Depletion interaction and active nematics

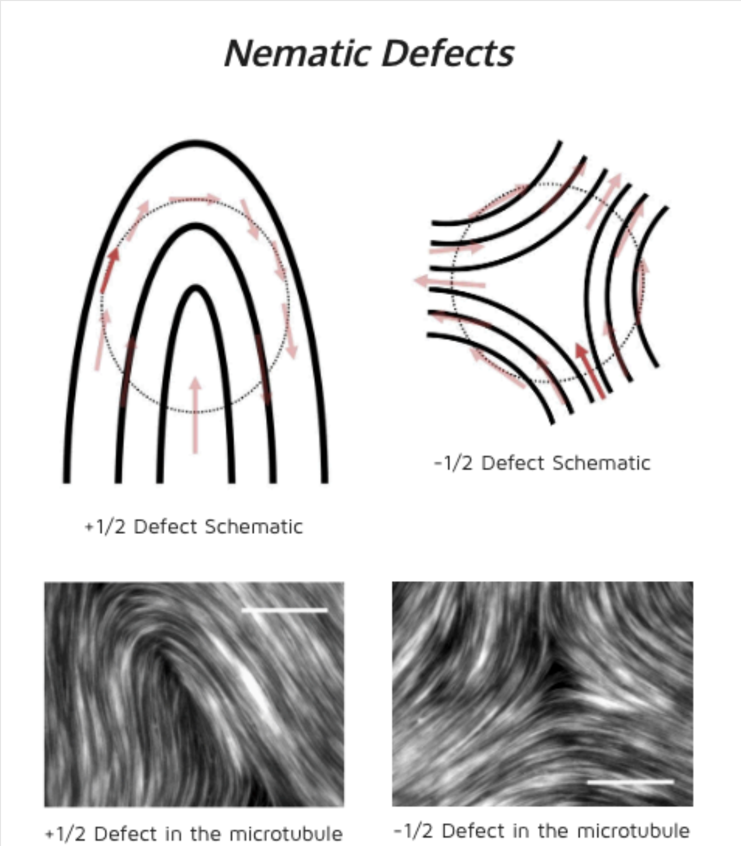




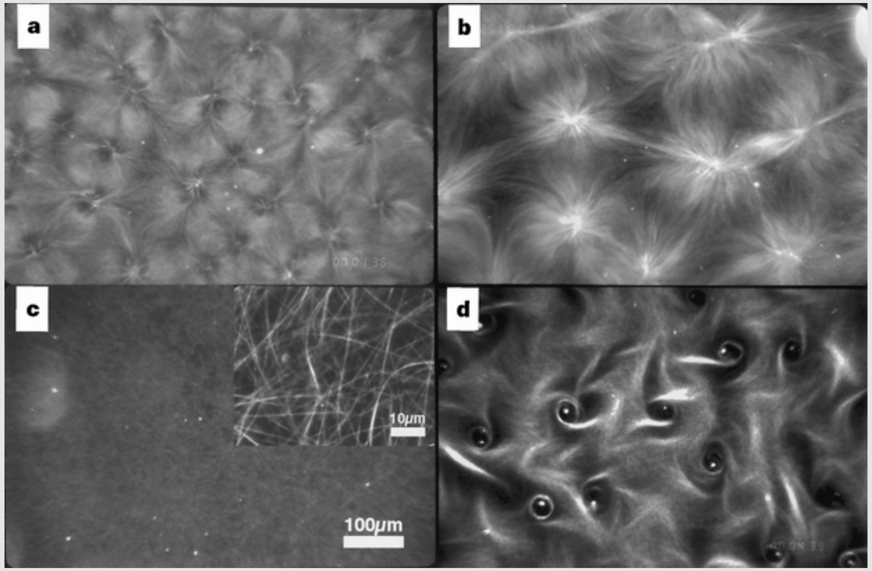
Scale bars: 50 µm

Sanchez *et al.*, *Nature* **(2012)** ; **DeCamp *et al.***, *Nat. Mat.* **(2015)**

Nematic topological defects and cytoskeleton patterns

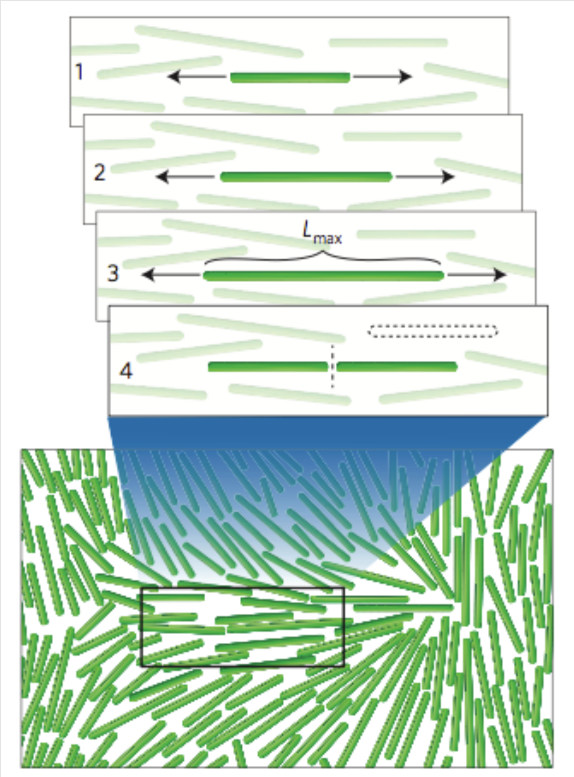


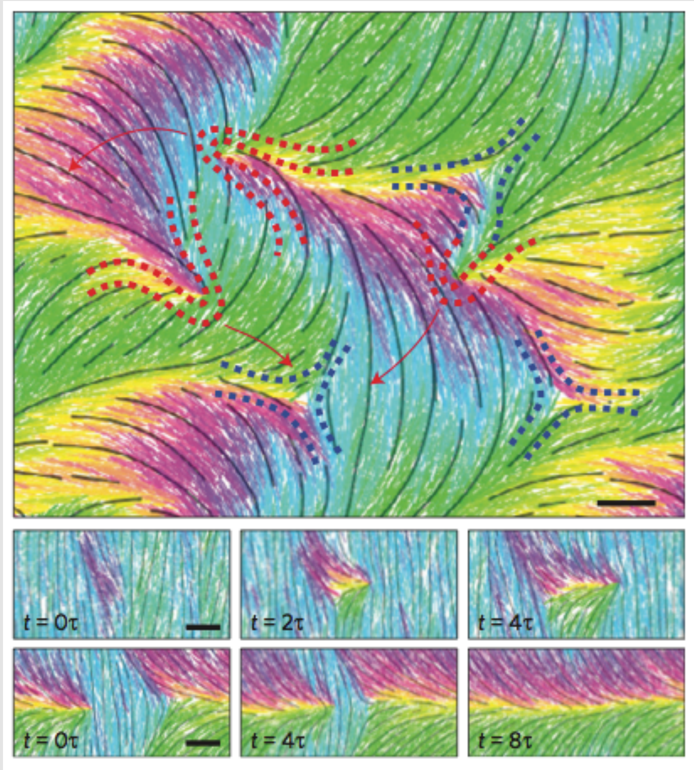
http://www.stephenjdecamp.com



Nedelec *et al.*, *Nature* (1997)

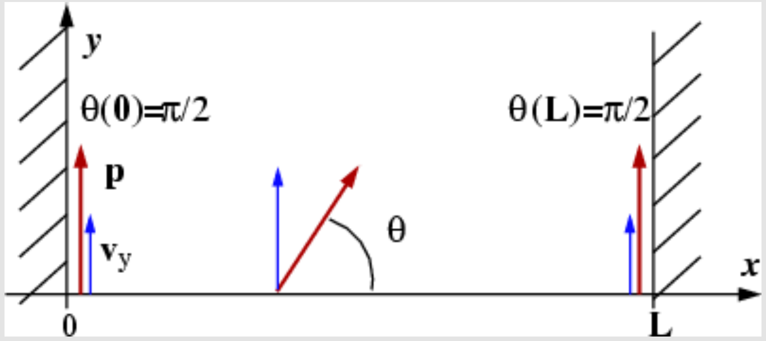
Numerical simulations



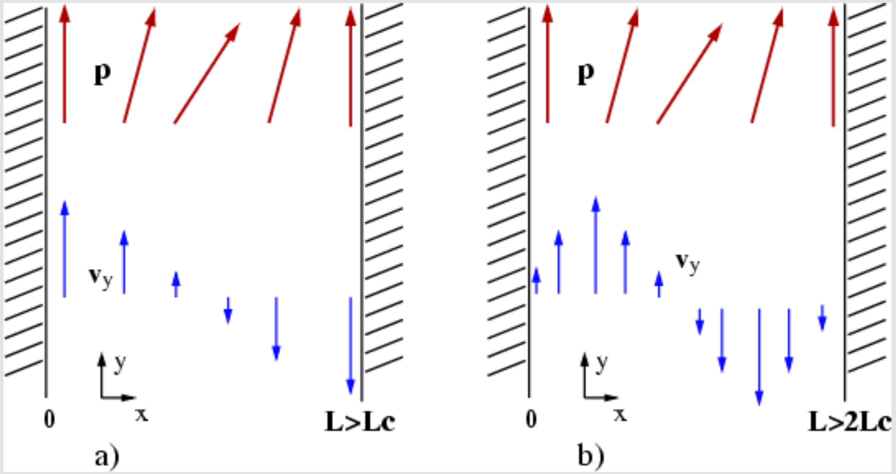


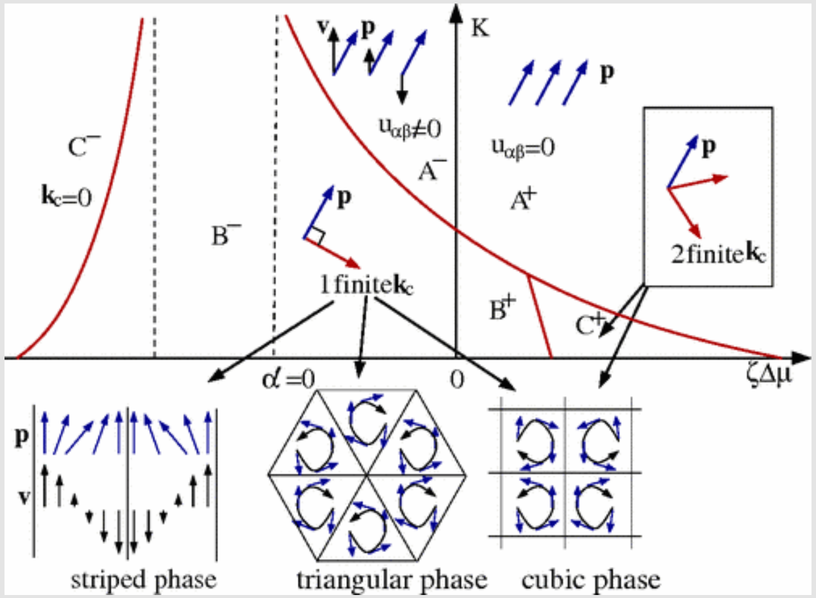
DeCamp *et al.*, *Nat. Mat.* **(2015)**

Example of active nematics



Voituriez *et al.*, *Europhys. Lett.* **(2005)**





Voituriez *et al.*, *PRL* **(2006)**

General framework of active gels

Kruse *et al.*, *EPJE* **(2005)**
Jülicher *et al.*, *Phys. Rep.* **(2007)**
Risler, *Springer Encyclopedia* **(2009)**

Sound detection out of equilibrium

The Hopf bifurcation revisited

F. Jülicher, J. Prost
Institut Curie, Paris
Max-Planck Institute, Dresden

Auditory performances

Frequency range: 20 Hz - 20 kHz (Human)
Up to 100 kHz (Bats; Wales)

Frequency discrimination: $\Delta f/f \approx 0.2 - 0.5$ %

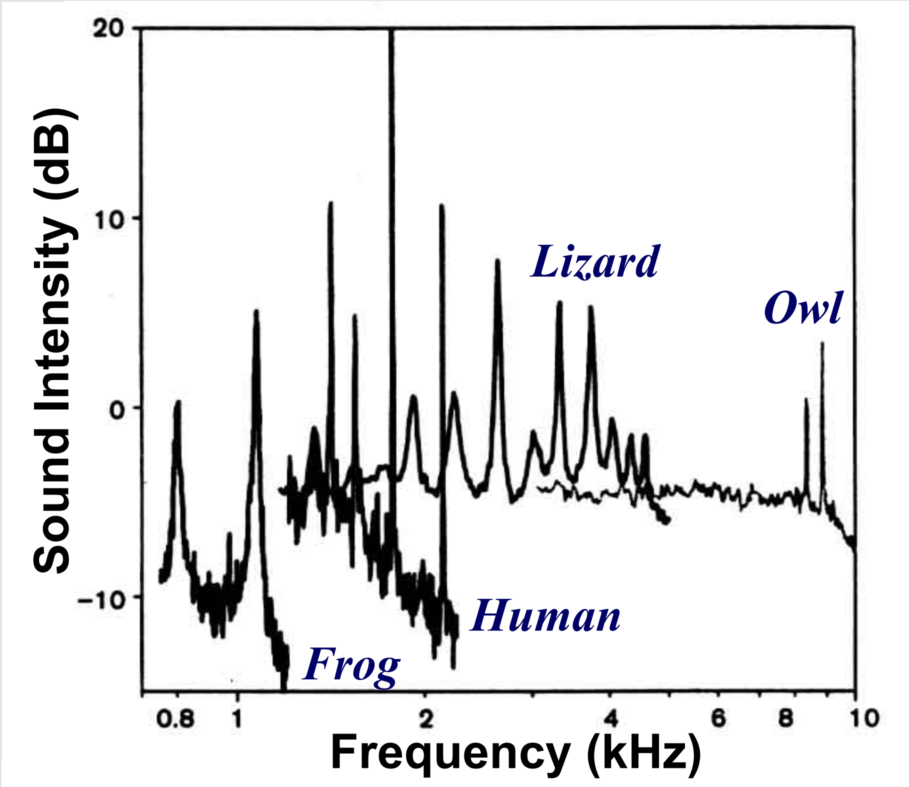
Dynamic range: Stimulus: 20 μPa - 20 Pa (1.000.000 fold)
Response: < 1 nm – 10s nm (100 fold)

Threshold: Thermal-noise limited
Vibrations < 1 nm

Nonlinear sensitivity ; Active amplification

Hearing and activity

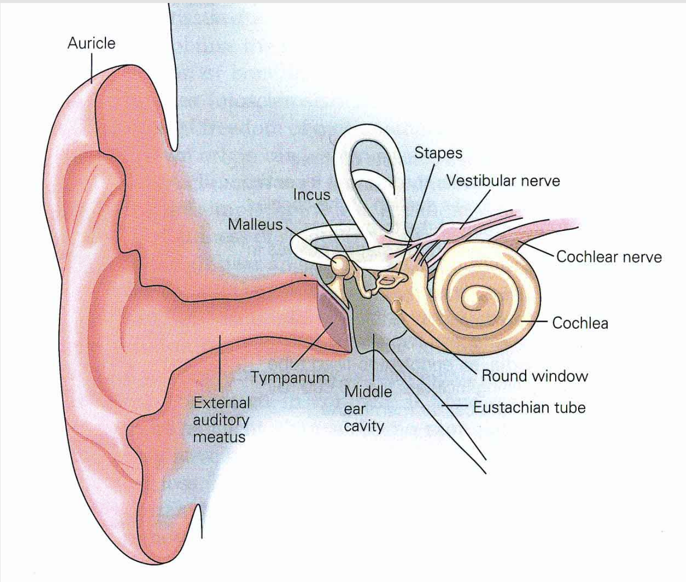
Spontaneous Oto-Acoustic Emissions (SOAE)



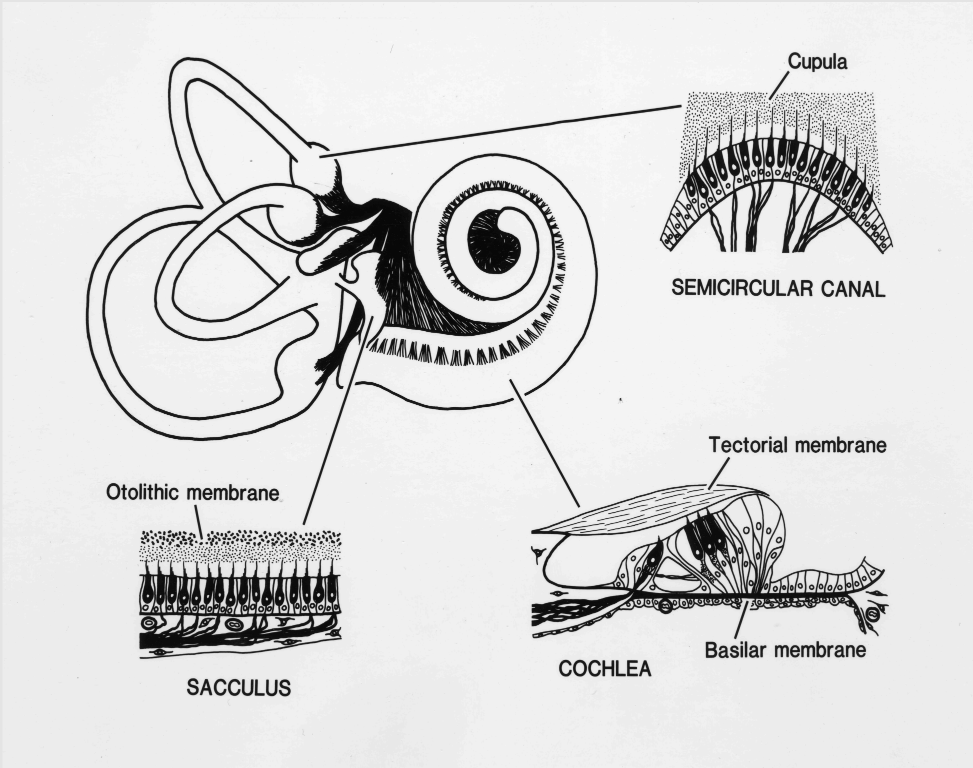
T. Gold, 1948

Manley & Köppel, *Cur. Op. Neurobiol.* **(1998)**

The human ear

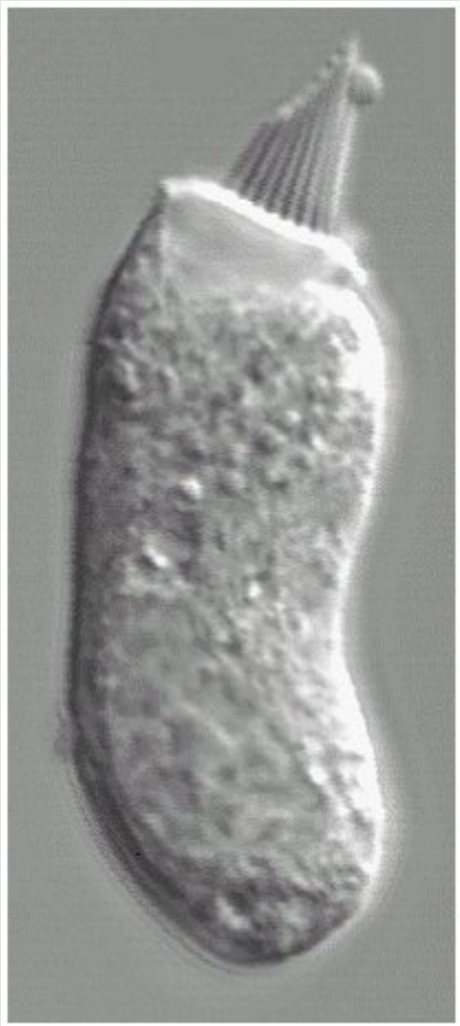


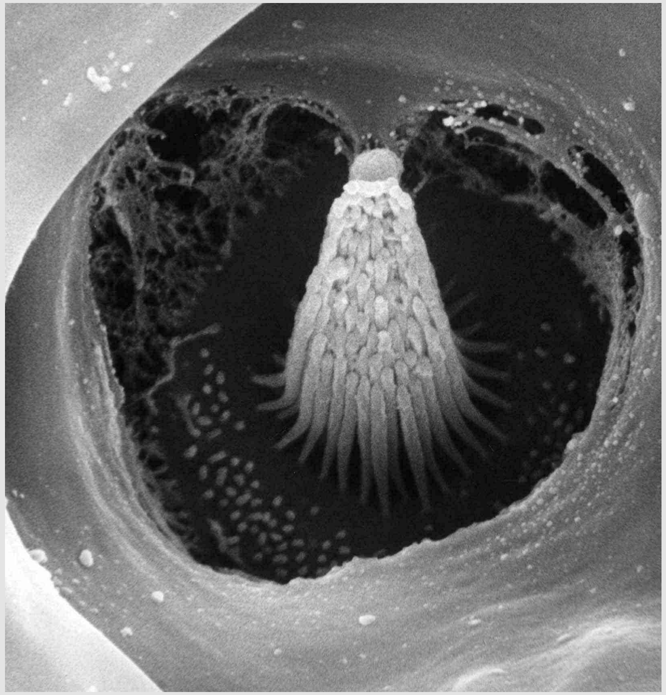
(**R. Pujol**, *http://www.iurc.montp.inserm.fr/cric/audition*)



Hudspeth, *Nature* **(1989) (review)**

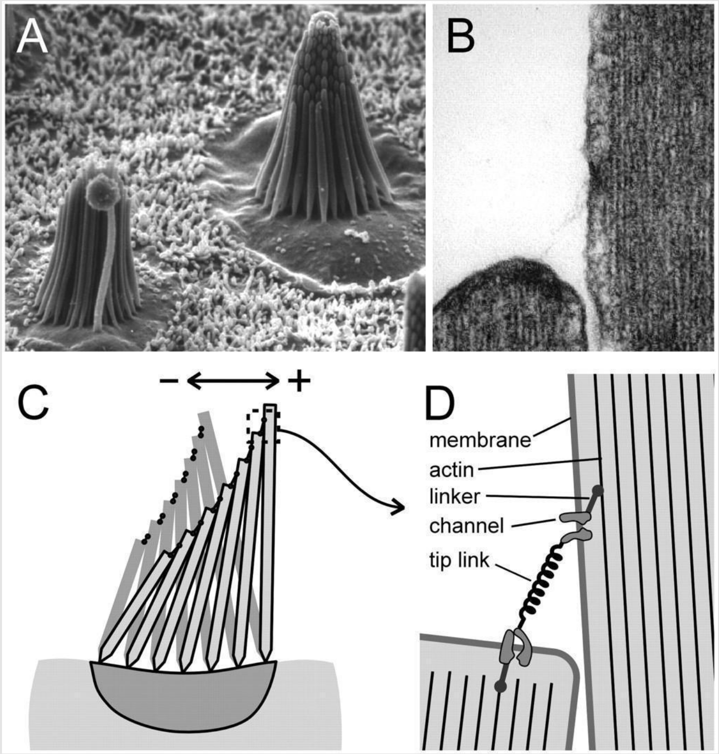
The sensory cells: the hair Cells



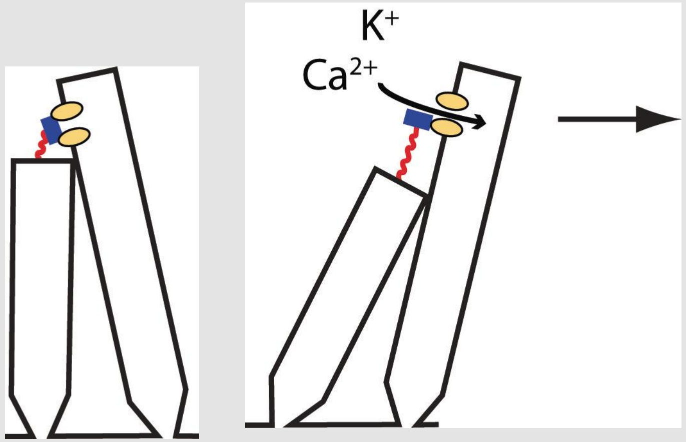


A.J. Hudspeth's Laboratory

Mechano-transduction

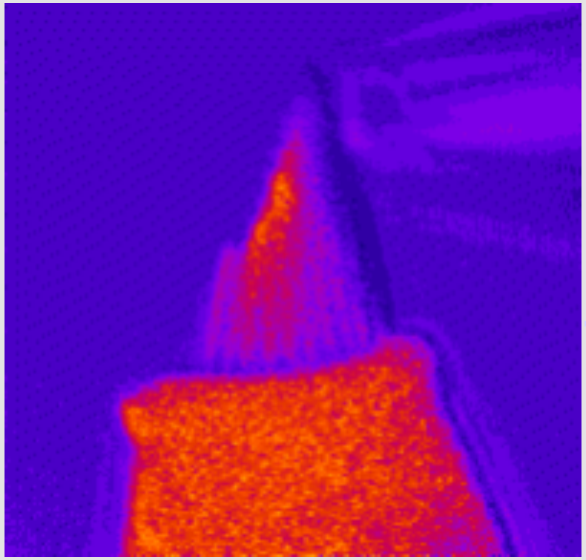


Holt & Corey, *PNAS* (2000)



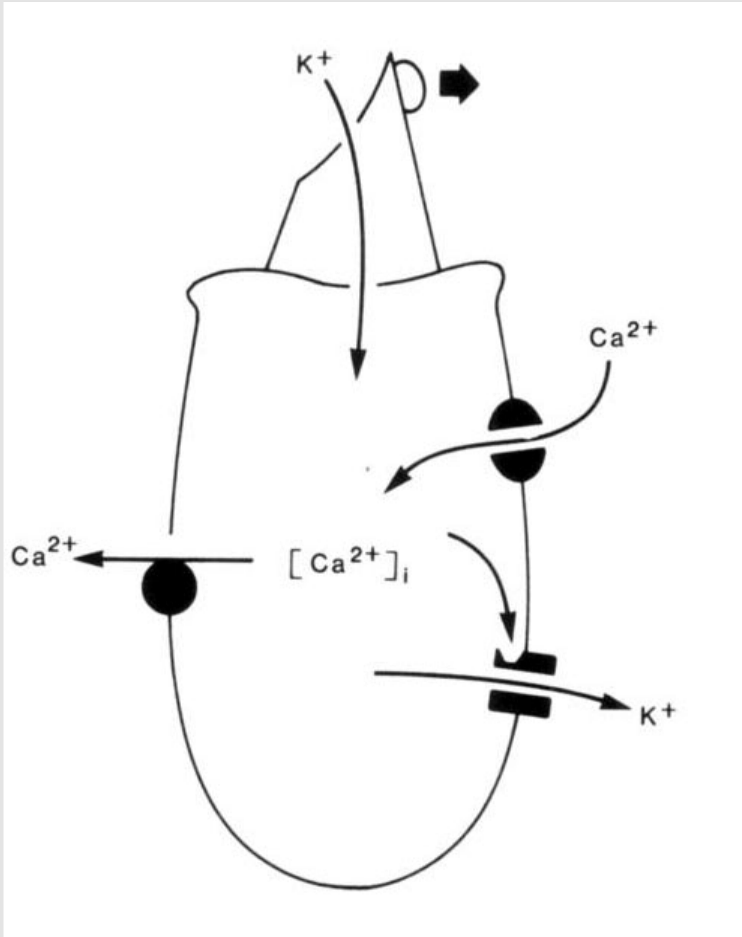
Corey & Hudspeth, *J. Neurosci.* (1983)
Howard & Hudspeth, *Neuron* (1988)

Ionic fluxes



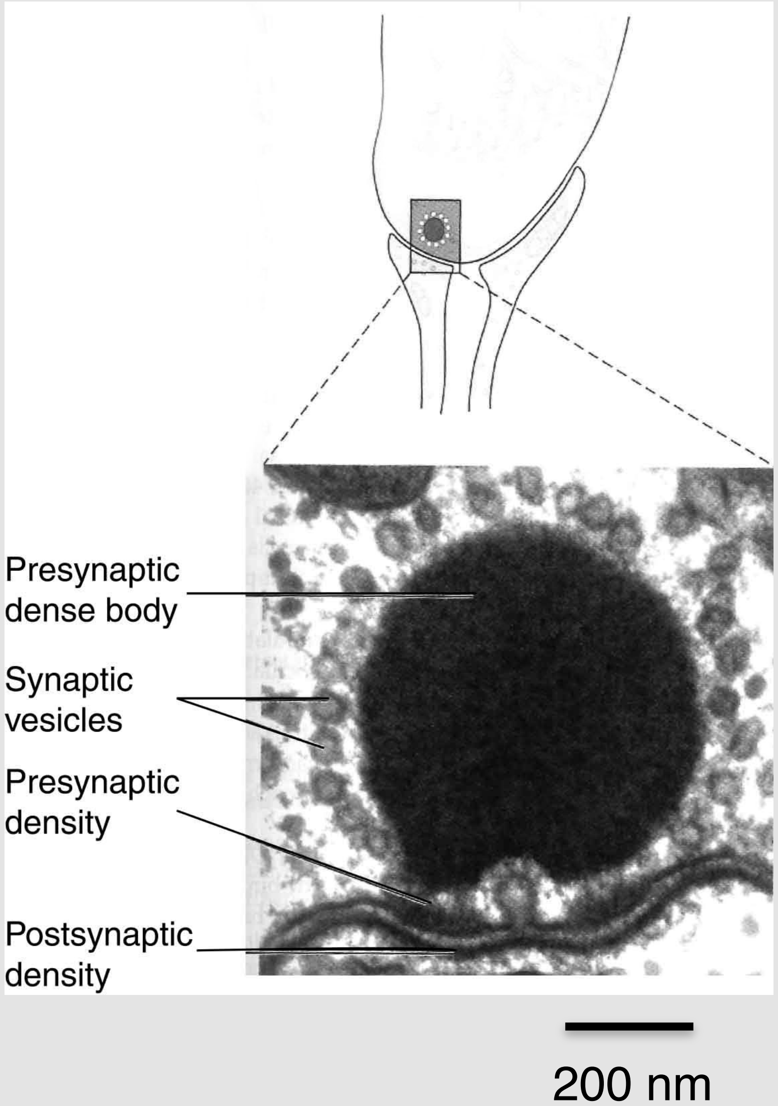
A.J. Hudspeth's Laboratory

Yamoah *et al.*, *J. Neurosci.* **(1998)**



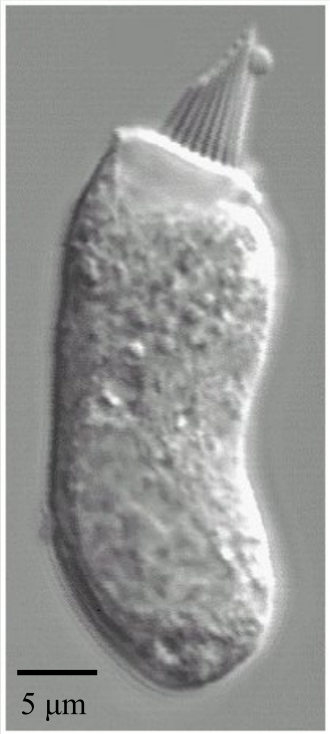
Hudspeth, *Science* **(1985)**

Ribbon synapse

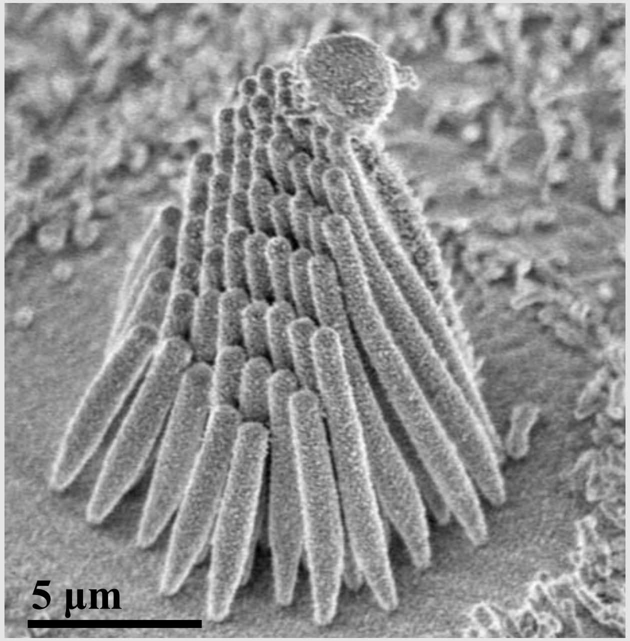


Jacobs & Hudspeth,
Cold Spring Harbor Symposia
(1990)

The degrees of freedom



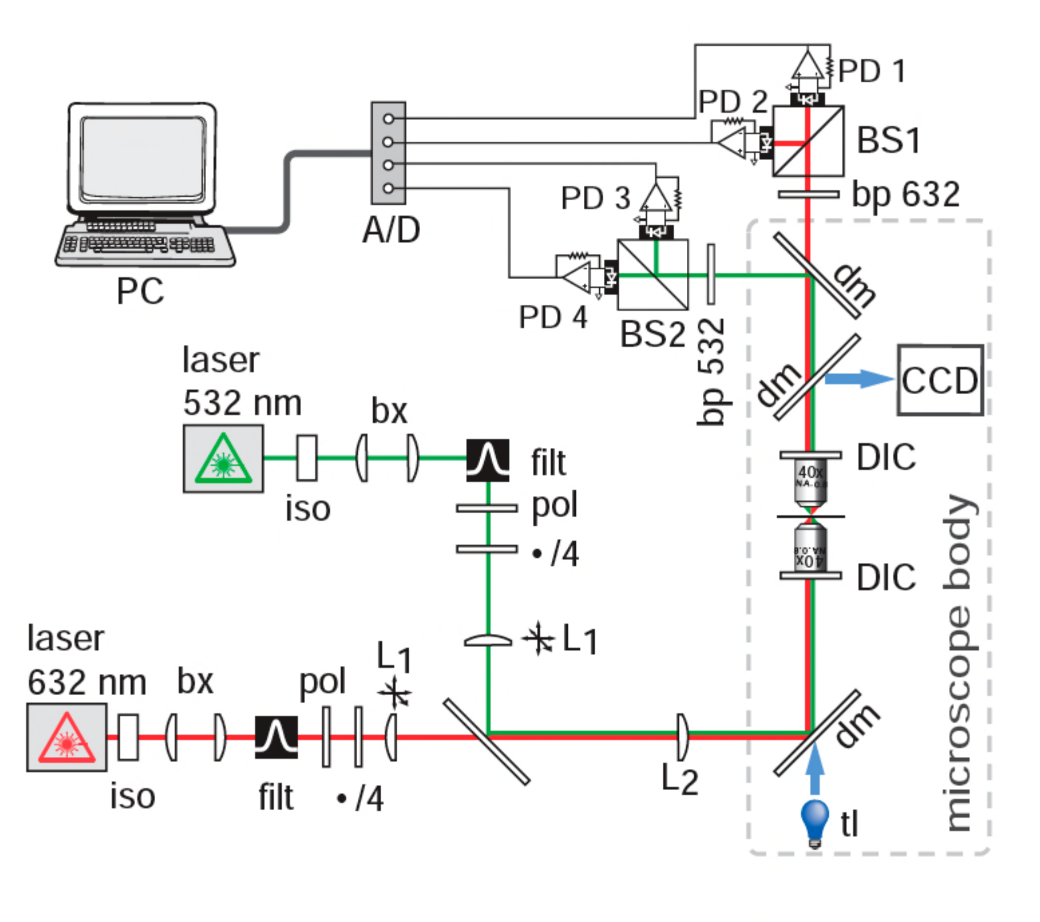
A.J. Hudspeth

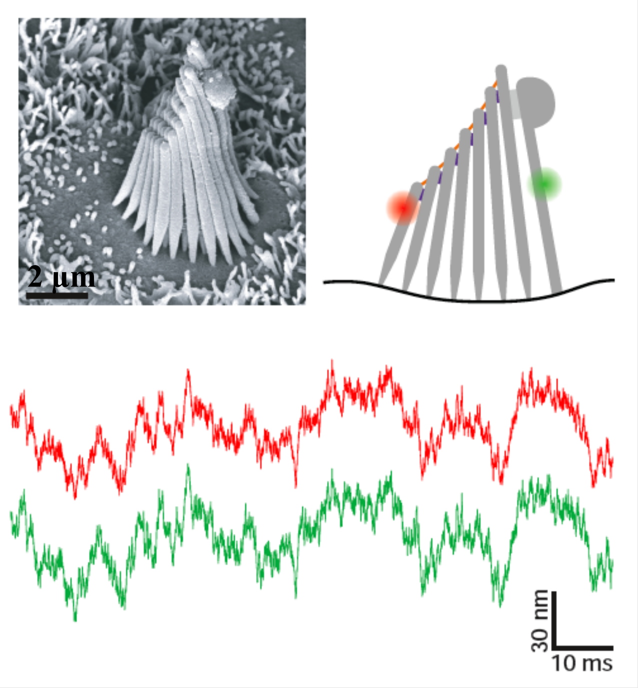


P. Gillespie

One or many degrees of freedom ?

Double-laser interferometer



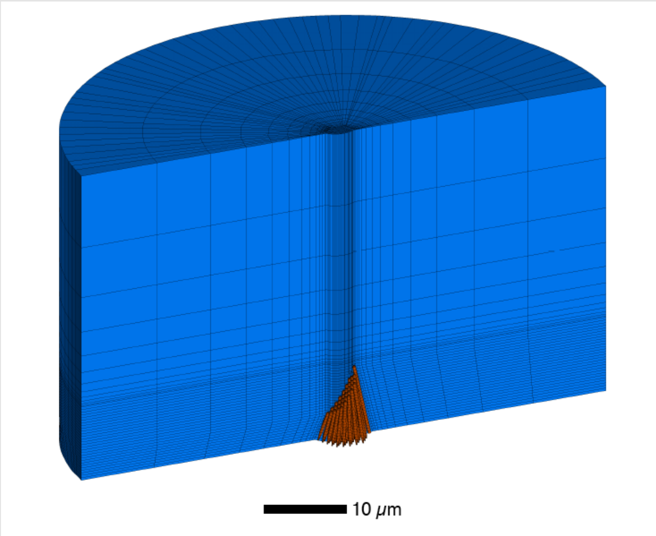


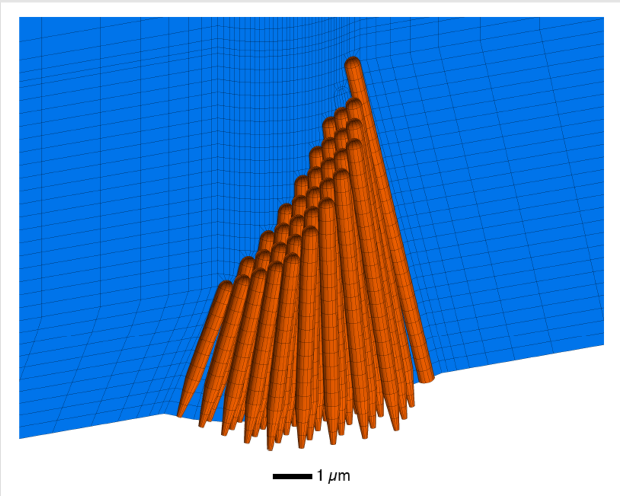
A. Kozlov, A. Hinterwirth

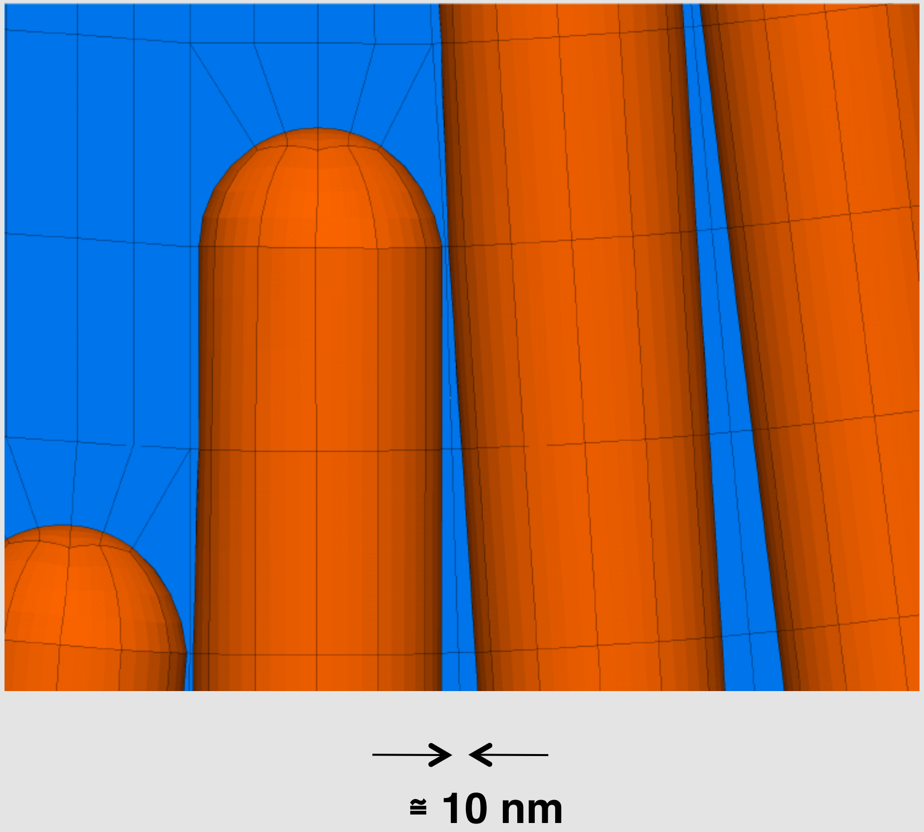
Kozlov *et al.*, *Nature* (2011)

Kozlov *et al.*, *J. Physiol.* (2012)

FEM model



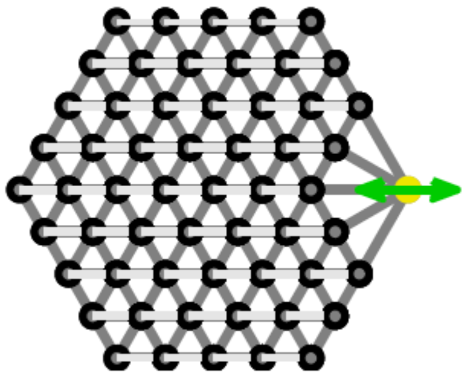




J. Baumgart

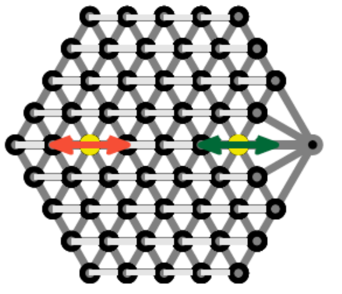
Observables

Drag



$$c_{HB}(f) = \mathrm{Re}\left(\frac{F_x}{v_x}\right)$$

Coherency

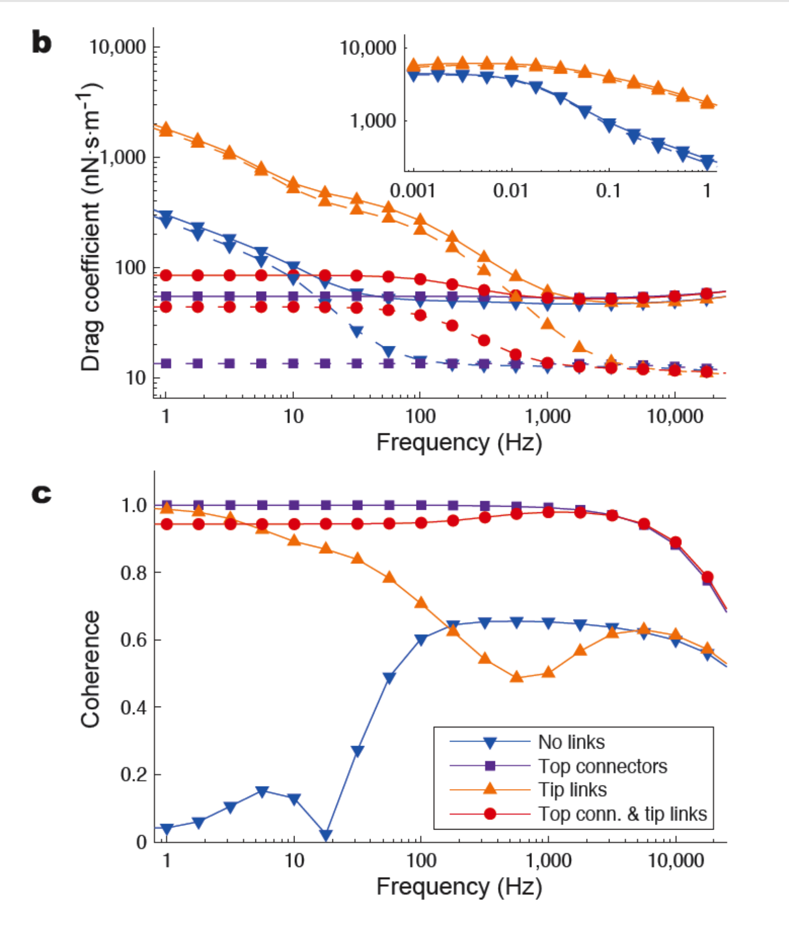


$$\underbrace{\begin{bmatrix} \chi_{ii} & \chi_{ij} \\ \chi_{ji} & \chi_{jj} \end{bmatrix}}_{\chi} \begin{bmatrix} F_i \\ F_j \end{bmatrix} = \begin{bmatrix} u_i \\ u_j \end{bmatrix}$$

$$\mathbf{G} = 2\, k_{\mathrm{B}}\, T\, \frac{\mathrm{Im}\left(\chi(\omega)\right)}{\omega}$$

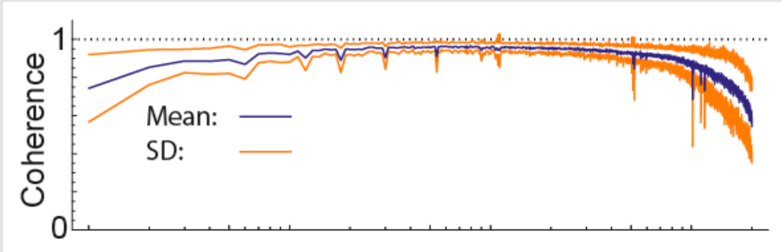
$$\gamma_{ij} = \frac{\mathbf{G}_{ij}}{\sqrt{\mathbf{G}_{ii}\, \mathbf{G}_{jj}}}$$

FEM results

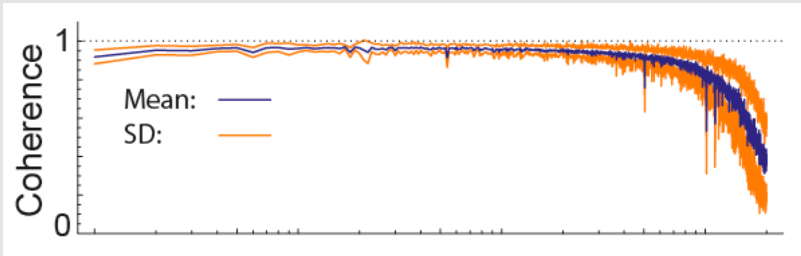


Kozlov *et al.*, *Nature* **474,** 376 **(2011)**

“Wild-type” cells



BAPTA cells

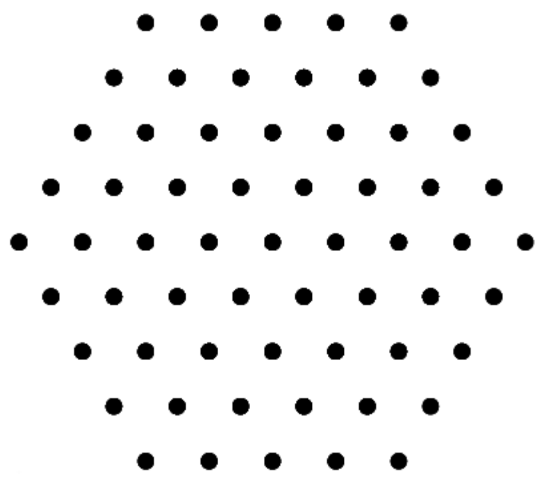


Kozlov *et al.*, *Nat. Neurosci.* **(2007)**

Stochastic model

Hair bundle of the bullfrog's sacculus

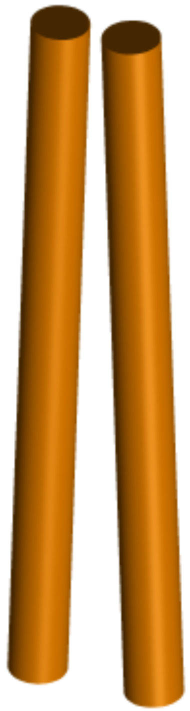
- 61 stereocilia in hexagonal arrangement
- 122 degrees of freedom (finite element model $\approx 350\,000$)

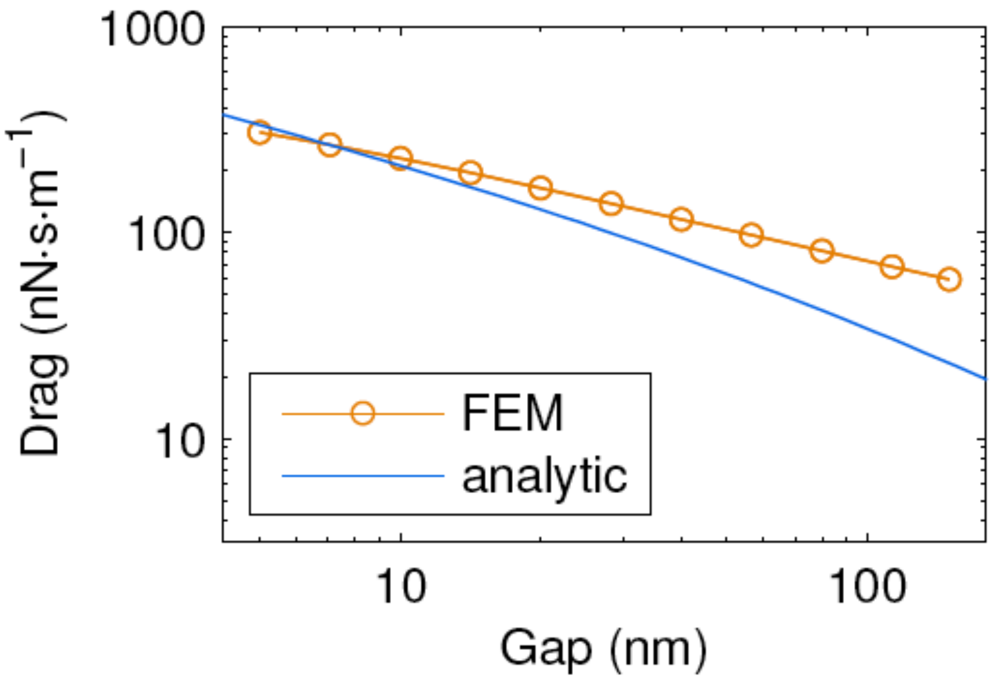


Formulation of stochastic model

Passive system: $D_{i,j} \frac{\partial x_j}{\partial t} + K_{i,j}\, x_j = f_i$

Comparison FEM - Analytic





- Lubrication approximation
- Very small axial flow

Numerical integration scheme

Formulation of stochastic model

Passive system: $D_{i,j}\,\frac{\partial x_j}{\partial t} + K_{i,j}\,x_j = f_i$

Euler time integration:

$$x_i^{t+\Delta t} = \Big(x_i - \Delta t\, D_{i,j}^{-1}\, K_{j,k}\, x_k + 2\sqrt{k_B\, T\, \Delta t}\; G_{i,j}\, \eta_j \\ \qquad\qquad - k_B\, T\, \Delta t\, D_{j,i}^{-1}\, \frac{\partial D_{j,l}}{\partial x_k}\, D_{l,k}^{-1}\Big)^t$$

D: Damping matrix

K: Stiffness matrix

x: Displacement vector

f: Force vector

t: Time

Δt: Time step

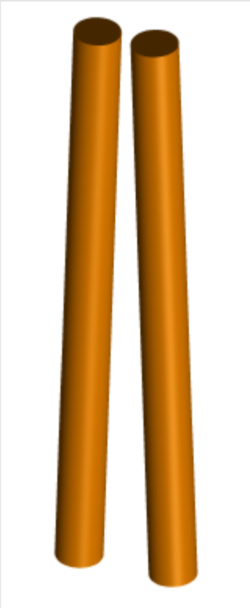
k_B: Boltzmann constant

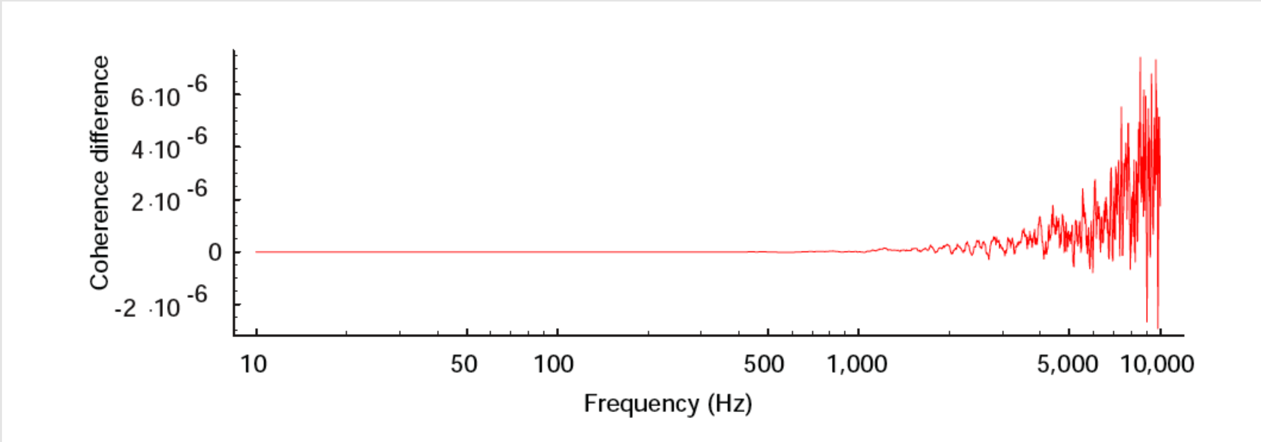
T: Temperature

G: $G_{k,i}G_{j,i} = D_{k,j}^{-1}$ and $G_{j,i} = G_{i,j}$

η: Noise with zero mean and variance of 1/2

Relative importance of the drift term

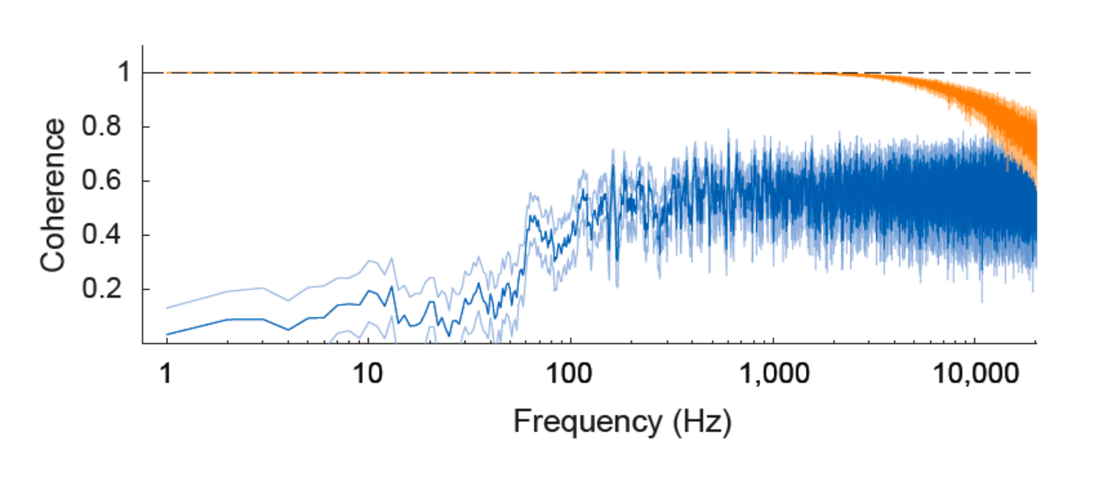


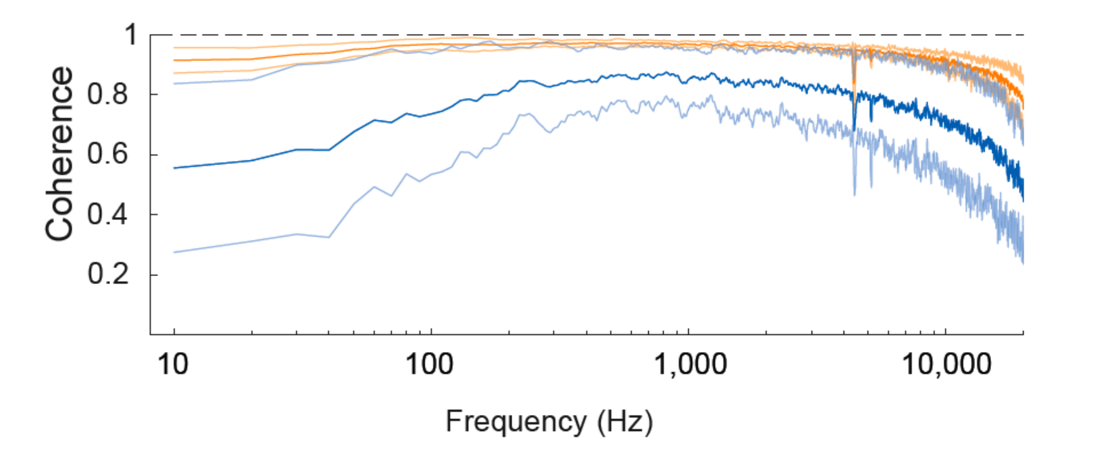


- Letting evolve for 5 times the largest eigenvalue (memory < 1%)

- Time step: gaps between adj. ster. vary by less than 5%

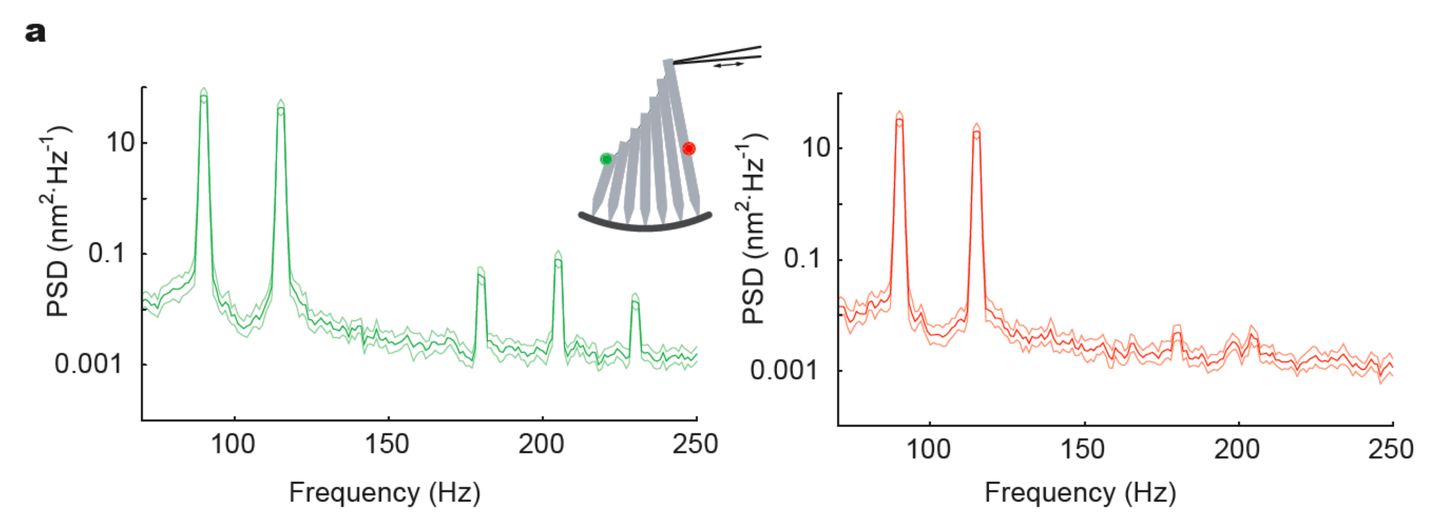
Stochastic model results





Kozlov *et al.*, (2011)

Splaying distances

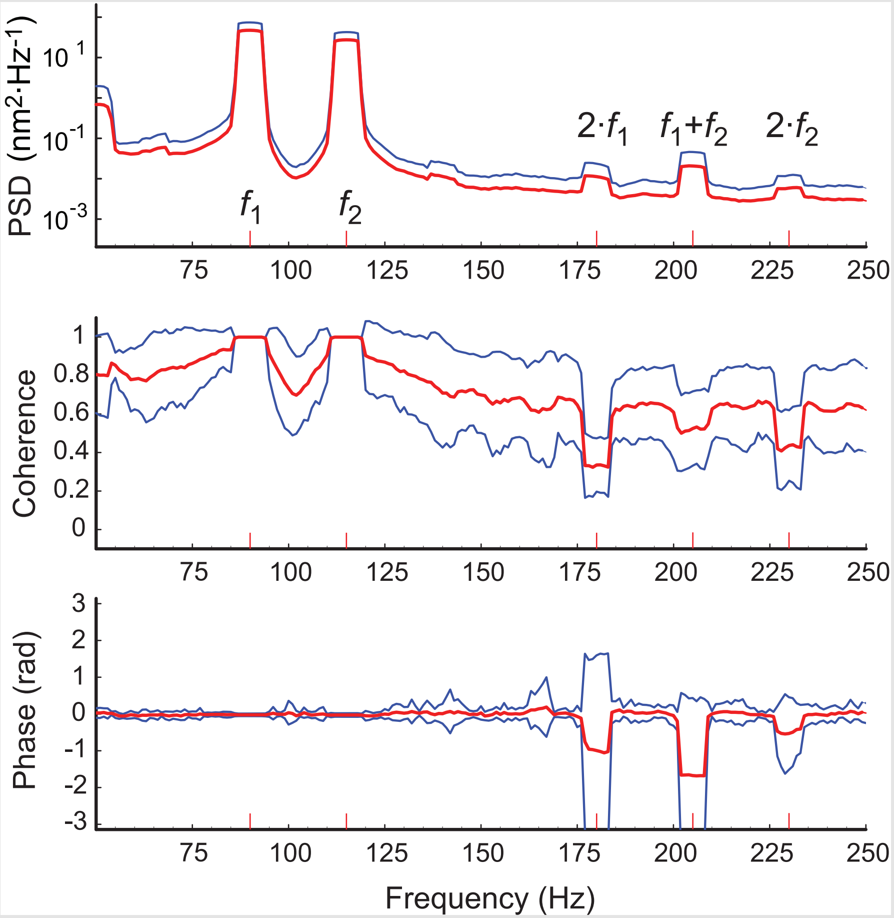


Kozlov *et al.*, *Nature* (2011)

Check of the FEM model

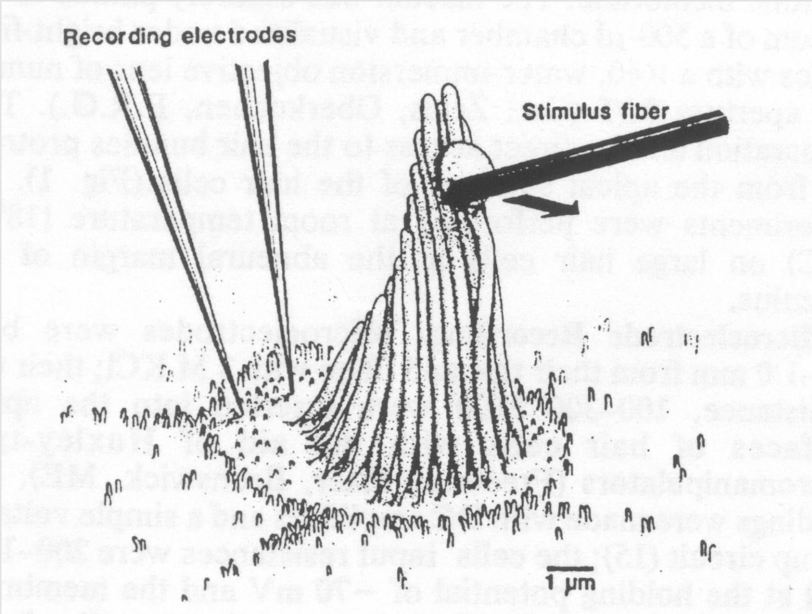
Splaying distances ≅ 1 nm or less

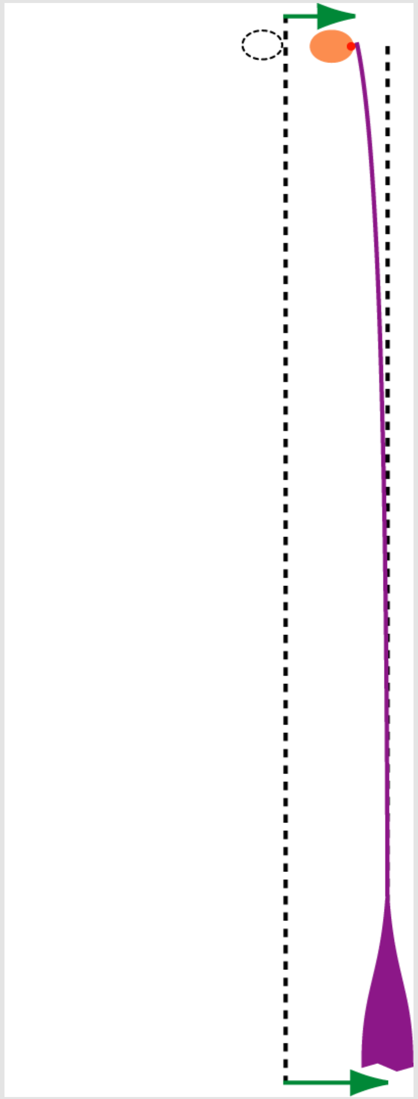
Relative phases



Kozlov *et al.*, *J. Physiol.* **(2012)**

Experiments



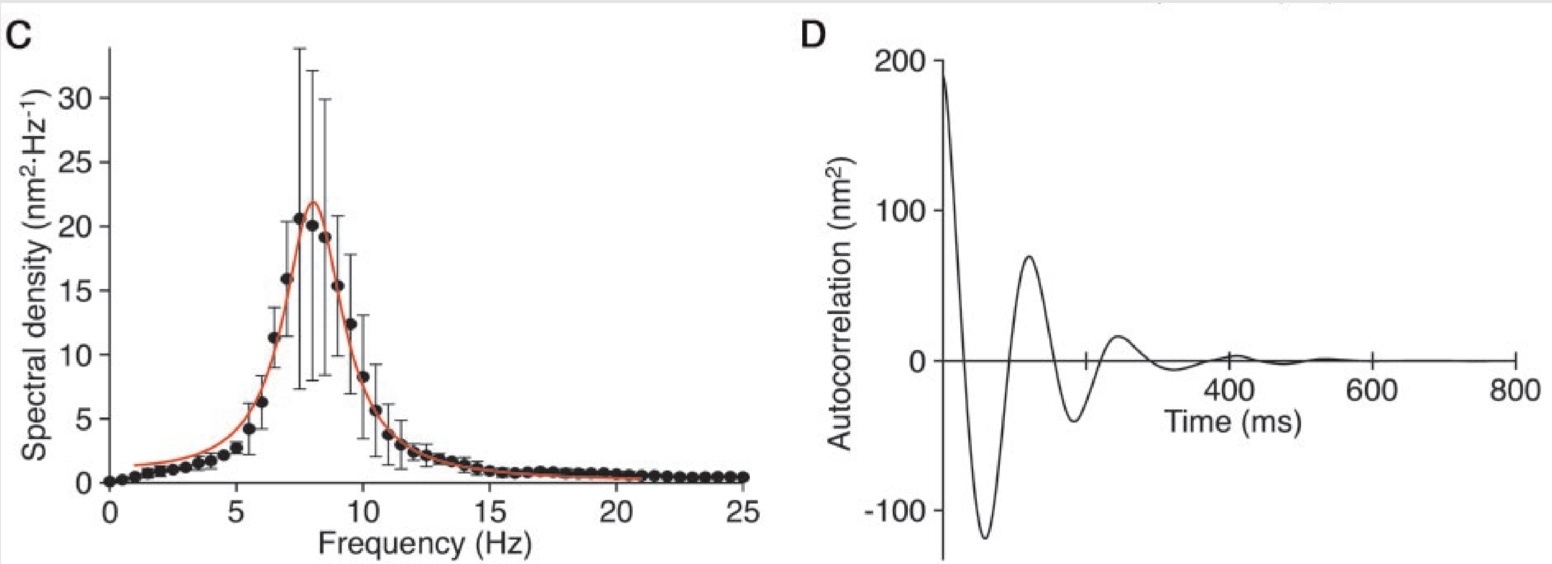


Howard, Hudspeth, *PNAS* (1987)

Fluctuation spectrum

$$\tilde{S}(\omega) = \left\langle X(\omega) X(-\omega) \right\rangle$$

Spontaneous oscillations with a preferred mean frequency

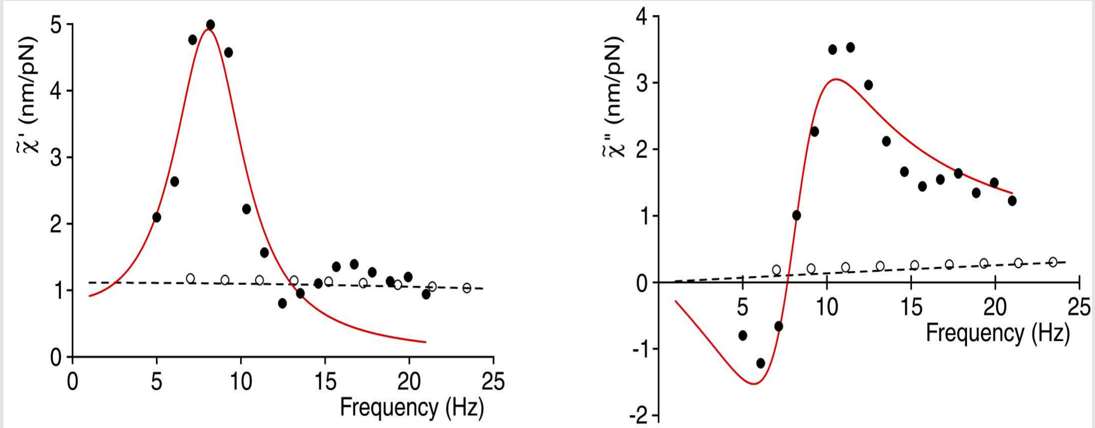


Martin et al., *PNAS* **(2001)**

Activity and fluctuation-dissipation

Linear response

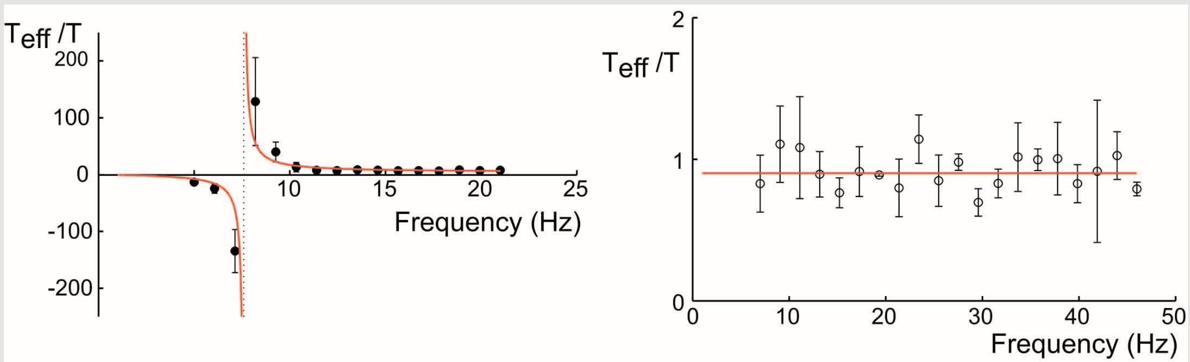
$$\tilde{\chi}(\omega) = \frac{\tilde{X}(\omega)}{\tilde{f}(\omega)}$$



Martin et al.,
PNAS **(2001)**

Effective temperature

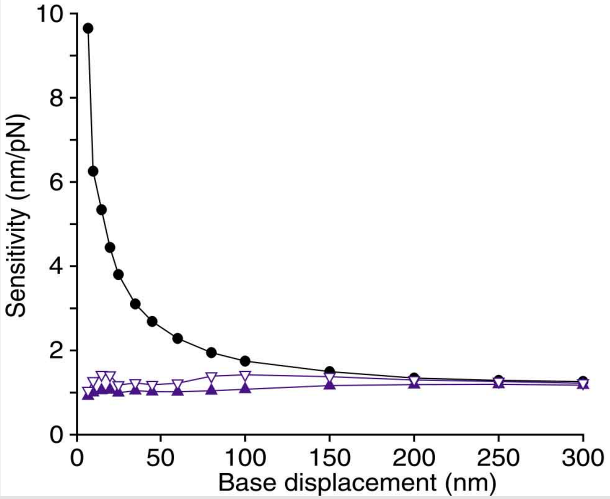
$$\boxed{\frac{T_{\mathrm{eff}}(\omega)}{T} = \frac{\omega\, \tilde{C}(\omega)}{2\, k_B T\, \tilde{\chi}''(\omega)}}$$

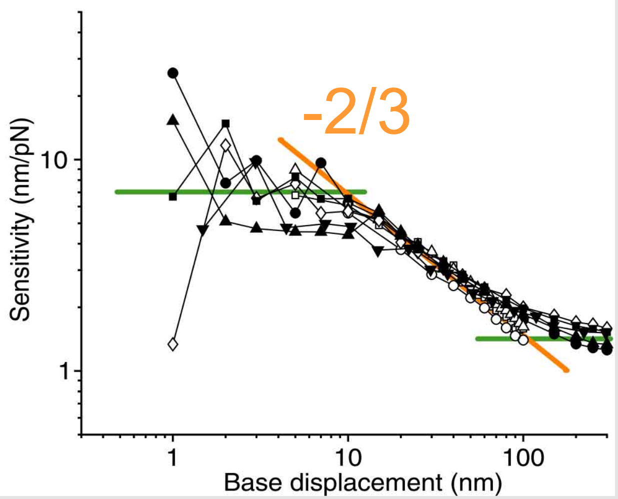


Martin et al.,
PNAS **(2001)**

The hair bundle: a critical oscillator

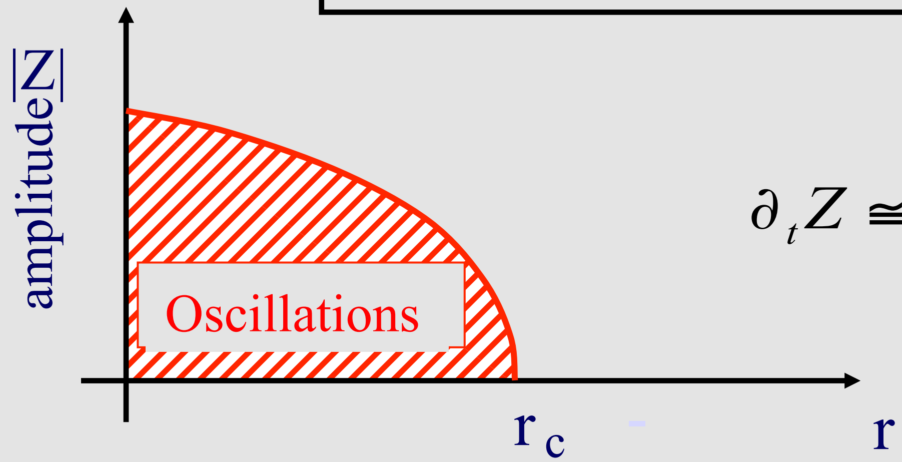
Sensitivity $$\left|\widetilde{\chi}(\omega)\right| = \left|\frac{\widetilde{X}(\omega)}{\widetilde{f}(\omega)}\right|$$





Martin, Hudspeth, *PNAS* **(2001)**

Hopf bifurcation and normal form



$$\partial_t Z \cong -(r + i\omega_0)Z - (u + iu_a)|Z|^2 Z$$

Poincaré, Andronov, Hopf

$$\partial_t Z \cong -(r + i\omega_0)Z - (u + iu_a)|Z|^2 Z + f$$

$$X \cong \mathrm{Re}(Z)$$

$$f \cong \Lambda^{-1} e^{i\theta} F$$

Bifurcation point

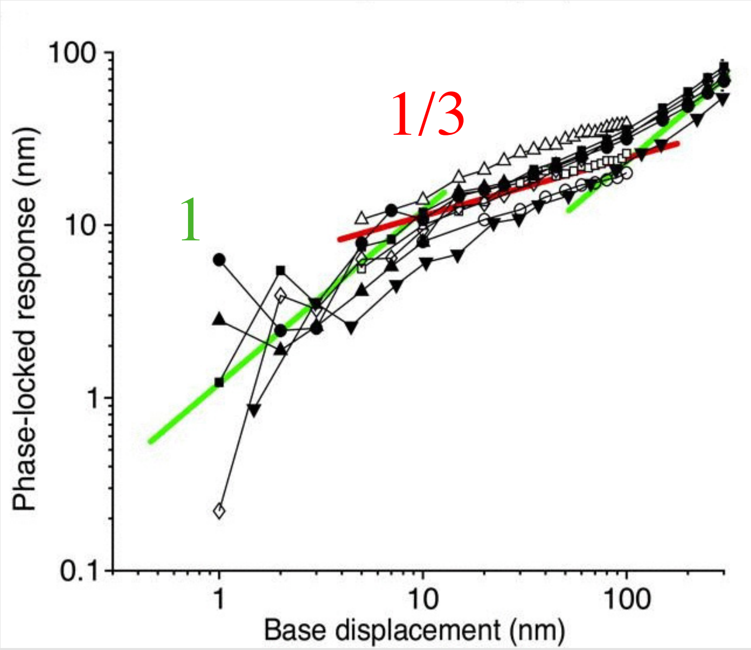
$$r = 0 \quad ; \quad \omega = \omega_0$$

$$\boxed{\frac{|X|}{|F|} \propto |F|^{-2/3}}$$

Choe et al., *PNAS* **(1998)**
Camalet et al., *PNAS* **(2000)**
Ospeck et al., *Biophys. J.* **(2001)**

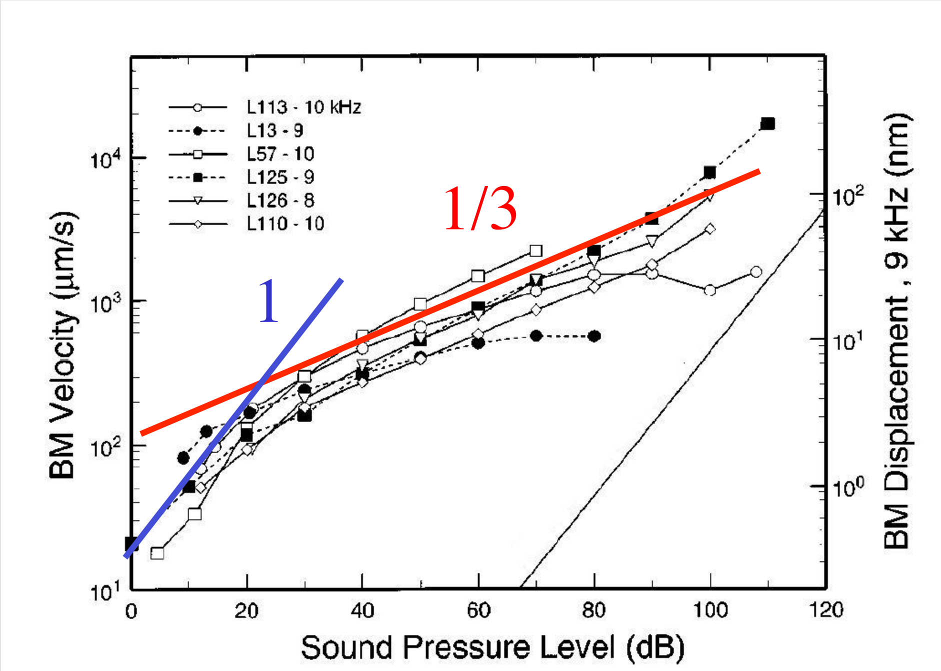
The cochlea: an ensemble of critical oscillators?

Frog Cells



Martin, Hudspeth, *PNAS* **(2001)**

Chinchilla Cochlea

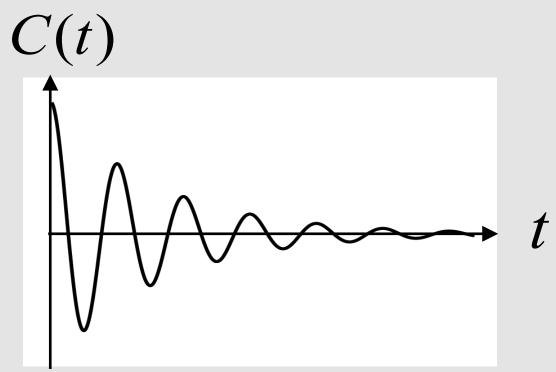


Ruggero et al., *J. Acoust. Soc. Am.* **(1997)**

Fluctuations and spontaneous oscillations

Noisy oscillator

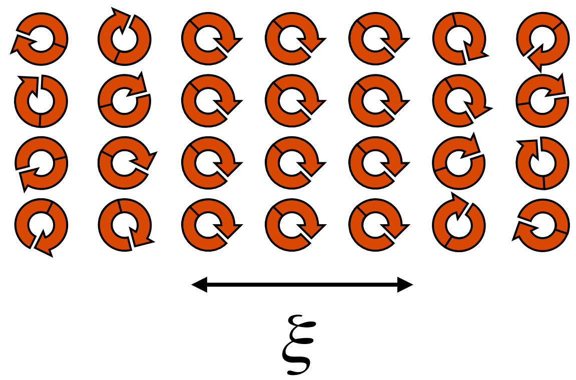
$$C(t) = \langle X(0)X(t) \rangle$$



Synchronization Transition
or
Hopf Bifurcation of
Coupled Oscillators

C(x,t)

Coupled Oscillators

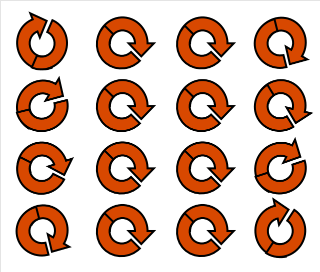


$$\xi, \tau \rightarrow \infty$$

Field theory for coupled oscillators

$$\partial_t Z = -(r + i\omega_0)Z - (u + iu_a)|Z|^2 Z$$
$$+ (c + ic_a)\Delta_d Z + \Lambda^{-1}e^{i\theta}F + \eta$$

CGLE: Aranson, Kramer, *Rev. Mod. Phys.* **(2002)**



$$\langle \eta(\mathbf{x},t) \rangle = 0$$
$$\langle \eta(\mathbf{x},t)\eta(\mathbf{x}',t') \rangle = 0$$
$$\langle \eta(\mathbf{x},t)\eta^*(\mathbf{x}',t') \rangle = 4D\delta(t-t')\delta^d(\mathbf{x}-\mathbf{x}')$$

Phase invariance $\quad Z \to Z\exp(i\varphi)$

A special case

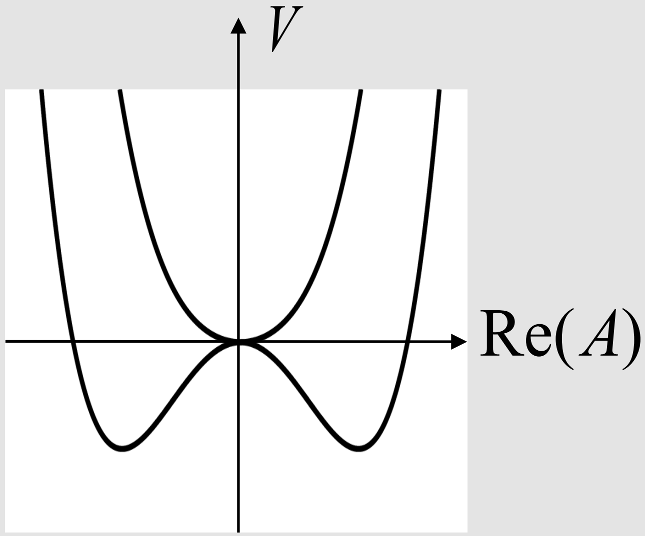
$$\partial_t Z = -(r + i\omega_0)Z - (u + \cancel{iu_a})|Z|^2 Z$$
$$+ (c + \cancel{ic_a})\Delta_d Z + \Lambda^{-1} e^{i\theta} F + \eta$$

Real case $\quad u_a = 0 \;\; ; \;\; c_a = 0$

$$A = e^{i\omega_0 t} Z$$

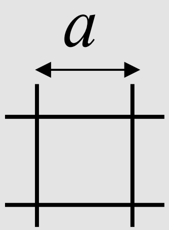
$$f = e^{i\omega_0 t} \Lambda^{-1} e^{i\theta} F$$

$$\partial_t A = -rA - u|A|^2 A + c\Delta_d A + f + \xi$$



Exact mapping to the XY model

Renormalization



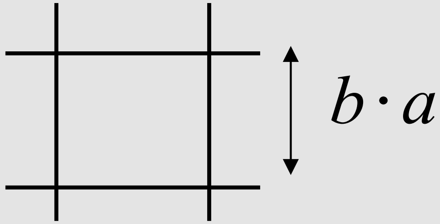
A

f

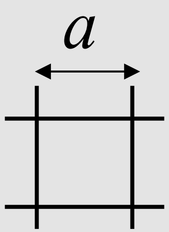
Integration

A'

f'



Rescaling: $x \rightarrow x/b$

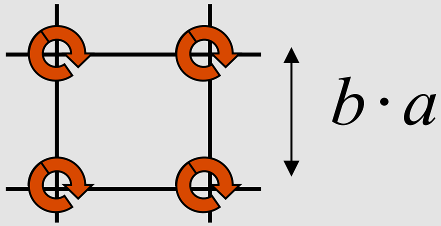


$$A = e^{i\omega_0 t} Z$$

$$f = e^{i\omega_0 t} \Lambda^{-1} e^{i\theta} F$$

A'

f'



$$\boxed{A^R = A' e^{i\delta\omega_0 t} \qquad f^R = f' e^{i(\delta\theta + \delta\omega_0 t)}}$$

Risler, Prost, Jülicher, *PRL* **(2004) &** *PRE* **(2005)**

Perturbation theory

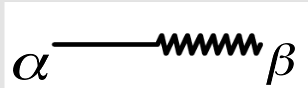
Elementary diagrams

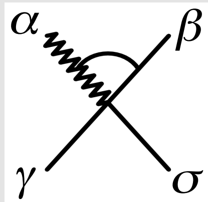
$$\left(Z = \psi_1 + i\psi_2\right)$$

$\psi_\alpha =$ 

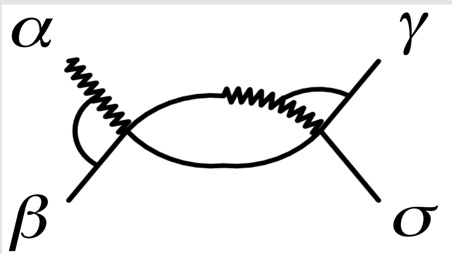
$C^0_{\alpha\beta} = \left\langle \psi_\alpha \psi_\beta \right\rangle_0 =$ 

$\tilde{\psi}_\alpha =$ 

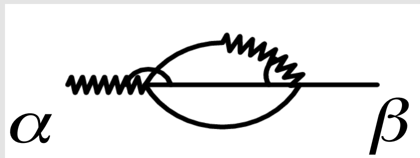
$\chi^0_{\alpha\beta} = \left\langle \psi_\alpha \tilde{\psi}_\beta \right\rangle_0 =$ 

$-\left(u\delta_{\alpha\beta} + u_a \varepsilon_{\alpha\beta}\right)\delta_{\gamma\sigma} =$ 

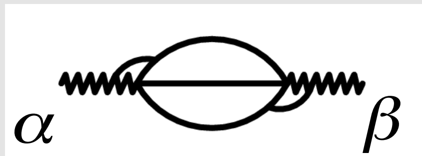
Feynman diagrams



$\rightarrow 6$



$\rightarrow 5$



$\rightarrow 2$

First order flow equations

$$\frac{\mathrm{d}r}{\mathrm{d}l} = 2r + 2\widetilde{D}u$$

$$\frac{\mathrm{d}u}{\mathrm{d}l} = \varepsilon u - \widetilde{D}\left[\frac{(u^2 + u_a^2) + 2uu_a c_a}{1 + c_a^2} + 4u^2\right]$$

$$\frac{\mathrm{d}u_a}{\mathrm{d}l} = \varepsilon u_a + \widetilde{D}\left[c_a \frac{(u^2 + u_a^2) + 2uu_a c_a}{1 + c_a^2} - 6uu_a\right]$$

$$\frac{\mathrm{d}c_a}{\mathrm{d}l} = 0$$

$$\varepsilon = 4 - d$$

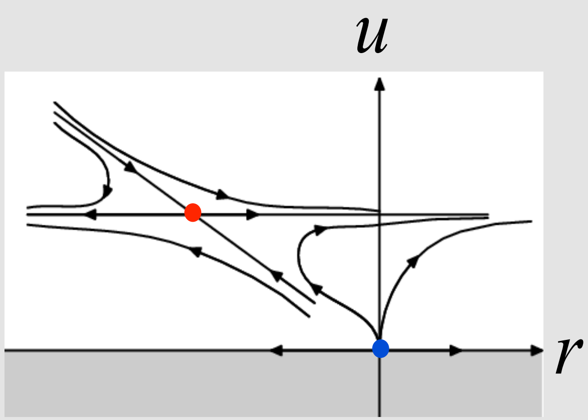
$$l = \ln b$$

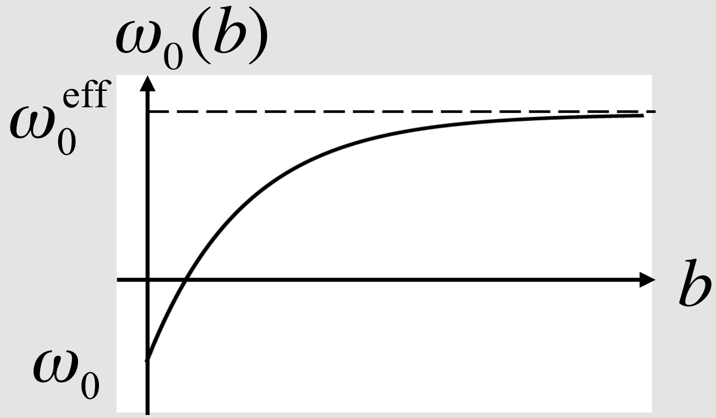
Fixed points $\quad r^*,\ u^* \propto \varepsilon \quad ; \quad u_a^* \propto \varepsilon\, c_a \quad ; \quad c_a$

Renormalization flow diagram

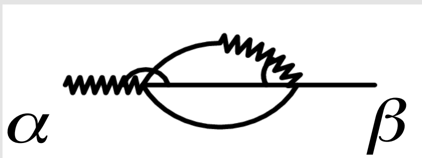
One-loop order

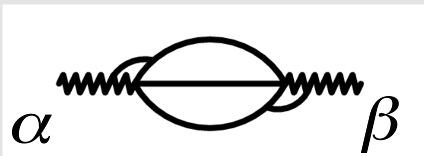
$$d = 4 - \varepsilon$$

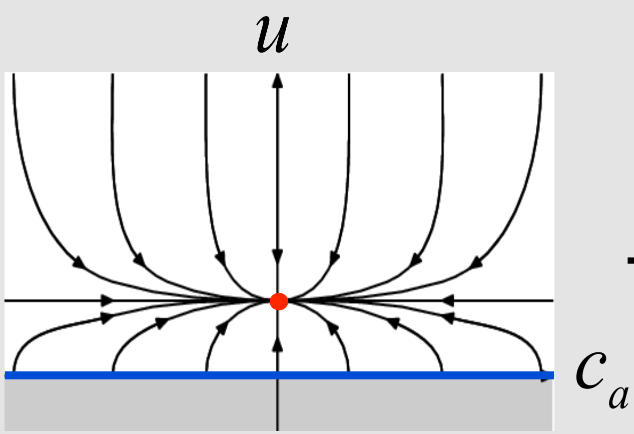




Two-loop order







$+\theta(b)..$

Risler, Prost, Jülicher, *PRL* **(2004) & ** *PRE* **(2005)**

Results

Fixed point

Dynamical XY model: Equilibrium fixed point!

$$\cos\theta_{\text{eff}}\ \chi''_{11} + \sin\theta_{\text{eff}}\ \chi''_{12} = \frac{1}{2\Lambda_{\text{eff}} D_{\text{eff}}}\left(\omega\, C_{11} + i\omega_0^{\text{eff}}\ C_{12}\right)$$

Response function

$$\chi(q,\omega=\omega_0^{\text{eff}}) \cong \frac{1}{2\Lambda_{\text{eff}}}\frac{1}{q^{2-\eta}}\left[\frac{e^{i\theta(q)}}{c+i\gamma(q)}\right]$$

$$\theta(q) \cong \theta_{\text{eff}} + \alpha_{\text{eff}} q^{\omega_1} + \beta_{\text{eff}} q^{\omega_2} \quad ; \quad \gamma(q) \cong \gamma_{\text{eff}} q^{\omega_2}$$

$$\eta \cong \varepsilon^2/50 \qquad \boxed{\omega_1 \cong \varepsilon/5 \quad ; \quad \omega_2 \cong \varepsilon^2/50}$$

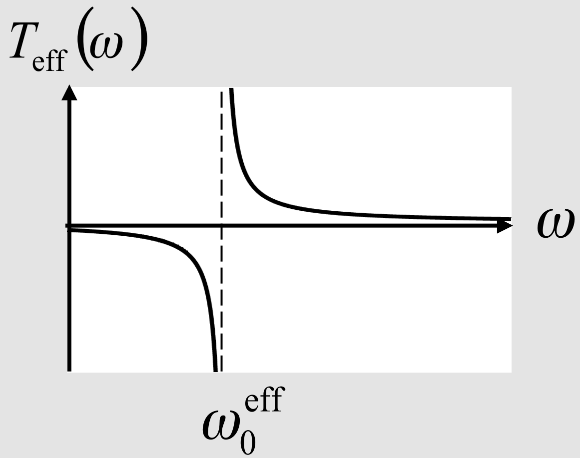
Risler, Prost, Jülicher, *PRE* **72,** 016130 **(2005)**

Fluctuation-dissipation

Effective temperature

$$\frac{T_{\text{eff}}(\omega)}{T} = \frac{\omega\,\tilde{C}(\omega)}{2\,k_B T\,\tilde{\chi}''(\omega)}$$

$$\boxed{\frac{T_{\text{eff}}(\omega)}{T} \propto \frac{1}{(\omega-\omega_0^{\text{eff}})^{\mu}} \qquad \mu \cong 1-\varepsilon/5}$$



Risler, Prost, Jülicher, *PRL* **(2004) &** *PRE* **(2005)**

Numerical verification

Wood, Broeck, Kawai, Lindenberg,
PRL **96,** 145701 **(2006)**
PRE **74,** 031113 **(2006)**

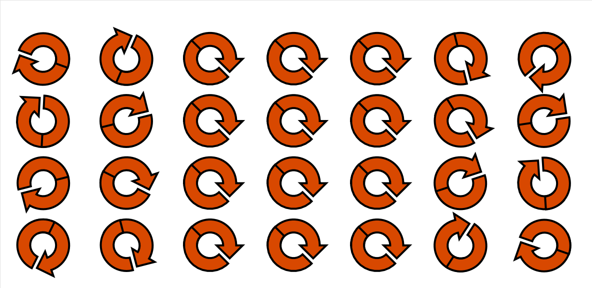
Summary

Synchronization Transition

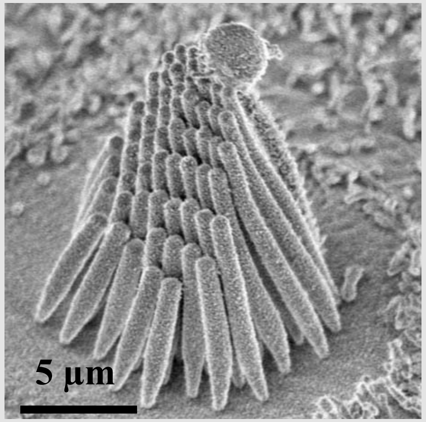
Hopf bifurcation of coupled oscillators:
An out-of-equilibrium phase transition

Renormalization group and flow

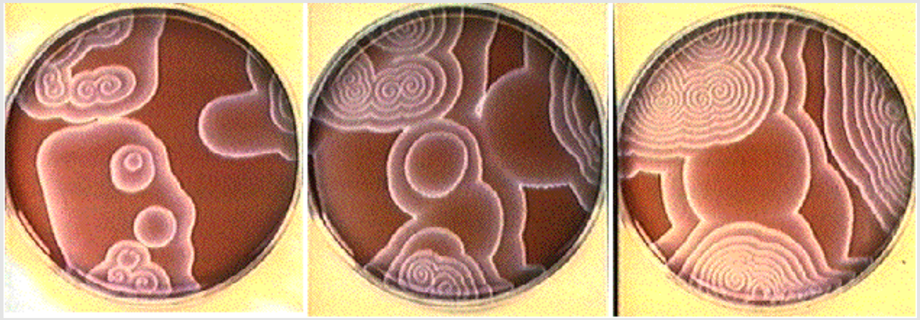
New universal properties



Real Systems?



P. Gillespie



http://www.ux.his.no/~ruoff/BZ_Phenomenology.html

Acknowledgements

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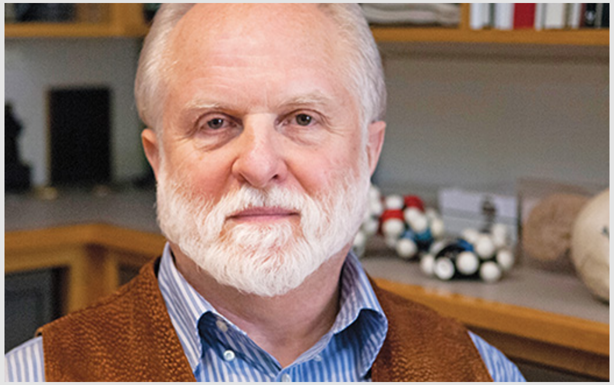
A. J. Hudspeth



Morphological instabilities in tissues

A hydrodynamic instability

M. Basan, J. Prost & J.-F. Joanny
ETH, Zürick
Institut Curie, Paris

Epithelia and carcinoma

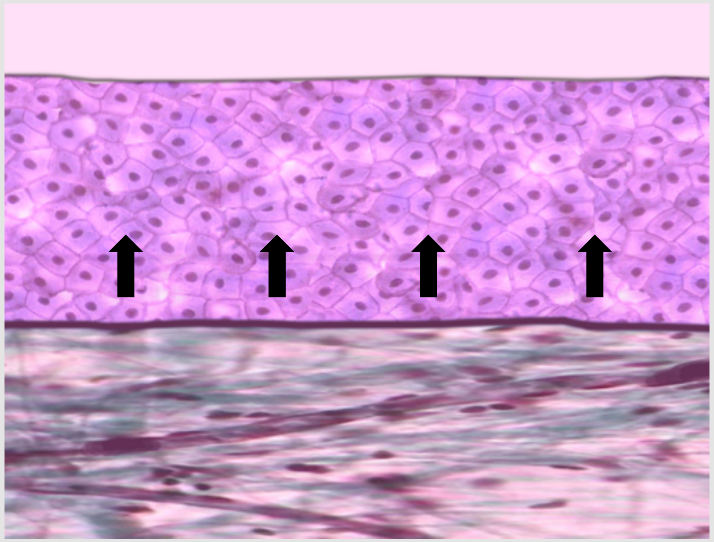
Epithelia constitute the most common tissue type throughout the body

Over 80% of human tumors originate from epithelia

Mutlilayred, stratified epithelium

Free surface

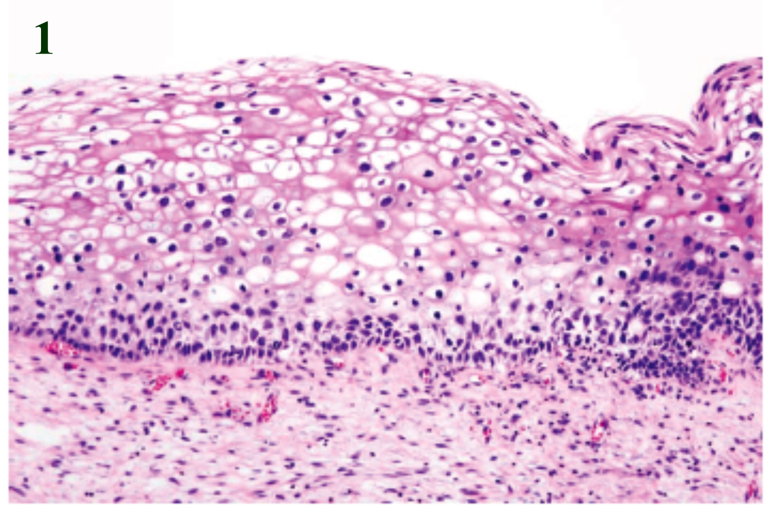
Basement membrane

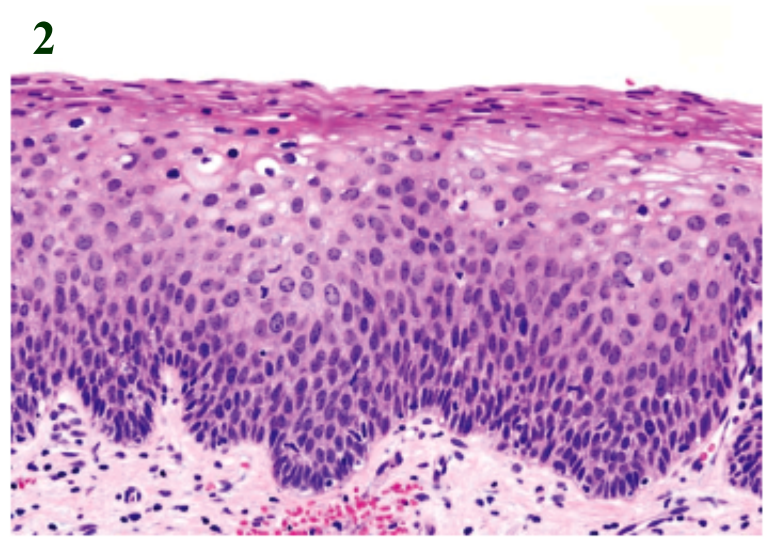


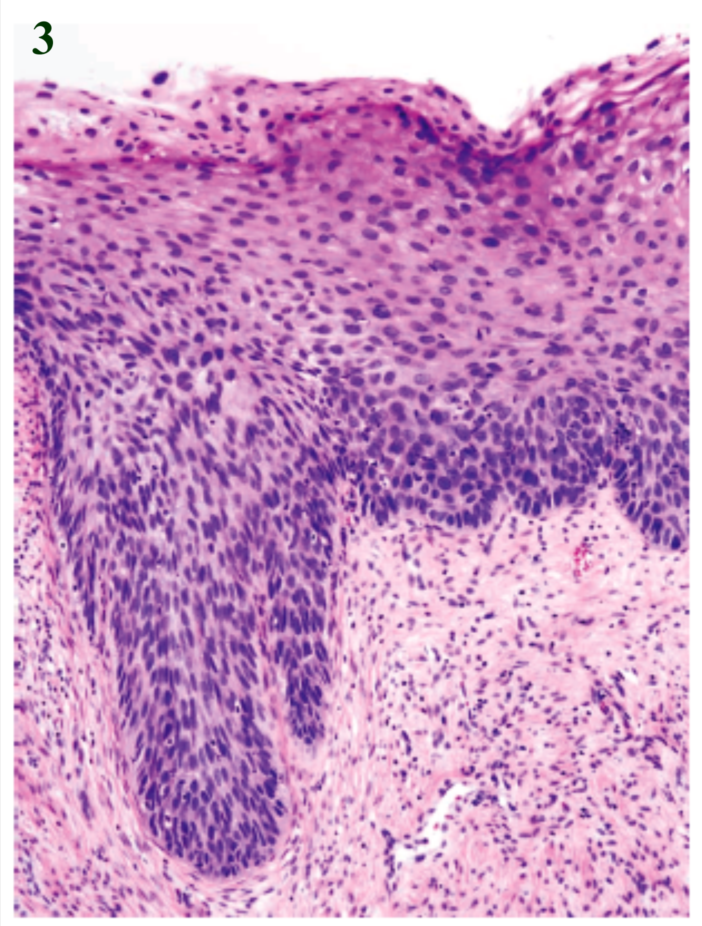
Epithelium

Connective tissue

Epithelial undulations

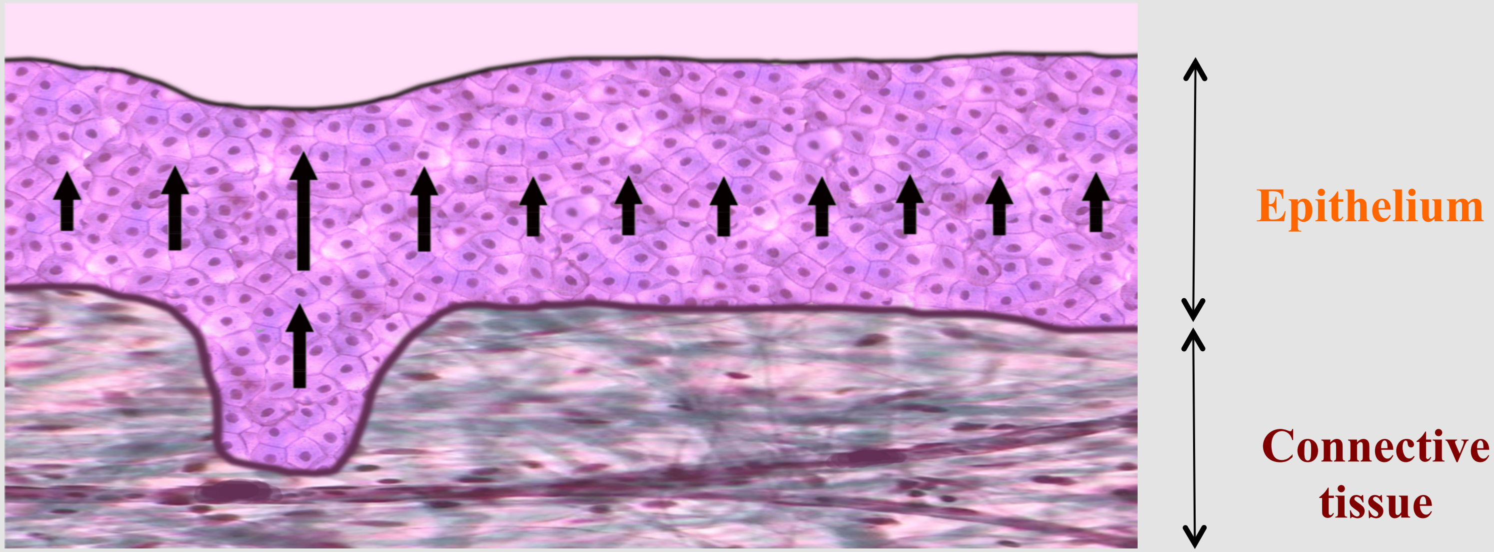






Wikipedia: Cervical dysplasia

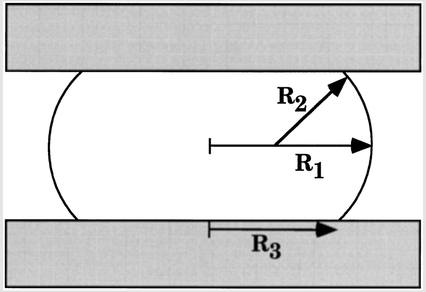
Epithelial instability

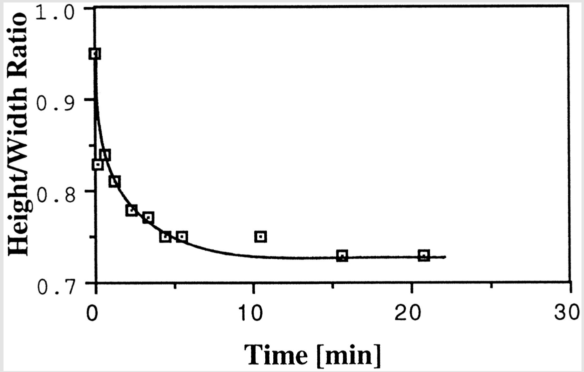


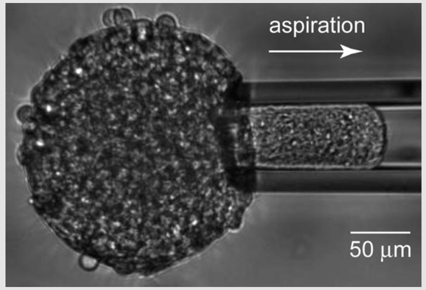
Basan *et al.*, *PRL* **(2011)**

Risler and Basan, *New J. Phys.* **(2013)**

Relaxation and rheology







Guevorkian *et al.*,
Phys. Rev. Lett. **(2010)**
PNAS **(2011)**

Foty *et al.*, *Development* **(1996)**
Forgacs *et al.*, *Biophys. J.* **(1998)**

Elastic modulus $E \simeq 10^2 - 10^4 \text{ Pa}$

Viscosity $\eta \simeq 10^3 - 10^5 \text{ Pa} \cdot \text{s}$

Relaxation time $\tau \simeq 10 \text{ s} - 10 \text{ mn}$

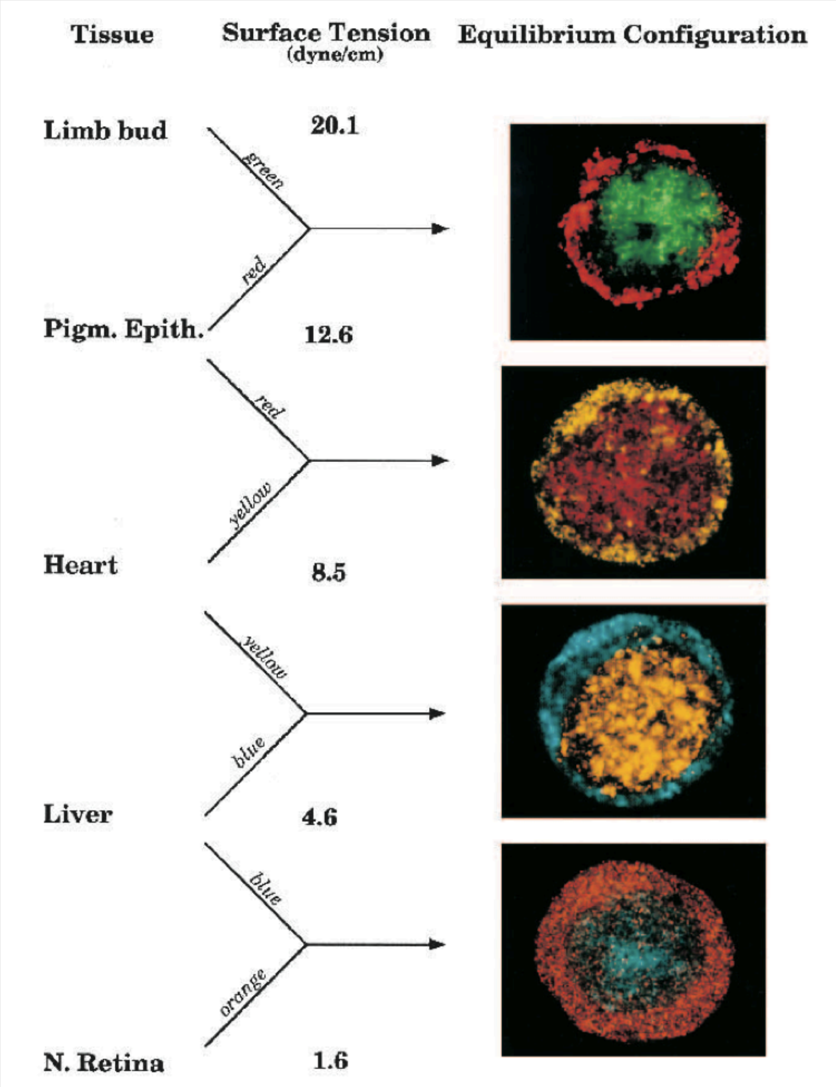
$\tau \simeq \text{hours}$

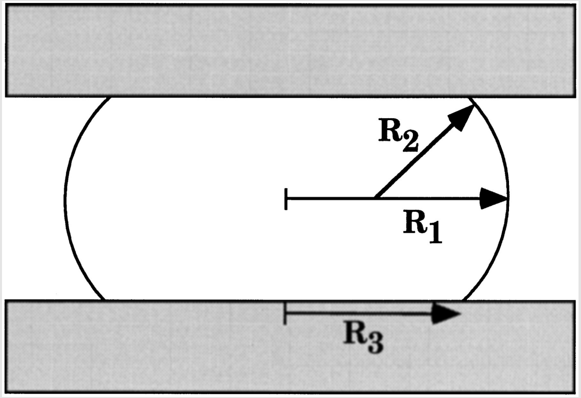
Marmottant *et al.*,
PNAS **(2009)**

Soft-matter models for tissues

Gonzalez-Rodriguez *et al.*,
Science **(2012)**

Surface tension

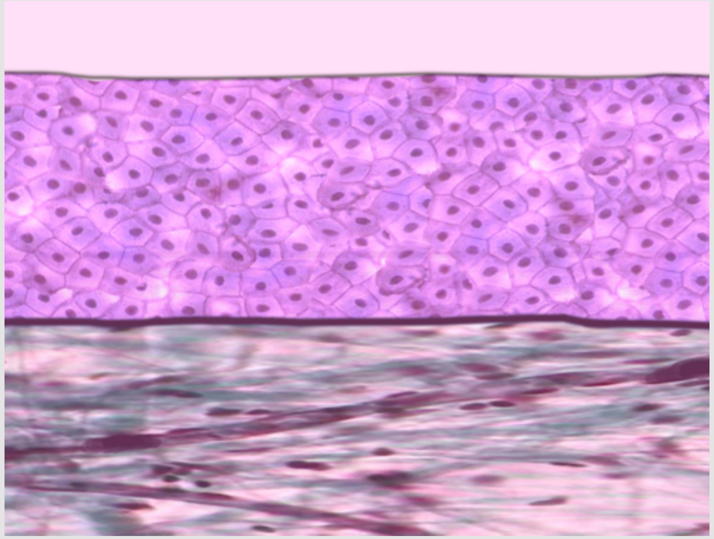




$$\frac{F_{\mathrm{eq}}}{\pi R_3^2} = \gamma \left(\frac{1}{R_1} + \frac{1}{R_2} \right)$$

Foty *et al.*, *Development* **(1996)**
M. Steinberg *et al.*

Constitutive equations



Epithelium:
Incompressible viscous medium with material production

$$\partial_\alpha v_\alpha = k_{\mathrm{d}} - k_{\mathrm{a}}$$

$$\partial_\alpha \sigma_{\alpha\beta} = 0$$

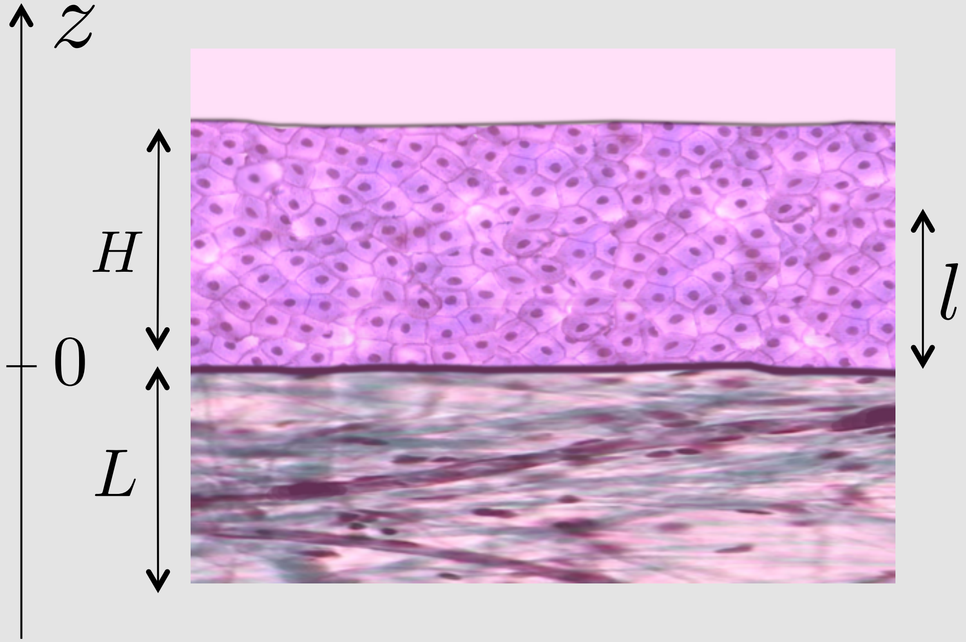
$$\sigma_{\alpha\beta} + P\delta_{\alpha\beta} = \eta \left(\partial_\alpha v_\beta + \partial_\beta v_\alpha \right)$$

Connective tissue (stroma): Standard viscoelastic medium

$$\partial_\alpha v^{\mathrm{s}}_\alpha = 0 \qquad \partial_\alpha \sigma^{\mathrm{s}}_{\alpha\beta} = 0$$

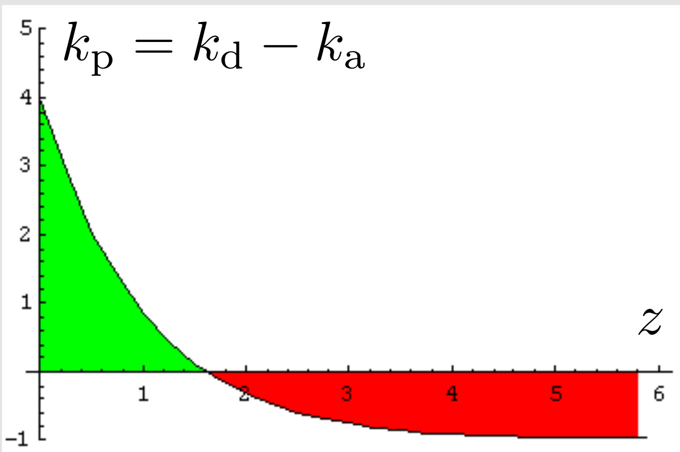
$$\left(\tau \partial_t + 1 \right) \left(\sigma^{\mathrm{s}}_{\alpha\beta} + P^{\mathrm{s}} \delta_{\alpha\beta} \right) = \eta^{\mathrm{s}} \left(\partial_\alpha v^{\mathrm{s}}_\beta + \partial_\beta v^{\mathrm{s}}_\alpha \right)$$

Epithelial source term



Epithelium: Incompressible viscous medium with material production

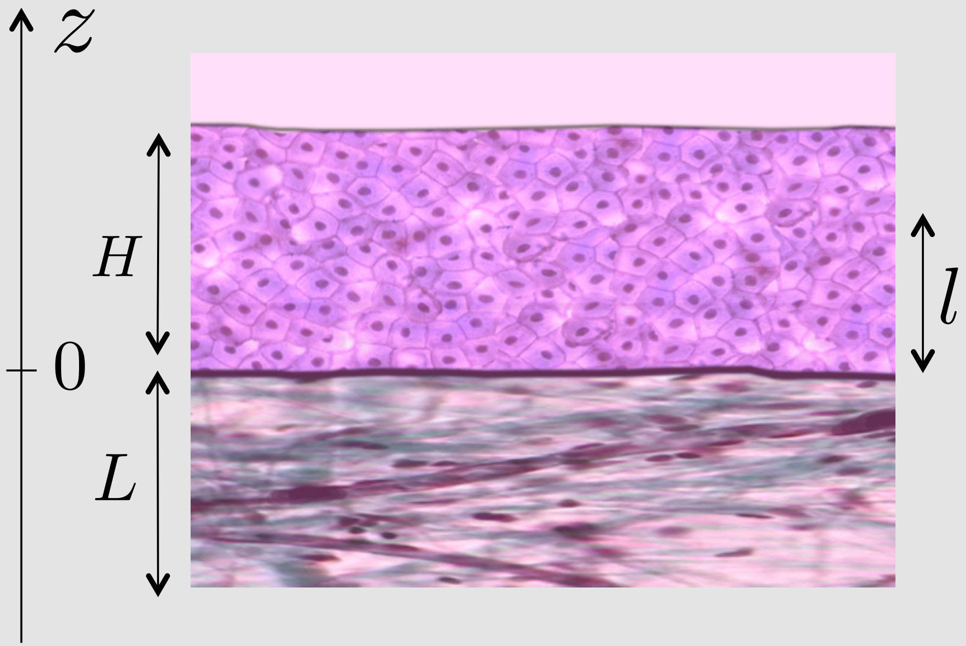
$$\partial_\alpha v_\alpha = k_\mathrm{d} - k_\mathrm{a}$$



Material production

$$\begin{aligned} k_\mathrm{p} &= k \exp\left(-z/l\right) - k_0 \\ v^0_{z\,|z=H} &= \int_0^H k_\mathrm{p}(z)\mathrm{d}z = 0 \end{aligned}$$

Boundary conditions



Upper surface of the epithelium

Free tangential stress $\sigma_{\rm nt} = 0$

Normal stress: Laplace's law

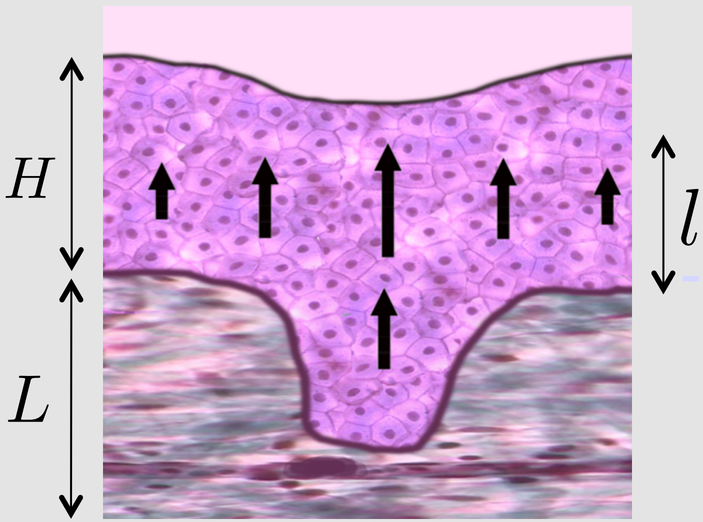
$$\sigma_{\rm nn} = \gamma_{\rm a}\, \delta H''$$

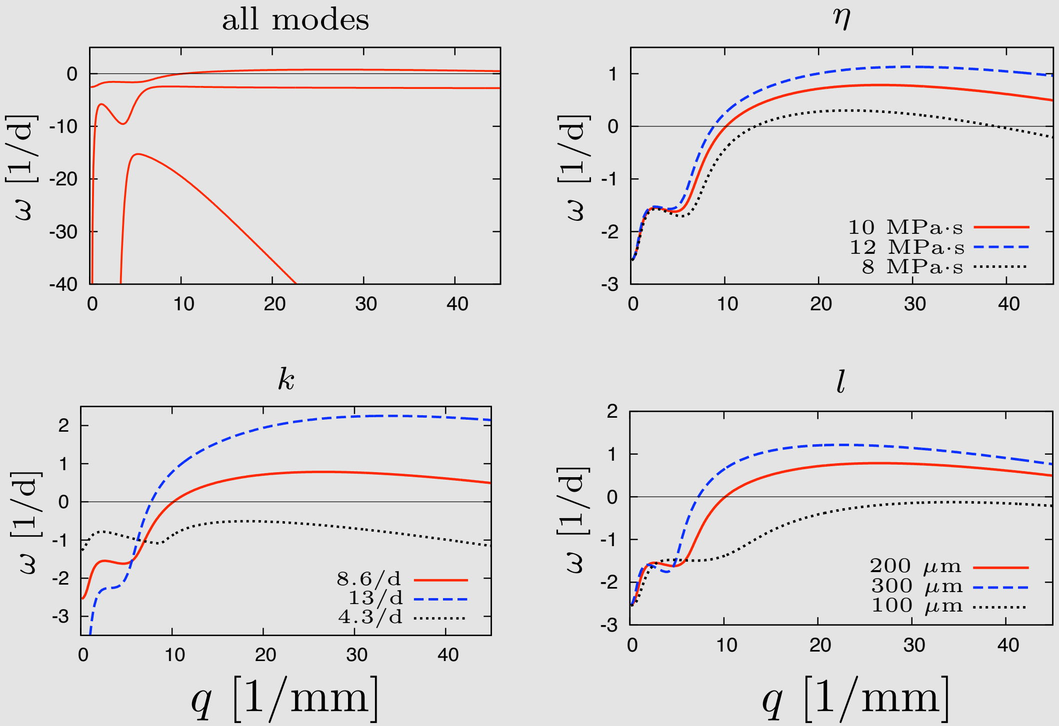
Opposite side **Hard-wall kinematic condition** $v^{\rm s}_{\alpha} = 0$

Interface **Normal stress: Laplace's law** $\sigma^{\rm s}_{\rm nn} = \sigma_{\rm nn} + \gamma_{\rm i}\, \delta h''$

Tangential stress: Friction term $\sigma^{\rm s}_{\rm nt} = \sigma_{\rm nt} = \xi(v_{\rm t} - v^{\rm s}_{\rm t})$

Modes: elastic connective tissue





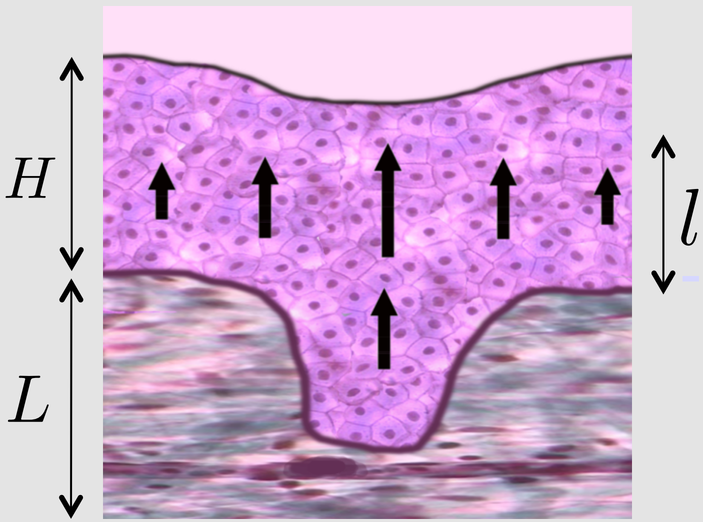
Basan *et al.*, *PRL* (2011)
Risler and Basan, *New J. Phys.* (2013)

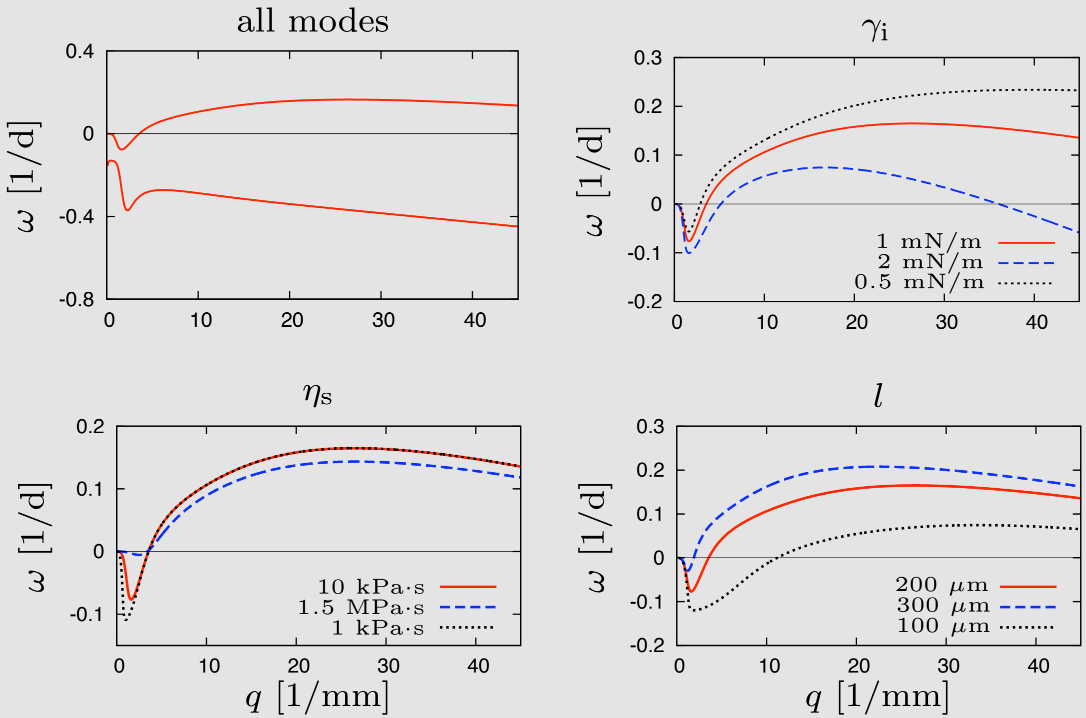
Epithelium viscosity η

Rate of cell division k

Thickness of dividing region l

Modes: viscous connective tissue





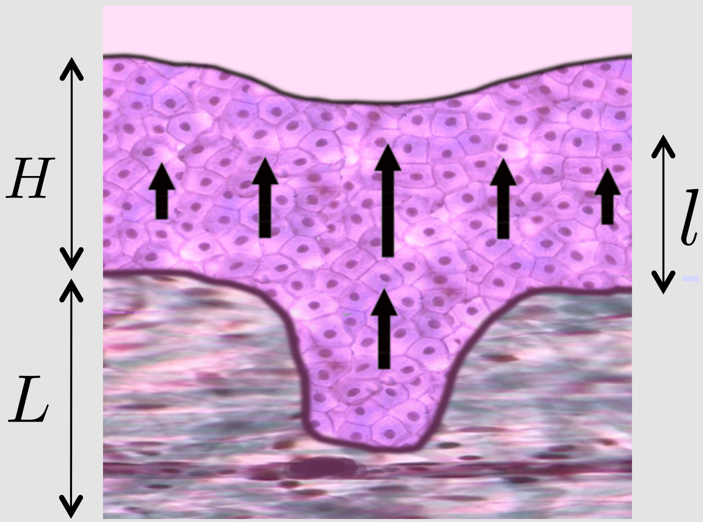
Basan *et al.*, *PRL* (2011)
Risler and Basan, *New J. Phys.* (2013)

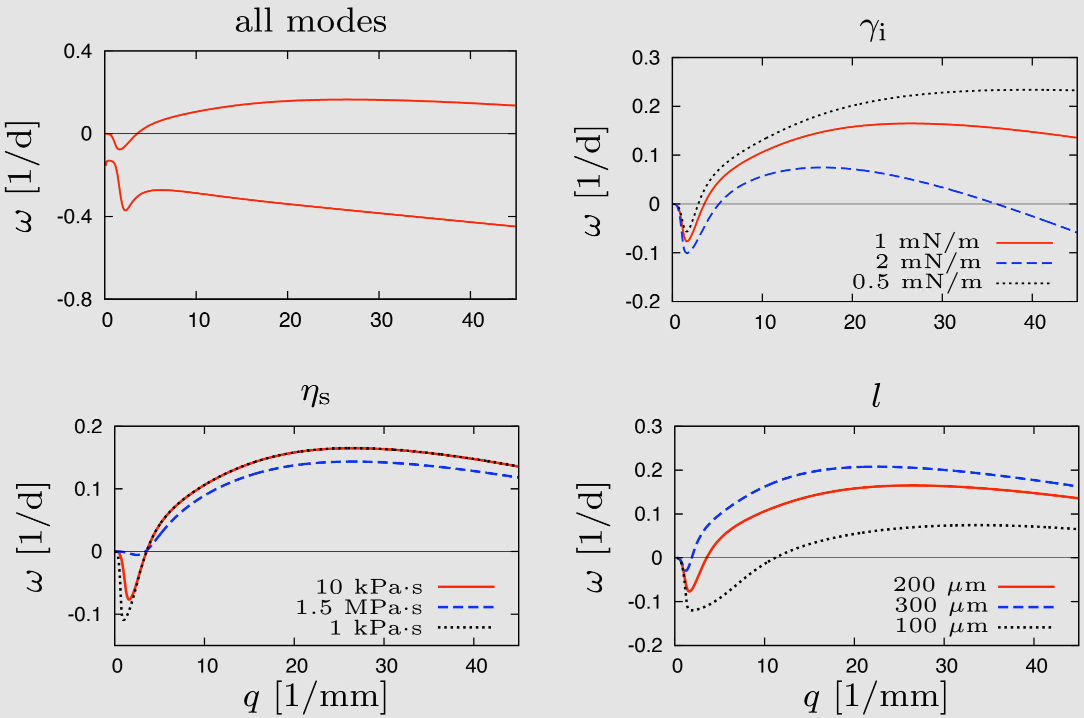
Interfacial tension γ_i

Stroma viscosity η_s

Thickness of dividing region l

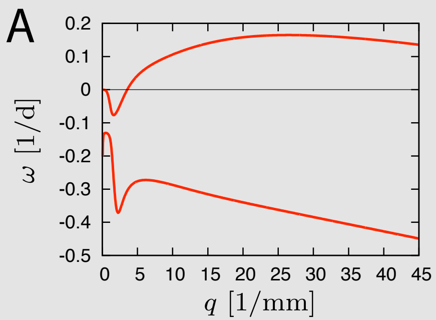
Modes: viscous connective tissue

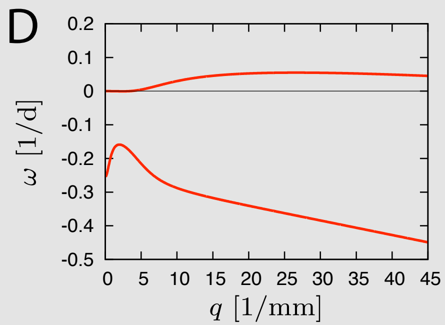




Relative viscosities $\eta = 10\ \mathrm{MPa \cdot s}$

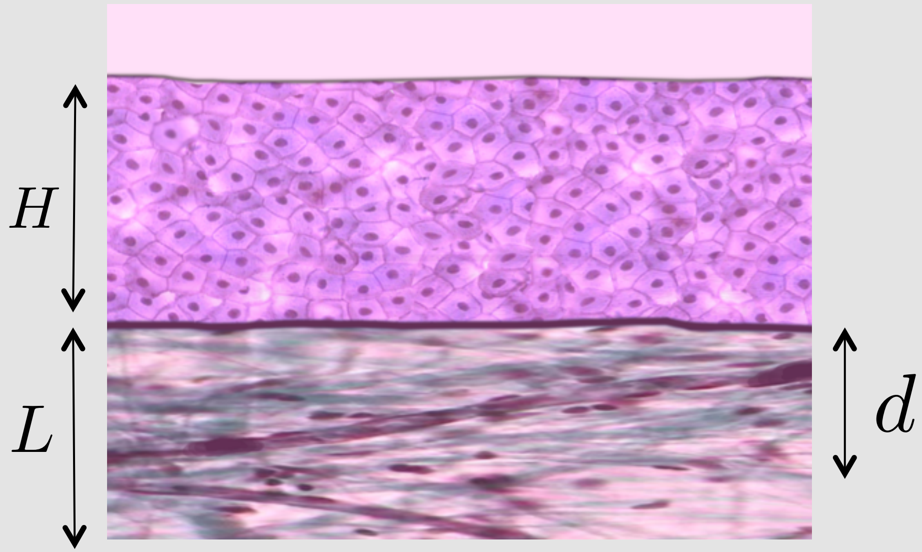
$\eta_{\mathrm{s}} = 10\ \mathrm{kPa \cdot s}$





$\eta_{\mathrm{s}} = 20\ \mathrm{MPa \cdot s}$

Coupling to nutrient diffusion



$$k_\mathrm{d} - k_\mathrm{a} = \kappa_1 \rho - \kappa_0$$

$$\begin{aligned} \partial_t \rho &= D \nabla^2 \rho - c\,\rho \\ \partial_t \rho^\mathrm{s} &= D^\mathrm{s} \nabla^2 \rho^\mathrm{s} \end{aligned}$$

Risler and Basan, *New J. Phys.* **(2013)**

Boundary conditions

Distance *d* from the interface $\quad \rho^\mathrm{s} = \bar{\rho}_0$

Apical surface of the epithelium $\quad -D\partial_\perp \rho = k_\mathrm{off}\,\rho$

Comparison of the two models

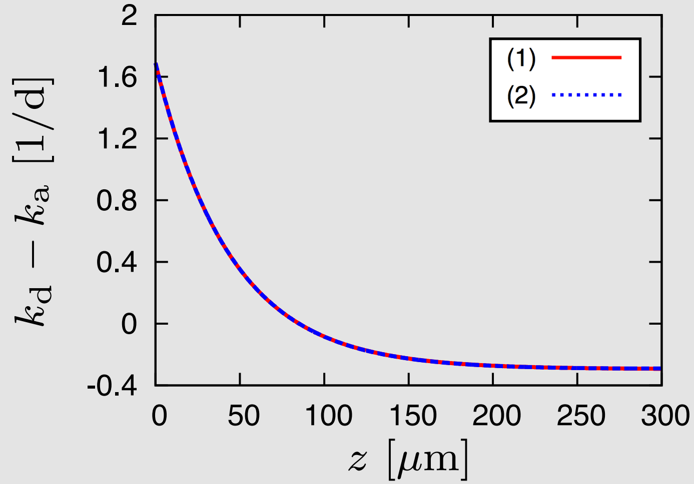
Fit the cell-production function

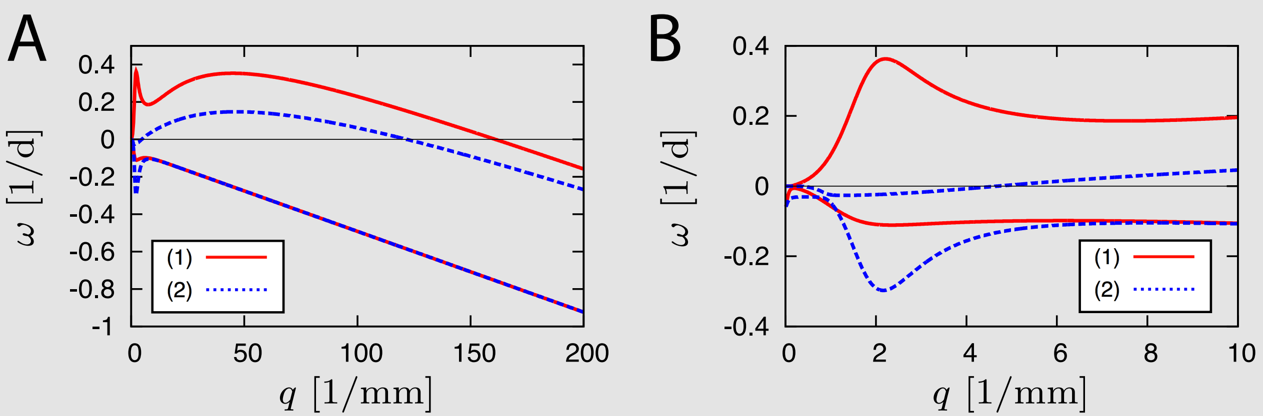
$$(1) \quad k_{\mathrm{d}} - k_{\mathrm{a}} = \kappa_1 \rho - \kappa_0$$

$$\partial_t \rho = D \nabla^2 \rho - c\rho$$

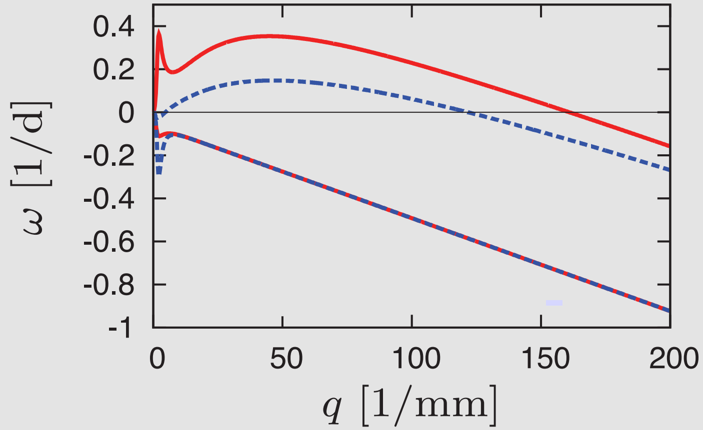
$$\partial_t \rho_{\mathrm{s}} = D_{\mathrm{s}} \nabla^2 \rho_{\mathrm{s}}$$

$$(2) \quad k_{\mathrm{d}} - k_{\mathrm{a}} = k \exp\left(-z/l\right) - k_0$$





New large-scale instability peak



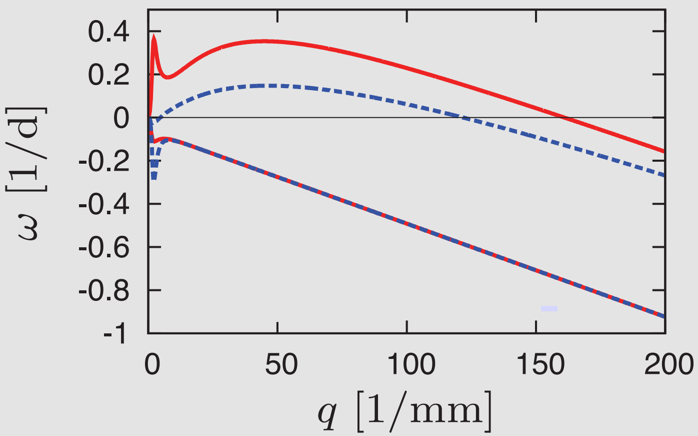
With coupling to diffusion

Without coupling to diffusion

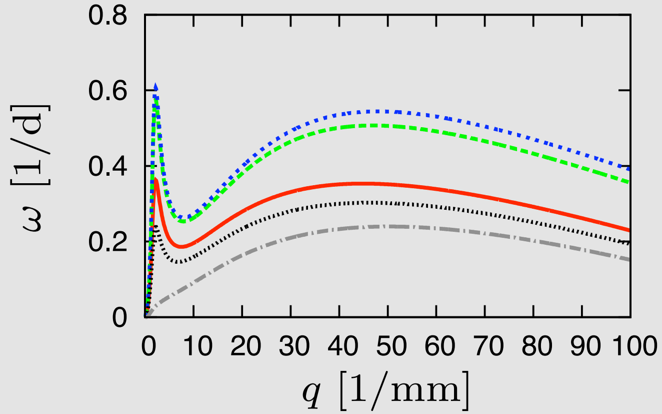
Instabilities in crystal growth

www.its.caltech.edu/~atomic/snowcrystals

Mullins-Sekerka type peak



www.its.caltech.edu/~atomic/
snowcrystals



$$D^{\mathrm{s}} = 2.10^{-11}\ \mathrm{m}^2 \cdot \mathrm{s}^{-1}$$

$$D^{\mathrm{s}} = 2.10^{-10}\ \mathrm{m}^2 \cdot \mathrm{s}^{-1}$$

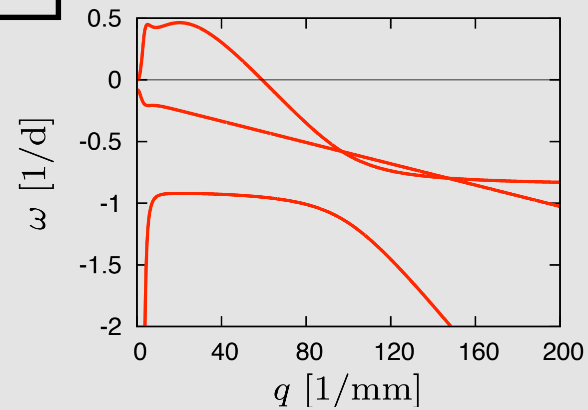
$$D^{\mathrm{s}} = 2.10^{-9}\ \mathrm{m}^2 \cdot \mathrm{s}^{-1}$$

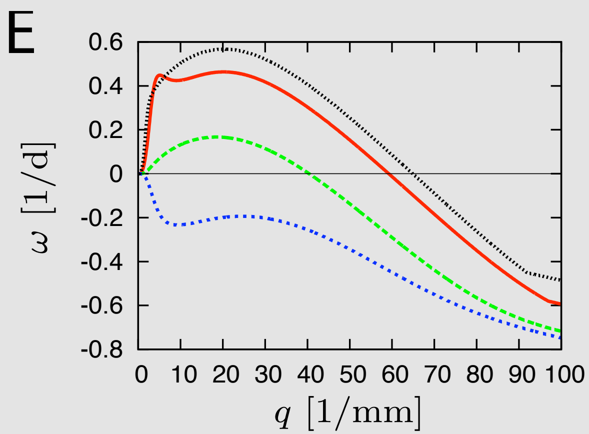
Risler and Basan, *New J. Phys.* **(2013)**

Viscoelastic stroma

Epithelium thickness $H = 300\ \mu\mathrm{m}$

Epithelium viscosity $\eta = 10\ \mathrm{MPa} \cdot \mathrm{s}$

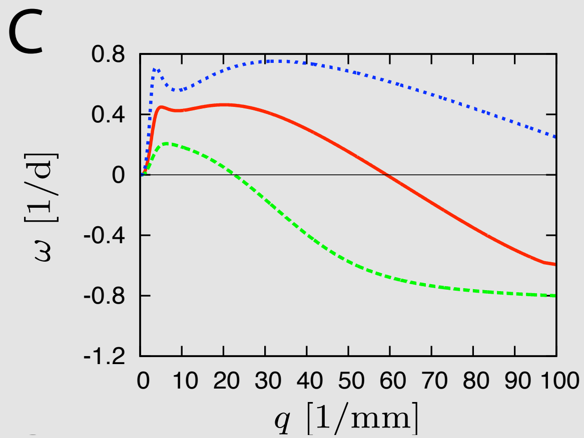




------ $H = 100\ \mu\mathrm{m}$

------ $H = 50\ \mu\mathrm{m}$

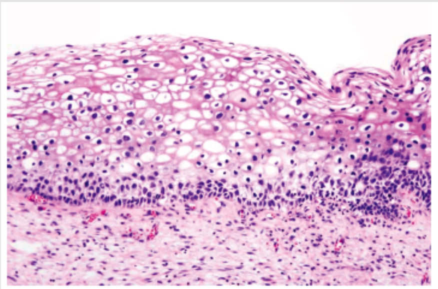
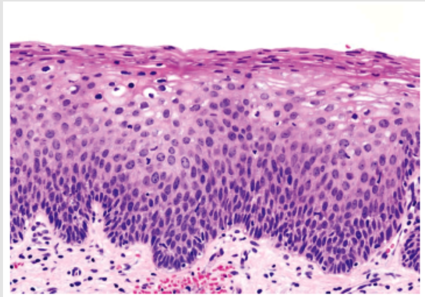
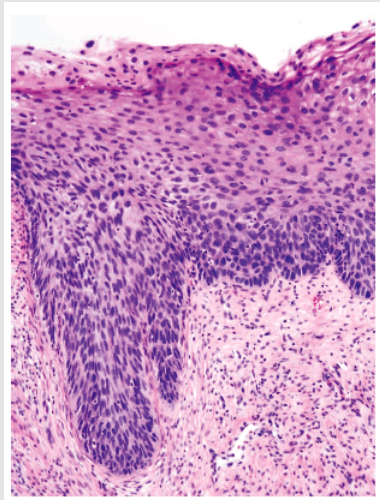
------ $H = 900\ \mu\mathrm{m}$



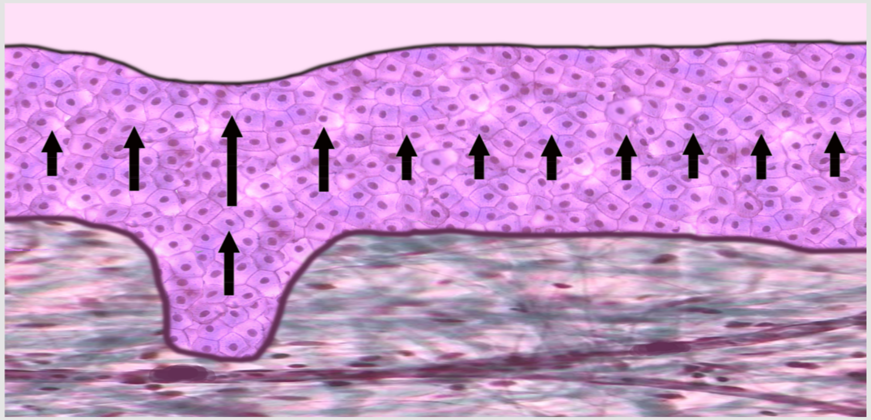
------ $\eta = 5\ \mathrm{MPa} \cdot \mathrm{s}$

------ $\eta = 20\ \mathrm{MPa} \cdot \mathrm{s}$

Epithelial undulations

http://en.wikipedia.org/wiki/Cervical_dysplasia



M. Basan
J.-F. Joanny
J. Prost

Basan *et al.*, *PRL* (2011)
Risler and Basan, *New J. Phys.* **(2013)**

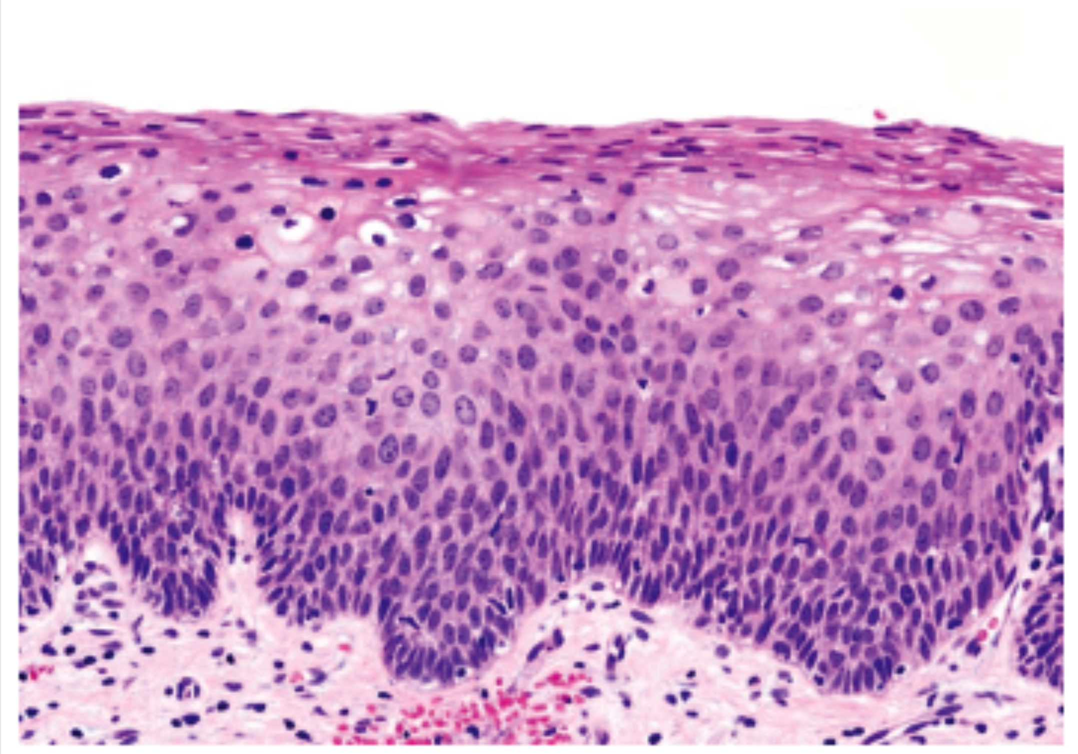
Review: Risler, *New J. Phys.* **(2015)**

Tissue alone with fluctuations

Homeostatic pressure and density
Surface fluctuations
Effective temperature

M. Basan, A. Peilloux, J.-F. Joanny & J. Prost
ETH, Zürick
Université Paris Diderot Paris VII
Institut Curie, Paris

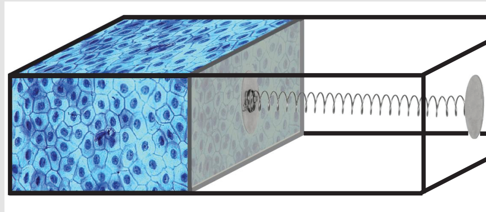
Epithelial undulations



http://en.wikipedia.org/wiki/
Cervical_dysplasia

Regulated pressure of tissue growth

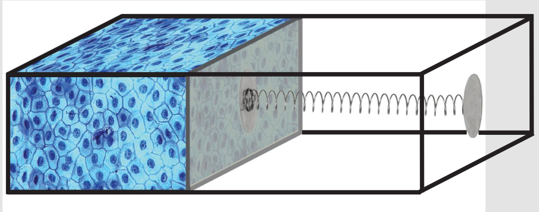
Homeostatic pressure P_{h}



Basan *et al.*, *HFSP J.* **(2009)**

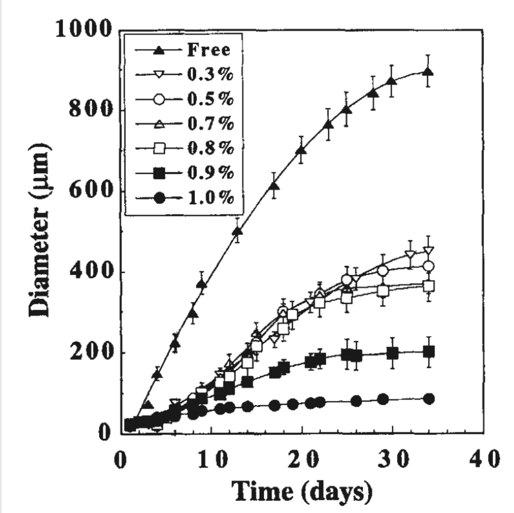
Regulated pressure of tissue growth

Homeostatic pressure P_{h}



Basan *et al.*, *HFSP J.* **(2009)**

Pressure regulation of tissue growth



Spheroids in an agarose gel

Helmlinger *et al.*, *Nature Biotech.* **(1997)**

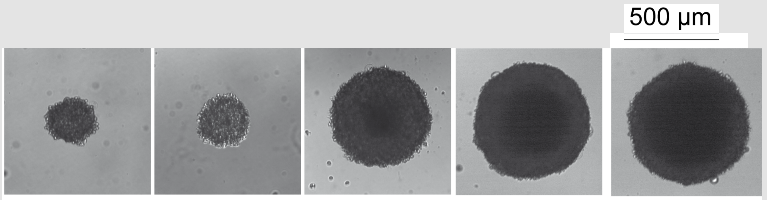
Mechanical feedback in development

B. Shraiman, *PNAS* **(2005)**

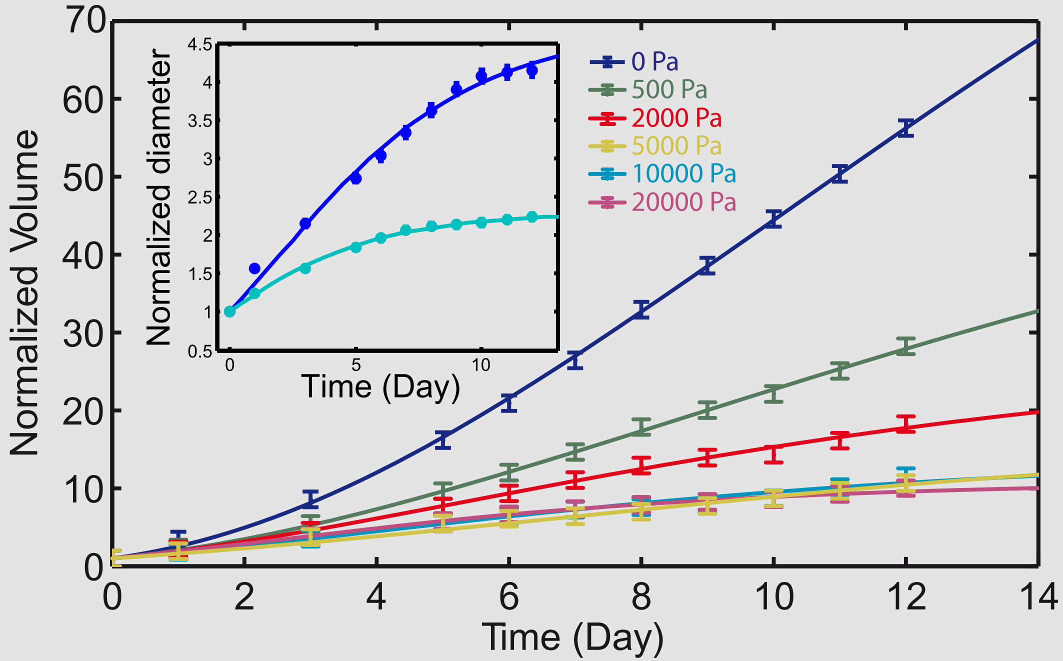
Experiments

Osmotic stress exerted by Dextran

F. Montel, M. Delarue. G. Capello, L. Malaquin, D. Vignjevic, *et al.*



Day 2 4 7 9 11

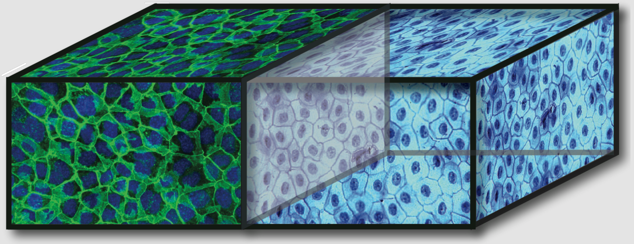


Montel, Delarue, Elgeti *et al.*,
Phys. Rev. Lett. **(2011)**
New J. Phys. **(2012)**

Tissue competition

Homeostatic pressure P_{h}

Tissue competition and tumor growth

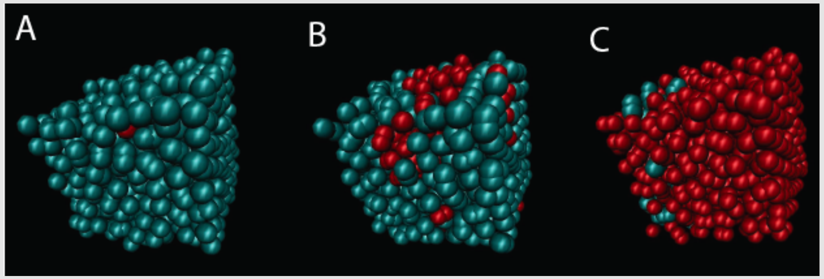


$$P_{\mathrm{h}}^{\mathrm{ct}} > P_{\mathrm{h}}^{\mathrm{ht}}$$

Dysplasic tissue | **Healthy tissue**

Basan *et al.*, *HFSP J.* **(2009)**

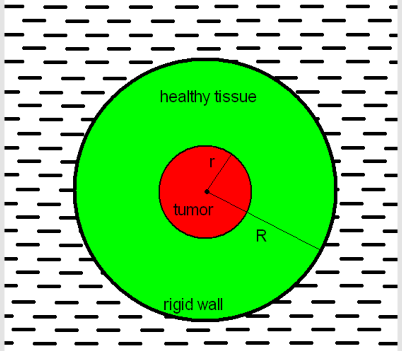
Dissipative particle dynamics



Basan *et al.*, *Phys. Biol.* **(2011)**

Dysplasic tissue **Healthy tissue**

Nucleation threshold



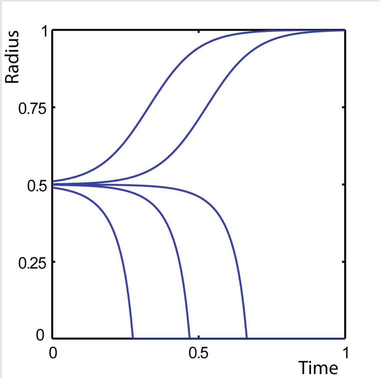
Surface tension

$$P^{\mathrm{ct}} - P^{\mathrm{ht}} = \frac{2\gamma}{r}$$

M. Steinberg *et al.*

Critical size

$$P_{\mathrm{h}}^{\mathrm{ct}} - P_{\mathrm{h}}^{\mathrm{ht}} = \frac{2\gamma}{r_{\mathrm{c}}}$$



$r > r_{\mathrm{c}}$ → **Tumor grows**

$r < r_{\mathrm{c}}$ → **Tumor shrinks**

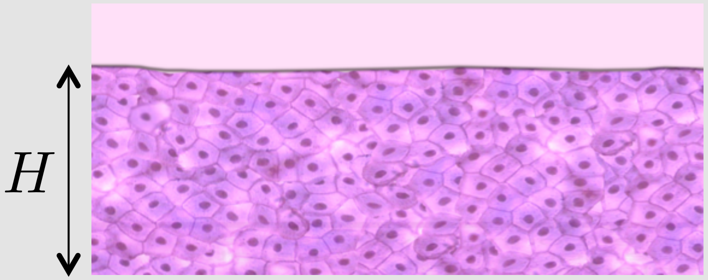
Nucleation and metastatic inefficiency **Fidler,** *Nature Rev. Cancer* **(2003)**

Basan et al., *HFSP J.* **(2009)**

Tissue alone with fluctuations

Epithelium

Compressible medium with stochastic source term



$$\partial_t \rho + \partial_\alpha(\rho v_\alpha) = (k_\mathrm{p} + \xi_\mathrm{c})\rho$$

$$\langle \xi_\mathrm{c}(\mathbf{r}, t)\rangle = 0$$

$$\langle \xi_c(\mathbf{r}, t)\xi_c(\mathbf{r}', t')\rangle = \frac{k_d + k_a}{\rho}\delta(\mathbf{r} - \mathbf{r}')\delta(t - t')$$

Close to homeostatic conditions

$$\delta\rho = \rho - \rho_\mathrm{h} \qquad \delta\sigma = \sigma - \sigma_\mathrm{h}$$

$$k_\mathrm{p} = -(1/\tau_\mathrm{i})\,(\delta\rho/\rho_\mathrm{h}) = (1/\tau_\mathrm{i})\,\chi_\mathrm{c}\,\delta\sigma$$

Tissue alone with fluctuations

Effective Maxwell model

$$(1+\tau_{\mathrm{i}}\partial_t)\delta\sigma = \zeta v_{\gamma\gamma} - \xi$$

$$\delta\sigma_{\alpha\beta} = \tilde{\sigma}_{\alpha\beta} + \delta\sigma\,\delta_{\alpha\beta}$$

$$(1+\tau_{\mathrm{a}}\partial_t)\,\tilde{\sigma}_{\alpha\beta} = 2\eta\tilde{v}_{\alpha\beta} - \tilde{\xi}_{\alpha\beta}$$

$$\partial_\alpha\delta\sigma_{\alpha\beta} = 0$$

Ranft *et al.*, *PNAS* **(2010)**

Correlation and response functions

$$C(\mathbf{r}-\mathbf{r}', t-t') = \langle \delta H(\mathbf{r},t)\delta H(\mathbf{r}',t')\rangle$$

$$\langle \delta H(\mathbf{r},t)\rangle = \int \chi(\mathbf{r}-\mathbf{r}', t-t')\delta P_e(\mathbf{r}',t')\,d\mathbf{r}'dt'$$

Effective temperature

$$k_{\mathrm{B}}T_{\mathrm{eff}}(q,\omega) = \frac{\omega}{2}\frac{C(q,\omega)}{\chi''(q,\omega)}$$

Thermodynamic limit

$$T_{\mathrm{eff}}(q,\omega) \equiv T \qquad \text{for} \qquad \theta = 2\eta k_{\mathrm{B}}T \quad \text{and} \quad \vartheta = 2\zeta k_{\mathrm{B}}T$$

η	**shear viscosity**	θ	**shear noise amplitude**
ζ	**bulk viscosity**	ϑ	**bulk noise amplitude**

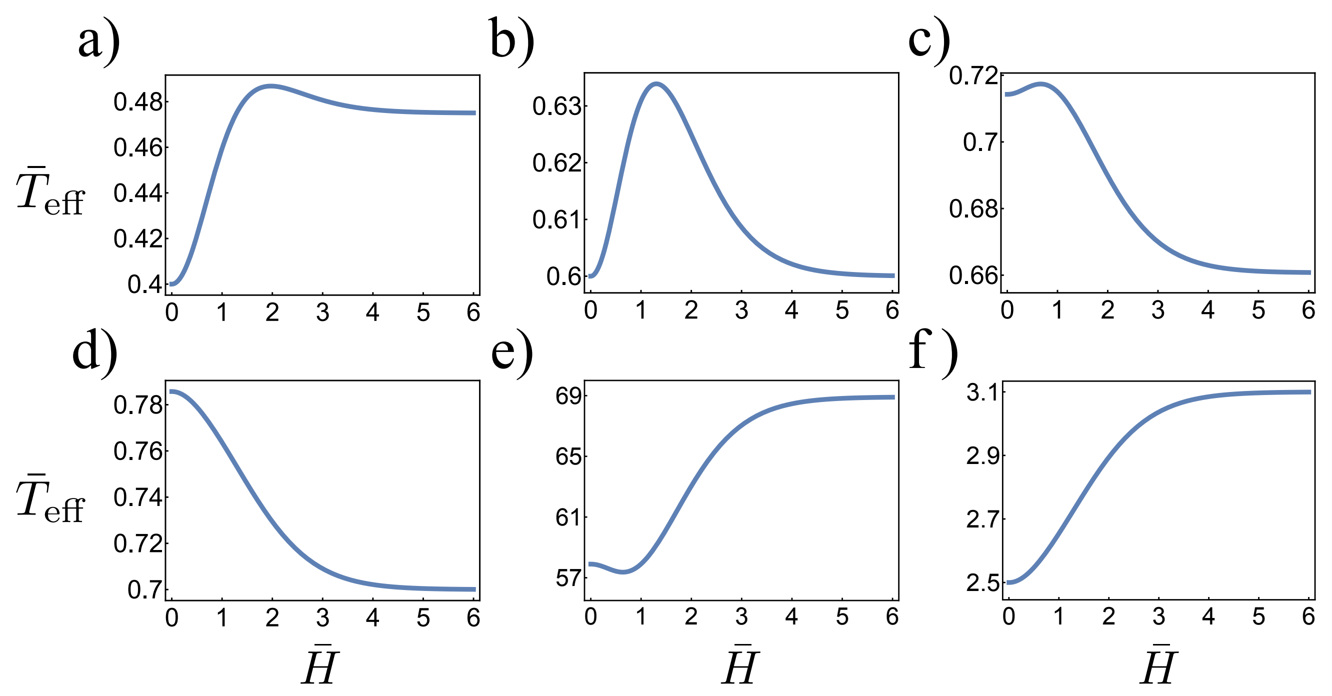
Infinite-thickness limit

Long-time limit	**Passive fluid at Teff, infinitely compressible**
Short-time limit	**Passive compressible Maxwell elastomere**

Effective temperature

$$k_{\mathrm{B}} T_{\mathrm{eff}}(q,\omega) = \frac{\omega}{2} \frac{C(q,\omega)}{\chi''(q,\omega)}$$

Finite thickness in the long-time limit



$$\bar{T}_{\mathrm{eff}} = \frac{2\zeta k_{\mathrm{B}} T_{\mathrm{eff}}}{\vartheta}$$

$$\bar{H} = qH$$

Risler, Peilloux, Prost, *PRL* (2015)

Generalized fluctuation-dissipation relation

In the long-time limit

$$\partial_t \, \delta H(q,t) = -\tau(q)^{-1} \, \delta H(q,t) + f(q,t) + \xi_H(q,t)$$

$$\langle \delta H(q,t) \delta H(q',t) \rangle = \Sigma(q) \, \delta(q+q')$$

Prost *et al.*, *PRL* (2009)

$$X(q,t) = -\tau(q)^{-1} \Sigma(q)^{-1} \, \delta H(q,t)$$

$$\boxed{\chi''_{XX}(q,\omega) = \frac{\omega}{2} C_{XX}(q,\omega)}$$

Risler, Peilloux, Prost, *PRL* (2015)

Analogy with membranes

In the long-time and long-wavelength limit

$$C(q,\omega) \simeq \frac{1}{H}\frac{\vartheta + \frac{4}{3}\theta}{(\gamma q^2 + \kappa q^4)^2 + \omega^2 \lambda_{\mathrm{p}}^{-2}}$$

$$\chi(q,\omega) \simeq -\frac{1}{\gamma q^2 + \kappa q^4 + \mathrm{i}\omega\lambda_{\mathrm{p}}^{-1}}$$

$$k_{\mathrm{B}}T_{\mathrm{eff}} \simeq \frac{1}{2}\frac{\vartheta + \frac{4}{3}\theta}{\zeta + \frac{4}{3}\eta}$$

Analogous to a membrane near a wall with permeation constant

$$\lambda_{\mathrm{p}} = \frac{H}{\zeta + \frac{4}{3}\eta}$$

Analogy with membranes

Equal-time correlation function

$$C(q, t - t' = 0) \simeq \frac{k_{\mathrm{B}} T_{\mathrm{eff}}}{\gamma q^2 + \kappa q^4}$$

Collision length

$$\langle \delta H(0,t) \delta H(l_{\mathrm{c}}, t) \rangle = H^2$$

Tension-dominated regime $\gamma H^2 \gg k_{\mathrm{B}} T_{\mathrm{eff}}$

$$l_{\mathrm{c}} \propto H \sqrt{\frac{\kappa}{k_{\mathrm{B}} T_{\mathrm{eff}}}} = l_\kappa \sqrt{\frac{\gamma H^2}{k_{\mathrm{B}} T_{\mathrm{eff}}}} \qquad l_\kappa = \sqrt{\kappa / \gamma}$$

Bending-dominated regime $\gamma H^2 \ll k_{\mathrm{B}} T_{\mathrm{eff}}$

$$l_{\mathrm{c}} \propto l_\kappa \exp\left(\frac{\pi \gamma H^2}{k_{\mathrm{B}} T_{\mathrm{eff}}} \right)$$

Risler, Peilloux, Prost, *PRL* (2015)

Acknowledgements

A. Peilloux

J. Prost

M. Basan

J.-F. Joanny

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