Biological Relevance of Active Gel Theory

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Actin-based dynamics

Hela cell, images Charras & al, JCB, 2006

Actin Intrinsic Treadmilling

ADP ATP

Pi

Actin Intrinsic Treadmilling
Many microscopic mechanisms
How to describe?

P.C. Martin, O. Parodi, P. Pershan

Generalized Hydrodynamics

Conserved quantities, Broken symmetries
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Generalized Hydrodynamics

Conserved quantities, Broken symmetries

• Actin (monomer+polymer)
How to describe?
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Generalized Hydrodynamics
Conserved quantities, Broken symmetries

- Actin (monomer+polymer)
- Myosin (bound, unbound)
How to describe?
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Generalized Hydrodynamics

Conserved quantities, Broken symmetries

- Actin (monomer+polymer)
- Myosin (bound, unbound)
- Momentum (force)
How to describe?

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Generalized Hydrodynamics

Conserved quantities, Broken symmetries

- Actin (monomer+polymer)
- Myosin (bound, unbound)
- Momentum (force)
- Polarization
Stress

Orientation dynamics

ATP consumption rate

Fluxes (myosin, actin, cytosol)

Velocity Gradients

Orientation direction gradients $\nabla P$

Chemical potential difference $= \Delta [ATP - ADP - Pi]$

Chemical potential gradients $\nabla [myo, act, cyt]$
\[
(1 + \tau \frac{D}{Dt}) \left\{ \tilde{\sigma}_{\alpha\beta} + \zeta \Delta \mu \ q_{\alpha\beta} + \frac{\nu_1}{2} (p_\alpha h_\beta + p_\beta h_\alpha - \frac{2}{3} p_\gamma h_\gamma \delta_{\alpha\beta}) \right\} = 2\eta \tilde{\nu}_{\alpha\beta} + \xi^{(s)}_{\alpha\beta}
\]

\[
(1 + \tau \frac{D}{Dt}) \{-p + \tilde{\zeta} \Delta \mu + \tilde{\nu}_1 p_\gamma h_\gamma \} = \eta \nu_{\gamma\gamma} + \xi
\]

\[
\frac{D}{Dt} p_\alpha = \left(1 + \tau \frac{D}{Dt}\right) \frac{1}{\gamma_1} h_\alpha + \lambda_1 p_\alpha \Delta \mu - \nu_1 p_\beta v_{\alpha\beta} - \tilde{\nu}_1 p_\alpha v_{\beta\beta} + \xi^{(p)}_\alpha
\]

\[
r = \lambda_1 p_\alpha h_\alpha + \Lambda \Delta \mu + \zeta q_{\alpha\beta} \tilde{\nu}_{\alpha\beta} + \tilde{\zeta} v_{\alpha\alpha} + \xi^{(r)}
\]

\[
< \xi^{(s)}_{\alpha\beta}(t, x) \xi^{(s)}_{\gamma\delta}(t', x') > = 2k_B T \eta \left[ (\delta_{\alpha\gamma} \delta_{\beta\delta} + \delta_{\alpha\delta} \delta_{\beta\gamma}) - \frac{2}{3} \delta_{\alpha\beta} \delta_{\gamma\delta} \right] \delta(t - t') \delta(x - x')
\]

\[
< \xi^{(r)}_{\alpha}(t, x) \xi^{(r)}_{\beta}(t', x') > = 2 \frac{k_B T}{\gamma_1} [\delta_{\alpha\beta} - p_\alpha p_\beta] \delta(t - t') \delta(x - x')
\]

\[
< \xi(t, x) \xi(t', x') > = 2k_B T \Lambda \delta(t - t') \delta(x - x')
\]

\[
< \xi^{(s)}_{\alpha\beta} \xi^{(s)}_{\gamma\delta} > = 0, \quad < \xi^{(s)}_{\alpha\beta} \xi^{(r)} > = 0,
\]

\[
< \xi^{(p)}_{\alpha}(t, x) \xi^{(r)}(t') > = 2k_B T \lambda_1 p_\alpha(x) \delta(t - t')
\]
K. Takiguchi, 1991
P.M. Bendix et al 2006

Contractility measured in units of Pascal
(like a pressure or an elastic modulus)

\[ 10^3 \text{ Pascal} \]
\[ 2u = \ldots + pp + \ldots \]
Nematic Hydrodynamics

(F.M. Leslie, F. Brochard, P.G. de Gennes, P. Pieranski, E. Guyon)

\[
\frac{Dp}{Dt} = \ldots + p + \ldots = \ldots + u_1 p + \ldots
\]

\[
\cos(2\theta) = \frac{1}{n_1}
\]
Spontaneous Frederiks transition

R. Voituriez et al
\[
\frac{\partial}{\partial t} = \frac{K}{1} \frac{\partial^2}{\partial z^2} + (1+n_1)u_{zx}
\]

\[
2 \sim u_{zx} \approx \sim \sin(2 \ ) + 1K \frac{\partial^2}{\partial z^2}
\]

\[
\frac{\partial}{\partial t} = \frac{K}{1} \frac{\partial^2}{\partial z^2} \sim \sin(2 \ )
\]

\[
(2 \sim )_c = \frac{K}{1}(\frac{1}{D})^2
\]
Topological Singularities

\[ F = \int d^2 x \left[ \frac{K}{2} (\nabla \cdot p)^2 + \frac{K + \delta K}{2} (p \cdot \nabla p)^2 
+ k \nabla \cdot p - h_{||} p^2 \right] \]

\[ K > 0 \quad K < 0 \quad K = 0 \]
Spontaneously moving topological singularity

\[ v_\theta(r) = \omega_0 r \log(r/r_0), \quad \omega_0 = \frac{2 \sin 2\psi_0}{4\eta + \gamma_1 v_1^2 \sin^2 2\psi_0} \zeta \Delta \mu \]
Microtubules + Motors

(François Nedelec et al)

+ A. Bernheim et al, A. Bausch et al
Actomyosin contractility rotates the cell nucleus
A. Kumar, A. Maitra, M. Sumit, G.V. Shivashankar, S. Ramaswamy
Pure Shear (Elongational Flow)

\[ t = \sin(2\theta) x v_x + \ldots \]

\[ t = 0 \text{ Stable if: } x v_x > 0 \]

\[ t = \frac{1}{2} \text{ Stable if: } x v_x < 0 \]
**Actin:** \( a = 0 \)
Xenopus Egg Wound healing

C.A. Mandato, W.M. Bement
Xenopus Egg Wound healing

C.A. Mandato, W.M. Bement
Want to describe?

- Why does it closes?
- Ring closure speed
- Flow pattern
- Alignment pattern

Equations for active isotropic liquid close to ordering transition

Excess contractility in the ring

Closure Time: $T \geq 30\text{ min}$  
Treadmilling Time: $1.5\text{ min}$  
$e \geq \text{ const}$
\[ 4\eta \partial_r (\partial_r + \frac{1}{r}) v_r + (\partial_r + \frac{2}{r})(\zeta \Delta \mu + \beta_1 \chi) \tilde{Q} = 0 \]
\[ \frac{\partial \tilde{Q}}{\partial t} = -\frac{\chi}{\beta_2} \tilde{Q} + \frac{\beta_1}{2} (\partial_r - \frac{1}{r}) v_r \]

\[ v_r(r_0) = -\frac{\zeta \Delta \mu_1^2 \beta_1 \beta_2}{16\eta^2 \chi} a + \frac{\zeta \Delta \mu r_0}{2\eta}, \quad v_r(r_1) = -\frac{\zeta \Delta \mu_1}{8\eta} a \]
Cytokinesis

L929 Cell, myosin GFP, J. Sedzinski, E. Paluch
Challenges

- Orientation pattern and flow
- Cell division failure
- Constriction dynamics (non monotonous)
- Constriction time independent of initial size
- Constriction speed decreases when turn over increases

Facts: Myosin and Actin densities constant
Width of extra contractility scales with size
Contractility generates flow

Simple balance:

Gel conservation law

\[ \frac{\partial e}{\partial t} + \nabla \cdot (e \nabla) = \bar{k}_d e + v_p \]

Stationary thickness:

\[ e_0 = \frac{v_p}{k_d} \]

Curvilinear dynamical equations

+ anisotropic Laplace’s Law

Flowtime: \( t = h \cdot z \cdot \Delta m \)

Cortex renewal time: \( k_d^{-1} \)
Sand-dollar zygote
G Von Dassow
Cell division success/failure

$\frac{\zeta}{\zeta_{\text{max}}}$

$t = 0.00 \ T_a$

$0 \text{ s}$

VX-680

0 s

Fig. 5. Cytokinesis duration is independent of initial cell size: Furrow radius $r_f$ as a function of time $t/T_a$ for four initial cell radii $R_0 = 0.5, 1, 2$ and 4. (Inset) Corresponding activity signals of width proportional to $R_0$, plotted as a function of the contour length $s$. 

$C. Elegans$
Non monotonic constriction rate
Non monotonic constriction rate

2 to 4 cells
Mean constant constriction rate
(47 to 23 μm) = 0.247 μm/s

4 to 8 cells
$y = 0.0107x$
$R^2 = 0.982$
Changing turnover

\[ kdTa = 30 \]

\[ kdTa = 40 \]

\[ kdTa = 80 \]
Why division time independent of initial size?

Dissipation due to cortex "viscosity":

\[ g \left( \frac{1}{R} \frac{dr}{dt} \right)^2 2A_r e \]

Work done upon contraction per unit time:

\[ \frac{\partial W}{\partial r} \frac{dr}{dt} \]

Area:

\[ 2A_r = \frac{4}{(1 + \frac{3}{2} \cos \frac{1}{2} \cos^3 )} \]

\[ a = a / 2 \quad R_0 \]

\[ g \left( a / t \right) = h( a / t ) \]

\[ a = \frac{g}{m} \quad E \]
Explains:

• Discontinuous character of the transition
• Constriction time independence if furrow width scales like initial radius
• Correct order of magnitude
• Effect of furrow width at constant extra contractility
• Non monotonic constriction rate
• Slowing down upon increasing turnover
Nematic Tissues?

Guillaume Duclos, Pascal Silberzan

P Friedl
Spontaneous Frederiks transition

R. Voituriez et al 2005
C B Mercader, J F Joanny, J P
A unique and robust approach to many different phenomena

- Cell motility
- Cell oscillations*
- Cell wound healing*
- Cytokinesis*
- Induced Blebs
- Spinning spindles, spinning nucleus
- mitotic spindle
- TISSUE MECHANICS, DEVELOPMENTAL BIOLOGY
Thank you!