Active motion with biological molecules

Reference
Alberts Molecular Biology of the cell
Howard Mechanism of motor protein and the cytoskeleton

F. Ibáñez et al. Active behavior of the cytoskeleton Phys Rep 449 3.28
IF Joanny and J. Bost Active gelo as a description of the actin myosin (2007)

Cytoskeleton
HEP 1-3
IF Joanny Contradict in red the description of cell dynamics

Joanny Seminar (2005) Birkhoer 2010

I Cytoskeleton

The cytoskeleton is the gel like structure made of filaments which control 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 filament as formed by assembly of actin monomers. Two protofilaments coil into a helix of 7.2 nm pitch. The filament is polar, it has a + and a - end. It is treaded by its polymerise at the + end with a velocity up and depolymerise at the - end with a velocity up.
The filament is semi-rigid with a persistence length \( l_p \approx 60 \mu m \).

Actins interact with many proteins with various roles: capping, branching, severing, and condensation.

Upon crosslinking, make a gel-like structure - typically denoted as a physical gel. The crosslinks in general have a finite life time (due to breaking and unbinding).

At times shorter than this life time, the actin gel behaves as solid with a finite shear modulus \( E \).

We estimate \( E \) via a scaling argument assuming that \( L \) and \( b \) are the only relevant length scales. \( E = \frac{kT}{L^2} \sqrt{\left( \frac{b}{L} \right)} \) from dimensional analysis.

If the bending mode of the filament dominates \( E \approx E_j \).

Eq.: Dimensional analysis \( E_j \approx \frac{E_j d^3}{kT} \)

\[ E = kT \frac{L_p^2}{L} \]

A.N. \( L_p = 16 \mu m \) \( L = 60 \mu m \) \( kT = 4 \mu N \cdot nm \)

\[ E = 85 \, Pa \]

If the stretching of the filaments dominates - eliminating fluctuations \( E \approx \frac{b^2}{l^4} \) \( E \approx kT \frac{b^2}{l^4} \approx 1000 \, Pa \)
When overlaid by passive contractions, the properties of actin gel are well described by classical equilibrium polymer physics. This is not obvious as the polymer-depolymeration process involves ATP. ATP hydrolysis inside the filament (required for the existence of treadmilling). In the cell actin interacts with the molecular motor myosin.

Myosin is a non-pressurer motor. In the cytoskeleton it works in aggregate which themselves are non-pressurer ad bind to actin.

7-tomoto (show movie on myosin) called mini-filaments.

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

\[ \text{ATP} \rightarrow \text{ADP} + \text{Phosphate} \quad \Delta \mu = \mu_{\text{ATP}} - \mu_{\text{ADP}} - \mu_e = 2.5 \text{kJ} \]

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

\[ \Delta \mu_r = \Delta \mu_{\text{reac}} + R \mathrm{T} \ln \frac{[\text{ATP}]}{[\text{ADP}]^{1/2}} \]

Muscle structure

A way to show that active acto-myosin gels are indeed non
Equilibrium systems is to check the fluctuation dissipation theorem. The group of C. Schmidt has shown that by adding beads inside the gel and by doing what they call active col-pair microrheology. In active microrheology, we measure the power $\alpha(t)$ of the bead and its correlating function

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

a its Fourier transform $\tilde{C}(\omega) = \int e^{-i\omega t} C(t) dt$

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

$$\chi''(\omega) = C(\omega)$$

If this is not satisfied, the system is not at thermal equilibrium. Except C. Schmidt also experiment on cells.

2. Microtubules

Hollow cylinders much stiffer than actin.

Polar objects, 13 microtubule. Kinesins are processive motors walking to the + end and dynein to the - end.

3. Active gels

- Slow Koenderink. Rheology experiments. Bacterial motility.

Other types of active systems.
II Active polar gels

There are always ways to describe active gels such as actinomyces gels at the microscopic level: we can use polymer physics to describe acta ad microscale through molecular scale ad the coarse grain to obtain the mesoscopic and microscopic property.

We do not follow the approach. We want to start directly at the macroscopic level and build up a hydrodynamic image. We decide only consider slow variables of the acts: myosin gel ad write Onagia-like constitutive equations.

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

- conserved quantities \( n \) (density), momentum
- Slow modes associated to broken symmetries \( f \) = polarizability (mode)
- 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 at temperature \( T \). The total entropy is \( dS = dS + dS_R \geq 0 \). The reservoir being at thermal equilibrium \( dS_R = \frac{du}{T} \)

\[
\frac{\partial}{\partial t} dS = dS - \frac{du}{T} = -\frac{\partial F}{\partial T} \quad F \text{ being the free energy} \quad F = k_B T S
\]
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 \( \overrightarrow{P} \) defined as the average of the local orientation of the filaments \( \overrightarrow{P} = \langle \overrightarrow{P} \rangle \)

\[
dF = \mu \, dN - V \overrightarrow{P} \cdot d\overrightarrow{p} \quad \overrightarrow{P} = -\frac{\partial F}{\partial \overrightarrow{P}} \text{ is the orientational field}
\]

We will work with the free energy per unit volume \( f = F/V \)

\[
df = \mu \, dN - \hbar \omega \, dp_x \quad \text{where} \quad n = \frac{N}{V} \text{ is the density}
\]

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 at interface \( \frac{1}{T} \frac{dS_e}{dt} = \frac{dF}{dt} = \int d\tau \int \rho \frac{\overrightarrow{p}}{dt} \cdot \frac{\partial \overrightarrow{P}}{\partial \overrightarrow{P}} + \frac{1}{2} n m v^2 \]

This would be the entropy production of a "nematic elastomer" in the absence of molecular motion. 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 \( -\int d\tau \, r \, d\mu \).
1. Conservation Laws

Number of particles \( \frac{\partial n}{\partial t} + \nabla \cdot \mathbf{J} = 0 \)

\( \mathbf{J} = n \mathbf{v} \)

Momentum \( \nabla \cdot \left[ \rho \left( \frac{\partial \mathbf{u}}{\partial t} + \mathbf{u} \cdot \nabla \mathbf{u} \right) \right] = \frac{\partial \rho}{\partial t} \mathbf{u} 
\)

Navier–Stokes

This looks like a conservation of the momentum density \( \rho n \mathbf{v} \)

\( \frac{\partial \rho n \mathbf{v}}{\partial t} + \nabla \cdot (\rho n \mathbf{v} \otimes \mathbf{v}) = \frac{\partial \rho}{\partial t} \mathbf{u} \)

The momentum flux is \( \sigma_{ij} = \delta_{ij} \rho \mathbf{v} - n m \mathbf{v} \mathbf{u} \)

At small Reynolds number, we ignore this Reynolds term.

3. Thermodynamics of Polar Systems

The slow modes associated to the phenomenology \( \mathbf{u} \) are associated to the angles of \( \mathbf{u} \). Except close to the critical point \( \mathbb{R} \mathbf{1} \) is not a hydrodynamic variable.

In the following without loss of generality we choose \( \mathbb{R} \mathbf{1} = 1 \).

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

\[ F = \int d\mathbf{r} \left[ \frac{k_3}{2} (\nabla \cdot \mathbf{F})^2 + \frac{k_4}{2} (\mathbf{F} \cdot \nabla \times \mathbf{F})^2 + \frac{k_5}{2} (\mathbf{F} \times (\nabla \times \mathbf{F}))^2 \right] \]

Splay \text{112} \quad \text{Twist} \text{0} \quad \text{Bend} \text{2} \quad \text{Twist} \frac{\theta}{2} \quad \text{Bend} \frac{\theta}{2}

In two dimensions if \( k_4 = k_3 \)

\[ F = \frac{1}{2} \int d\mathbf{r} k (\nabla \mathbf{B})^2 \]

It is often useful to distinguish the components of \( \mathbf{h} \) \( \mathbf{h}_{\parallel} \) parallel to \( \mathbf{u} \)
and \( \mathbf{h}_{\perp} \perp \mathbf{u} \). \( \mathbf{h}_{\parallel} \) monitors the degree of alignment \( \mathbf{p} \) and \( \mathbf{h}_{\perp} \) the extent of the perpendicular components, respectively.
In order to ensure that $|p_i^2| = 1$ we add a Lagrange multiplier $\lambda_{ii}$ and a term in the energy $\int \lambda_{ii} p_i^2 dt$.
In a non-isotropic medium, the stress is not symmetric. The asymmetric component is associated to torques that do not vanish. (The right-hand symmetry is broken.) The antisymmetric component of the stress can be calculated by

\[ \sigma_{xy} = \frac{1}{2} (\sigma_{yx} - \sigma_{xy}) \]

It depends only on \( \mathbf{b}_1 \). See de Gennes and Prost. The physics of liquid crystals.

4. Phase and space, time reversal

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

\[ T \frac{dS}{dt} = -\int d^3 x \left\{ \sigma_{\alpha\beta} \dot{\nabla}_{\alpha\beta} + P_{\alpha} \dot{\nabla}_{\alpha} + \nabla \Delta P \right\} \]

\( \sigma_{\alpha\beta} \) is the symmetric part of the stress

\[ \sigma_{\alpha\beta}^S = \sigma_{\alpha\beta} - \frac{1}{2} \delta_{\alpha\beta} \nabla \cdot \mathbf{u} \]

\( \nabla \cdot \mathbf{u} \) is the strain rate tensor

\[ \nabla \cdot \mathbf{u} = \frac{1}{2} (\nabla \mathbf{u}_{\alpha} + \nabla \mathbf{u}_{\alpha}) \]

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

\[ \omega_{\alpha\beta} = \frac{1}{2} (\nabla \mathbf{u}_{\alpha} \times \nabla \mathbf{u}_{\beta}) \]

\( \omega_{\alpha\beta} \) is the connected derivative of \( \mathbf{u} \)

\[ \gamma_{\alpha\beta} = \partial_{\alpha} \mathbf{u}_{\beta} + \partial_{\beta} \mathbf{u}_{\alpha} + \omega_{\alpha\beta} \]

\( \gamma_{\alpha\beta} \) is the rate of deformation tensor

\[ \dot{P} = \frac{DF}{D_t} = \frac{\partial F}{\partial t} + (\mathbf{v} \cdot \nabla) F + \nabla \times \mathbf{v} \times F \]

\( \mathbf{v} = \frac{1}{2} \nabla (\nabla \cdot \mathbf{u}) \) is the local velocity

\( \mathbf{F} \) is the external force density
Following Onsager we identify 3 faces and 3 fluxes.

\[ \nabla \psi \quad \text{time reversal symmetry (1)} \quad \text{conjugated flux } \delta_{\psi} \]

\[ h_{\psi} \quad +1 \quad \delta_{\psi} \]

\[ \Delta \mu \quad +1 \quad \gamma \]

The constitutive equations are obtained by writing the most general linear equation between flux and fluxes respectively, respecting the symmetry of the problem: Translational symmetry, 1 vector \( \mathbf{T} \), 1 tensor \( g_{\mu \nu} = \rho \mu \nu - \frac{1}{3} \delta_{\mu \nu} \) and \( \delta_{\mu \nu} \).

The fluxes must be separated into a reactive component with a negative part, similar to that of the conjugate face, and a dissipative component with the same negative as the face. 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 just consider an active polar liquid where the relationship between fluxes and faces is local in time.
We split all terms into a diagonal part (the shear in the shear) and a diagonal part

\[ \sigma_{\alpha\beta} = \sigma_{\alpha\alpha} \delta_{\alpha\beta} \]

\[ \sigma_{\alpha\alpha} = \nabla_x p + \mu \nabla_x u_x \]

a. Dissipative fluids

Only fluids with the same sign signature are coupled and \( \sigma_{\alpha\beta} \) as only coupled to \( \nabla_x p \)

\[ \text{diagonal part} \quad \sigma_d^d = \eta \nabla_x u_x \]

\[ \text{travelling part} \quad \sigma_d^t = \eta \nabla_x u_x \]

There are the equations of a simple fluid

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

\[ P_d^d = \frac{\rho d}{\gamma} + \lambda \Delta p \mu \]

\[ P_d^t = \lambda \Delta p + \lambda \rho d \mu \]

b. Reactive fluids

The crossed coefficients in the Onsager Matrix have opposite signs. The "matrix" couple fluids with forces of opposite signature. The Onsager matrix is anti-symmetric

\[ \sigma_r = \sigma_{\alpha\beta} \]

\[ \sigma_{\alpha\beta} = \left[ \mu \rho d \sigma_{\alpha\beta} + \mu \rho d \sigma_{\alpha\beta} - \frac{1}{2} \rho d \sigma_{\alpha\beta} \right] \]
\[ P_q = -\nabla_i \mu \frac{\mu_i}{\nabla} - \nabla_i \tilde{\eta} \nabla_i \mu_i \]

In the following, we consider only incompressible fluids, \( \mu = \nabla \cdot \tilde{v} = 0 \). In this case the diagonal part of the tensor can be included in the pressure, which is a diagonal multiplier and we can ignore \( \tilde{\eta} = \tilde{v}_i = 0 \).

6. Microscopic interpretation of the transport coefficients

- \( \gamma_0 > 0 \) is a rotational viscosity associated to disentanglement of the polymer. It exists for simple liquid crystals.
- \( \gamma_1 \) measures the coupling between flow and polymer. It has also been measured for liquid crystals.

\[ B \sim \frac{1}{\gamma_1} \quad \cos 2\theta = \frac{1}{\gamma_1} \]

Note that \( |V_0| > 5 \) otherwise there is no stationary state. The polymer tumble.

- \( \gamma_1 \) is an active longitudinal field that tends to align the active filaments.

\[ S \mu \] is the active stress that we discussed before. It is contractile and \( S > 0 \).
It is a normal stress difference contracting along the direction of \( \pi \)
and dilating it in the perpendicular direction. By comparing to expermental cells \( 5 \Delta p \mu \) \( \approx 10^3 \) Pa. Note that this stress is derived only from symmetry arguments.

If \( |\beta| = 1 \) we can always set \( \lambda \to \infty \) and change the value of \( S \)
\( S \to S + \lambda_\pi \gamma_1 \gamma_2 \). In the following, we set \( \lambda \to \infty \).

7. Viscelastic active polymer gel

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

\[
\frac{D \delta_{wp}}{Dt} + \frac{1}{\tau} \delta_{wp} = \lambda E \delta_{wp}
\]

\( E \) is the shear modulus, and the effective viscosity is \( \eta = E \tau \).

The measured relaxation time \( \tau \approx 100 \) ms and the viscosity is huge \( \eta \approx 10^5 \) Pa.

The constitutive equation are

\[
2D_{wp} = (1 + 2 \frac{D}{Dt}) \left[ \delta_{wp} + 5 \Delta \mu \phi_{wp} - \frac{\gamma_1}{2} (h_{wp} + p + h_{wp}) \right]
\]

The memory of the system also plays a role for the dynamics of the acto-myosin

\[
\frac{D\mu_\pi}{Dt} = \frac{1}{\gamma_1} \left( 1 + 2 \frac{D}{Dt} \right) h_{\pi} - \frac{\gamma_1}{\gamma_1} \nu_{wp} \mu_\beta 
\]

(\( \lambda \to \infty \) and incompressible system)
8. Possible geure kigation

- Nematic active gel \( \tau_{ij} = \langle \mu_{ij} \pi_{ij} - \frac{1}{3} \delta_{ij} \pi > \rangle < \mu > 0 \)

- In fact the equatic ions are not polar. One could add "non linear" polar terms to the polarigita equations

\[ W_1 \Delta \pi \cdot (\hat{r} \cdot \hat{V}) \hat{r} , \quad W_2 \hat{r} \cdot (\hat{V} \pi) \quad \text{and} \quad W_3 \hat{V} \pi . \]

These terms have been studied in detail by C. Houdt and others.

- Two conorunt systems

- Breading can be introduced as a boundary condition

- Active gel theory of chains (cells can die and divide)

III. Spontaneous flow of active liquids

\[ \vec{V} \]

Anchoring of the polarigita along \( \mathbf{u} \). Obvious steady state \( \mathbf{u} = 0 \), \( \mathbf{p} = 0 \).

We now study the stability of this state by looking for a solution \( \mathbf{v} \) along \( \mathbf{u} \) and \( \mathbf{p} = \rho \cos \theta \). The basic state is \( \mathbf{u} = \frac{1}{2} \left( \frac{\partial}{\partial y} \right) \mathbf{p} \).

The constitutive equation on the axis is

\[ \sigma^t = -P \delta_{ij} \pi_{ij} + \sigma_{ij} \]

The damping equation reads \( \partial_t \sigma^t \sigma^t = 0 \). As there is no shear in the
We calculate \( \sigma_{xy} = \sigma_{xy} + \sigma_{yz} = \sigma_{xy} - \sigma_{xy} = 2 \sigma_{xy} = -h_1 \)

where \( h_1 = h_2 \sin \theta - h_2 \cos \theta \)

The new gives the symmetric part of \( \sigma_{xy} = 4\mu - 5A\mu \sin 2\theta + \nu_1 \)

\( (h_1 \sin \theta + h_2 \cos \theta) \) where \( h_1 = h_2 \cos \theta + h_2 \sin \theta \)

so that \( h_1 = 4\mu - 5A\mu \sin 2\theta + \nu_1 \left[ h_1 \sin \theta + h_2 \cos \theta \right] \)

The constitutive equation for the plasma gives

\[
\begin{align*}
\mu \sin \theta &= \frac{1}{Y_2} h_2 - \nu_1 \sin \theta \mu \quad \text{and} \quad h_1 = \nu_1 \sin \theta \mu, \\
\mu \cos \theta &= \frac{h_2}{Y_2} - \nu_1 \cos \theta \mu \quad \text{and} \quad h_1 = \nu_1 \cos \theta \mu.
\end{align*}
\]

This gives

\[
h_1 = \frac{5A\mu \sin 2\theta (1 + \nu_1 \cos ^2 \theta)}{\left( \frac{4\nu_1 + 1 + \nu_1^2 + 2\nu_1 \cos 2\theta}{Y_2} \right)} \quad \text{and} \quad \mu = \frac{5A\mu \sin 2\theta}{\left( \frac{4\nu_1 + 1 + \nu_1^2 + 2\nu_1 \cos 2\theta}{Y_2} \right)}
\]

In the approximation where the Frank constants are equal, the free energy is

\[
F = \frac{1}{2} \int \left( \frac{\partial \theta}{\partial y} \right)^2 dy \quad \text{and} \quad h_1 = -\frac{\partial F}{\partial \theta} = K \frac{\partial \theta}{\partial y}
\]

If \( \theta \) is small the equations are \( h_1 \) gives \( \nabla ^2 \theta + \frac{1}{L^2} \theta = 0 \) where

\[
\frac{1}{L^2} = -\frac{5A\mu}{k} \frac{1 + \nu_1}{4\nu_1 + 1 + \nu_1^2} > 0
\]

The solution is \( \theta = \theta_0 \sin \frac{y}{L} \) with \( \theta(0) = 0 \).
If $h < \eta h$ there is no motion.

If $h > \eta h$ there is a solution with finite $\Theta_0$, but one needs to include $\Theta^3$ terms to find $\Theta_0$. In this case the film is unstable by varying along $y$ and the velocity gradient $\mu$ is finite.

Thick enough film (at constant active $5A\mu$) a active enough film at constant thickness ($5A\mu$ large) are therefore spontaneously flowing. The flux $Q = \int_0^h \mu dy$ is finite.

Eq. - Analogy with the Frederico transition of nemotic liquid crystal.

- $\frac{1}{B}$. Any gradient in $\mu$ creates a gradient in active flow and thus a flow.
- $\Theta_0$ and $-\Theta_0$ are possible even for polar systems (symmetry breaking).
- $5A\mu > \mu$ goes out of plane Ramanarany.
- Biological relevance.
Critical actin layer

In many cells, actin forms a thin layer at the center 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 filament grows from the membrane where there are actin nucleators and they are almost parallel to the membrane.
- They are oriented randomly in the target plane to the cell.

Fig. 1 can do an active gel theory for a nemotic but non-polar "gel". Exercise do it.

- Depolymerization occurs at the surface of the actin and the depolymerization rate depends on the local "tension".

\[ \xi \]

\[
\begin{array}{c}
\text{membrane}
\end{array}
\]

In the language of nemotic liquid crystals it corresponds to a nemotic order parameter \( \xi \) = membrane. The contractility is along the filament, \( 54 \xi > 0 \).

For a uniaxial layer \( \gamma_2 (\delta y - P) = 0 \), \( \delta y = \text{const} \) as the \( u \) to zero on the surface. For an incompatible layer \( \gamma_2 = 0 \) is a long 3 and nothing depend on a by symmetry.
The velocity \( \mathbf{v} \) (polymerization velocity)

**Constitutive equations in a steady state**

\[
(D + 2 \eta_0 \frac{\partial}{\partial t}) \left[ \sigma_{xx} - \epsilon \Delta \epsilon \right] = 0, \quad D \epsilon = \frac{\partial \sigma_{yy}}{\partial t} \left( \epsilon_{yy} + \frac{\Delta \epsilon}{2} \right).
\]

In the following we assume that \( \Delta \epsilon \) depends on \( \epsilon \): \( \Delta \epsilon = \Delta \epsilon (\epsilon) \). This assumption, together with the polymerization kinetics,

\[
\sigma_{xx} + \sigma_{yy} = \sigma_{zz} \text{ as the trace of the total stress} \quad \sigma = 2 \tau
\]

Active stress \( \Delta \epsilon (\epsilon, \frac{\epsilon}{\epsilon} - \frac{1}{2} \epsilon_{ij}) = \left( \begin{array}{cc} -\frac{1}{2} & 0 \\ 0 & \frac{1}{2} \end{array} \right) \Delta \epsilon \)

\[
\sigma_{xx} = \frac{\Delta \epsilon (\epsilon)}{2} + a e^{-3/\nu} \quad \sigma_{zz} = \frac{\Delta \epsilon (\epsilon)}{2} + b e^{-3/\nu}
\]

with \( a + b = 0 \)

When \( \epsilon \to 0 \), \( \sigma_{zz} \to 0 \), the active stress is created with zero tension

\[
\epsilon = 0 \quad \sigma_{zz} \to 0 \quad \text{the active stress creates tension at the film}
\]

so that

\[
\sigma_{xx} = \frac{\Delta \epsilon (\epsilon)}{2} = \frac{\Delta \epsilon (\epsilon)}{2} (1 - e^{-3/\nu})
\]

\[
\theta = \frac{\sigma_{zz}}{\Delta \epsilon (\epsilon)} = \frac{\Delta \epsilon (\epsilon)}{2} (1 - e^{-3/\nu})
\]

so that

\[
\sigma_{xx} = \Delta \epsilon (\epsilon) (1 - e^{-3/\nu})
\]

If the tension is large, the depolymerization velocity increases. Inspired by

Knudson law, we assume

\[
\frac{\Delta \epsilon (\epsilon)}{2} = \frac{\Delta \epsilon (\epsilon)}{2} e^{\left( \frac{\sigma_{xx} - \theta}{\frac{\Delta \epsilon (\epsilon)}{2}} \right) (\epsilon - 2)}
\]
In a steady state \( \mathcal{N}_d = \mathcal{V}_p \)

\[
(\sigma_{xx} - \bar{p})(r) = \sigma_0 \log \frac{\mathcal{V}_p}{\mathcal{V}_d} = \sigma_0 \frac{g > 0}{g} \text{ is the free energy of the polymeric mesh}
\]

\[
e = -\sigma_0 \mathcal{V}_m \log \left[ 1 + \frac{g \sigma_0}{5\Delta \mu} \right]
\]

\[
\frac{e}{\mathcal{V}_p} \mathcal{V}_m \longrightarrow \Delta \mu
\]

\( \Delta \mu \) very large the layer is very thin \( \mathcal{N}_d > \mathcal{V}_p \) if \( e \) is large \( \Delta \mu \rightarrow \mathcal{V}_p \) always larger than \( \mathcal{V}_d \) and the cortical layer invades the cell

The tension in the cortex is \( T = \int_0^e (\sigma_{xx} - \bar{p}) \, dr \)

\[
T = 5\Delta \mu \sigma_0 \left[ 1 + \frac{g \sigma_0}{5\Delta \mu} \log \left( 1 + \frac{5\sigma_0}{5\Delta \mu} \right) \right] \approx 5\Delta \mu \sigma_0 
\]

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

A possible measurement is to overclose the cell through a micropipette

\[
\Delta P \sim \sigma \frac{r}{r} \Rightarrow \mathcal{P} < \frac{1}{6} \text{ (if } \Delta P > 2T (\frac{A}{b} - \frac{A}{b})\text{)}
\]
Cell motility: lamellipodium motion.

We now discuss the motion of tumor cells. The cell has a very flat lamellipodium and a third cell body at the back. It moves fast in and out of focus.

\[ c = \frac{u}{3} \mu m \]

In order to make a single snapshot, we assume that the lamellipodium is invariant along \( y \). This grows like a wobbly little eddy.

The flow of actin and the thin on the surface has 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 WAVE located at the beak. We assume its profile to decay exponentially \( p_{w} = p_{0} e^{-z} \) corresponding to advection by a motion \( \vec{v} \) and diffusion \( D_{p} \).

\[ \lambda = \frac{D_{p}}{v_{m}} \]

In dimensions, we assume that the flow at the wall is parallel to the motion \( \vec{p}_{w} = -\vec{v} \).
They polymerize with a velocity $v_1$ for $N_p = v_1 \rho_v$ and depolymerize at the bead with a velocity $v_2$.

We are a thin film desorptive where acting glide on the surface. The adherence of the depository is non-specific and we describe it by a friction $F_2$ per unit area.

Face before a thin direction:

$$\frac{d}{dx} \left( \overline{\sigma}_{xx} - F_2 \right) h = \gamma v_x (z = 0)$$

The local force is $F = h \left( \overline{\sigma}_{xx} - F_2 \right)$, $\overline{\sigma}_{xx} = \frac{1}{h} \int_{0}^{h} \sigma_{xx} \, dy$

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

The constitutive equations are:

$$\sigma_{xx} + \frac{5 \sigma_{xx}}{2} = 4 \eta \frac{dv_x}{dx} \quad \left( \sigma_{yy} = \frac{5 \sigma_{xx}}{2} \right) = - \frac{\eta dv_y}{dx} = - \frac{\eta dv_z}{dx}$$

We consider the cytoskeleton as liquid and incompressible so that $C_{22} v_z + C_{23} v_z = 0$.

On the surface $\sigma_{yy} = 0$: $F_2 = \frac{5 \sigma_{xx}}{2} - 2 \eta \frac{dv_x}{dx}$

This gives $\sigma_{xx} - F_2 = 4 \eta \frac{dv_x}{dx} - \frac{5 \sigma_{xx}}{2}$

In terms of $F$ and $F = \frac{F}{h} \frac{5 \sigma_{xx}}{2} - 4 \eta \frac{dv_x}{dx}$

In a steady state, the velocity profile does not change with time at a reference face moving at velocity $u$. $\frac{\partial}{\partial z} h (M + v) = N_p (z)$ gives nano conversion.

$$L = \int_{-L}^{L} v_p (x) \, dx \cdot \frac{1}{N_p (z)}$$

Note that the integral is roughly constant.
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 $x = L, z = h_0$
- Continuity of the fluxes at the back $N_D = M = 0$.

The last equation gives the advective velocity $u$:

- We find numerically a lamellipodium jet 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 that $\bar{h}$

$$4\pi h \frac{\partial v}{\partial z} = f \quad N = v_0 \ e^{-2a} \quad d^2 = \frac{4\pi h}{5}$$

The approximation are consistent of $d > \bar{h}$. We obtain $d = 5 \mu m > 2, \bar{h} = 4 \mu m$

$$F(x=0) = \bar{h} \quad \sigma(x=0) = -5 \Delta \mu + 4\pi h \frac{dv}{dz} = -N_0 = \frac{d^3 \Delta \mu}{4\pi}$$

The advective velocity is $u = d\Delta \mu$

- Polymeric and depolymericize motion the velocity
- Contractility monochrome the retrograde flow $N_0 = 2 \mu m, \ll \Delta = 10 \mu m$ (experimentally). Many no we estimate $154 \mu m = 10^{-3} \mu m$

- The cytoskeleton is mesoelastic at the edge over a region of $x = L$. The
- Not so clear what fixes to a T