Active mechanics of cells

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100μm

(HeLa cells)
Table of contents

Multicellular scale (>>10μm)

My research subjects

Epithelial tissue dynamics

Cellular scale (~ several 10μm)

Chemotactic migration of eukaryotic cells

Subcellular scale (< 10μm)

Contractility in actin-myosin cytoskeleton

[Bray et al. Science ‘88.]

[Salbreux et al., TCB ‘13]
Cytoskeleton, controlling cell shape

\[ \text{Persistence length} \approx 17\mu m \]

[Image from: http://csls-db.c.u-tokyo.ac.jp/search/detail?image_repository_id=341]

\[G. \text{ Charras et al., J. Cell Biol. '06}\]

\[G. \text{ Salbreux et al., Trends in Cell Biol. 22, 536 (2013).}\]

Contractility in actomyosin network
Mechanics of cortical cytoskeleton

Myosin (Motor) + F-actin → Motor-induced force → Contractile

[Bray et al. Science ‘88.]

“How act.-myo. cytosk. gets contractile??”

J.Sedzinski, M.Biro et al., Nature 476, 462 (2011).]
Theoretical model


Myosin heads try to move twd. determined dirs. alg. F-act.,
\[
\left( \mu ds_i / dt = -dU / ds_i \right.
\text{with the potential } U = -f_0 \sum_i s_i \right)
\]
Numerical results

**Without passive crosslinkers**

→ Extensile (Diffusive)

**With passive crosslinkers**

→ Contractile

[TH and G. Salbreux, PRL 116, 188101 (2016).]

Details will be discussed on the poster
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Chemotactic migration of a eukaryotic cell

Chemotaxis of *Dictyostelium discoideum* (aca-)

[ C. McCann et al., J. Cell Science, 2010. ]

Every 30 seconds for 90 minutes.

Using phase-contrast microscopy with a 5 × objective.

“*Theor. model describing chemotaxis trajectory*?”
EoM of a cell as a self-driven object

\[
\frac{d}{dt} q = I_q (1 - q^2) q + \overline{fg.s.} + \xi
\]

Deterministic bias due to chem. grad. (Mechanical process)

\[
\mu \frac{d}{dt} x = \chi q
\]

Force balance btw. friction and momentum generation alg. polarity (q) (Biol. pr.)

Polarity dynamics

\[
v = \frac{dx}{dt}
\]

\[v_s: \text{constant speed } (= \frac{\nu}{\mu})\]

Responsiveness \(f_q\)

\[v = \frac{dx}{dt}\]

\[k_{on}, k_{off}\]

\[\nu_s: \text{constant speed } (= \frac{\nu}{\mu})\]

\[\nu\]

\[I_q\]

\[\chi\]

\[\xi\]

\[\text{White Gaussian noise}\]

\[\text{Distribution } P_s(\theta_v)\]

\[\text{Gradient direction when polarity } q \text{ is spontaneously formed}\]

\[\text{w/o spontaneous formation of polarity}\]

\[\text{using realistic Dicty. Parameters}\]

[TH et al., Physical Biology 11, 056002 (2014).]

Chemotactic migration

(Experiment)

[Fuller et al, 2009]

(\(fg.s. = (0, S)\) with chemotact. bias \(S = 0.1\), Dispers. \(D\) of noise \(\xi = 0.5\))

\[l_q = 100\]

\[P_s(\theta_v)\]

\[\text{Distribution } P_s(\theta_v)\]

\[\text{migration direction } \theta_v/\pi\]

7/11/2016

10/18
Toward many cell system

\[
\mu \frac{d}{dt} x_i = \chi q_i + K_i(\{x_j\})
\]

\[
\frac{d}{dt} q_i = I_q(1 - q_i^2)q_i + J_i(\{x_j\}, \{q_j\}) + f^g.s. + \xi_i
\]

Cell-cell avoidance

Alignment

Xenopus Neural Crest cells

Chemotactic migration
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  - Chemotactic migration of eukaryotic cells

- Contractility in actin-myosin cytoskeleton

- [Bray et al. Science ‘88.]
- [Salbreux et al., TCB ‘13]
Multicellular organism are covered by epithelial tissue

Drosophila embryogenesis

Adhesion molecules (E-cadherin-GFP)

Basal membrane

Lateral view

Adherence junction and Actomyosin bundle

Top view

[Y. Wang et al., Dev. Cell 25, 299 (2013).]
Epithelial tissue dynamics

"How can this long-term motion be realized?"

[ E. Kuranaga et al., Curr. Biol '10.]

[ M. Suzanne et al., Development 138, 1493 (2011).]
Model — Cellular vertex model

\[ \mathbf{r}_i \approx 10\mu m \]

- Variational dynamics:

\[ \mu \frac{d}{dt} \mathbf{r}_i = - \frac{\partial E(\mathbf{r}_i)}{\partial \mathbf{r}_i} \]

\[ E(\{\mathbf{r}_\alpha\}) = \frac{K}{2} \sum_{\alpha:\text{cells}} (A_\alpha - A^{(0)})^2 + \frac{K^p}{2} \sum_{\alpha:\text{cells}} (L_\alpha - L^{(0)})^2 + \sum_{<i,j>:\text{bonds}} \Lambda_{ij} l_{ij} \]

  \hline
  \text{Cell area (}A_\alpha\text{) control} \hline
  \text{Cell perimeter (}L_\alpha\text{) control} \hline
  \text{Bond-specific tension (}l_{ij}: \text{length of the bond }<i,j>\text{)} \hline

- Junctional remodeling

\[ [\text{T. Nagai and H. Honda, Phil. Mag. 81, 699 (2001).}] \]
Introducing chirality in tension

**Bond specificity in tension** $\lambda_{ij}(t)$
(chirality in tension strength)

$$\lambda_{ij}(t) = \gamma_1(t) \times \cos^2 (\theta_{ij} - \theta_0)$$

with $\theta_0 = 45^\circ$ and $\gamma_1(t) = \gamma_1(0) \left[ \frac{1 + \cos(2\pi f_{ij}t)}{2} \right]$

Model: Implementation

\[ \mu \frac{d}{dt} \vec{r}_j = - \left. \frac{\partial E(\{\vec{r}_\alpha\}, \{\Lambda_{ij}\})}{\partial \vec{r}_i} \right|_{\Lambda_{ij} = \lambda_{ij}(t)} \]

with \( \lambda_{ij}(t) = \gamma_1(t) \times \cos^2(\theta_{ij} - \theta_0) \)

The direction in which tension is maximally strengthened

“Mechano-active” coupling

Mechanical process:
\[ \mu \frac{d}{dt} \vec{r}_j = - \left. \frac{\partial E(\{\vec{r}_\alpha\}, \{\Lambda_{ij}\})}{\partial \vec{r}_i} \right|_{\Lambda_{ij} = \lambda_{ij}(t)} \]

Active process:
\[ \left( \tau \frac{d\Lambda_{ij}}{dt} = \right) 0 = -(\Lambda_{ij} - \lambda_{ij}(t)) \]
Numerical results

Comp. with *in vivo* data
(ex) bond angle distribution around AP axis

*In vivo*

Before rotation

*Sim.*

During rotation

Describing living cells’ dynamics

Mechanics on active, dynamic motions of living cells

(Cl.) Mechanical eq. of motion + Finding the minimal “biological” assumption
## Acknowledgements

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Thank you for your attention.