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Active matter with Biological molecules

References Alberts Molecular Biology of the cell
Howard Mechanics of motor proteins and the cytoskeleton
F. Jülicher et al. Active behavior of the cytoskeleton Phys. Rep. 449 3.28 (2007)
JF Joanny and J. Prost Active gels as a description of the actin myosin cytoskeleton HFSP J 3, 94 (2009)
J. Prost J.F. Joanny Constructing tools for the description of cell dynamics
Poincaré Seminar (2009) Birkhauser 2010

I Cytoskeleton

The cytoskeleton is the gel like structure made of filaments which controls the mechanical properties of cells. There are 3 types of filaments actin microtubules and intermediate filaments. Show images of actin + microtubules

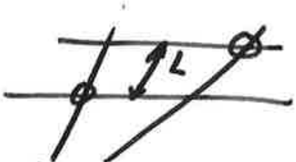
1. Actin - myosin cytoskeleton

Actin filaments are formed by assembly of actin monomers. Two protofilaments coil into a helix of 72 nm pitch. The filament is polar; it has a + barbed end and a - pointed end. It is treadmilling it polymerizes at the + end with a velocity v_p and depolymerizes at the - end with a velocity v_d

$v_p = 1\,\mu m/s$

The filament is semi rigid with a persistence length $l_p \sim 10\,\mu m$.

Actin interact with many proteins with various roles: capping - branching - severing - crosslinking.

Upon crosslinking makes a physical gel  typically $L \simeq 60\,nm$

The crosslinks in general have a finite life time (due to binding and unbinding)

At times shorter than this life time actin gels behave as solids with a finite shear modulus E

We estimate E via a scaling argument assuming that L and l_p are the only relevant length scales $E = \frac{kT}{L^3} f\left(\frac{L}{l_p}\right)$ from dimensional analysis

If the bending mode of the filament dominate $E \sim E_f \sim l_p$

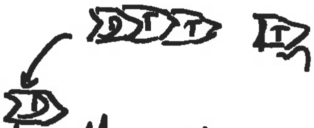
Rq: Dimensional analysis $l_p \sim \frac{E_f d^4}{kT}$

$E = kT \frac{l_p}{L^4}$ A.N. $l_p = 10\,\mu m$ $L = 60\,nm$ $kT = 4\,pN.nm = 4\,10^{-21}\,J$

$E = 25\,Pa$

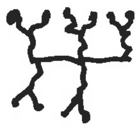
If the stretching of the filaments dominate  unwinding of fluctuations $E \sim l_p^2$ $E \sim kT \frac{l_p^2}{L^5} \sim 600\,Pa$

When crosslinked by passive crosslinkers, the properties of actin gels are well-described by classical equilibrium polymer physics. This is not obvious as the polymerization depolymerization process involve ATP



ATP hydrolysis inside the filament (required for the existence of tread-milling). In the cell actin interacts with the molecular motor myosin

Myosin is a non processive motor. In the cytoskeleton it works in aggregate which themselves are more processive and bind on actin



7-10 motors (show movie on myosin) called minifilaments

Myosin minifilaments bind to the actin filaments and induce internal active stress by moving to the + end . Myosin consume energy in the form of ATP. An actin myosin gel is a non-equilibrium gel where energy is consumed all the time in the form of ATP (chemical energy)

ATP ⟶ ADP + Phosphate $\quad \Delta\mu = \mu_{ATP} - \mu_{ADP} - \mu_{P} \approx 25\,kT$

Rq. In the cell ADP is recycled to ATP in mitochondria

$$\Delta\mu = \Delta\mu_0 + kT \operatorname{Log} [ATP]/[ADP][P_i]$$

. Muscle structure

We assume that $\Delta\mu$ does not vary with space

A way to show that active acto-myosin gels are indeed non

Equilibrium systems is tested the fluctuation dissipation theorem. The group of C. Schmidt has obtained that by adding beads inside the gel and by doing what they call active and passive microrheology. In ~~acti~~ passive microrheology we measure the position $x(t)$ of the bead and its correlation function $C(t) = \langle x(0)\, x(t) \rangle$ and its Fourier transform $\tilde{C}(\omega) = \int e^{+i\omega t} C(t)\,dt$

In an active experiment, we exert a force $f(\omega)$ and measure the response function $\tilde{x}(\omega) = \tilde{\chi}(\omega)\, f(\omega)$. For an equilibrium system

$$\frac{2kT\,\chi''(\omega)}{\omega} = \tilde{C}(\omega).$$

If this is not satisfied the system is not at thermal equilibrium. - Expt C. Schmidt also experiments on cells.

2. Microtubules

Hollow cylinders much stiffer than actin

Polar objects, 13 p. filaments. Kinesins are processive motors walking to the + end and dyneins to the - end. Z. Dogic Science (2011)

3. Active gels

- Show Koenderink. Rheology experiments. Keratocyte motion

Other types of active systems

II Active polar gels

There are 2 ways to describe active gels such as actomyosin gels: at the microscopic level we can use polymer physics to describe actin and microscopic theories of molecular motors and then coarse grain to obtain the mesoscopic or macroscopic properties.

We do not follow this approach. We want to start directly at the macroscopic level and build up a hydrodynamic theory. We therefore only consider slow variables of the actin-myosin gel and write Onsager-like constitutive equations.

In a hydrodynamic theory the slow variables are of 2-3 types

- conserved quantities n (density), momentum
- Slow modes associated to broken symmetries $\vec{p}$ = polarization (2 modes)
- critical variables

There is a systematic way using symmetries to construct the constitutive equations.

1. Entropy production

We consider a system at a constant temperature T i.e. a system in contact (exchanging energy) with a reservoir R at temperature T. The total entropy is $dS_t = dS + dS_R \geq 0$. The reservoir being at thermal equilibrium $dS_R = \frac{dU_R}{T}$ $= -\frac{dU}{T}$ $\quad dS_t = dS - \frac{dU}{T} = -\frac{dF}{T}$ F being the free energy. $F = U - TS$

As a first approximation, we make a one component theory lumping actin and myosin in a single component. A more complex 2 or 3 fluid model is doable but leads to much more complex equations.

The free energy is a function of 2 variables (slow), the number of molecules (actin) and the polarization $\vec{p}$ defined as the average of the local orientation of the filaments

$$\vec{p} = \langle \vec{n} \rangle$$

$$dF = \mu\, dN - V \vec{h}\, d\vec{p} \qquad \vec{h} = -\frac{\partial F/V}{\partial \vec{p}}$$ is the orientational field

We will work with the free energy per unit volume $f = F/V$

$$df = \mu\, dn - h_\alpha\, dp_\alpha$$ where $n = \frac{N}{V}$ is the density

If there is a global motion, the density of kinetic energy is $\frac{1}{2}\rho v^2 = \frac{1}{2} n m v^2$

The entropy production is therefore $-T\frac{dS_t}{dt} = \frac{dF}{dt} = \int d\vec{r} \left[\mu \frac{\partial n}{\partial t} - \vec{h}\frac{\partial \vec{p}}{\partial t}\right.$

$\left. \frac{\partial}{\partial t}\left(\frac{1}{2} n m v^2\right)\right]$

This would be the entropy production of a "nematic elastomer" in the absence of molecular motors. The motors are maintained out of equilibrium by consumption of ATP

If r is the number of ATP molecules consumed per unit time and per unit volume we must add a term $-\int d\vec{r}\;\, r\,\Delta\mu$.

Rq We assume $\Delta\mu = ct$

2. Conservation laws

Number of molecules $\frac{\partial n}{\partial t} + \vec\nabla \vec J = 0 \quad \vec J = n\vec v$

Momentum $nm\left[\frac{\partial \tilde v_\alpha}{\partial t} + v_\beta \partial_\beta v_\alpha\right] = \partial_\beta \sigma^t_{\alpha\beta}$ Navier-Stokes

This looks like a conservation of the momentum density $\vec g = nm\vec v$

$\frac{\partial \vec g}{\partial t} - \vec\nabla \tilde\sigma_t = 0$ - the momentum flux is $\tilde\sigma_{t\alpha\beta} = \sigma^t_{\alpha\beta} - nm v_\alpha v_\beta$

At small Reynolds number, we ignore this Reynolds stress.

3. Thermodynamics of polar systems

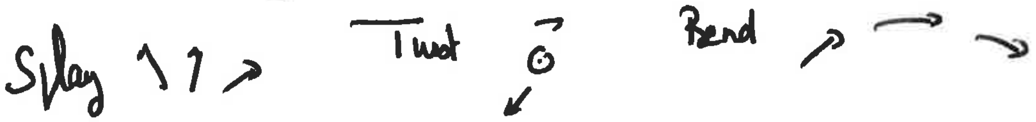
The slow modes associated to the polarization $\vec p$ are associated to the rotations of $\vec p$. Except close to the critical point $|\vec p|$ is not a hydrodynamic variable.

In the following without loss of generality we choose $|\vec p| = 1$

The free energy is the Frank free energy of polar liquid crystals

$$F = \int d\vec r \left\{ \frac{K_1}{2}(\vec\nabla \cdot \vec p)^2 + \frac{K_2}{2}(\vec p \cdot \vec\nabla \times \vec p)^2 + \frac{K_3}{2}\left[\vec p \times (\vec\nabla \times \vec p)\right]^2 \right.$$

Discuss $h\vec\nabla p$ term



In two dimensions if $K_1 = K_3$ $\quad F = \frac{1}{2}\int d\vec r\, K(\nabla\theta)^2$

It is often useful to distinguish the components of h: $h_\parallel$ parallel to $\vec p$ and $h_\perp \perp$ to $\vec p$. $h_\parallel$ monitors the degree of ordering $|\vec p|$ and $h_\perp$ is the torque that drive the orientation of $\vec p$ to its equilibrium value

In order to ensure that $|\vec{p}| = 1$ we add a Lagrange multiplier $h_{\parallel}^{0}$ and a term in the free energy $-\int \frac{h_{\parallel}^{0}}{2} p^2 \, d\vec{r}$

Gibbs Duhem relation $n\, d\mu = dP - h_\alpha \, dp_\alpha$

In a non isotropic medium the stress is not symmetric. The asymmetric component is associated to torques that do not vanish. (the rotational symmetry is broken). The antisymmetric component of the stress can be calculated by conservation of angular momentum in the fluid $\sigma^a_{\alpha\beta} = \frac{1}{2}(p_\beta h_\alpha - p_\alpha h_\beta)$

It depends only on $h_\perp$. See de Gennes and Prost The physics of liquid crystals.

4. Fluxes and forces, time reversal

After using conservation laws and integrating by parts, the entropy production can be rewritten as

$$T\frac{dS_t}{dt} = \int d\vec{r}\left\{\sigma_{\alpha\beta} v_{\alpha\beta} + P_\alpha h_\alpha + r\Delta\mu\right\}$$

$\sigma_{\alpha\beta}$ is the symmetric part of the stress $\sigma^t_{\alpha\beta} = \sigma^a_{\alpha\beta} - P\delta_{\alpha\beta} + \sigma_{\alpha\beta}$

$v_{\alpha\beta}$ is the strain rate tensor $v_{\alpha\beta} = \frac{1}{2}(\partial_\alpha v_\beta + \partial_\beta v_\alpha)$

we also define the antisymmetric part of the velocity gradient associated to vorticity

$$\omega_{\alpha\beta} = \frac{1}{2}(\partial_\alpha v_\beta - \partial_\beta v_\alpha)$$

P_α is the convected derivative of p_α $P_\alpha = \frac{\partial p_\alpha}{\partial t} + v_\beta \partial_\beta p_\alpha + \omega_{\alpha\beta} p_\beta$

$\vec{P} = \frac{D\vec{p}}{Dt} = \frac{\partial\vec{p}}{\partial t} + (\vec{v}\cdot\vec{\nabla})\vec{p} + \vec{\omega}\times\vec{p}$ $\quad\vec{\omega} = \frac{1}{2}(\vec{\nabla}\times\vec{v})$ is the local rotation

Rq More complex if the system is chiral S. Fürthauer F. Jülicher.

Following Onsager we identify 3 forces and 3 fluxes

$v_{\alpha\beta}$	time reversal signature (-1)	conjugated flux $\sigma_{\alpha\beta}$
h_α	+1	P_α
$\Delta\mu$	+1	r

The constitutive equations are obtained by writing the most general linear equation between forces and fluxes respectively, respecting the symmetries of the problem: translational symmetry, 1 vector $\vec{p}$ 1 tensor $q_{\alpha\beta} = p_\alpha p_\beta - \frac{1}{3}\delta_{\alpha\beta}$ and $\delta_{\alpha\beta}$

The fluxes must be separated into a reactive component with a signature opposite to that of the conjugate force and a dissipative component with the same signature as the force. For the stress the reactive component is the "elastic" stress and the dissipative component the viscous stress. Only the dissipative stress contributes to the entropy production

5. Liquid active polar gel

We first consider an active polar liquid where the relationship between fluxes and forces is local in time

We split all tensors into a traceless part (the ~~[illegible]~~ shear for the stress) and a diagonal part

$$\sigma_{\alpha\beta} = \sigma\,\delta_{\alpha\beta} + \tilde{\sigma}_{\alpha\beta} \qquad \tilde{\sigma}_{\alpha\alpha} = 0 \qquad v_{\alpha\beta} = \frac{u}{3}\delta_{\alpha\beta} + \tilde{v}_{\alpha\beta} \quad u = \partial_\gamma v_\gamma$$

a. Dissipative fluxes

Only fluxes and forces with the same time signature are coupled and $\sigma_{\alpha\beta}$ is only coupled to $v_{\alpha\beta}$

diagonal part $\sigma^d = \bar{\eta}\, u$ These are the equations of a

traceless part $\tilde{\sigma}^d_{\alpha\beta} = 2\eta\,\tilde{v}_{\alpha\beta}$ simple fluid

For simplicity we ignore the tensorial character of the viscosity: there are 3 independent viscosities for an incompressible fluid

$P^d_\alpha = \dfrac{h_\alpha}{\gamma_1} + \lambda\Delta\mu\, p_\alpha$ We use here Onsager symmetry, the

$r^d = \Lambda\Delta\mu + \lambda h_\alpha p_\alpha$ "dissipative matrix" is symmetric

b. Reactive fluxes

The crossed coefficients in the Onsager Matrix have opposite signs. The "matrix" couple fluxes and forces of opposite signature. The Onsager matrix is antisymmetric

$$\sigma^r = -\bar{\zeta}\Delta\mu + \bar{\nu}_1\, p_\alpha h_\alpha$$

$$\tilde{\sigma}^r_{\alpha\beta} = -\zeta\Delta\mu\, q_{\alpha\beta} + \frac{\nu_1}{2}\left[p_\alpha h_\beta + p_\beta h_\alpha - \frac{2}{3} p_\gamma h_\gamma \delta_{\alpha\beta}\right]$$

$$P_\alpha^r = -\bar{\nu}_1 p_\alpha \frac{u}{3} - \nu_1 \tilde{u}_{\alpha\beta} p_\beta$$

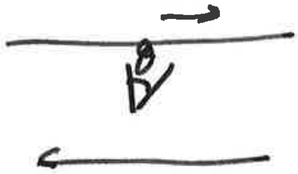
$$r^r = \bar{\zeta} \frac{u_{\gamma\gamma}}{3} + \zeta q_{\alpha\beta} \tilde{u}_{\alpha\beta}$$

In the following, we consider only incompressible fluids, $u = 0$ $\vec{\nabla}.\vec{v} = 0$.

In this case the diagonal part of the stress can be included in the pressure which is a Lagrange multiplier and we can ignore $\bar{\zeta} = \bar{\nu}_1 = \bar{\eta} = 0$

6. Microscopic interpretation of the transport coefficients

- $\gamma_1 > 0$ is a rotationnal viscosity associated to dissipation during the rotation of the polarization. It exists for simple liquid crystals
- ν_1 measures the coupling between flow and polarization. It has also been measured for liquid crystals



$$\cos 2\theta = \frac{1}{\nu_1}$$

Note that $|\nu_1| > 1$ otherwise there is no stationnary state the polarization tumbles

- λ is an active longitudinal field that tends to align the active filaments

- $\zeta \Delta\mu$ is the active stress that we discussed before. It is contractile and $\zeta < 0$

It is a normal stress difference contracting along the direction of $\vec{p}$ and dilating it in the perpendicular direction. By comparing to experiments on cells $|\zeta\Delta\mu| \sim 10^3$ Pa. Note that this stress is derived only from symmetry arguments.

If $|\vec{p}| = 1$ we can always set $\lambda = 0$ and change the value of ζ

$\zeta \to \zeta + \lambda_1 \nu_1 \gamma_1$. In the following, we set $\lambda = 0$

7. Viscoelastic active polar gel

In order to take into account the passive crosslinks, we consider the acto-myosin cytoskeleton as viscoelastic and describe it by a Maxwell model

$$\frac{D\tilde{\sigma}_{\alpha\beta}}{Dt} + \frac{1}{\tau}\tilde{\sigma}_{\alpha\beta} = 2E\tilde{v}_{\alpha\beta}$$

E is the shear modulus and the effective viscosity is $\eta = E\tau$

The measured relaxation time $\tau \sim 10 - 100$ s and the viscosity is huge $\eta \sim 10^5$ Pa.s

The constitutive equations are

$$2\eta v_{\alpha\beta} = \left(1 + \tau\frac{D}{Dt}\right)\left[\tilde{\sigma}_{\alpha\beta} + \zeta\Delta\mu\, q_{\alpha\beta} - \frac{\nu_1}{2}\left(p_\alpha h_\beta + p_\beta h_\alpha\right)\right]$$

The memory of the system also plays a role for the dynamics of the orientation

$$\frac{Dp_\alpha}{Dt} = \frac{1}{\gamma_1}\left(1 + \tau\frac{D}{Dt}\right)h_\alpha - \nu_1 v_{\alpha\beta}\, p_\beta$$

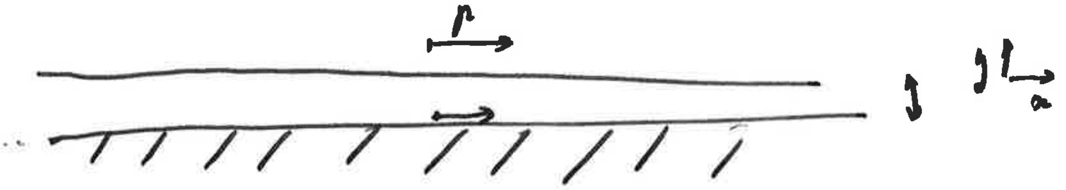
($\lambda = 0$ and incompressible system)

8. Possible generalization

- Nematic active gel $q_{\alpha\beta} = \langle p_\alpha p_\beta - \frac{1}{3}\delta_{\alpha\beta} \rangle$ $\langle p_\alpha \rangle = 0$

- In fact the equations proposed are not polar. One could add "non linear" polar terms in the polarization equation
$w_1 \Delta\mu \, (\vec{p}.\vec{\nabla})\vec{p}$, $w_2 \, \vec{p}(\vec{\nabla}\vec{p})$ and $w_3 \, \vec{\nabla}\vec{p}^2$. These terms have been studied in details by C. Marchetti and coworkers.
- Noise in active gels.
- Two component systems
- treadmilling can be introduced as a boundary condition
- Active gel theory of tissues (the cells die and divide)

III Spontaneous flow of active liquids



Anchoring of the polarization along x. Obvious steady state $\vec{v} = \vec{0}$ $\vec{p} = \vec{e}_x$

We now study the stability of this state by looking for a solution v along x and $p = \begin{vmatrix} \cos\theta \\ \sin\theta \end{vmatrix}$ The shear rate is $u = \frac{1}{2}(\partial_y v_x$

All derivatives with respect to x vanish

The ~~constitutive equation on~~ total the stress is

$$\sigma^t_{\alpha\beta} = -P\delta_{\alpha\beta} + \sigma_{\alpha\beta} + \sigma'^a_{\alpha\beta}$$

The force balance equation reads $\partial_y \sigma^t_{yx} = 0$, As there is no shear on the surface $\sigma^t_{yx} = 0$

We calculate $\sigma^t_{xy} - \sigma^t_{xy} + \sigma^t_{yx} = \sigma^t_{xy} - \sigma^t_{yx} = 2\sigma^a_{xy} = -h_\perp$
$= (-\mu_x h_y + \mu_y h_x)$

where $h_\perp = h_y \cos\theta - h_x \sin\theta$

The sum gives the symmetric part of $\sigma^t_{xy} = 4\eta u - \zeta\Delta\mu \sin 2\theta + \nu_1$ $(h_\parallel \sin 2\theta + h_\perp \cos 2\theta)$ where $h_\parallel = h_x \cos\theta + h_y \sin\theta$

so that $-h_\perp = 4\eta u - \zeta\Delta\mu \sin 2\theta + \nu_1 \left[h_\parallel \sin 2\theta + h_\perp \cos 2\theta\right]$

The constitutive equation for the polarisation gives

$-u\sin\theta = \frac{1}{\gamma_1} h_x - \nu_1 \sin\theta\, u$ or $h_\parallel = \nu_1\gamma_1 \sin 2\theta\, u$

$u\cos\theta = \frac{h_y}{\gamma_1} - \nu_1 \cos\theta\, u$ $h_\perp = \gamma_1(1 + \nu_1 \cos 2\theta)\, u$

Cela donne $h_\perp = \dfrac{\zeta\Delta\mu \sin 2\theta\,(1 + \nu_1 \cos 2\theta)}{\left(\frac{4\eta}{\gamma_1} + 1 + \nu_1^2 + 2\nu_1 \cos 2\theta\right)}$ et $u = \dfrac{\zeta\Delta\mu \sin 2\theta/\gamma_1}{\frac{4\eta}{\gamma_1} + 1 + \nu_1^2 + 2\nu_1 \cos 2\theta}$

In the approximation where the Frank constants are equal, the free energy is $F = \frac{1}{2} K \int \left(\frac{\partial\theta}{\partial y}\right)^2 dy$ and $h_\perp = -\frac{\partial F}{\partial\theta} = K \frac{\partial^2\theta}{\partial y^2}$

If θ is small the equation on $h_\perp$ gives $\nabla^2\theta + \frac{1}{L^2}\theta = 0$ where

$$\frac{1}{L^2} = -\frac{2\zeta\Delta\mu}{K} \frac{1+\nu_1}{\frac{4\eta}{\gamma_1} + (1+\nu_1)^2} > 0$$

The solution is $\theta = \theta_0 \sin\frac{y}{L}$ with $\theta(h) = 0$

If $h < \pi L$ there is no solution.

If $h > \pi L$ There is a solution with finite θ_0 but one needs to include θ^3 terms to find θ_0. In this case the film is unstable

p_y varies along y and the velocity gradient u is finite.

Thick enough films (at constant active stress $\zeta\Delta\mu$) or active enough films at constant thickness ($\zeta\Delta\mu$ large) are therefore spontaneously flowing. The flux $Q = \int_0^h v\,dy$ is finite

Rq - Analogy with the Fredericks transition of nematic liquid crystal

- Any gradient on $\vec{p}$ creates a gradient in active stress and thus a flow
- No experimental verification. Numerical simulation Marenduzzo
- θ_0 and $-\theta_0$ are possible even for polar systems (symmetry breaking)
- $\zeta\Delta\mu > 0$ $\vec{p}$ goes out of plane Ramaswamy
- Biological relevance

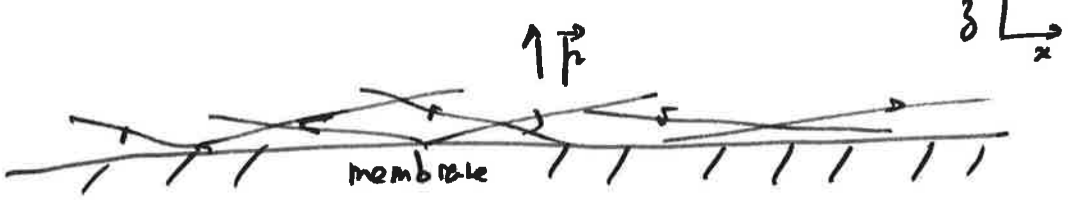
IV Cortical actin layer

In many cells, actin forms a thin layer at the cortex of the cell. The thickness of this layer is of order 0,5 → 1 μm. We give here a very naive model of this layer based on 3 assumptions

- The filaments grow from the membrane where there are actin nucleators and they are almost parallel to the membrane
- They are oriented randomly in the tangent plane to the cell

Rq One can do an active gel theory for nematic but non polar "gels"
Exercise do it

- Depolymerization occurs at the surface of the cortex and the depolymerization rate depend on the local "tension"



In the language of nematic liquid crystals it corresponds to a nematic order parameter $\vec p$ ⊥ membrane. The contractility is along the filaments $\zeta\Delta\mu > 0$

For a uniform layer $\partial_z(\sigma_{zz} - P) = 0$, $\sigma_{zz} = P$ as there is no stress on the surface. For an incompressible layer $\partial_z v = 0$ v is along z and nothing depend on x by symmetry

The velocity is $v = v_p$ (polymerization velocity)

Constitutive equation in a steady state

$$\Big(1 + \tau \underset{\nearrow \atop \frac{D}{Dt}}{v_p \frac{\partial}{\partial z}}\Big)\Big[\tilde{\sigma}_{xx} - \frac{\zeta\Delta\mu}{2}(z)\Big] = 0 \qquad 1 + \tau v_p \frac{\partial}{\partial z}\Big(\tilde{\sigma}_{zz} + \frac{\zeta\Delta\mu}{2}\Big) = 0$$

In the following we assume that $\zeta\Delta\mu$ depends on z $\quad \zeta\Delta\mu = \overline{\zeta\Delta\mu}\big(1 - e^{-\frac{z}{v\tau_m}}\big)$

The new born filaments do not carry any myosins. $\zeta\Delta\mu(z=0) = 0$. This law assumes then that myosins bind with a first order kinetics

$\tilde{\sigma}_{xx} + \tilde{\sigma}_{zz} = 0$ as the trace of the total stress is $-2P$

Active stress $\zeta\Delta\mu\big(p_i p_j - \frac{1}{2}\delta_{ij}\big) = \begin{pmatrix} -1/2 & 0 \\ 0 & \frac{1}{2} \end{pmatrix} \zeta\Delta\mu$

$\tilde{\sigma}_{xx} = \frac{\zeta\Delta\mu(z)}{2} + a\, e^{-z/v_p\tau}$ and $\tilde{\sigma}_{zz} = -\frac{\zeta\Delta\mu(z)}{2} + b\, e^{-z/v_p\tau}$

with $a + b = 0$

When $z = 0$ $\sigma_{\cancel{zz}\,xx} - P = 0$ the actin filaments are created with zero tension

so $a = 0$ if $z > 0$ the active stress creates tension in the filaments

$\tilde{\sigma}_{xx} = \frac{\zeta\Delta\mu(z)}{2} = \frac{\overline{\zeta\Delta\mu}}{2}\big(1 - e^{-z/v_p\tau_m}\big)$

$P = \tilde{\sigma}_{zz} = -\frac{\overline{\zeta\Delta\mu}}{2}\big(1 - e^{-z/v_p\tau_m}\big)$

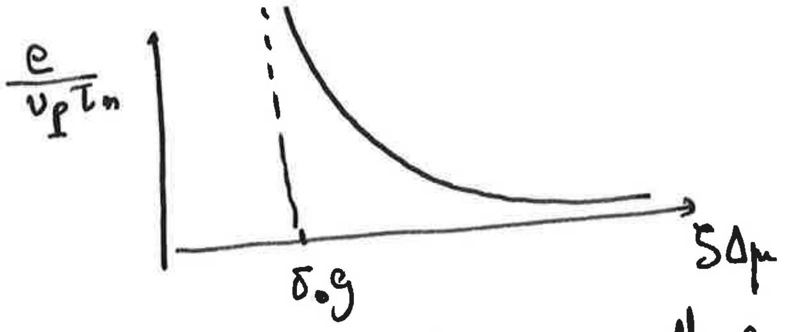
So that $\sigma_{xx} - P = \overline{\zeta\Delta\mu}\big(1 - e^{-z/v_p\tau_m}\big)$

If the tension is large the depolymerization velocity increase. Inspired by Kramers law, we assume $v_d = v_d^0 \exp + \frac{(\sigma_{xx} - P)(z=e)}{\sigma_0}$

In a steady state $v_d = v_p$

$$(\sigma_{xx} - P)(e) = \sigma_0 \,\text{Log}\, \frac{v_p}{v_d^0} = \sigma_0 g > 0$$ g is the free energy of the polymerization reaction

or $e = -v_p \tau_m \,\text{Log}\left[1 - \frac{g\sigma_0}{(\zeta\Delta\mu)}\right]$



$\overline{\zeta\Delta\mu}$ very large the layer is very thin as $v_d > v_p$; if e is large

$\overline{\zeta\Delta\mu} = \sigma_0 g$, v_p always larger than v_d and the cortical layer invades the cell

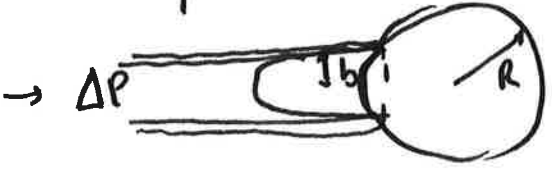
The tension in the cortex is $T = \int_0^e (\sigma_{xx} - P)(z)\, dz$

$$T = \overline{\zeta\Delta\mu}\, e \left[1 + \frac{\sigma_0 g}{\overline{\zeta\Delta\mu}} \frac{1}{\text{Log}\left(1 - \frac{g\sigma_0}{\overline{\zeta\Delta\mu}}\right)}\right] \sim \overline{\zeta\Delta\mu}\, e$$

$\zeta\Delta\mu \simeq g\sigma_0$

- The cortical layer has a finite tension that adds up to the membrane tension. Its order of magnitude is $T \sim 10^{-3}$ N/m. During mitosis, the cortical tension increases and the cell becomes round

A possible measurement is to swallow the cell through a micropipette

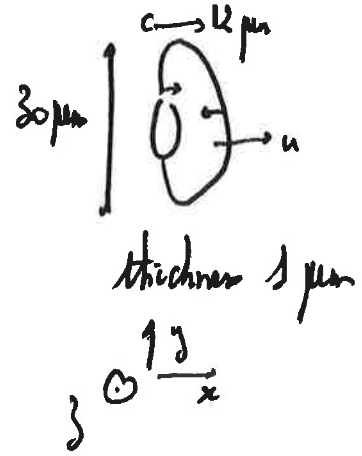


the cell enters the pipette if $\Delta P > 2T\left(\frac{1}{b} - \frac{1}{R}\right)$

- Blebs oscillations and contractile rings

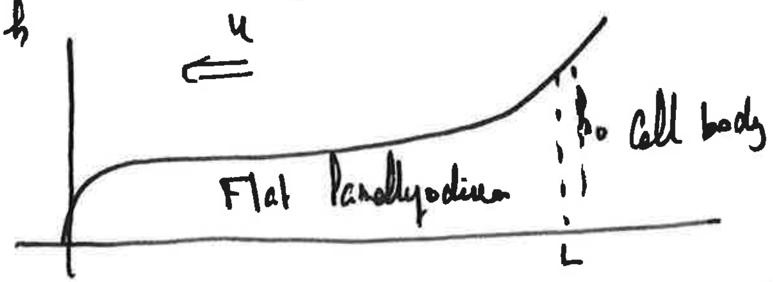
V Cell motility: lamellipodium motion.

We now discuss the motion of keratocyte cells. The cell has a very flat lamellipodium and a thick cell body at the back. It moves fast for a cell $u \simeq 10\,\mu m/min$

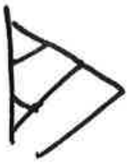


In order to make a simple description, we assume that the lamellipodium is invariant along z. This ignores the motion on the sides behaving like edges

The flow of actin and the stress on the surface have been measured: actin has been observed to have a retrograde flow.



The structure of the actin gel close to the tip has been directly observed



There is a "branching" protein called ~~WASP~~ ARP2/3 and a nucleating protein WASP located at the membrane. We assume its profile to decay exponentially $\rho_W = \rho_0 e^{-x/\lambda}$ corresponding to advection by a motor (v_m) and diffusion D_p $\lambda = D_p / v_m$

In 2 dimensions, we assume that the filaments are parallel to the motion $\vec{p} = -\vec{e}_x$

They polymerize with a velocity $\propto \rho_w$ $v_p = v_p^0\, \rho_w(x)$ and they depolymerize at the back with a velocity v_d.

We use a thin film description where actin glides on the surface. The adhesion of the keratocyte is non specific and we describe it by a friction ξv per unit area

Force balance in the x direction

$$\frac{d}{dx}\left(\bar{\sigma}_{xx} - P\right)h = \xi v_x(z=0)$$

The local force is $F = h\left(\bar{\sigma}_{xx} - P\right)$ $\bar{\sigma}_{xx} = \frac{1}{h}\int_0^h \sigma_{xx}\,dz$

both $\bar{\sigma}_{xx}$ and $v = v_x$ depend hardly on z and can be considered as constant

The constitutive equations are

$$\sigma_{xx} + \frac{\zeta\Delta\mu}{2} = 2\eta\frac{\partial v}{\partial x} \qquad \left(\sigma_{zz} - \frac{\zeta\Delta\mu}{2}\right) = 2\eta\frac{dv_z}{dz} = -2\eta\frac{dv_x}{dx}$$

We consider the cytoskeleton as liquid and incompressible so that $\partial_x v_x + \partial_z v_z = 0$

On the surface $\sigma_{zz} - P = 0$ $P = \frac{\zeta\Delta\mu}{2} - 2\eta\,\partial_x v$

This gives $\sigma_{xx} - P = 4\eta\,\partial_x v - \zeta\Delta\mu$

In terms of F $\partial_x F = \xi v$ $\frac{F}{h} + \zeta\Delta\mu = 4\eta\,\partial_x v$

In a steady state, the velocity profile does not change with time in a reference frame moving at velocity $-U$ $\frac{\partial}{\partial x} h(U+v) = v_p(x)$ gives mass conservation

$$h = \int_0^x v_p(x')\,\frac{dx'}{\cancel{U+v(x')}}\,\frac{1}{U+v(x)}$$ Note that the integral is roughly constant $\lambda v_p^0 \rho_w^0$

3. Equations for h, F, v

Boundary conditions
- No external force at the front and at the back
- Profile matches with the cell body if $x = L$ $h = h_0$
- Continuity of the fluxes at the back $v_d = U + v(L)$

This last equation gives the advancing velocity U

- We find numerically a lamellipodium flat at the center $h = \bar{h}$
- Retrograde flow at the front and anterograde flow at the back

A very simple approximation is to consider the central part $h \approx \bar{h}$

$$4\eta \bar{h} \frac{\partial^2 v}{\partial x^2} = \xi v \qquad v = v_0 e^{-x/d} \qquad d^2 = \frac{4\eta \bar{h}}{\xi}$$

. The approximations are consistent if $d \gg \bar{h}$. We obtain $d = 5\,\mu m > \lambda, \bar{h} \sim 1\,\mu m$

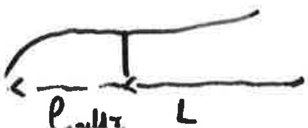
$$F(x=0) = \bar{h}\,\sigma(x=0) \Rightarrow -\zeta\Delta\mu + 4\eta \frac{dv_x}{dx} = 0 \qquad v_0 = -\frac{d\,\zeta\Delta\mu}{4\eta}$$

The advancing velocity is $U \approx v_d$

- Polymerization and depolymerization monitor the velocity
- Contractility monitors the retrograde flow. $v_0 \approx 1\,\mu m/s \ll U = 10\,\mu m/s$

(experimentally). Using v_0 we estimate $|\zeta\Delta\mu| = 10^3$ Pa

- The cytoskeleton is viscoelastic at the edge over a region of size $\ell = U\tau$



- Not so clear what fixes to a Th