Spontaneous polarization and deformation of active layers:

modelling bio- and biomimetic materials with polar and nematic order parameters

Michael Köpf
Département de Physique
École Normale supérieure

Len Pismen
Department of Chemical Engineering
Technion – Israel Institute of Technology

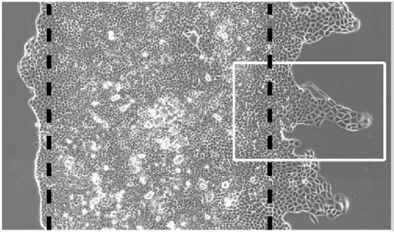
HUMAN FRONTIER SCIENCE PROGRAM
FUNDING FRONTIER RESEARCH INTO COMPLEX BIOLOGICAL SYSTEMS

LabEx ENS-ICFP

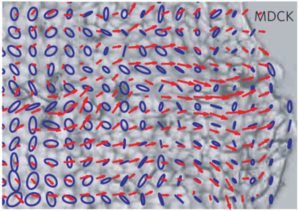
Outline

- Polar medium
  - Chemo-mechanical instabilities driven by deformation – polarisation – concentration feedback
  - Application and modification: epithelial spreading
- Nematic medium
  - Deformation and ordering in doped nematic elastomers
  - Chemo-mechanical instabilities in an active layer

Defining the scope of the model



L. Petitjean, M. Reffay, E. Grasland-Mongrain, M. Poujade, B. Ladoux, A. Buguin, and P. Silberzan
Biophysical Journal 98(9) 1790–1800

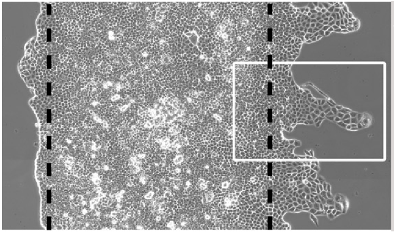


Stress ellipses and velocity vectors

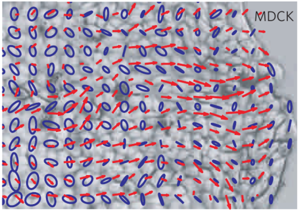
Dhananjay T. Tambe, C. Corey Hardin, Thomas E. Angelini, Kavitha Rajendran, Chan Young Park, Xavier Serra-Picamal, Enhua H. Zhou, Muhammad H. Zaman, James P. Butler, David A. Weitz, Jeffrey J. Fredberg and Xavier Trepat
NATURE MATERIALS | VOL 10 | JUNE 2011 | **469**

- Mechanics: elasticity, traction, stresses

Defining the scope of the model



L. Petitjean, M. Reffay, E. Grasland-Mongrain, M. Poujade, B. Ladoux, A. Buguin, and P. Silberzan
Biophysical Journal 98(9) 1790–1800



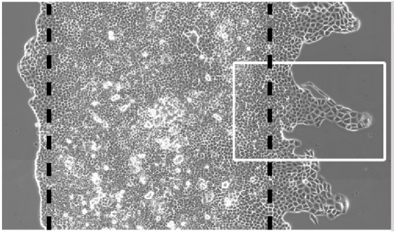
Stress ellipses and velocity vectors

Dhananjay T. Tambe, C. Corey Hardin, Thomas E. Angelini, Kavitha Rajendran, Chan Young Park, Xavier Serra-Picamal, Enhua H. Zhou, Muhammad H. Zaman, James P. Butler, David A. Weitz, Jeffrey J. Fredberg and Xavier Trepat
NATURE MATERIALS | VOL 10 | JUNE 2011 | **469**

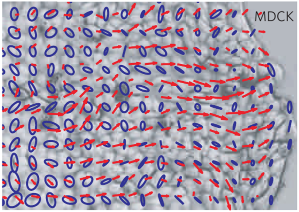
- Mechanics: elasticity, traction, stresses

How does collective behavior emerge?

Defining the scope of the model



L. Petitjean, M. Reffay, E. Grasland-Mongrain, M. Poujade, B. Ladoux, A. Buguin, and P. Silberzan
Biophysical Journal 98(9) 1790–1800



Stress ellipses and velocity vectors

Dhananjay T. Tambe, C. Corey Hardin, Thomas E. Angelini, Kavitha Rajendran, Chan Young Park, Xavier Serra-Picamal, Enhua H. Zhou, Muhammad H. Zaman, James P. Butler, David A. Weitz, Jeffrey J. Fredberg and Xavier Trepat
NATURE MATERIALS | VOL 10 | JUNE 2011 | **469**

- Mechanics: elasticity, traction, stresses

How does collective behavior emerge?

- Communication: Chemical signals, mechanosensitivity
- Action: Polarization, active forces

A simple macroscopic model

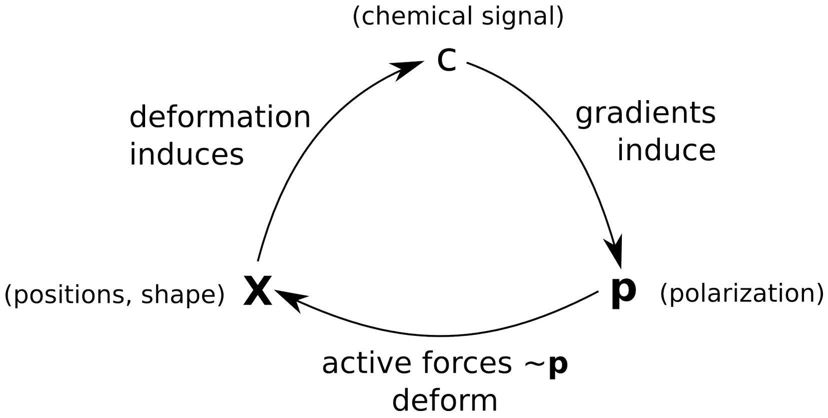
(chemical signal)

c

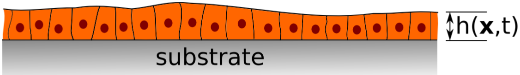
(positions, shape) **X**

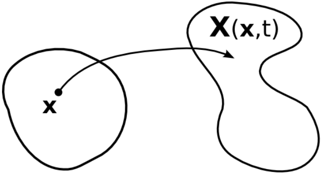
p (polarization)

A simple macroscopic model



Weakly nonlinear description of cell monolayers





Elasticity:

$$F_{ij} = \frac{\partial X_i}{\partial x_j} \qquad \omega_{ij} = F_{ki}F_{kj} - \delta_{ij}$$

$$\mathcal{F}_{\text{el}} = \frac{\mu}{4}\int h\omega_{ij}\omega_{ij}\mathrm{d}^2\mathbf{x} \qquad \sigma_{ij} = \frac{\partial \mathcal{L}_{\text{el}}}{\partial F_{ij}}$$

Incompressibility (in 3D): $h = h_0/J$ with $J = \det \mathbf{F}$

Overdamped dynamics:

$$\eta D_t X_i = \partial_j \sigma_{ij} + qp_i$$

Polarization

Polarization:

$$\mathcal{F}_{\mathrm{p}} = \int \mathrm{d}^2\mathbf{X}\,\frac{\kappa h}{2a_x^2}\left[\alpha^2|\mathbf{p}|^2\left(1+\frac{\kappa_0}{2}|\mathbf{p}|^2\right) - c\nabla_i p_i + (\nabla_i p_i)^2 + \kappa_2(\epsilon_{ik}\nabla_i p_k)^2 + \kappa_3|\mathbf{p}|^2\nabla_i p_i\right].$$

$$\begin{aligned}\gamma\mathcal{D}_{ij}p_j &= \nabla_i(h\nabla_j p_j) + \kappa_2\nabla_j\left[h\left(\nabla_j p_i - \nabla_i p_j\right)\right] \\ &- \nabla_i(hc) - \alpha^2 h\left(1+|\mathbf{p}|^2\right)p_i\end{aligned}$$

Corotational derivative $\mathcal{D}_{ij} = D_t\delta_{ij} + \frac{1}{2}(\nabla_j v_i - \nabla_i v_j)$

Chemical signal

- Diffusive flux depends on the local monolayer thickness
- The chemical species decays with time (linearly)

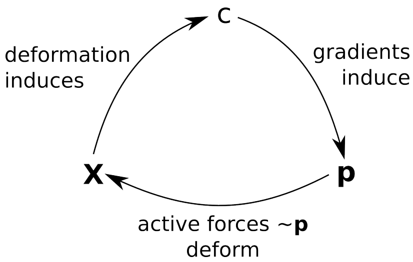
$$\mathrm{D}_t c = h^{-1}\nabla_i(h\nabla_i c) - c + \beta\psi, \qquad \psi = \frac{\mathrm{d}A}{\mathrm{d}A_0} - 1 = J - 1$$

- Strain dependence

Examples from biology:

- MAPK activation
  [Matsubayashi et al. *Curr. Biol.* **14** 2004, 731–735]
- Compression dependent myosin attachment
  [Fernandez-Gonzales et al. *Developmental Cell* **17** 2009, 736–743]
- Ectopic expression of Twist
  [Farge *Curr. Biol.* **13** 2003, 1365–1377]

Closing the feedback loop



Chemical signal:

$$\mathrm{D}_t c = h^{-1}\nabla_i(h\nabla_i c) - c + \beta\psi$$

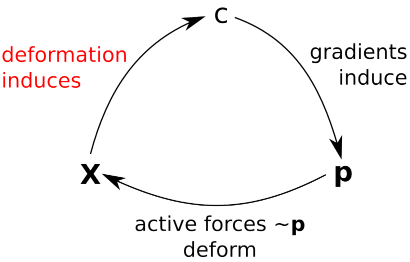
Polarization:

$$\begin{aligned}\gamma\mathcal{D}_{ij}p_j &= \nabla_i(h\nabla_j p_j) + \kappa_2\nabla_j\left[h\left(\nabla_j p_i - \nabla_i p_j\right)\right] \\ &- \nabla_i(hc) - \alpha^2 h\left(1+|\mathbf{p}|^2\right)p_i\end{aligned}$$

Mechanics with active force (traction):

$$\eta\partial_t X_i = \partial_j\sigma_{ij} + q\mathbf{p}$$

Closing the feedback loop



Chemical signal:

$$\mathrm{D}_t c = h^{-1}\nabla_i(h\nabla_i c) - c + \beta\psi$$

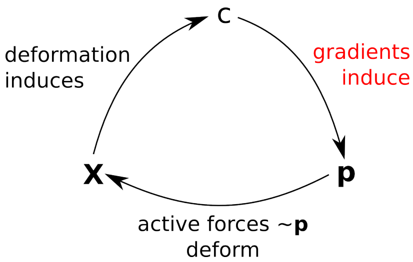
Polarization:

$$\begin{aligned}\gamma\mathcal{D}_{ij}p_j &= \nabla_i(h\nabla_j p_j) + \kappa_2\nabla_j\left[h\left(\nabla_j p_i - \nabla_i p_j\right)\right] \\ &- \nabla_i(hc) - \alpha^2 h\left(1+|\mathbf{p}|^2\right)p_i\end{aligned}$$

Mechanics with active force (traction):

$$\eta\partial_t X_i = \partial_j\sigma_{ij} + q\mathbf{p}$$

Closing the feedback loop



Chemical signal:

$$D_t c = h^{-1}\nabla_i(h\nabla_i c) - c + \beta\psi$$

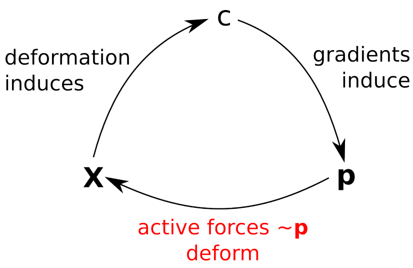
Polarization:

$$\begin{aligned}\gamma\mathcal{D}_{ij}p_j &= \nabla_i(h\nabla_j p_j) + \kappa_2\nabla_j\left[h\left(\nabla_j p_i - \nabla_i p_j\right)\right] \\ &- \nabla_i(hc) - \alpha^2 h\left(1+|\mathbf{p}|^2\right)p_i\end{aligned}$$

Mechanics with active force (traction):

$$\eta\partial_t X_i = \partial_j\sigma_{ij} + q\mathbf{p}$$

Closing the feedback loop



Chemical signal:

$$\mathrm{D}_t c = h^{-1}\nabla_i(h\nabla_i c) - c + \beta\psi$$

Polarization:

$$\begin{aligned} \gamma\mathcal{D}_{ij}p_j &= \nabla_i(h\nabla_j p_j) + \kappa_2\nabla_j\left[h\left(\nabla_j p_i - \nabla_i p_j\right)\right] \\ &- \nabla_i(hc) - \alpha^2 h\left(1+|\mathbf{p}|^2\right)p_i \end{aligned}$$

Mechanics with active force (traction):

$$\eta\partial_t X_i = \partial_j\sigma_{ij} + q\mathbf{p}$$

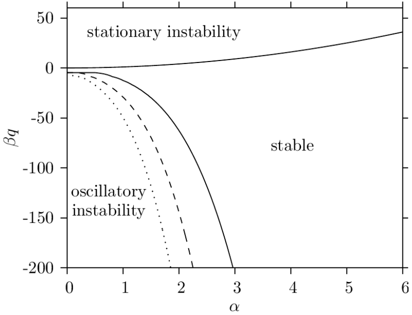
Linear stability of homogeneous states

Linear dynamics around solution $\mathbf{p} = 0, c = 0, \mathbf{X} = \mathbf{x}$

$$\begin{aligned} \eta\, \partial_t \psi &= \nabla^2 \psi + q\phi, \\ \gamma\, \partial_t \phi &= \nabla^2 \phi - \alpha^2 \phi - \nabla^2 c, \\ \partial_t c &= \nabla^2 c - c + \beta\psi, \end{aligned}$$

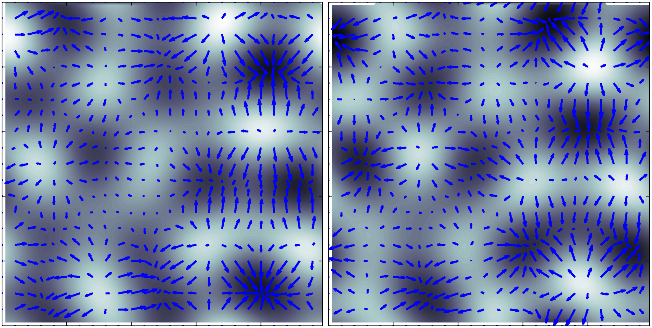
with strain ψ and splay ϕ

$$\begin{aligned} \psi &= \nabla \cdot (\mathbf{X} - \mathbf{x}), \\ \phi &= \nabla \cdot \mathbf{p}. \end{aligned}$$



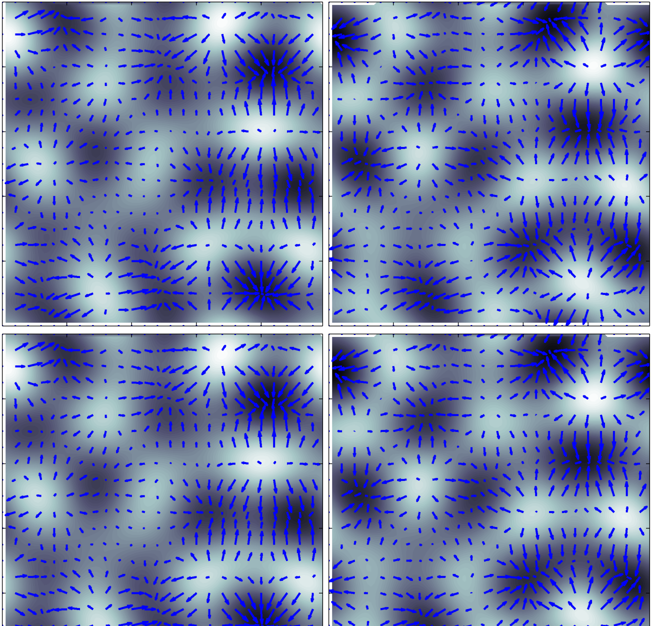
M.H. Köpf, L.M. Pismen / Physica D 259 (2013) 48–54

Oscillatory instability

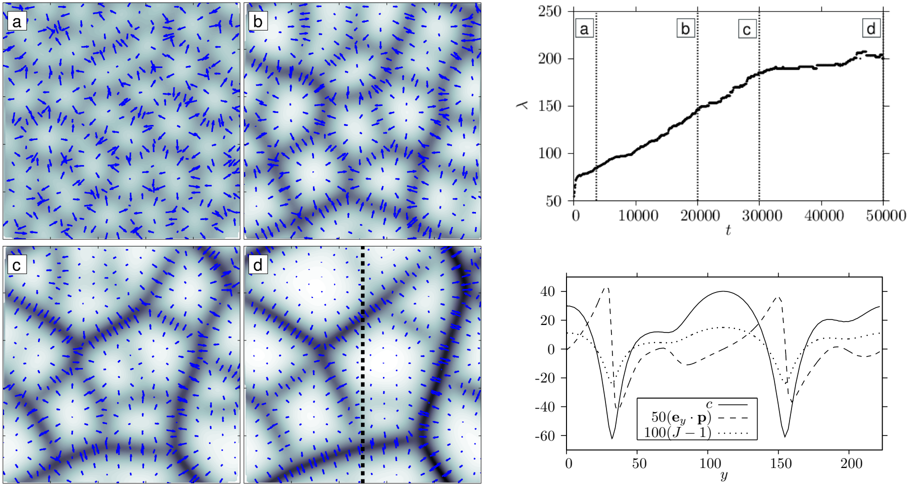


M.H. Köpf, L.M. Pismen / Physica D 259 (2013) 48–54

Oscillatory instability

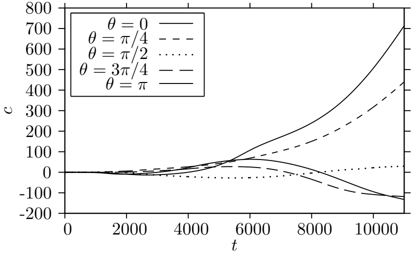


Stationary instability & coarsening

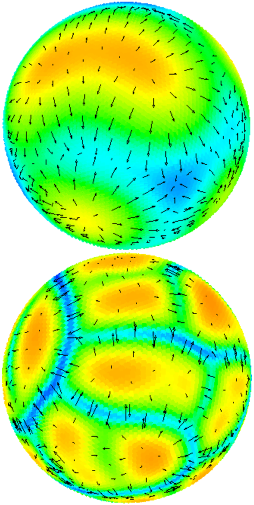


M.H. Köpf, L.M. Pismen / Physica D 259 (2013) 48–54

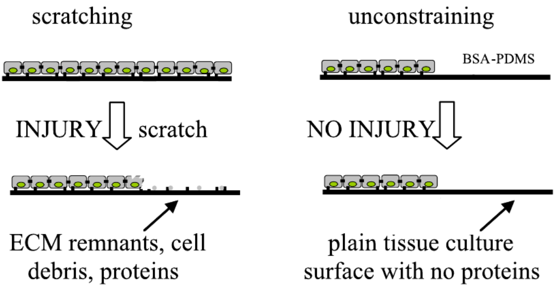
Coarsening in spherical cortices: Establishment of polarity



M.H. Köpf, L.M. Pismen / Physica D 259 (2013) 48–54

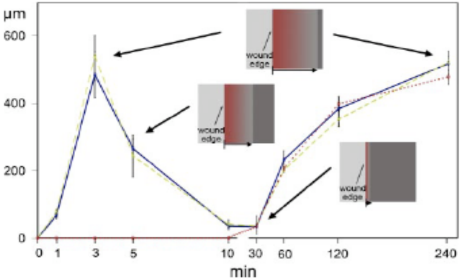


Wound healing experiments



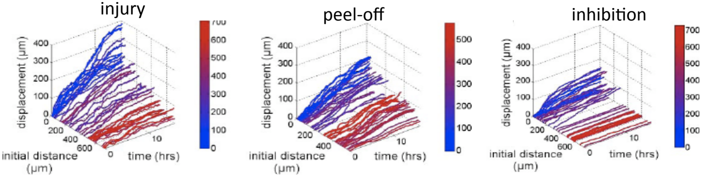
Nikolić, Djordje L., Alistair N. Boettiger, Dafna Bar-Sagi, Jeffrey D. Carbeck, and Stanislav Y. Shvartsman.
Am J Physiol Cell Physiol 291: C68–C75, 2006.

Wound healing experiments

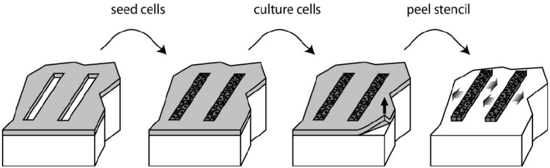


2 activation waves

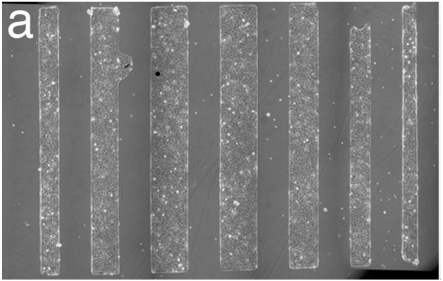
Shvartsman et al, 2006



Unconstrained spreading



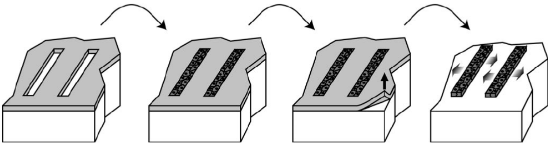
M. Poujade, E. Grasland-Mongrain, A. Hertzog, J. Jouanneau, P. Chavrier, B. Ladoux, A. Buguin, and P. Silberzan
PNAS | **October 9, 2007** | vol. 104 | no. 41 | **15988–15993**



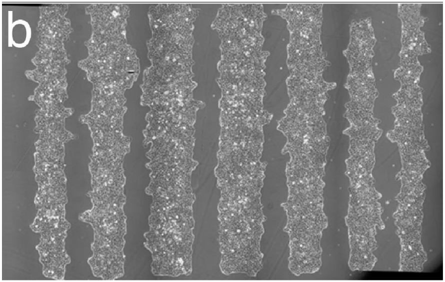
t=0

M. Poujade, E. Grasland-Mongrain, A. Hertzog, J. Jouanneau, P. Chavrier, B. Ladoux, A. Buguin, and P. Silberzan
PNAS | **October 9, 2007** | vol. 104 | no. 41 | **15988–15993**

Unconstrained spreading



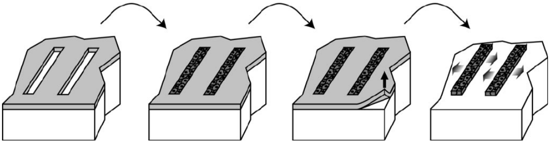
M. Poujade, E. Grasland-Mongrain, A. Hertzog, J. Jouanneau, P. Chavrier, B. Ladoux, A. Buguin, and P. Silberzan
PNAS | **October 9, 2007** | vol. 104 | no. 41 | **15988–15993**



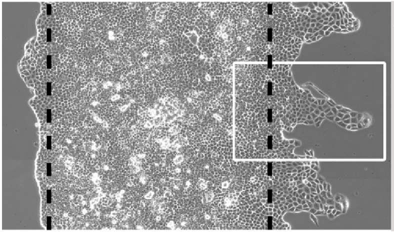
M. Poujade, E. Grasland-Mongrain, A. Hertzog, J. Jouanneau, P. Chavrier, B. Ladoux, A. Buguin, and P. Silberzan
PNAS | **October 9, 2007** | vol. 104 | no. 41 | **15988–15993**

t=13 h

Unconstrained spreading

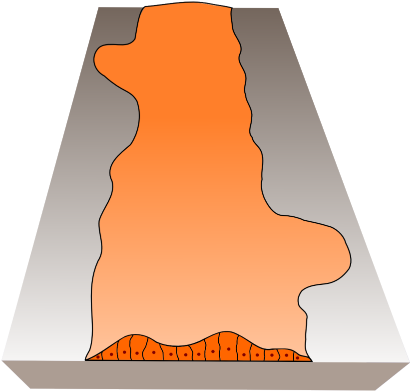


M. Poujade, E. Grasland-Mongrain, A. Hertzog, J. Jouanneau, P. Chavrier, B. Ladoux, A. Buguin, and P. Silberzan
PNAS | **October 9, 2007** | vol. 104 | no. 41 | **15988–15993**



L. Petitjean, M. Reffay, E. Grasland-Mongrain, M. Poujade, B. Ladoux, A. Buguin, and P. Silberzan
Biophysical Journal 98(9) 1790–1800

Unconstrained spreading



Boundary conditions

- Free boundaries

$$n_j \sigma_{ij}|_{\partial A} = 0$$

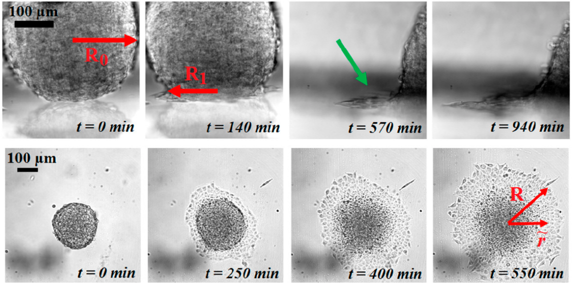
- No chemical flux through the boundaries

$$N_i \nabla_i c|_{\partial A} = 0$$

- Vanishing directional derivative of $\mathbf{p}$

$$N_j \partial_j p_i|_{\partial A} = 0$$

Wetting and spreading

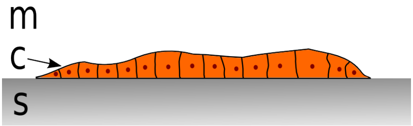


Douezan et al. PNAS | **May 3, 2011** | vol. 108 | **7315–7320**

Spreading coefficient

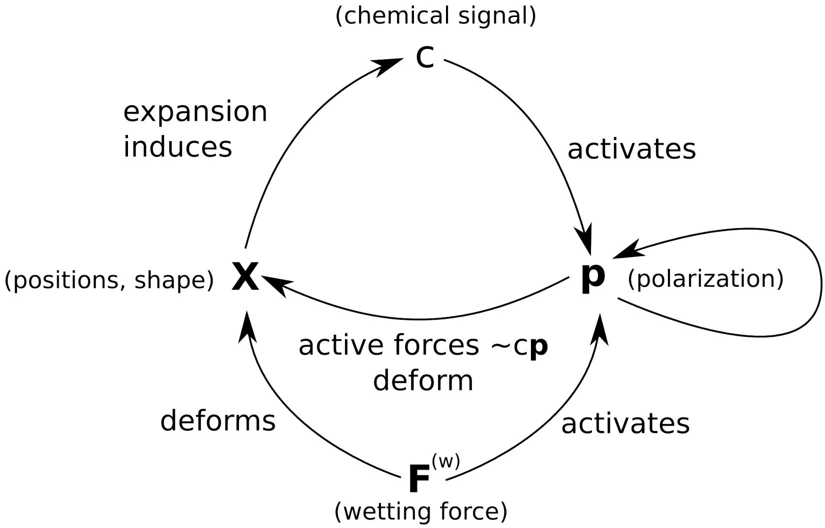
$$S = \gamma_{sm} - (\gamma_{cs} + \gamma_{cm})$$

$$\mathcal{F}_{\mathrm{w}} = SA$$



$$-\left.\frac{\delta \mathcal{F}_{\mathrm{w}}}{\delta X_i(\mathbf{x})}\right|_{\mathbf{x}\in\partial A} = f^{(\mathrm{w})}(\mathbf{x})N_i$$

The feedback loop in wound healing

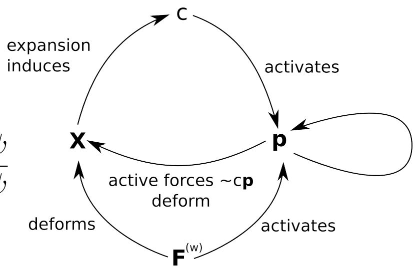


Salm, Pismen. *Phys. Biol.* **9** (2012) 026009

The feedback loop in wound healing

Chemical signal:

$$\mathrm{D}_t c = J\nabla_i(J^{-1}\nabla_i c) - c + \frac{\theta(\psi)\beta\psi}{1+s_c\psi}$$



Polarization:

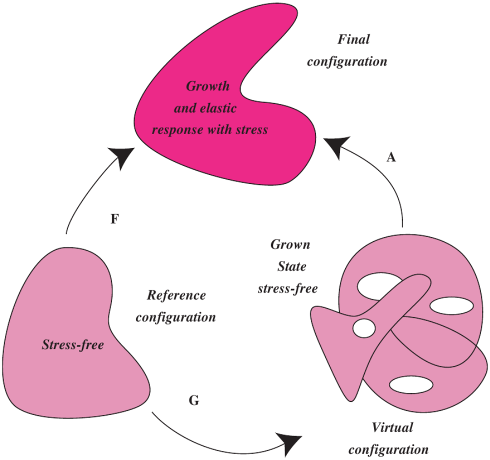
$$\gamma\mathcal{D}_{ij}p_j = \nabla_i(J^{-1}\nabla_j p_j) + \kappa_2\nabla_j\left[J^{-1}\left(\nabla_j p_i - \nabla_i p_j\right)\right] - \alpha^2 J^{-1}\left(1+|\mathbf{p}|^2\right)p_i + q\left(\frac{J^{-1}cp_i}{(1+s_a|\mathbf{p}|)} + F_i^{(\mathrm{w})}\right)$$

Mechanics with active force (traction):

$$\eta\partial_t X_i = \partial_j\sigma_{ij} + F_i^{(\mathrm{w})} + \frac{cp_i}{J}$$

Tissue growth and elasticity

How to separate growth from elastic deformation?



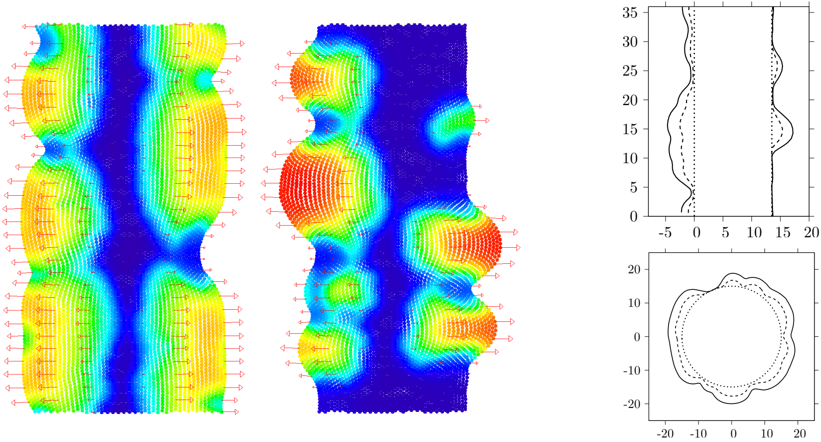
M. Ben Amar, A. Goriely / J. Mech. Phys. Solids 53 (2005) 2284–2319

$$\partial_j X_i = A_{ik} G_{kj}$$

$$\omega_{ij} = (A_{ki} A_{kj} - \delta_{ij})$$

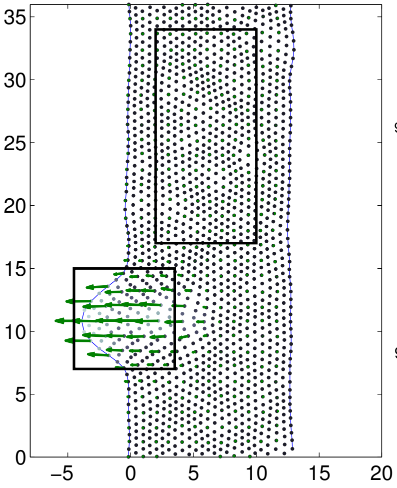
$$\mathcal{F}_{\mathrm{el}} = \frac{\mu h_0}{4} \int \mathrm{d}^2 \mathbf{X} \frac{\omega_{ij}\omega_{ij}}{J}$$

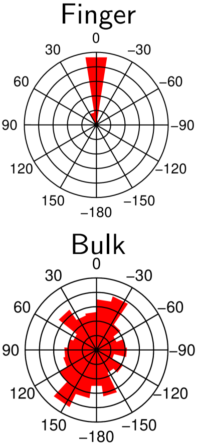
Strongly non-uniform deformation

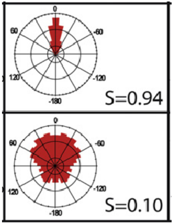


M. H. Köpf and L. M. Pismen | *Soft Matter*, 2013, **9**, 3727

Velocity orientation: Bulk vs. Finger



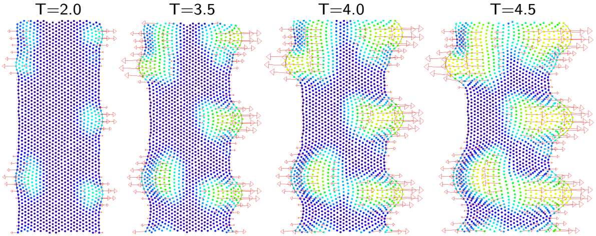


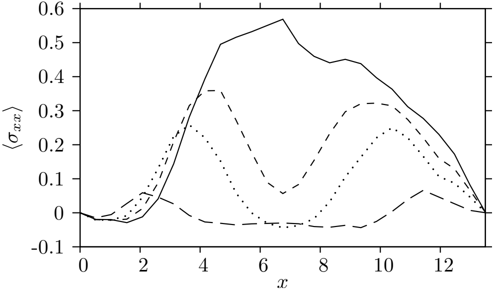


M. Reffay, L. Petitjean, S. Coscoy, E. Grasland-Mongrain, F. Amblard, A. Buguin, and P. Silberzan*
Biophysical Journal 100(11) 1–10

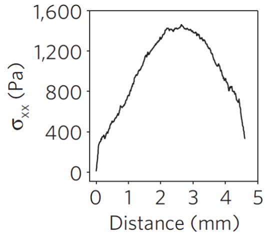
M. H. Köpf and L. M. Pismen | *Soft Matter*, 2013, **9**, 3727

Mechanical waves and the global tug of war





M. H. Köpf and L. M. Pismen | *Soft Matter*, 2013, **9**, 3727



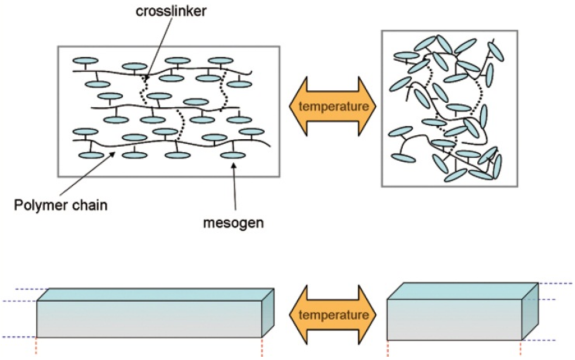
Xavier Trepat, Michael R. Wasserman, Thomas E. Angelini, Emil Millet, David A. Weitz, James P. Butler and Jeffrey J. Fredberg
NATURE PHYSICS | VOL 5 | JUNE 2009 | **426**

Xavier Serra-Picamal, Vito Conte, Romaric Vincent, Ester Anon, Dhananjay T. Tambe, Elsa Bazellieres, James P. Butler, Jeffrey J. Fredberg and Xavier Trepat
NATURE PHYSICS | VOL 8 | AUGUST 2012 | **628**

Summary & Remarks: polar order

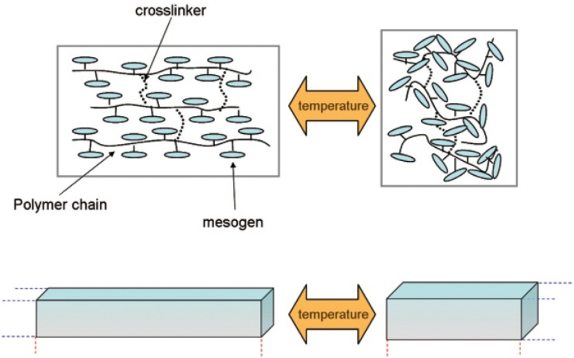
- We developed continuum models of active tissue with weakly nonlinear elasticity describing the dynamics of $\mathbf{X}$, $\mathbf{p}$, and concentration
- A simple feedback mechanism leads to two basic types of chemo-mechanical instabilities:
  - Stationary instability for expansive activation
  - Oscillatory instability for compressive activation
- Coarsening provides a natural mechanism to establish a permanent polarity in spherical systems (closed surfaces)
- Unconstrained spreading is described using a free interface approach and a wetting force
- The spreading is strongly non-uniform and exhibits *fingering*
- *global tug of war*
- Mechanical waves travel from the wound edge inwards

Biomimetic materials: Nematic elastomers



Dorkenoo et al. in *Advanced Elastomers - Technology, Properties and Applications* (2012)

Biomimetic materials: Nematic elastomers

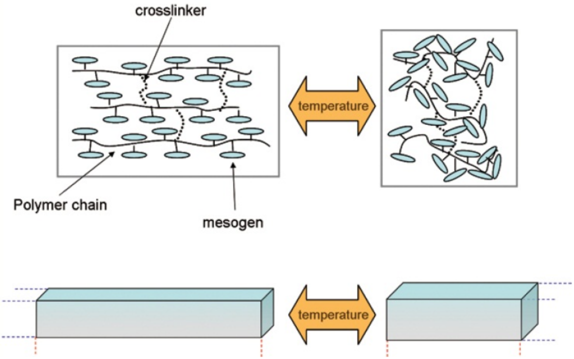


Dorkenoo et al. in *Advanced Elastomers - Technology, Properties and Applications* (2012)

Analogy to growth:

$$F_{ij} = A_{ik} G_{kj} \qquad G_{ij} = N^{-1/2}(\delta_{ij} + g\widetilde{Q}_{ij}),$$

Biomimetic materials: Nematic elastomers



Dorkenoo et al. in *Advanced Elastomers - Technology, Properties and Applications* (2012)

What is the effect of dopants?

Doped nematic elastomers

Free energy:

$$\mathcal{F}[\mathbf{F},\mathbf{Q},c] = \mathcal{F}_{\mathrm{el}}[\mathbf{F},\mathbf{Q},c] + \mathcal{F}_{\mathrm{n}}[\mathbf{F},\mathbf{Q},c] + \mathcal{F}_{c}[\mathbf{F},\mathbf{Q},c].$$

Energy densities:

$$\mathcal{L}_{\mathrm{el}} = \frac{1}{2}\left(\nu\, u_{ij}^2 - \lambda u_{ii}^2\right)$$

$$\begin{aligned}\mathcal{L}_{\mathrm{n}} = &-\frac{\alpha_1 - \alpha_c c}{4} Q_{ij}Q_{ij} + \frac{\alpha_2}{16}\left(Q_{ij}Q_{ij}\right)^2 + \beta c \nabla_i \nabla_j Q_{ij} \\ &+ \frac{\kappa_1}{2}\left|\nabla_i Q_{ij}\right|^2 + \frac{\kappa_2}{4}\sum_{ijk}\left(\nabla_i Q_{jk}\right)^2\end{aligned}$$

$$\mathcal{L}_c = \frac{\chi}{2}\left(\nabla c\right)^2 + c\ln c + (1-c)\ln(1-c)$$

Biomimetic materials: Nematic elastomers

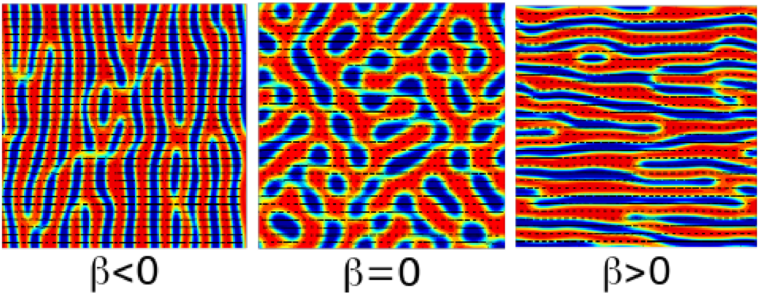
Dynamics:

$$
\begin{aligned}
\Gamma_{\mathrm{el}}^{-1}\mathrm{D}_t X_i &= \partial_j \sigma_{ij} - \delta(\mathcal{L}_\mathrm{n} + \mathcal{L}_c)/\delta X_i \\
\mathcal{D}_{ijkl} Q_{kl} &= -\Gamma_\mathrm{n} \delta\mathcal{F}/\delta Q_{ij} \\
\mathrm{D}_t c &= \Gamma_c \nabla_i \left[c(1-c)\nabla_i \mu\right] \\
\mu &= -\chi \nabla^2 c + k_\mathrm{B} T \ln\frac{c}{1-c} + \frac{\alpha_c}{4} Q_{ij}Q_{ij} + \beta \nabla_i \nabla_j Q_{ij}.
\end{aligned}
$$

Elastic-nematic coupling:

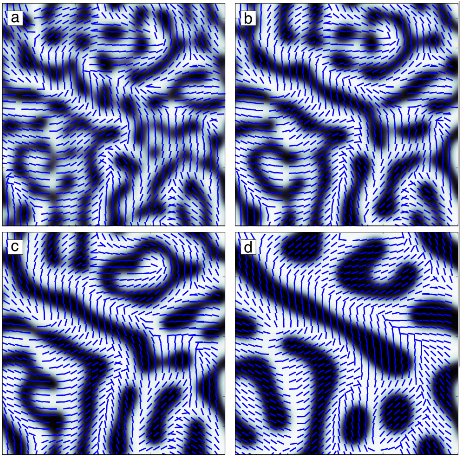
$$
\begin{aligned}
\frac{\partial \mathcal{L}_\mathrm{el}}{\partial Q_{ij}} = -gN^{-1/2} \Big[& \sigma_{kj}^{(A)} F_{ki} + \sigma_{ki}^{(A)} F_{kj} \\
& - \sigma_{kl}^{(A)} \left(F_{kl}\delta_{ij} + gN^{-1/2} \widetilde{Q}_{ij} A_{kl} \right) \Big]
\end{aligned}
$$

Dependence on the coupling parameter β



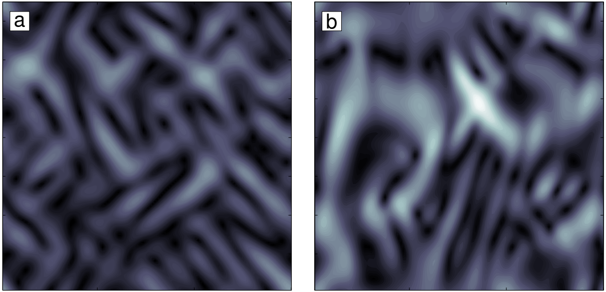
Köpf and Pismen | *Eur. Phys. J. E* **36** (2013)

Quenched states



Köpf and Pismen | *Eur. Phys. J. E* **36** (2013)

The displacement field



Köpf and Pismen | *Eur. Phys. J. E* **36** (2013)

Active nematic elastomers

Free energy:

$$\mathcal{F} = \mathcal{F}^{\mathrm{el}} + \mathcal{F}^{\mathrm{n}} = \int \left(\mathcal{L}^{\mathbf{el}} + \mathcal{L}^{\mathrm{n}}\right) \mathrm{d}^2\mathbf{x}.$$

Energy densities:

$$\mathcal{L}^{\mathrm{el}} = \mu \left(u_{ij} - \frac{1}{2} u_{kk}\delta_{ij}\right)^2 + \frac{K}{2} u_{ii}^2$$

$$\begin{aligned}\mathcal{L}^{\mathrm{n}} = {} & \frac{\alpha_1}{4} Q_{ij}Q_{ij} + \frac{\alpha_2}{16} \left(Q_{ij}Q_{ij}\right)^2 \\ & + \frac{\kappa_1}{2} \left|Q_{ij,j}\right|^2 + \frac{\kappa_2}{4} \sum_{ijk} \left(Q_{jk,i}\right)^2 .\end{aligned}$$

Active nematic elastomers

Deformation dynamics:

$$\begin{aligned} \eta^{\mathrm{el}} \mathrm{D}_t u_i =& \partial_j \left[\sigma_{ij}^{\mathrm{el}} + \sigma_{ij}^{\mathrm{E}} - \chi Q_{ij} \right] \\ \sigma_{ij}^{\mathrm{el}} =& \mu(2u_{ij} - u_{kk}\delta_{ij}) + K u_{kk}\delta_{ij}, \\ \sigma_{ij}^{\mathrm{E}} =& 2\kappa_1 Q_{kl,k} Q_{jl,i} + \kappa_2 Q_{kl,i} Q_{kl,j} \end{aligned}$$

χ is an activity parameter (or function)

Nematic dynamics:

$$\eta^{\mathrm{n}} \mathcal{D}_{ijkl} Q_{kl} = h_{ij} + H_{ij}, \qquad h_{ij} = -\delta \mathcal{L}^{\mathrm{n}} / \delta Q_{ij}$$

H_{ij} is a non-equilibrium source of ordering

Active nematic elastomers

Direct feedback: $H_{ij} = \beta(2u_{ij} - u_{kk}\delta_{ij}),\ \chi =$ const

At $\beta > 0$, the medium polarises in the direction of uniaxial stretch or normally to the direction of uniaxial compression

concentration-dependent feedback: $H_{ij} = \beta(2\rho_{,ij} - \Delta\rho\,\delta_{ij})$

$$\mathrm{D}_t\rho = D\Delta\rho + C(1-\rho) + \gamma u_{ii}$$

ρ is concentration of an active or signaling species

Linear stability analysis

Direct feedback:

Disordered state is stable at $\beta\chi < \mu$

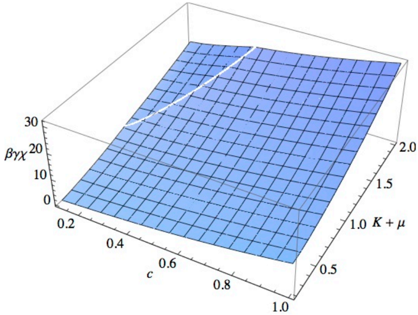
Deformed ordered state is stable at $\beta\chi > \mu$

Quenched state undergoes coarsening

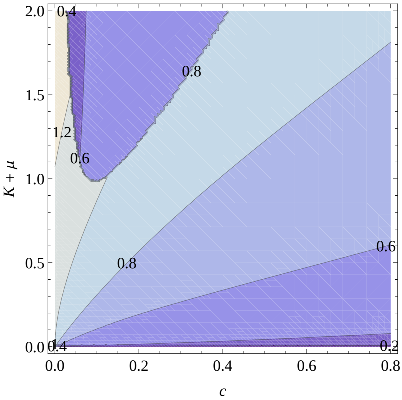
concentration-dependent feedback:

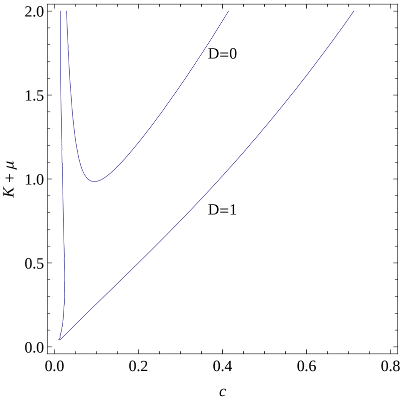
Monotonic instability at $\beta\gamma\chi < -(\mu + K)(C + D + 2\sqrt{CD})$ on a finite wavenumber $k = \sqrt{C/D}$

Wave instability at positive $\beta\gamma\chi$

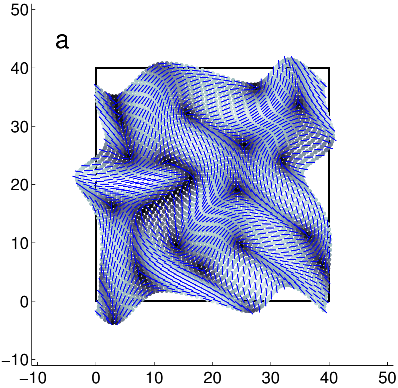


Wavenumber jump

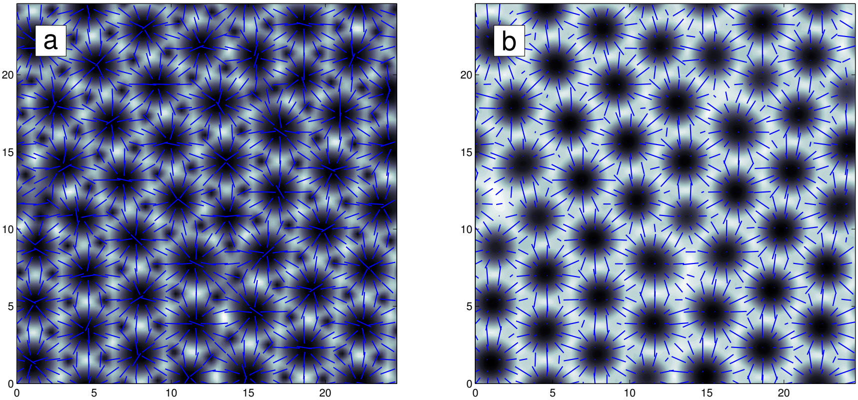




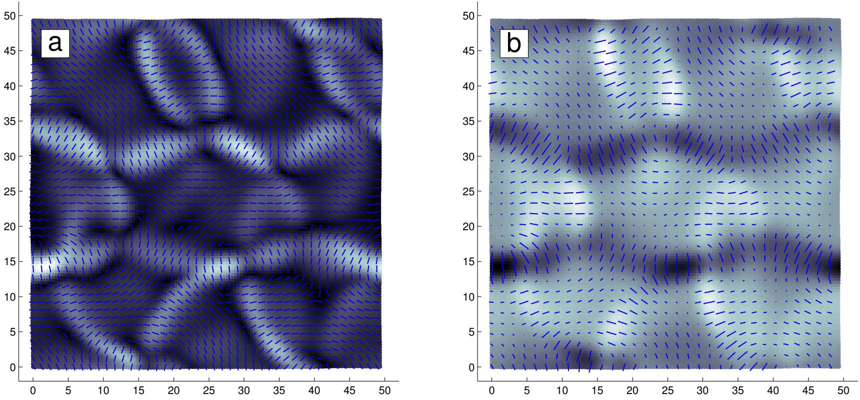
Coarsening



Stationary pattern



Wave pattern



Summary & Remarks: nematic media

- Deformation and ordering in doped nematic elastomers are described by a model with weakly nonlinear elasticity and couplings between $\mathbf{X}$, $\mathbf{Q}$, and concentration
- A biphasic region between isotropic and nematic phases emerges at temperatures below NIT
- Development of the patterns in biphasic region depends on the material properties, in particular, on anisotropic plasticity quantified by the parameter g and the coupling between the gradients of concentration and nematic alignment quantified by the parameter β
- The patterns undergo slow coarsening
- Two models of active elastomers: coarsening, stationary and wave patterns

This work was funded by the Human Frontier Science Program

Thank you for your attention!