# Active matter with biological molecules

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# Outline

1. Acto-myosin gels
   - Active systems

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2. Cortical layer
   - Cell Instabilities
   - Bleb formation
   - Static properties
   - Dynamics of Bleb Growth
   - Contractile rings
   - Wound Healing in Xenopus eggs
   - Cytokinesis

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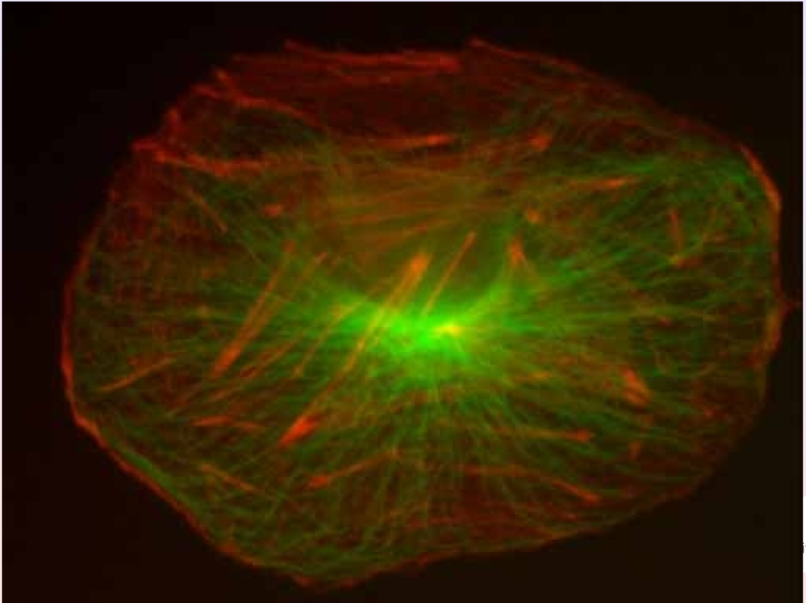
# Cytoskeleton

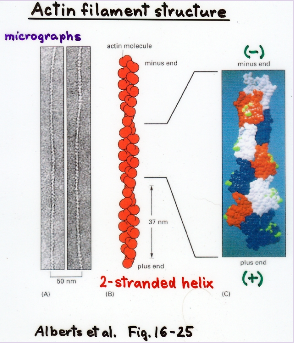


# Actin polymerization

## Actin monomers

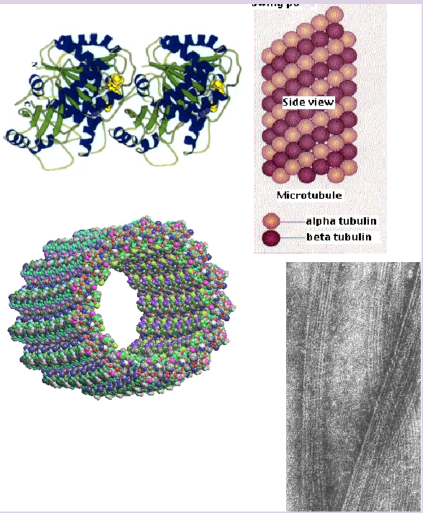

- molecular weight $45kDa$
- size $\delta = 5.5$nm
- ATP binding pocket
- polar monomer

## Actin polymers




- 2 protofilaments
- right-handed helix, 72nm pitch, 24 monomers per turn

## Tubulin polymerization




## Microtubule properties

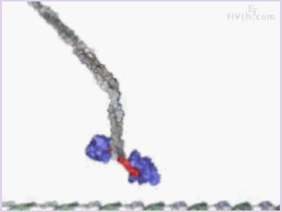
- 13 parallel protofilaments
- GTP binding
- Polar filaments
- Very rigid: persistence length 5$mm$
- Holow cylinders, radius 24$nm$

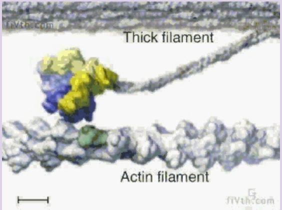
# Molecular motor functions

## Motor proteins

- Muscle contraction (myosin II)
- Cilia and axonemes (Dynein)
- Mitosis
- Intracellular transport (kinesin, myosinV)
- Inner ear hair cells (Myosin 1c)
- Rotating motors

## Motor structure

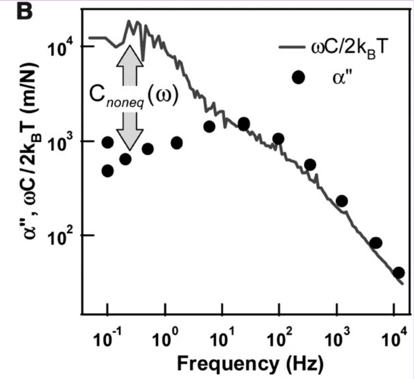





Vale

# Violation of the fluctuation dissipation theorem

## Fluctuations of acto-myosin networks




Mizuno et al.

- Microrheology experiment: active and passive
- Similar experiment with cells

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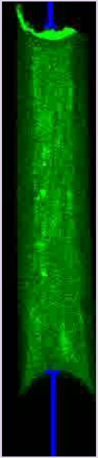
# In vitro active gels, G.Koenderink

## Actin Myosin gel



## Build-up of contractile stress

- Actin-myosin gel in a 400$\mu m$ diameter capillary
- Accelerated 180 times
- ATP introduced at time $t = 0$. Tensile stress increases with time

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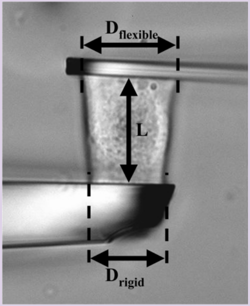
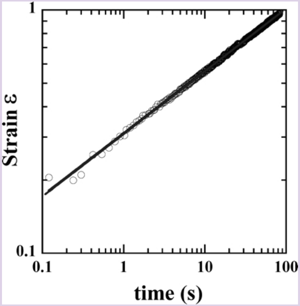
# Single cell elasticity, Asnacios

## Creep measurement

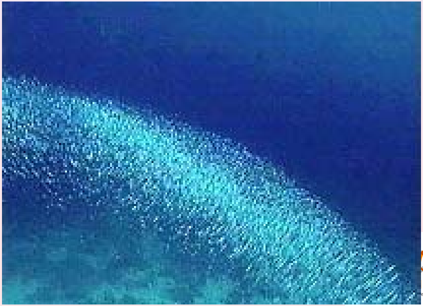



- Weak power law increase of creep compliance $J(t) \sim t^{0.24}$
- Complex elastic modulus $G(\omega) \sim \omega^{0.24}$. Large distribution of relaxation times
- Active effect
- Cell regulation at times larger than 100s

# Active Systems

- Tissues
- Bacterial colonies Kessler, Goldstein
- Vibrated granular materials Menon et al.
- Active colloids, Active nematics Ramaswamy et al.
- Bird flocks, Fish shoals Vicsek, Toner, Chaté, Carere



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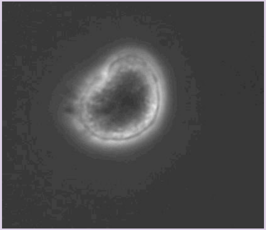
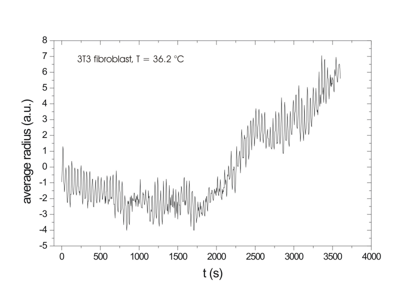
# Non-adhering cells, P. Pullarkat

## Cell oscillations (T3 fibroblasts)



- Oscillations depend on actin contractility
- Oscillations depend on calcium (threshold density)

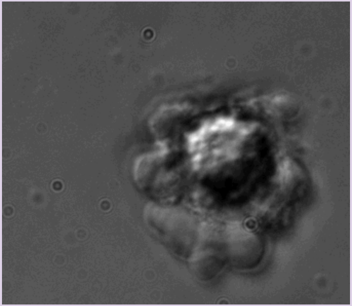
## Period




- Oscillation period $\simeq$ 30s
- Oscillation period decreases with myosin activity

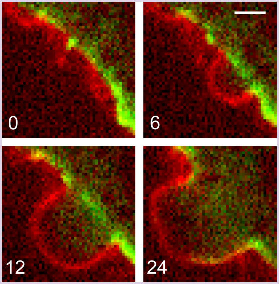
# Blebs induced by laser ablation E. Paluch, J.Y. Tinnevez

## Blebs on spreading cells



D.Cuvelier

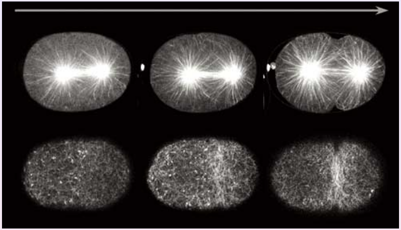
## Membrane detachment from the cortical layer




Charras

- Detachments of the membrane form the cortical layer
- Bleb lifetime 30s

# Formation of contractile rings



## Actin contractile rings

- Cell Cytokinesis
- C.Elegans embryo first division
- Wound healing
- Drosophila dorsal closure

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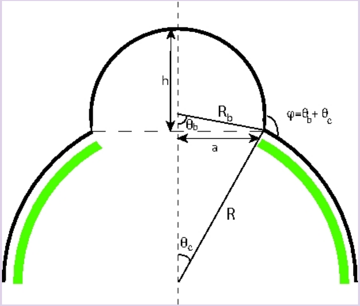
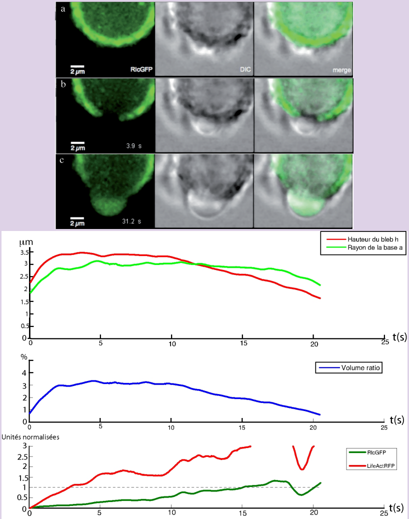
# Bleb Geometry E. Paluch, J.Y. Tinnevez

## Geometrical parameters




- Bleb volume $\frac{V_b}{V_c} = 3\frac{\Delta R}{R}$
- Total volume $V_b + V_c = V$
- Opening angle $a = a_0 + R\Delta\theta_c$

## Bleb growth and Shrinkage

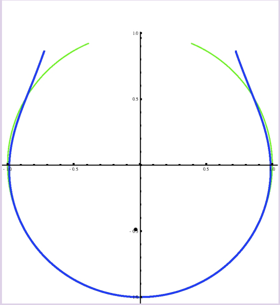


# Equilibrium blebs

## Pressure Equilibria

- Elastic thin shell theory of the cortical layer
- Pressure inside the cell
  $P_c = P_0 + \frac{2(\gamma + e\zeta\Delta\mu)}{R} - 12E\frac{e\Delta R}{R^2}$
- Effective tension $\gamma + e\zeta\Delta\mu$
- Elastic deformation
- Pressure inside the bleb
  $P_b = \frac{2\gamma}{R_b}$
- Bleb Volume
  $\frac{V_b}{V_c} = \frac{\zeta\Delta\mu}{2E} + \frac{\gamma}{2eE}(1 - \frac{R}{R_b})$

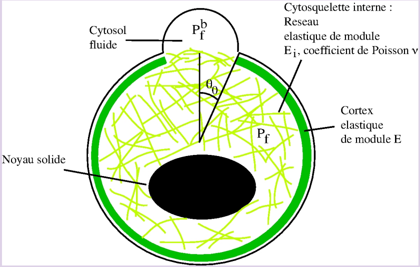
## Cortex deformation



- $\Delta\theta_c = \frac{\gamma}{2Ee}\sin\phi$
- too small to explain experimental results

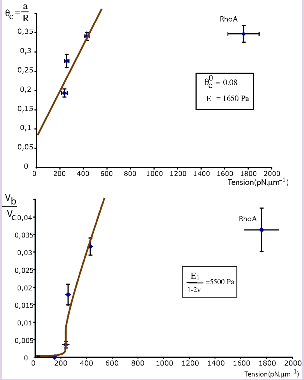
# Internal cell elasticity

## Internal cell compression




- Bleb volume $\left(\frac{E_i}{1-2\nu}+12E\frac{e}{R}\right)\frac{V_b}{3V_c}=\frac{2(\gamma+e\zeta\Delta\mu)}{R}-\frac{2\gamma}{R_b}$
- Opening angle $\Delta\theta_c=\frac{\zeta\Delta\mu}{4E}\theta_c$

## Comparison to experimental data




Cell tension measured by micropipette aspiration

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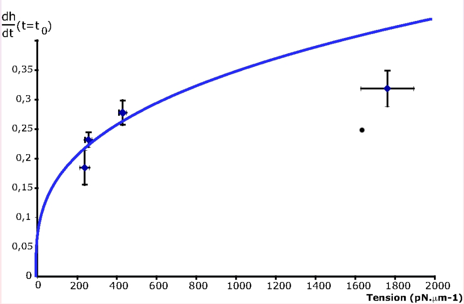
# Bleb Growth

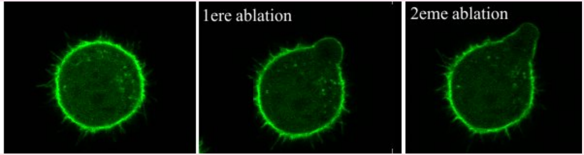
- Dissipation mechanisms during bleb growth
  - Solvent permeation through the cytoplasm
  - Dissipation due to membrane flow toward the bleb $\alpha$
- Initial bleb growth $\frac{dh}{dt} = \left(\frac{a^2 \zeta \Delta\mu e}{18 R \alpha t^2}\right)^{1/3}$

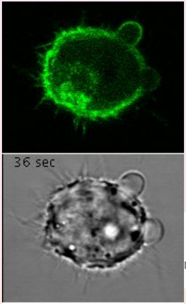


# Repolymerization and Bleb healing

## Growth saturation and collapse of the bleb

- Actin polymerization at the bleb membrane stops bleb growth
- Bleb growth stops before the equilibrium state
- Bleb collapse is induced by myosin recruitment after actin repolymerization



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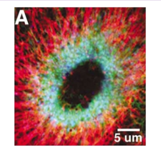
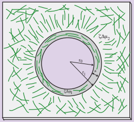
# Ring closure in Xenopus eggs Mandato, Bement

## Wound closure




- Laser Ablation
- Myosin accumulation in a rim around the edge of wound
- Slow contraction velocity $0.04\mu m/s$
- Maximum velocity outside the rim $0.12\mu m/s$

## Filament orientation



- Nematic order parameter change sign
- Actin flow induced by activity gradient
- Filament orientation due to actin flow

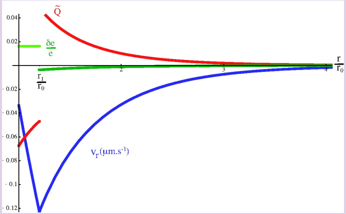
# Active gel theory of contractile rings G.Salbreux

## Active gel Thin film Equations

$$4\eta\partial_r(\partial_r + \frac{1}{r})v_r \quad + \quad (\partial_r + \frac{2}{r})(\zeta\Delta\mu + \beta_1\chi)\tilde{Q} = 0$$

$$\frac{\partial\tilde{Q}}{\partial t} \quad = \quad -\frac{\chi}{\beta_2}\tilde{Q} + \frac{\beta_1}{2}(\partial_r - \frac{1}{r})v_r$$

## Velocity and order parameter profiles




## Critical activity threshold

- $\zeta\Delta\mu_1 > \left(\frac{8\zeta\Delta\mu\eta\chi r_0}{a\beta_1\beta_2}\right)^{1/2}$

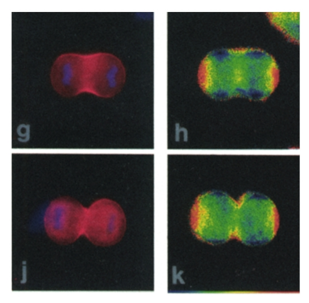
## Filament orientation

- $\tilde{Q} < 0$ parallel to rim
- $\tilde{Q} > 0$ perpendicular to rim

# Outline

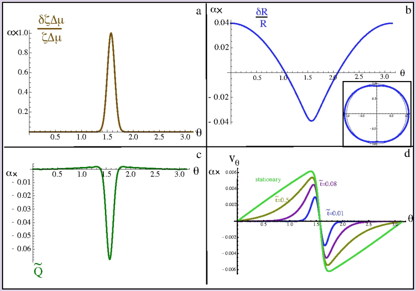
# Ring formation during cytokinesis

## Cleavage furrow Y. Wang et al.




- Enhanced myosin activity at the equator
- Actin flow

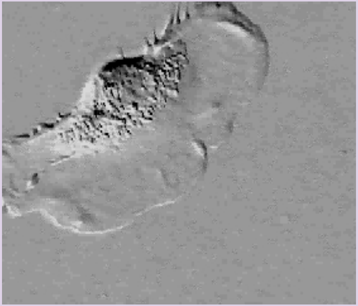
## Active gel theory




- C.Elegans embryos S.Grill

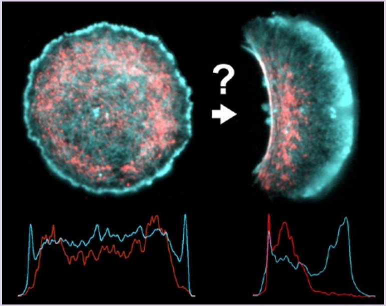
# Motion of Keratocyte cells, Verkhovsky

## Lamellipodium motion



Fast motion: 10$\mu$m/min.
Flat lamellipodium

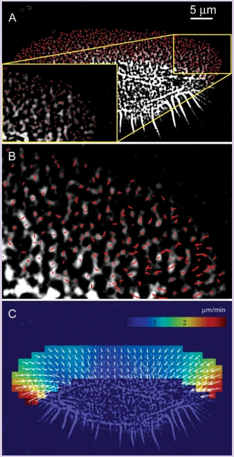
## Cell fragments




Keratocyte fragments: actin +myosin *II*

# Lamellipodium motion Verkhovsky

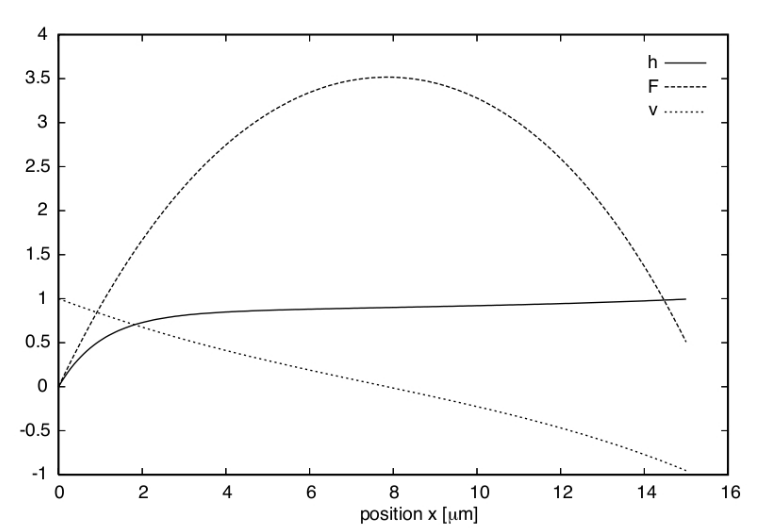
## Actin velocity field




## Stress distribution

- Velocity field obtained by speckle microscopy Valloton et al.
- Advancing velocity $u = 10\mu m/min.$
- Retrograde flow $v = 1\mu m/min.$
- Stress distribution on the substrate $\sigma_{xz} = 4 \quad 10^2 N/m^2$ Oliver et al.
- Actin viscosity $\eta = 10^5 \quad Pa.s$ Kaes et al.

# Active gel description



# Aknowledgements

## Active gels

Frank Juelicher

Karsten Kruse

Jacques Prost

## Theory

R.Voituriez
M.Basan
T.Risler

G.Salbreux
Y.Kafri
A.Callan-Jones

T. Guérin
K.Sekimoto
A.Basu

## Experiments

C.Sykes
J.Plastino
A. Roux

P. Bassereau
E.Paluch
J.Y. Tinevez

P.Martin
M.Balland
P.Y.Placais

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