Active matter with biological molecules

J.F. Joanny

Physico-Chimie Curie
Institut Curie

Boulder school
Outline

1. Acto-myosin gels
   - Active systems
Outline

1. Acto-myosin gels
   - Active systems

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

1. Acto-myosin gels
   - Active systems

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

3. Lamellipodium Motion
Actin polymerization

Actin monomers

- molecular weight 45kDa
- size $\delta = 5.5\text{nm}$
- 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 5mm
- Holow cylinders, radius 24nm
Molecular motor functions

Motor proteins

- Muscle contraction (myosin II)
- Cilia and axonemes (Dynein)
- Mitosis
- Intracellular transport (kinesin, myosin V)
- Inner ear hair cells (Myosin 1c)
- Rotating motors
Violation of the fluctuation dissipation theorem

Fluctuations of acto-myosin networks

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

Mizuno et al.
Outline

1. Acto-myosin gels
   - Active systems

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

3. Lamellipodium Motion
In vitro active gels, G. Koenderink

**Actin Myosin gel**

### Build-up of contractile stress

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

1. Acto-myosin gels
   - Active systems

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

3. Lamellipodium Motion
Non-adhering cells, P. Pullarkat

**Cell oscillations (T3 fibroblasts)**

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

**Period**

- Oscillation period $\approx 30s$
- Oscillation period decreases with myosin activity
Blebs induced by laser ablation

E. Paluch, J.Y. Tinnevez

Blebs on spreading cells

Membrane detachment from the cortical layer

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
Outline

1. Acto-myosin gels
   - Active systems

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

3. Lamellipodium Motion
Acto-myosin gels

- Active systems

Cortical layer

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

Lamellipodium Motion
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

![Bleb growth and Shrinkage images and graphs]

- Volume ratio
- Segment of bleb height
- Volume changes over time
- Units normalized
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
  \[ \frac{V_b}{V_c} = \frac{\zeta \Delta \mu}{2E} + \frac{\gamma}{2eE} \left( 1 - \frac{R}{R_b} \right) \]

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
Acto-myosin gels
- Active systems

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

Lamellipodium Motion
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

![Images showing bleb stages]
Outline

1. Acto-myosin gels
   - Active systems

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

3. Lamellipodium Motion
Ring closure in Xenopus eggs

**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

\[ 4\eta \frac{\partial}{\partial r}(\frac{\partial}{\partial r} + \frac{1}{r})v_r + (\frac{\partial}{\partial r} + \frac{2}{r})(\zeta \Delta \mu + \beta_1 \chi)\tilde{Q} = 0 \]

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

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

Velocity and order parameter profiles
Outline

1. Acto-myosin gels
   - Active systems

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

3. Lamellipodium Motion
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: 10μm/min.
Flat lamellipodium

Cell fragments

Keratocyte fragments: actin + myosin //
Lamellipodium motion

**Actin velocity field**

- 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
  - \( \sigma_{xz} = 4 \times 10^2 N/m^2 \) Oliver et al.
- Actin viscosity
  - \( \eta = 10^5 \ Pa.s \) 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. Ballard
P. Y. Placais