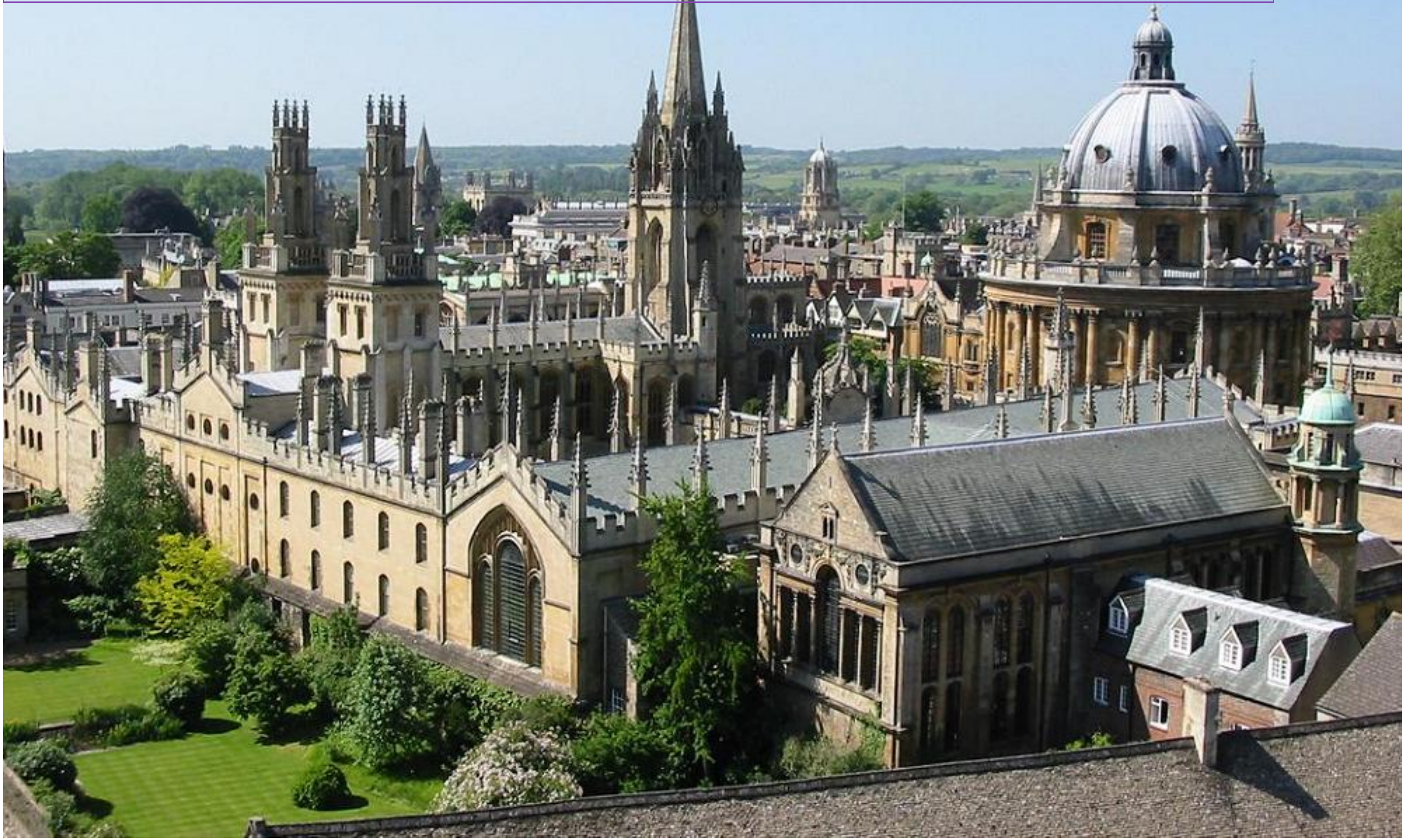
Topology in Biology

Julia Yeomans
University of Oxford



Amin Doostmohammadi
University of Oxford

Tyler Shendruk
Oxford =>Rockefeller

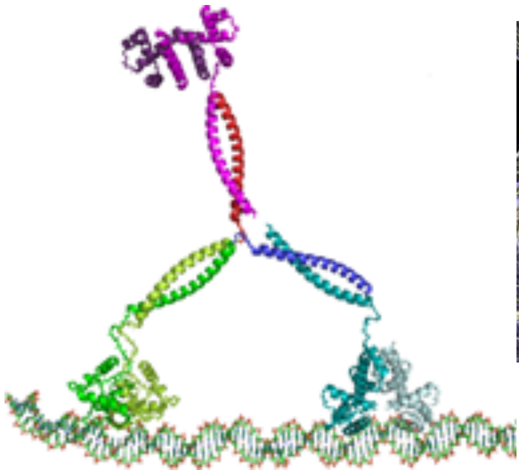
Kristian Thyssen
Eindhoven

Sumesh Thampi
Matthew Blow
Benoit Ladoux
Thuan Beng Saw
Vincent Nier
Philippe Marcq

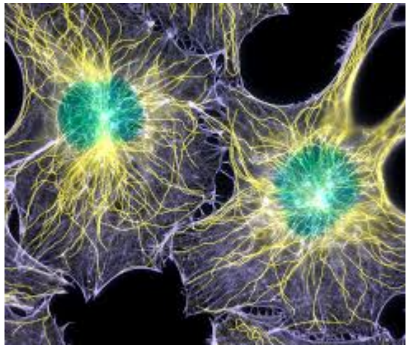
Funding: ERC

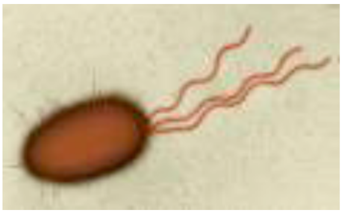
Active particles convert energy to motion

Energy enters the system on a single particle level

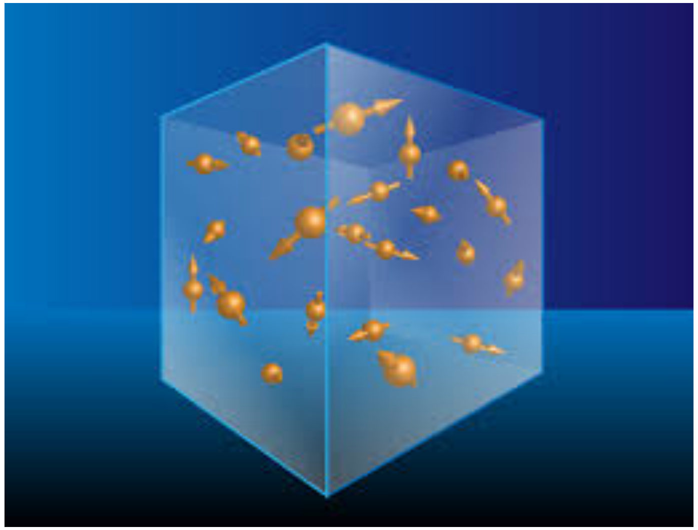


molecular motors





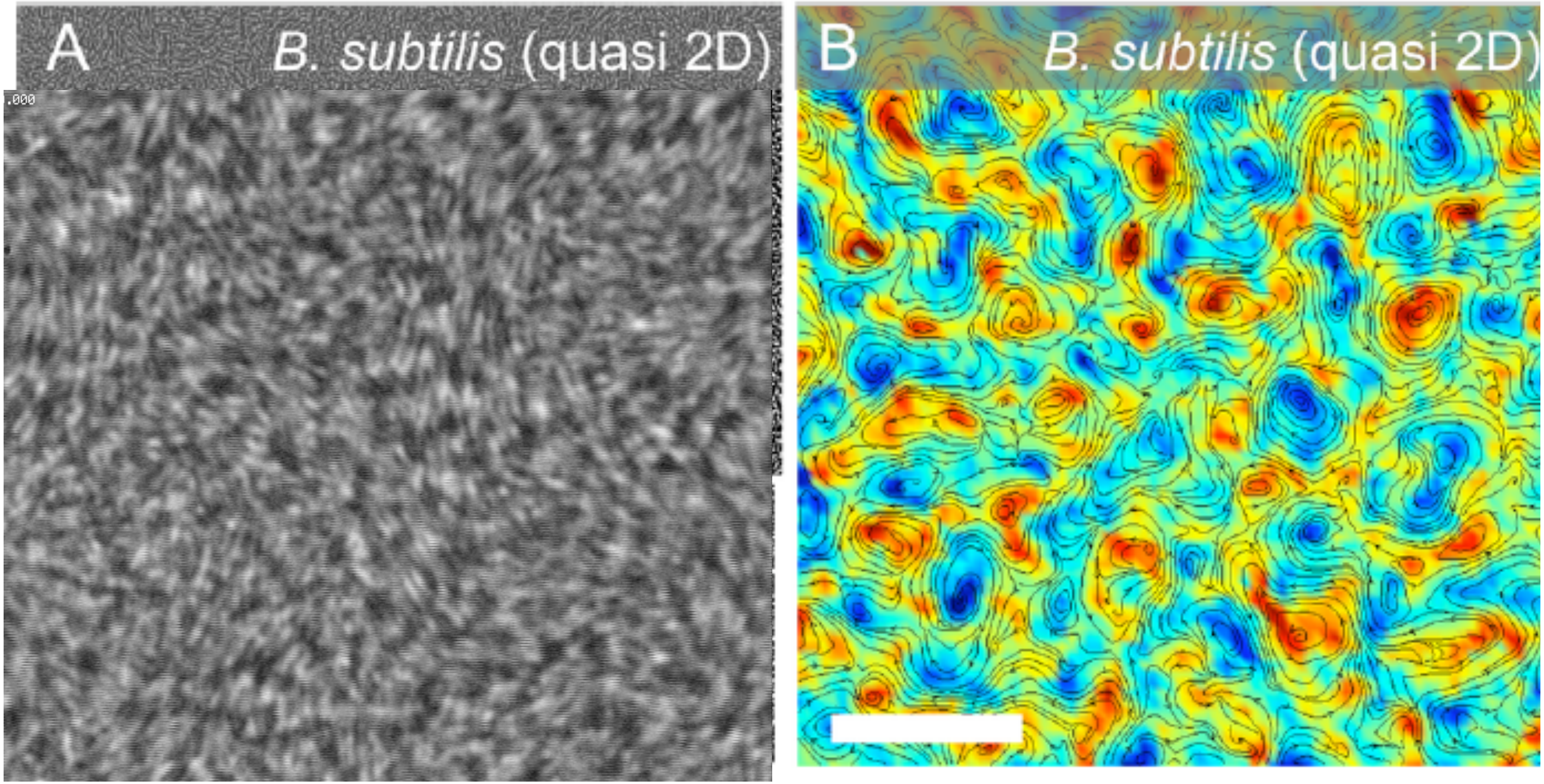
cells



active colloids

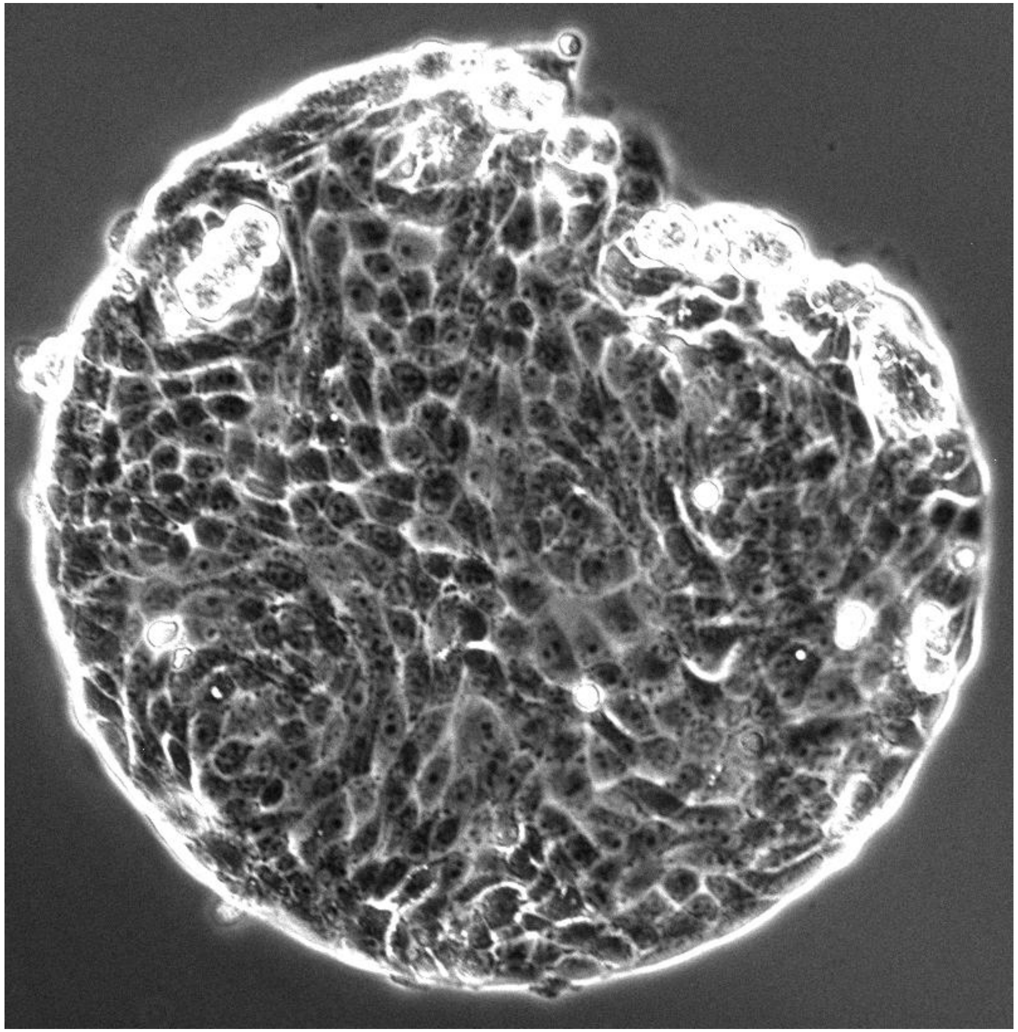
Active turbulence

vorticity



Wensink, Dunkel, Heidenreich, Dresher, Goldstein, Lowen, Yeomans, PNAS 2012

Active turbulence of cells?



1. Dense active matter and active turbulence

2. Confining active matter

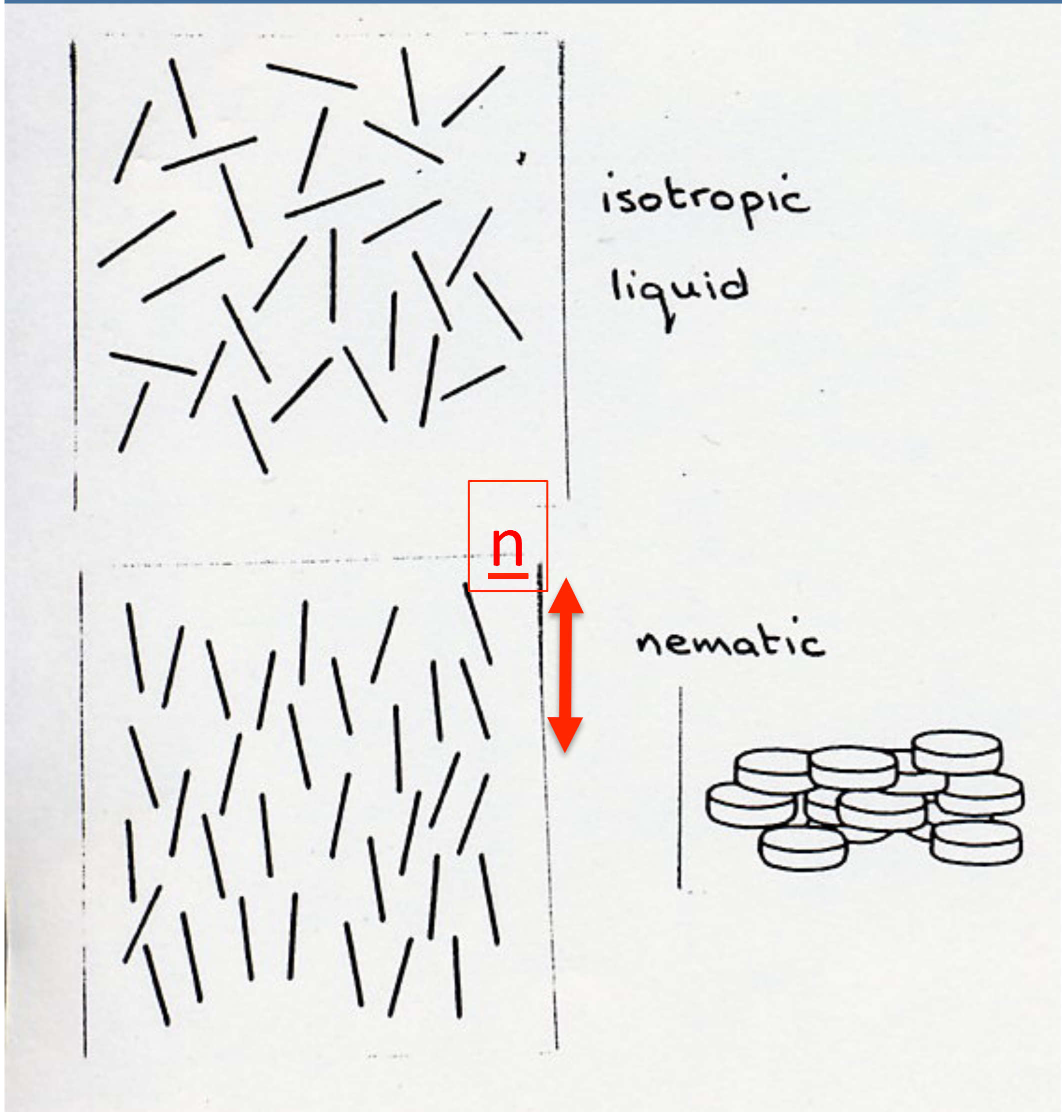
   Ceilidh dance and transition to active turbulence

3. Cells as active nematics

   Topological defects in confluent cell layers

4. Cells in channels

Liquid crystals

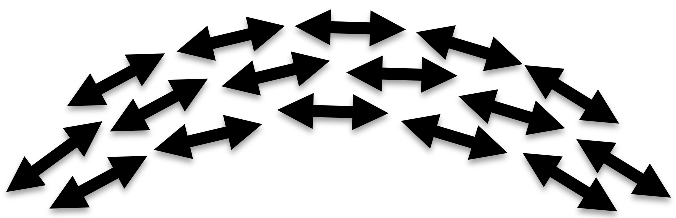


nematic symmetry

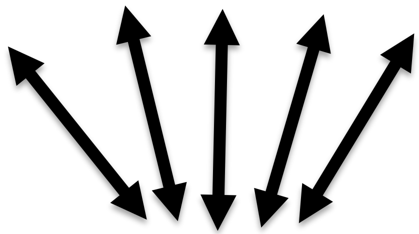
nematic order parameter n
tensor order parameter Q

$$Q_{ij} = \langle n_i n_j - \frac{\delta_{ij}}{3} \rangle$$

Viscoelastic



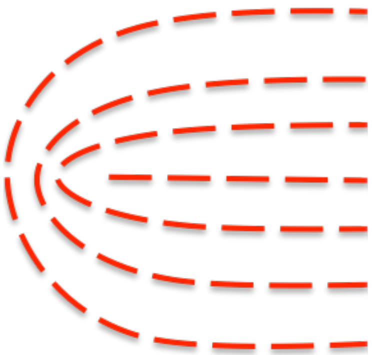
Bend



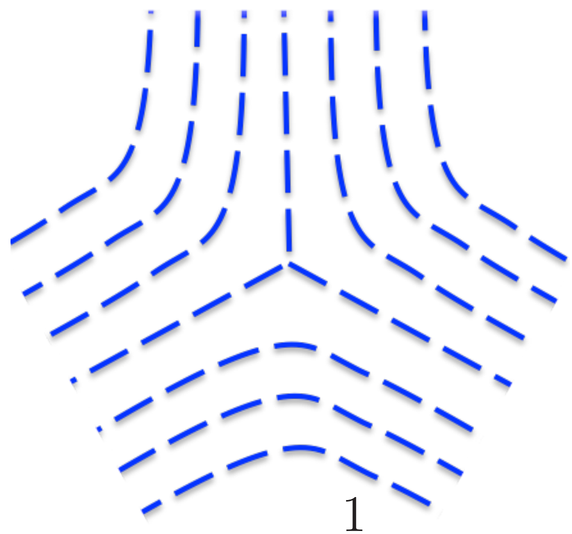
Splay

$$\mathcal{F} = K(\partial_k Q_{ij})^2/2 + AQ_{ij}Q_{ji}/2 + BQ_{ij}Q_{jk}Q_{ki}/3 + C(Q_{ij}Q_{ji})^2/4$$

Topological defects



$m = +\frac{1}{2}$



$m = -\frac{1}{2}$

Continuum equations of liquid crystal hydrodynamics

$$(\partial_t + u_k \partial_k) Q_{ij} - S_{ij} = \Gamma H_{ij}$$

$$S_{ij} = (\lambda E_{ik} + \Omega_{ik})(Q_{kj} + \delta_{kj}/3) +$$

$$(Q_{ik} + \delta_{ik}/3)(\lambda E_{kj} - \Omega_{kj}) - 2\lambda(Q_{ij} + \delta_{ij}/3)(Q_{kl}\partial_k u_l)$$

$$E_{ij} = (\partial_i u_j + \partial_j u_i)/2$$

$$\Omega_{ij} = (\partial_j u_i - \partial_i u_j)/2$$

$$H_{ij} = -\delta \mathcal{F}/\delta Q_{ij} + (\delta_{ij}/3)\mathrm{Tr}(\delta \mathcal{F}/\delta Q_{kl})$$

$$\mathcal{F} = K(\partial_k Q_{ij})^2/2 + AQ_{ij}Q_{ji}/2 + BQ_{ij}Q_{jk}Q_{ki}/3 + C(Q_{ij}Q_{ji})^2/4$$

Continuum equations of liquid crystal hydrodynamics

$$\rho(\partial_t + u_k\partial_k)u_i = \partial_j\Pi_{ij}$$

$$\Pi_{ij}^{viscous} = 2\mu E_{ij}$$

$$\begin{aligned}\Pi_{ij}^{passive} = & -P\delta_{ij} + 2\lambda(Q_{ij} + \delta_{ij}/3)(Q_{kl}H_{lk}) - \lambda H_{ik}(Q_{kj} + \delta_{kj}/3) \\ & -\lambda(Q_{ik} + \delta_{ik}/3)H_{kj} - \partial_i Q_{kl}\frac{\delta\mathcal{F}}{\delta\partial_j Q_{lk}} + Q_{ik}H_{kj} - H_{ik}Q_{kj}\end{aligned}$$

Continuum equations of liquid crystal hydrodynamics

$$(\partial_t + u_k \partial_k) Q_{ij} - S_{ij} = \Gamma H_{ij}$$

couples nematic order and shear flows

relaxation to minimum of Landau-de Gennes free energy

$$\rho(\partial_t + u_k \partial_k) u_i = \partial_j \Pi_{ij}$$

viscous + passive

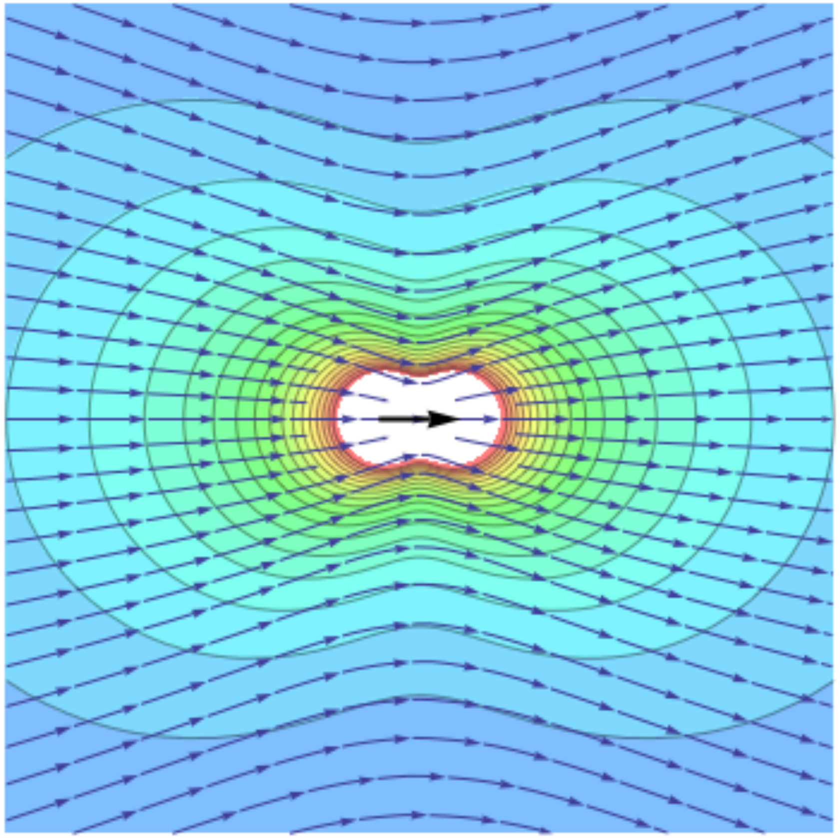
Hydrodynamics of active systems

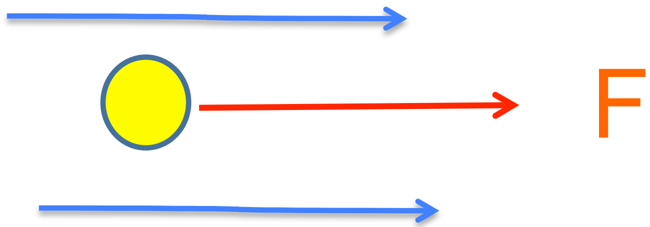
Stokes equations

$$\nabla p = \mu \nabla^2 \mathbf{v} + \mathbf{f}$$

Stokeslet

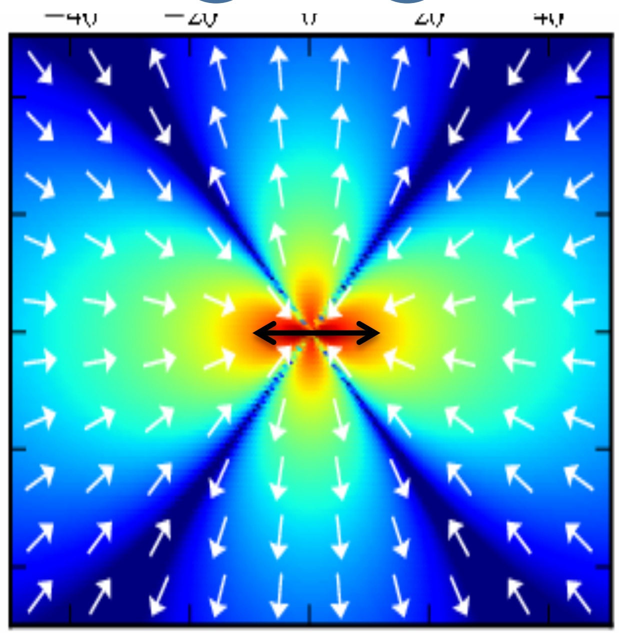
$$\mathbf{v} = \frac{\mathbf{f}}{8\pi\mu} \cdot \left(\frac{\mathbf{I}}{r} + \frac{\mathbf{rr}}{r^3} \right)$$



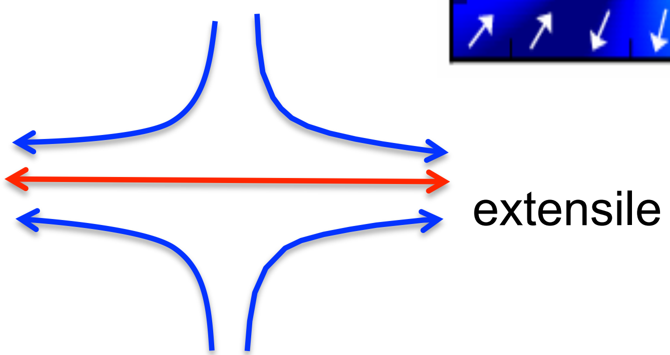


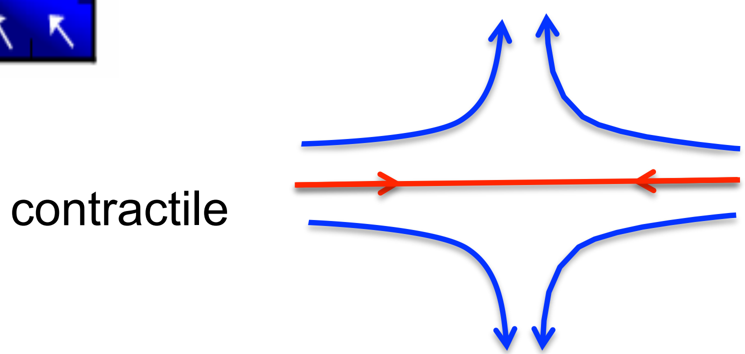
Hydrodynamics of active systems

Swimmers are force free => flow field is dipolar (stresslet)



nematic
symmetry





Continuum equations of liquid crystal hydrodynamics

$$(\partial_t + u_k \partial_k) Q_{ij} - S_{ij} = \Gamma H_{ij}$$

couples nematic order and shear flows

relaxation to minimum of Landau-de Gennes free energy

$$\rho(\partial_t + u_k \partial_k) u_i = \partial_j \Pi_{ij}$$

viscous + passive

Continuum equations of active liquid crystal hydrodynamics

$$(\partial_t + u_k \partial_k) Q_{ij} - S_{ij} = \Gamma H_{ij}$$

couples nematic order and shear flows

relaxation to minimum of Landau-de Gennes free energy

$$\rho(\partial_t + u_k \partial_k) u_i = \partial_j \Pi_{ij}$$

viscous + passive + active stress

$$\Pi_{ij}^{active} = -\zeta Q_{ij}$$

1. Active stress => active turbulence

Active contribution to the stress $-\zeta \mathbf{Q}$

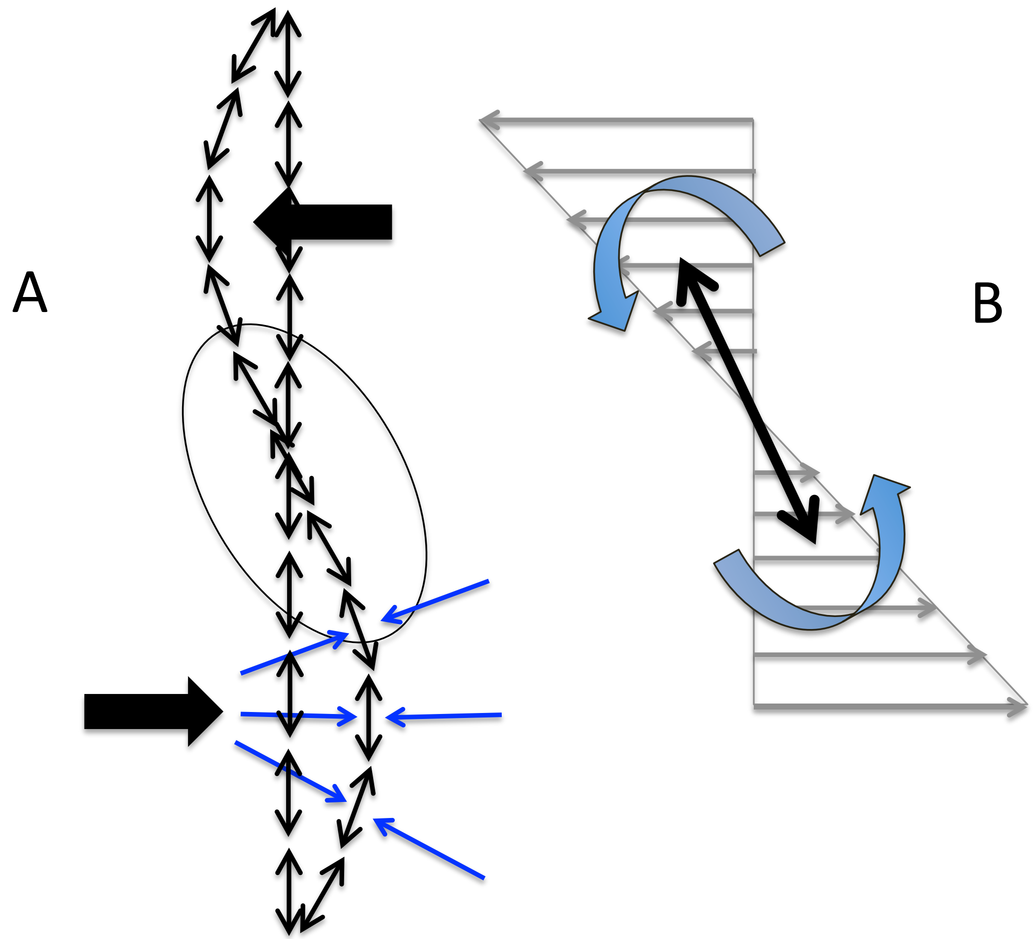
Gradients in the magnitude or direction of the order parameter induce flow.

➡

nematic state is unstable to vortical flows

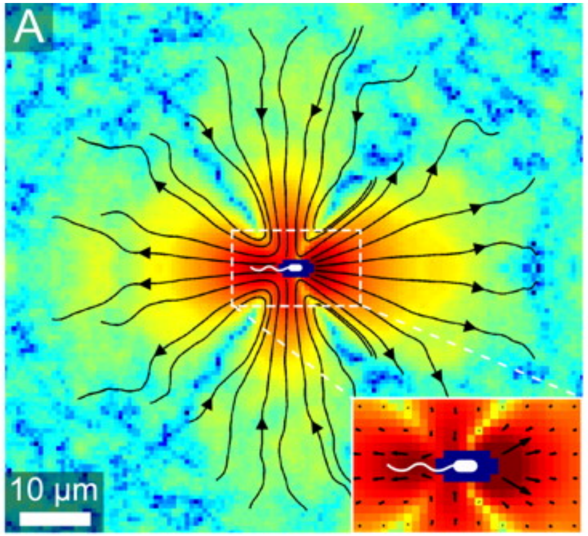
Hatwalne, Ramaswamy, Rao, Simha, PRL 2004

Instabilities in active nematics



Extensile active nematics – unstable to bend deformations
Contractile active nematics – unstable to splay deformations

Active turbulence



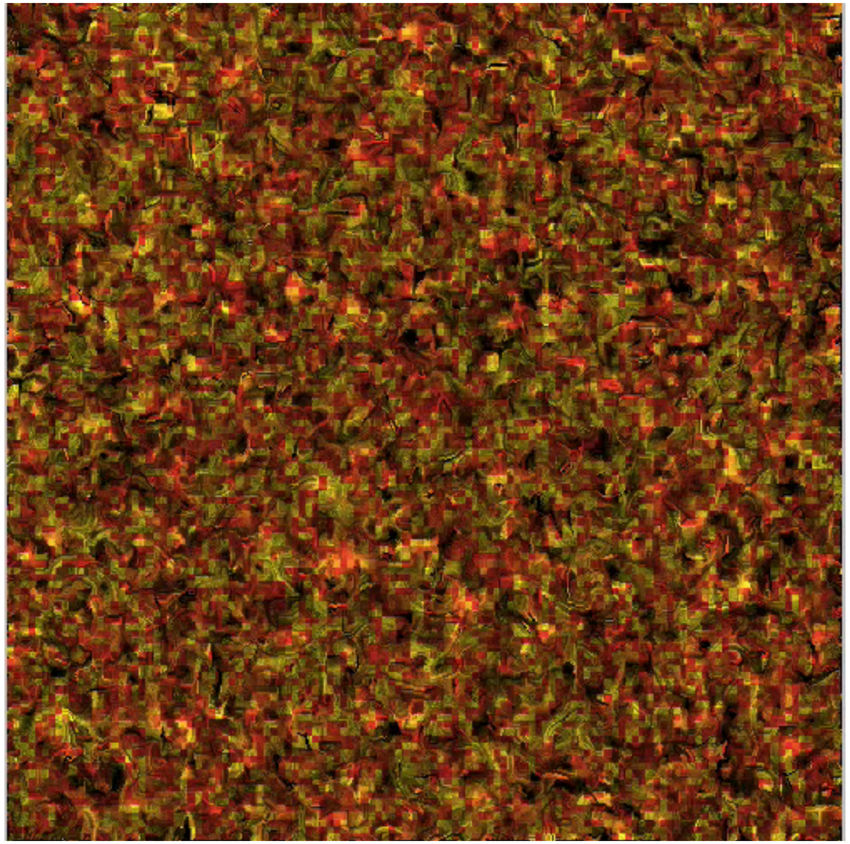
Active systems have nematic symmetry because they are force free

Ordered nematic state is unstable to flow

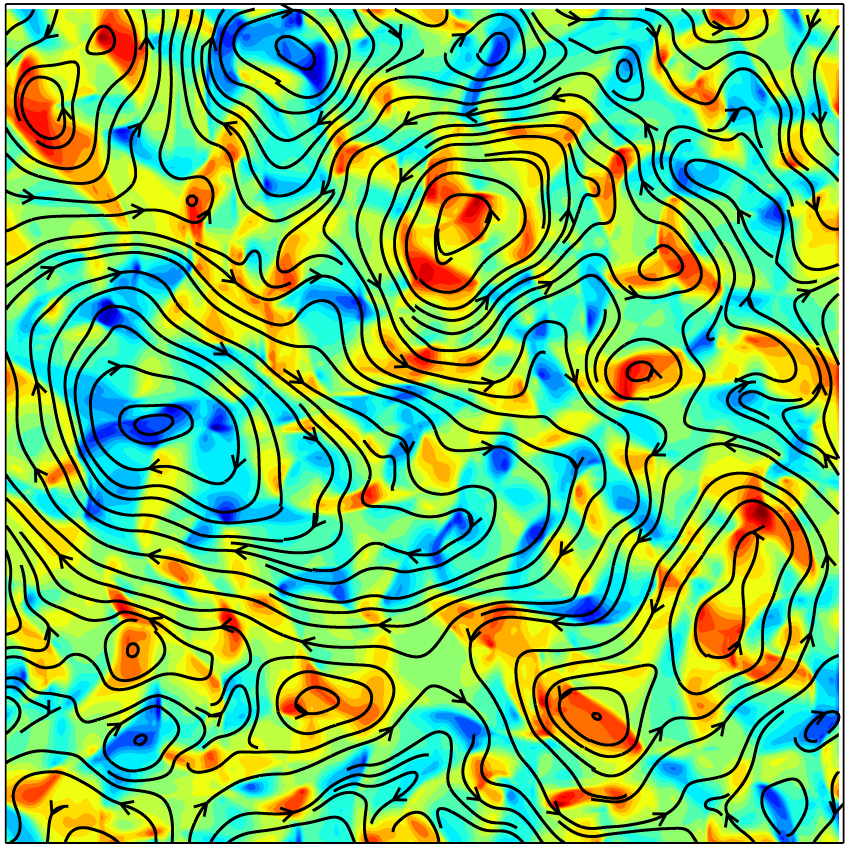
What happens instead is active turbulence

Hatwalne, Ramaswamy, Rao, Simha, PRL 2004

Active turbulence is characterised by

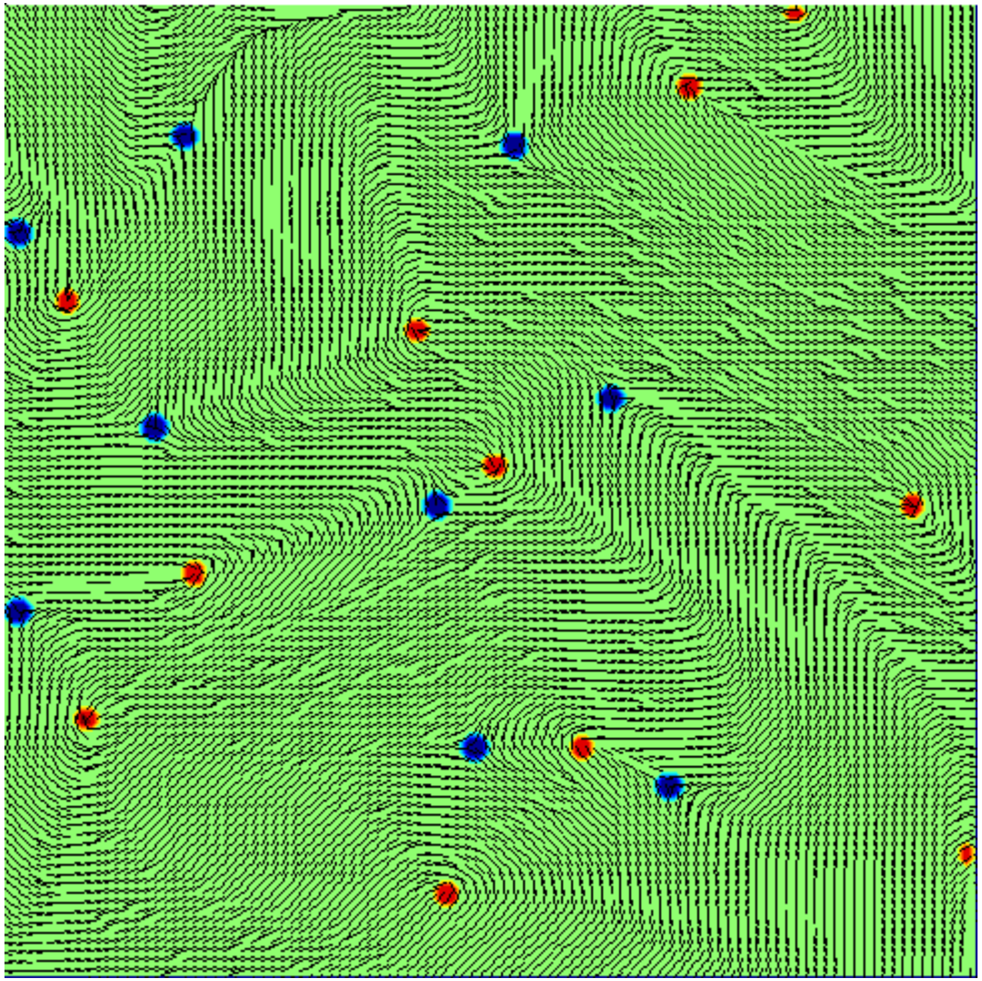


Flow jets

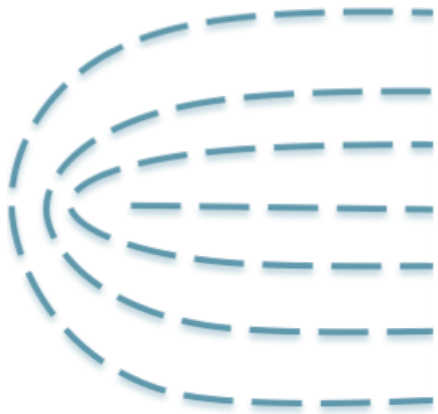


Vorticity

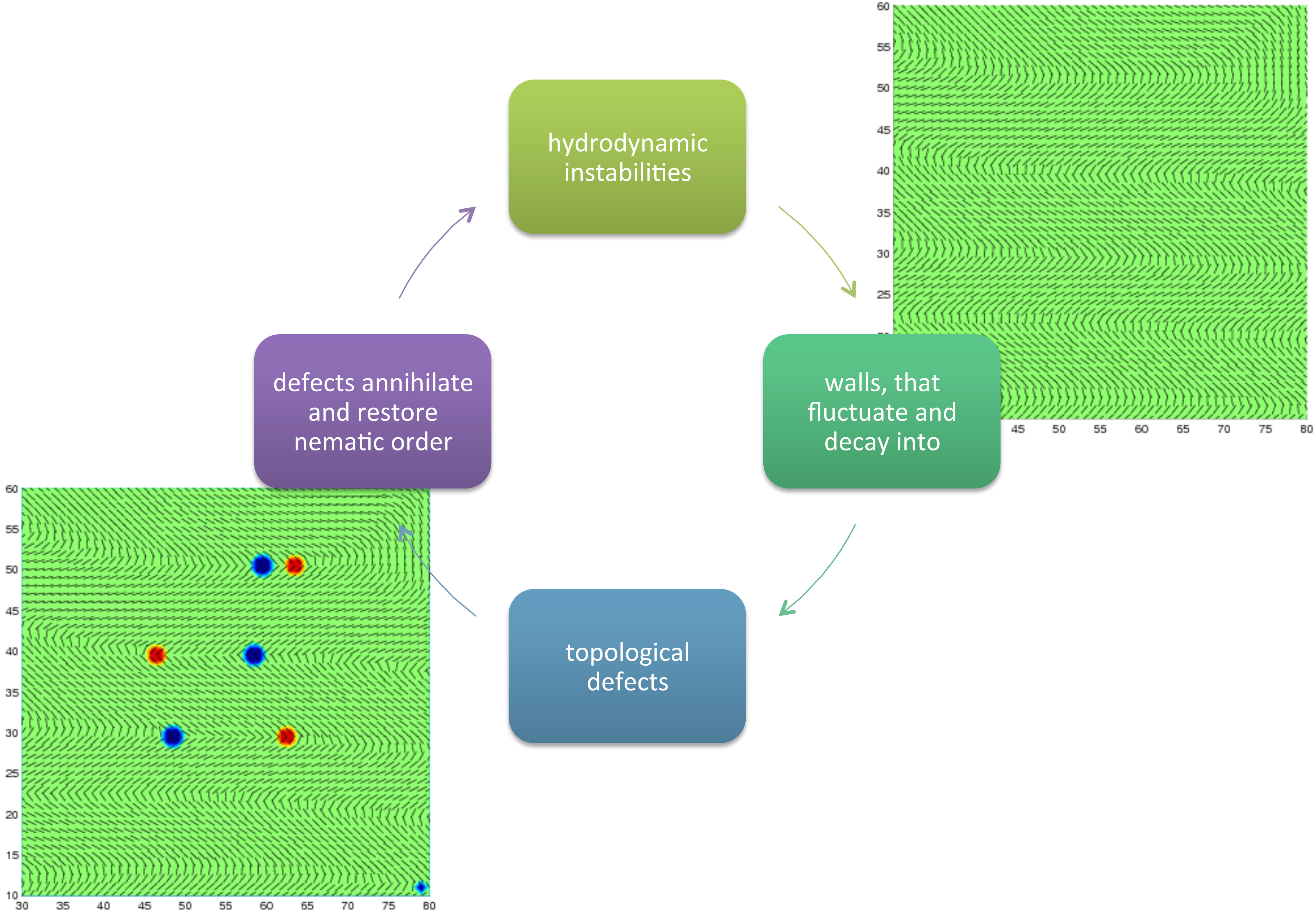
Active turbulence: topological defects are created and destroyed



Topological defects



Active turbulence



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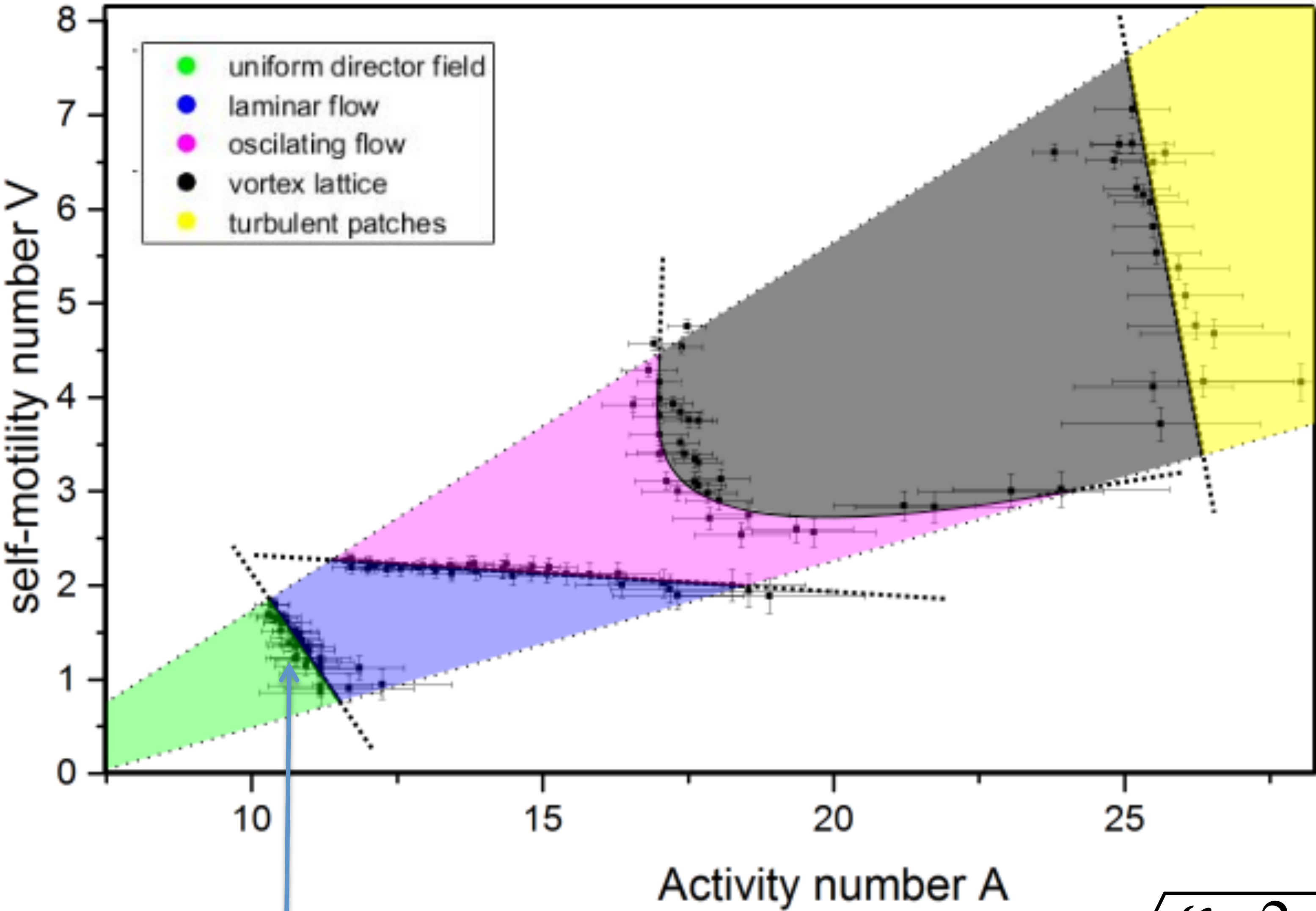
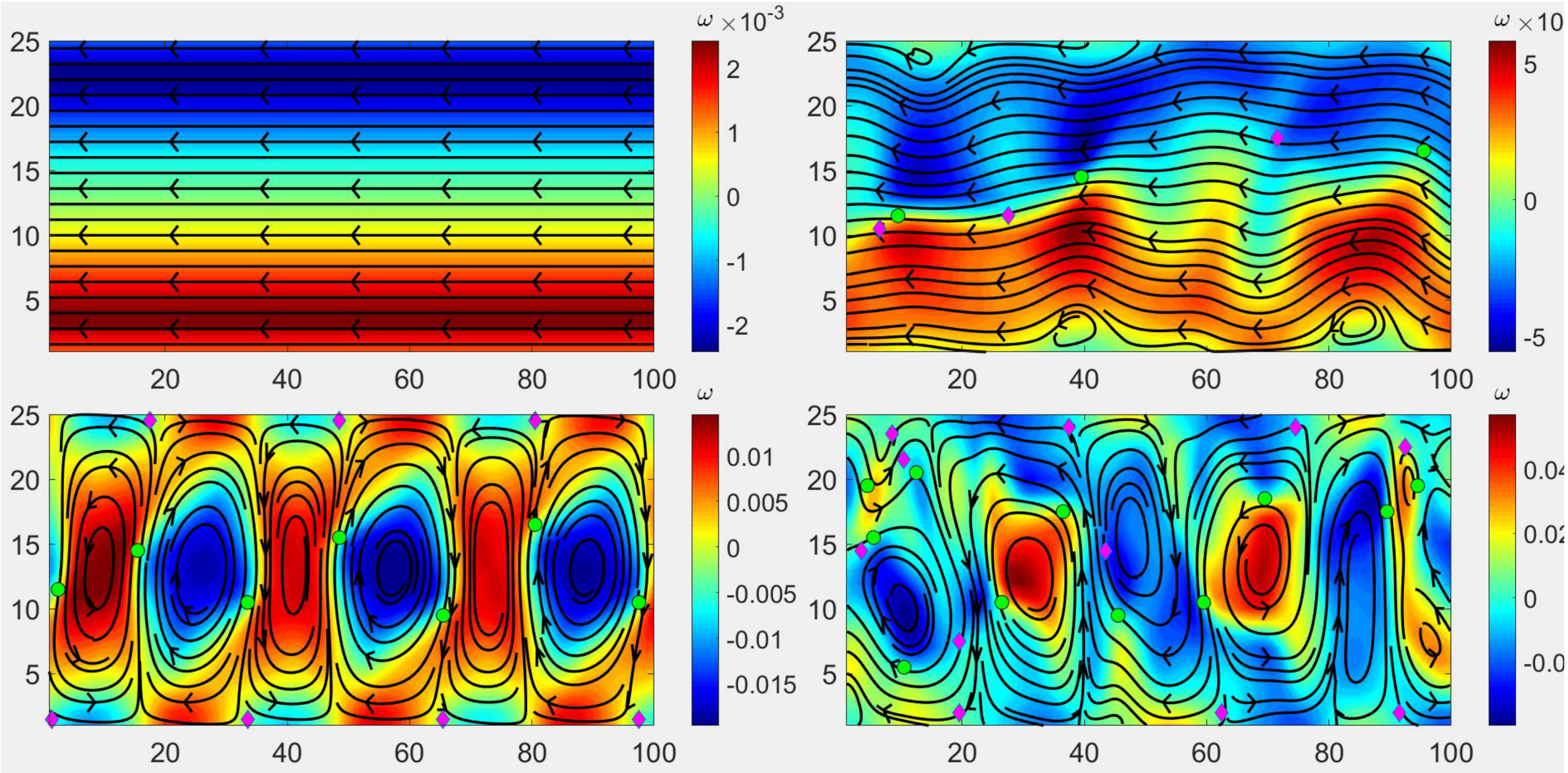
States of an Active Nematic in a Channel



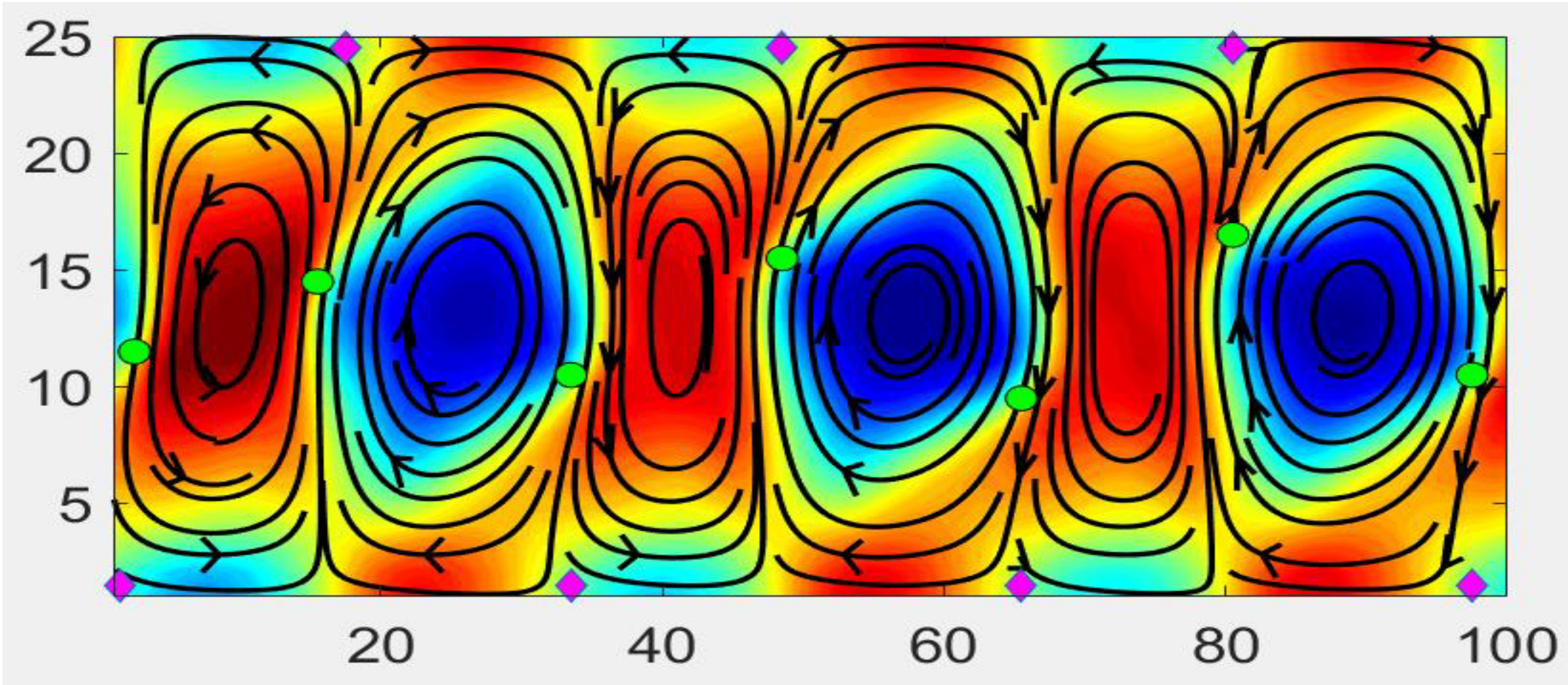
Voituriez et al
EPL (2005)

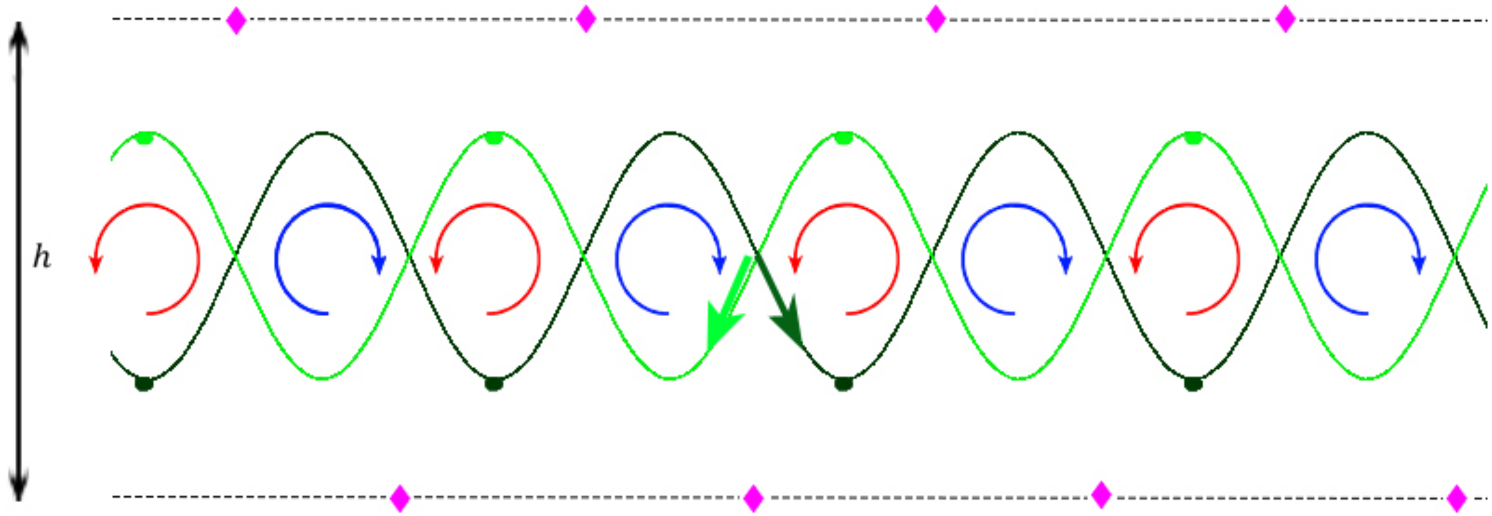
$$= \sqrt{\zeta h^2 / K}$$

States of an Active Nematic in a Channel

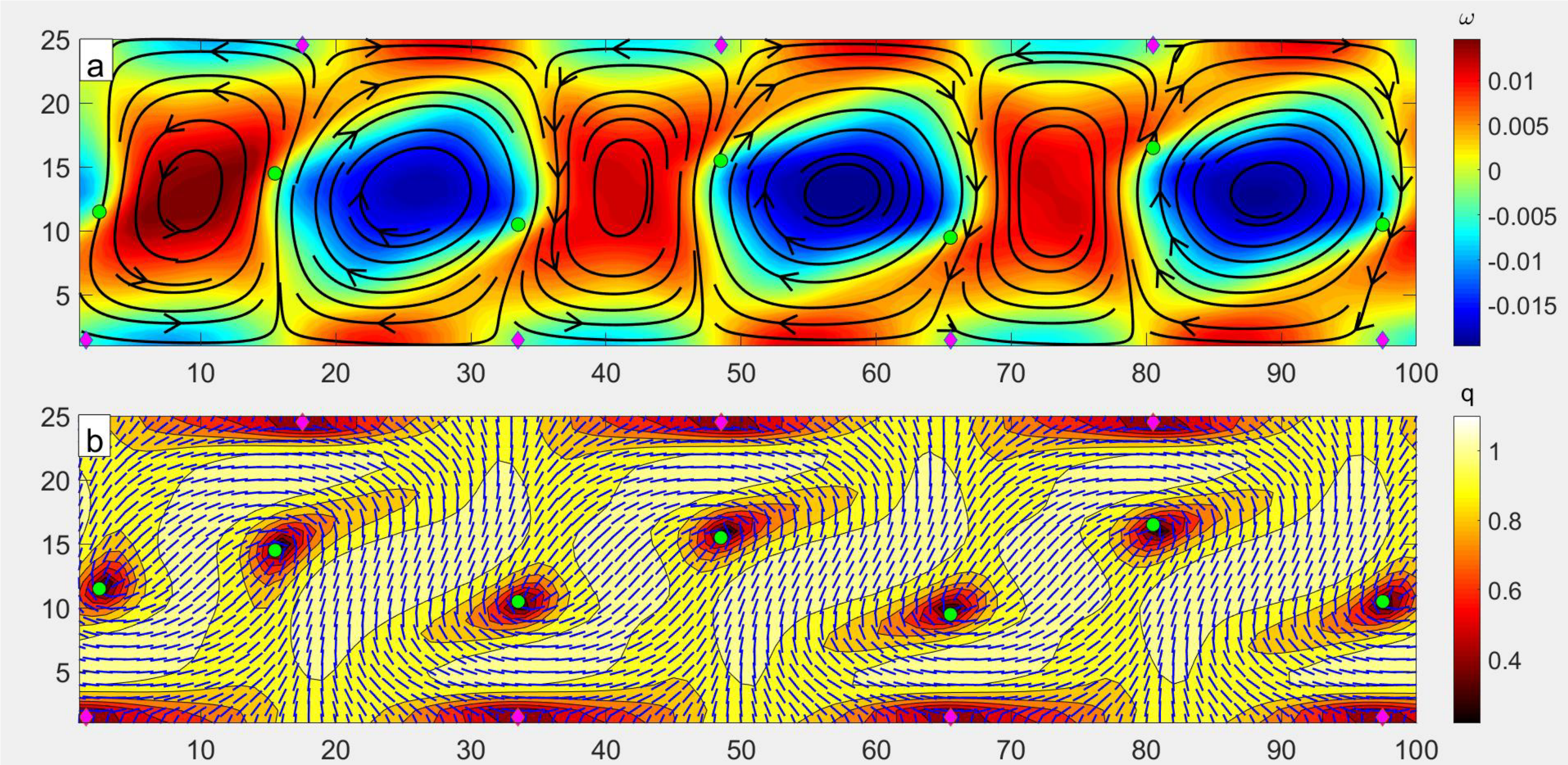


Ceilidh Dance

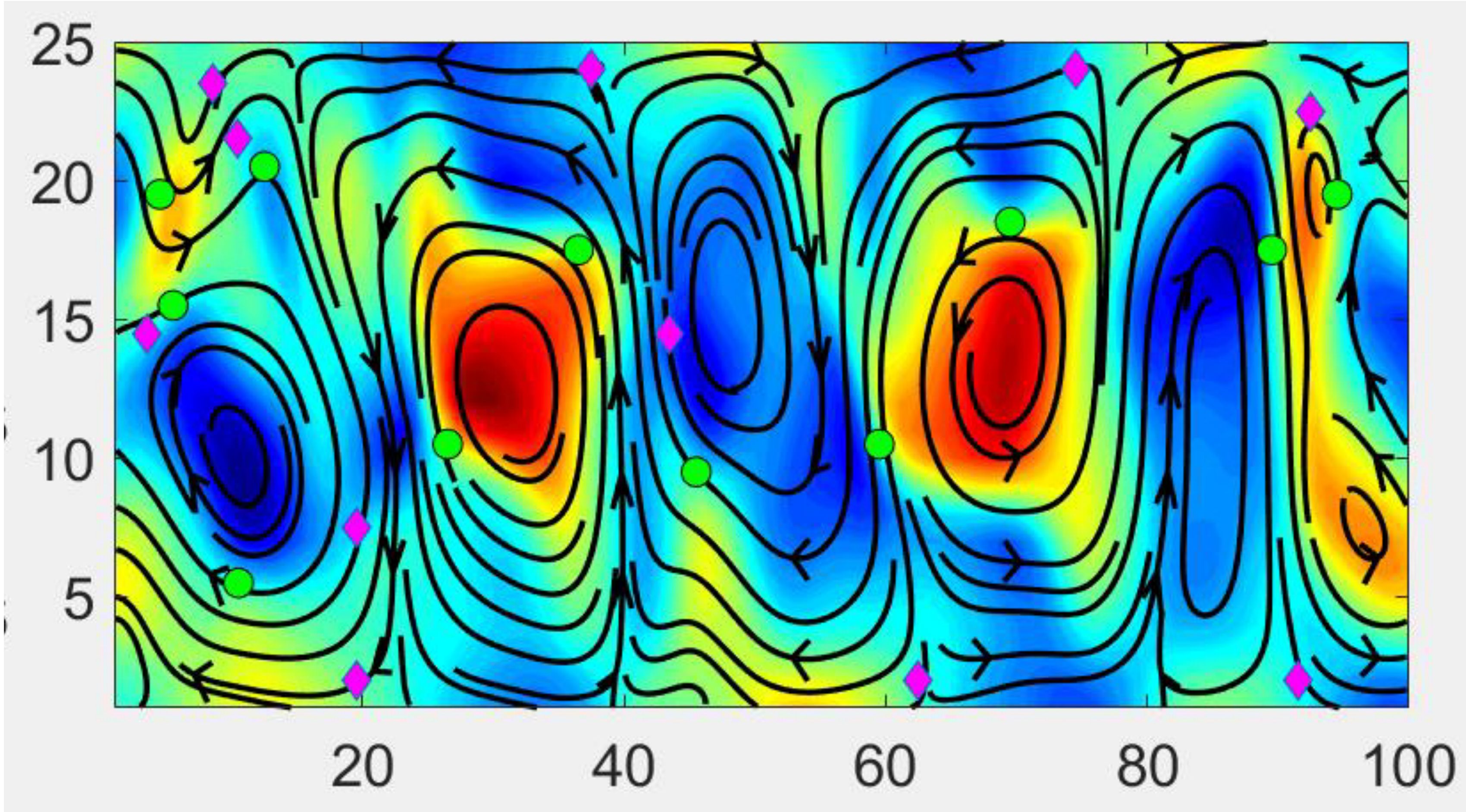




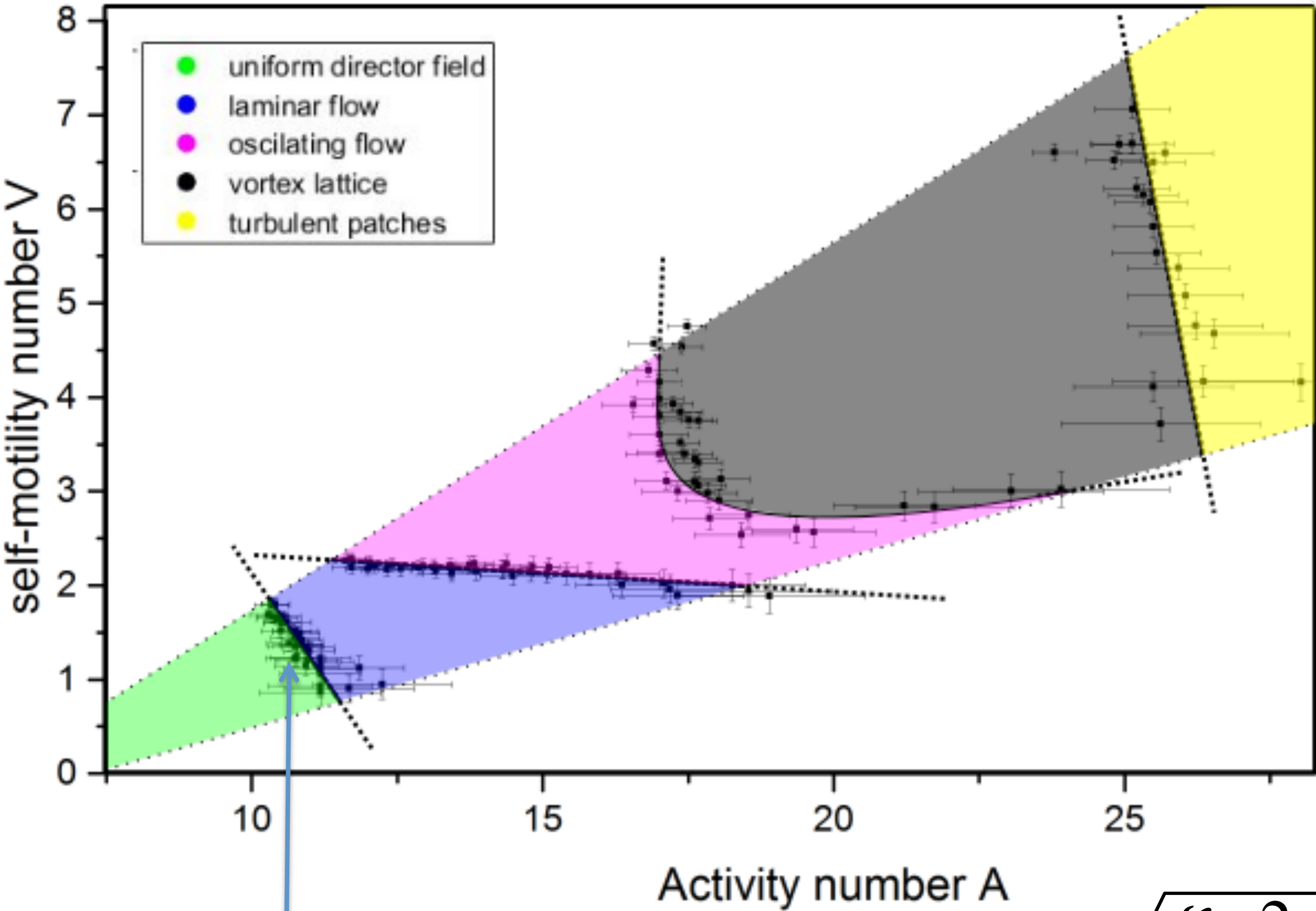
Vortex lattice and active topological microfluidics



Transition to Turbulence



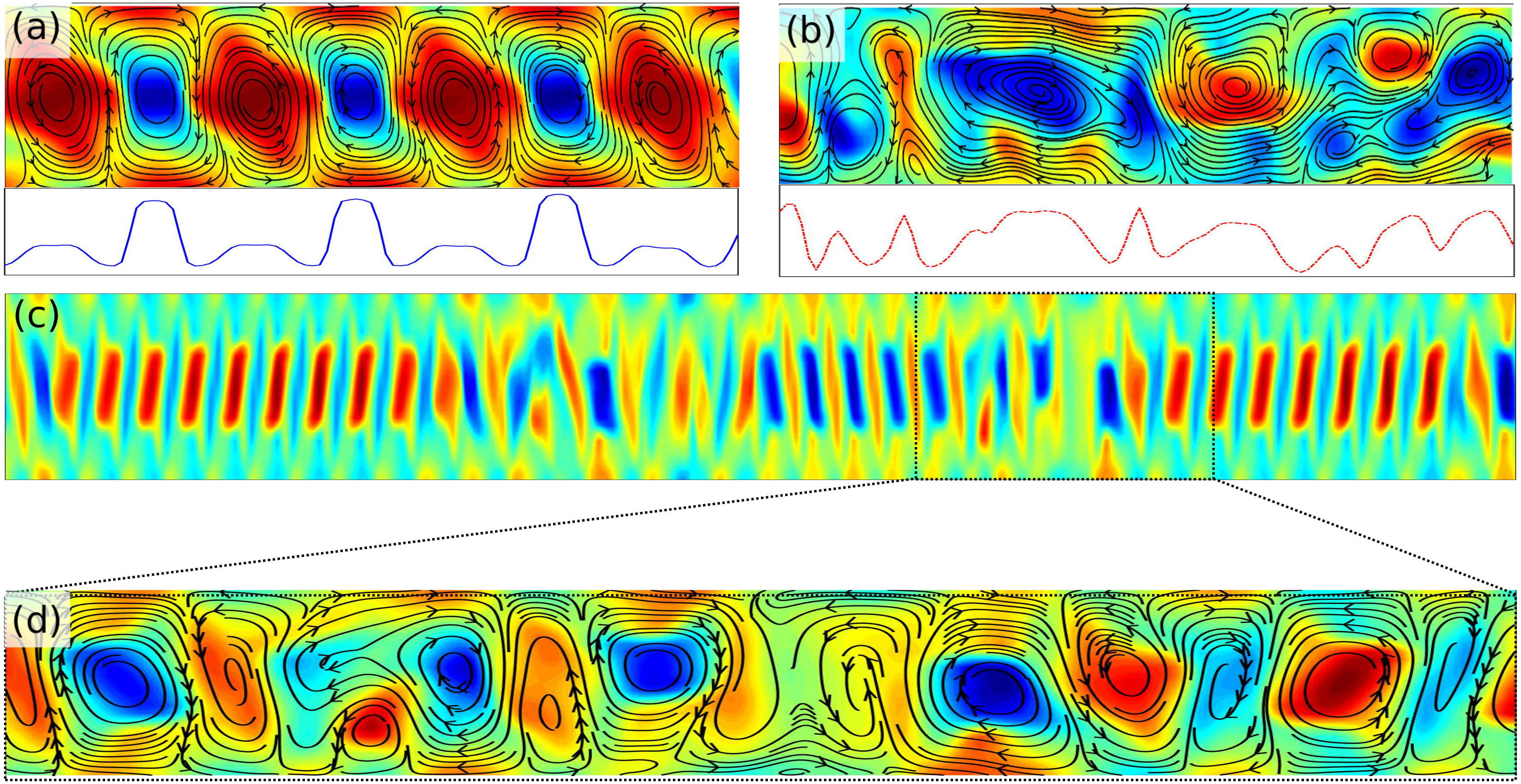
States of an Active Nematic in a Channel



Voituriez et al
EPL (2005)

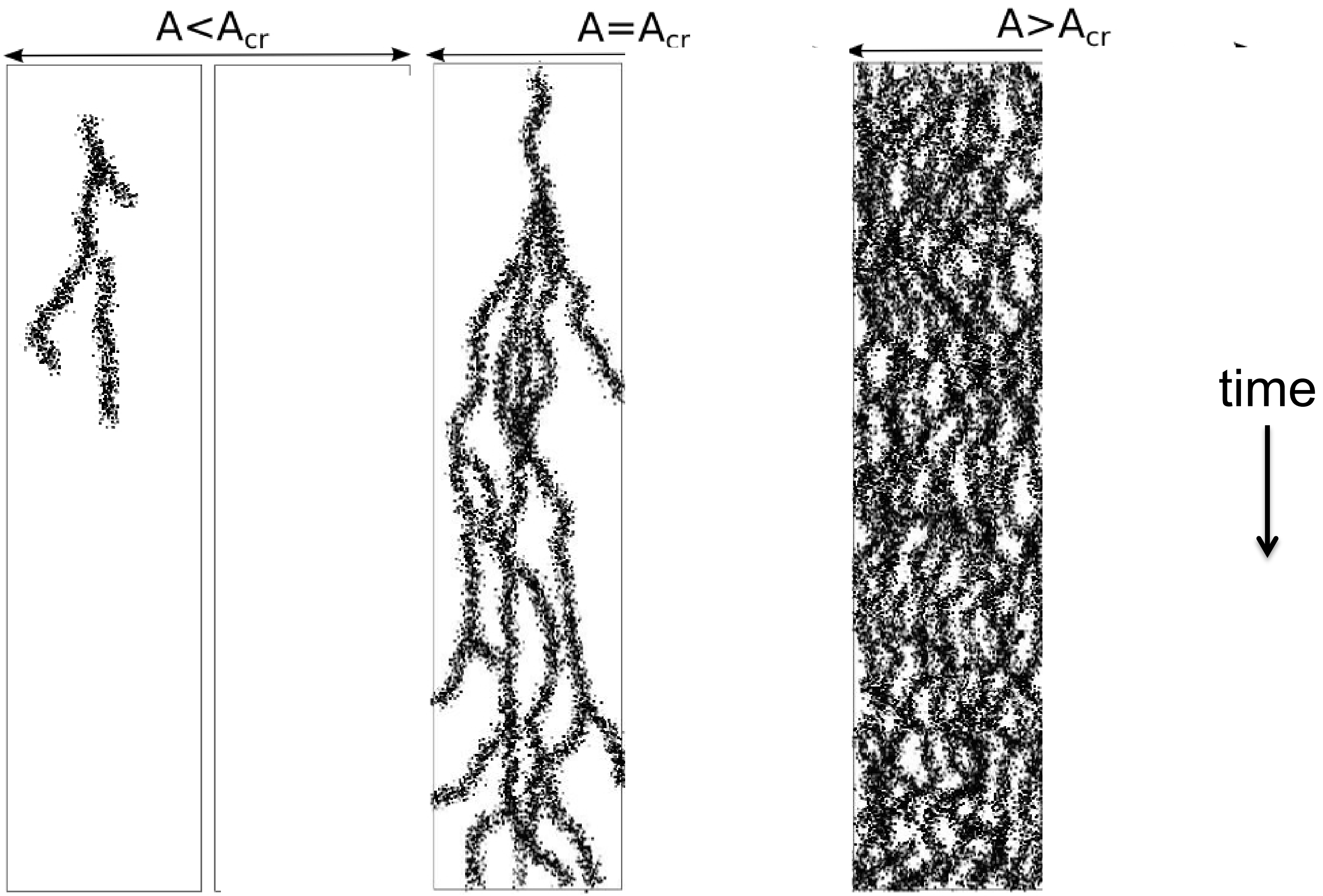
$$= \sqrt{\zeta h^2 / K}$$

Vorticity distribution



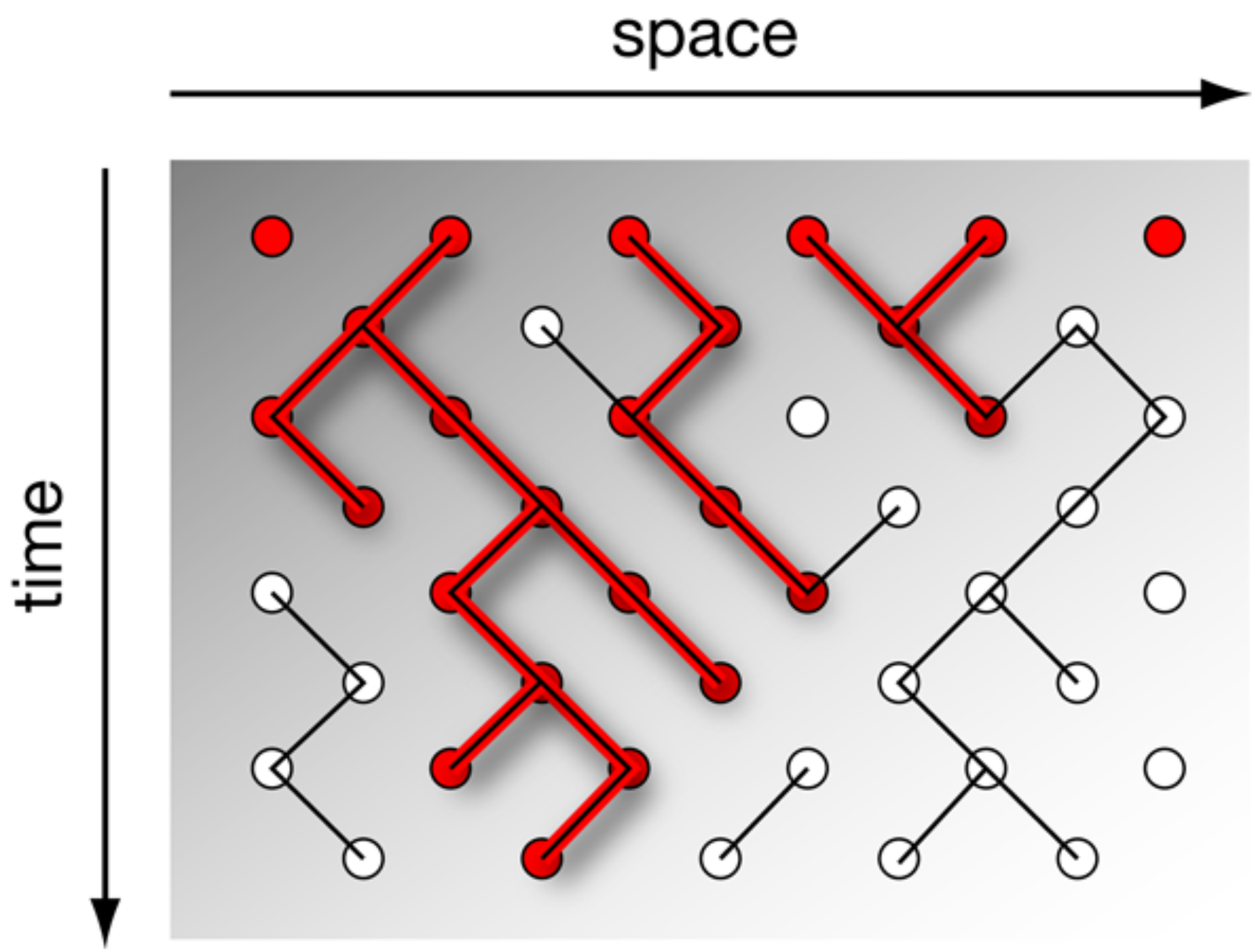
Measure the enstrophy – $|\text{vorticity}|^2$

Enstrophy kymograph



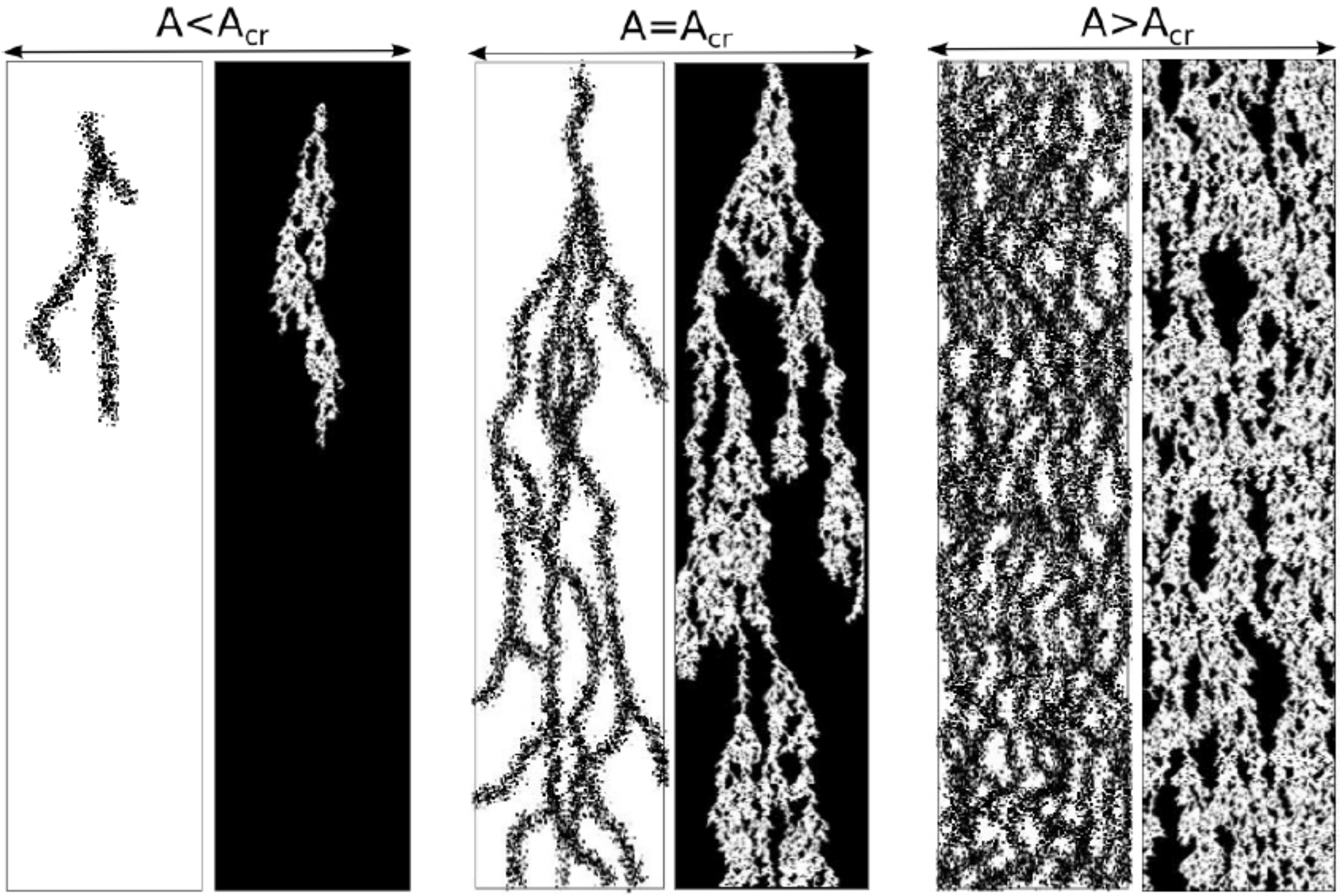
left hand panels: active nematic

Directed percolation



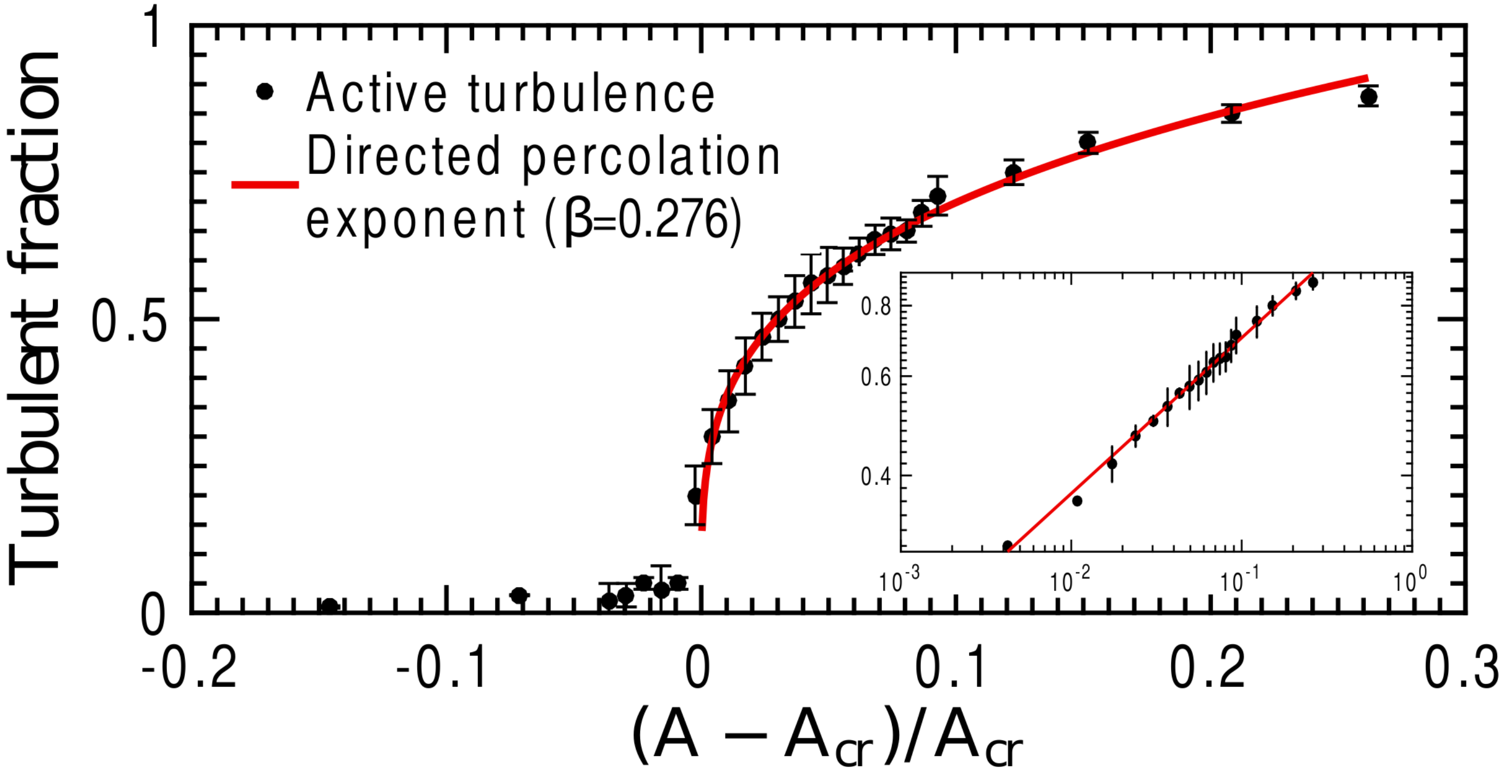
probability p that
a site is occupied

enstrophy kymograph



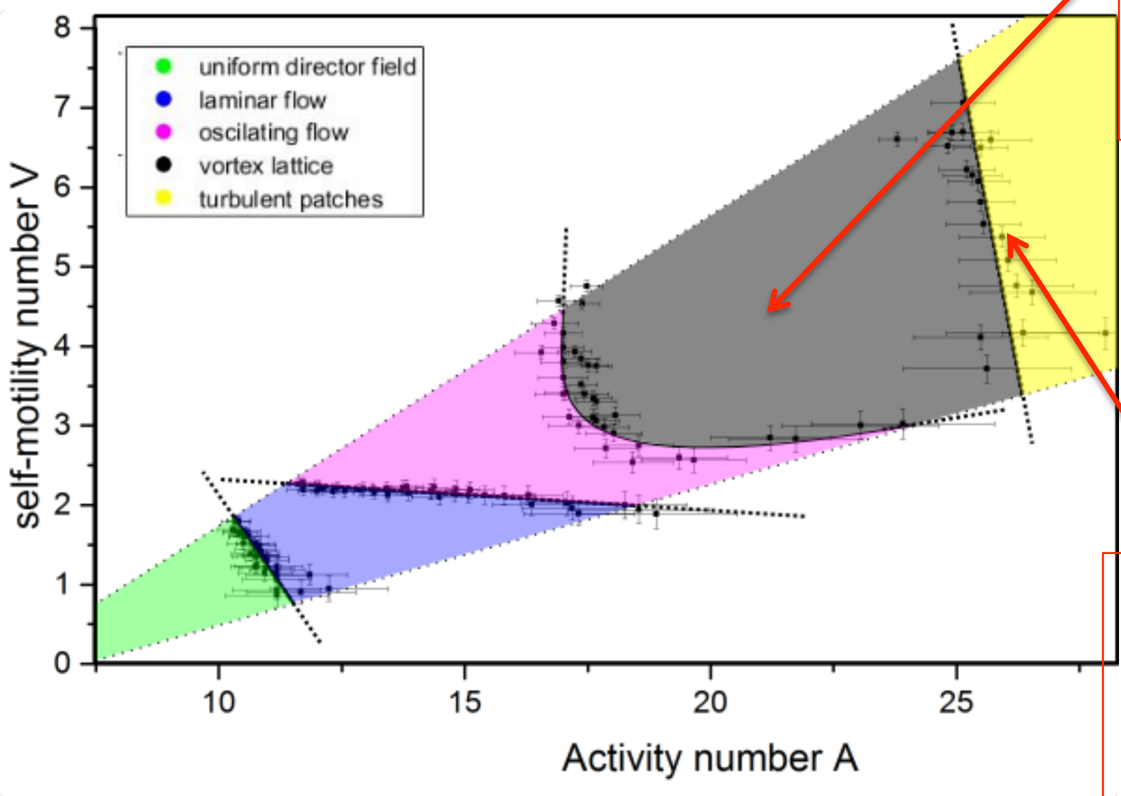
left hand panels: active nematic
right hand panels: directed percolation

Turbulent fraction as a function of activity



Critical exponents	β
Active turbulence at zero-Reynolds number	0.275±0.043
Couette experiments for inertial turbulence (*12*)	0.28±0.03
$(1+1)$ directed percolation (*28*)	0.276

Confinement is a way of harnessing active energy



Ceilidh Dance
Vortex lattice and
disclination orbits

Transition to active
turbulence in the
directed percolation
universality class

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Continuum equations of liquid crystal hydrodynamics

Hydrodynamic variables:
density, concentration, liquid crystal order parameter, velocity

$$(\partial_t + u_k \partial_k) Q_{ij} - S_{ij} = \Gamma H_{ij}$$

Active stress – cells moving

$$\rho(\partial_t + u_k \partial_k) u_i = \partial_j \Pi_{ij}$$

$$\Pi_{ij}^{active} = -\zeta Q_{ij}$$

$\zeta > 0 \Leftrightarrow$ extensile

$\zeta < 0 \Leftrightarrow$ contractile

Continuum equations of lyotropic liquid crystal hydrodynamics

Hydrodynamic variables:
density, concentration, liquid crystal order parameter, velocity

$$(\partial_t + u_k \partial_k) Q_{ij} - S_{ij} = \Gamma H_{ij}$$

Active stress – cells moving

$$\rho(\partial_t + u_k \partial_k) u_i = \partial_j \Pi_{ij}$$

$$\Pi_{ij}^{active} = -\zeta Q_{ij}$$

$$\partial_t \phi + \partial_i (u_i \phi) = \Gamma_\phi \nabla^2 \mu$$

Continuum equations of lyotropic liquid crystal hydrodynamics

Hydrodynamic variables:
density, concentration, liquid crystal order parameter, velocity

$$(\partial_t + u_k \partial_k) Q_{ij} - S_{ij} = \Gamma H_{ij}$$

Active stress – cells moving

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$$\Pi_{ij}^{active} = -\zeta Q_{ij}$$

$$\partial_t \phi + \partial_i (u_i \phi) = \Gamma_\phi \nabla^2 \mu$$

$$+ \alpha \phi$$

Cells dividing

Continuum equations of lyotropic liquid crystal hydrodynamics

Hydrodynamic variables:
density, concentration, liquid crystal order parameter, velocity

$$(\partial_t + u_k \partial_k) Q_{ij} - S_{ij} = \Gamma H_{ij}$$

$$f_0 u_i$$

Friction

$$\rho(\partial_t + u_k \partial_k) u_i = \partial_j \Pi_{ij}$$

Active stress – cells moving

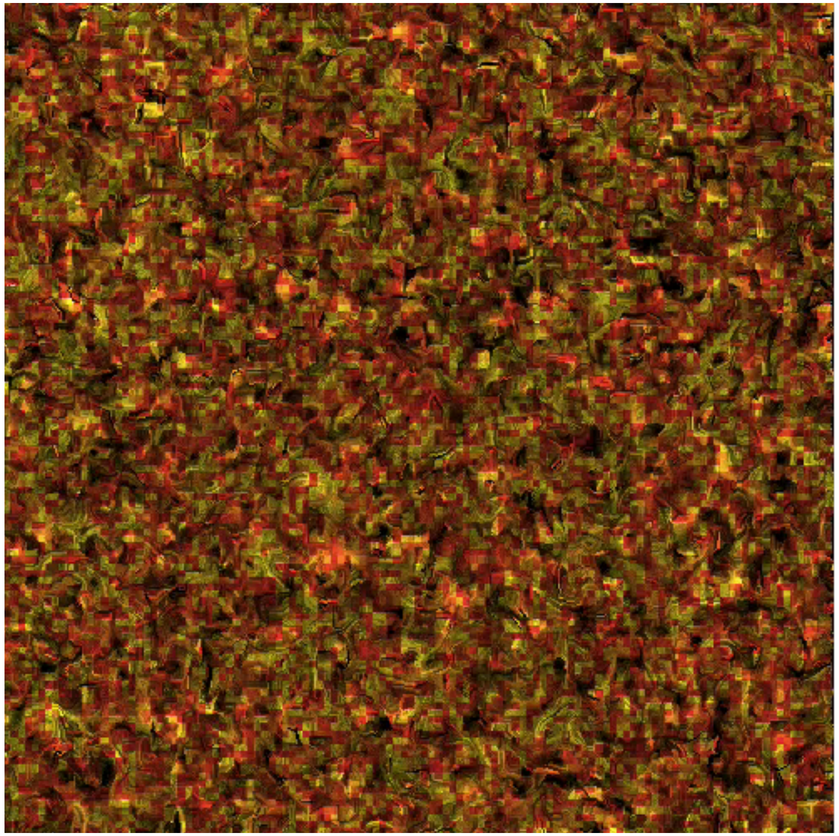
$$\Pi_{ij}^{active} = -\zeta Q_{ij}$$

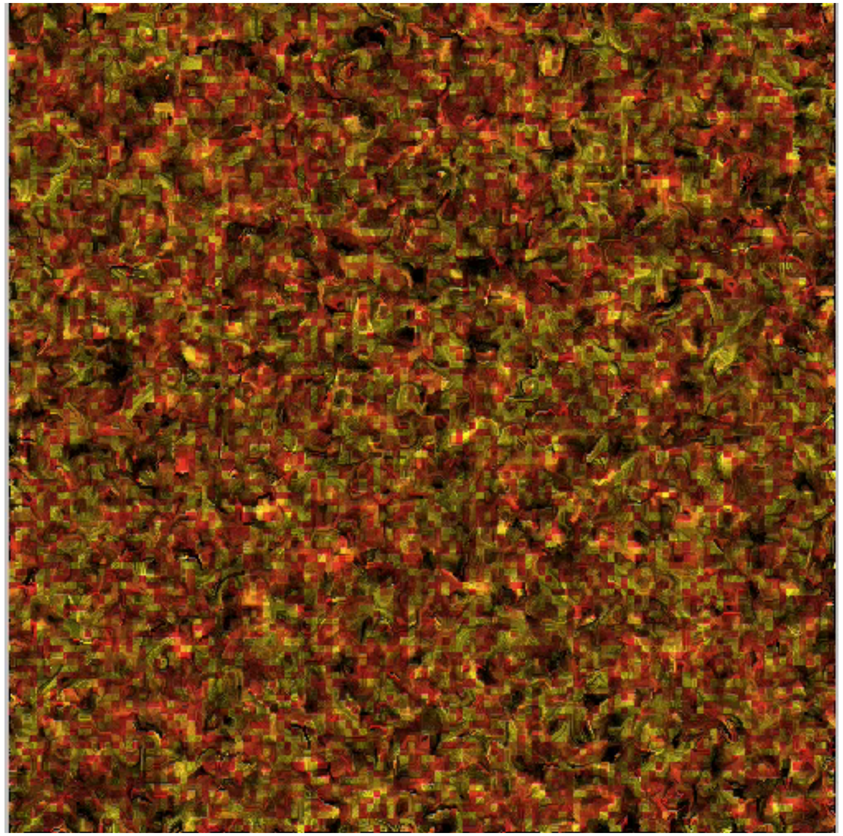
$$\partial_t \phi + \partial_i (u_i \phi) = \Gamma_\phi \nabla^2 \mu$$

$$+ \alpha \phi$$

Cells dividing

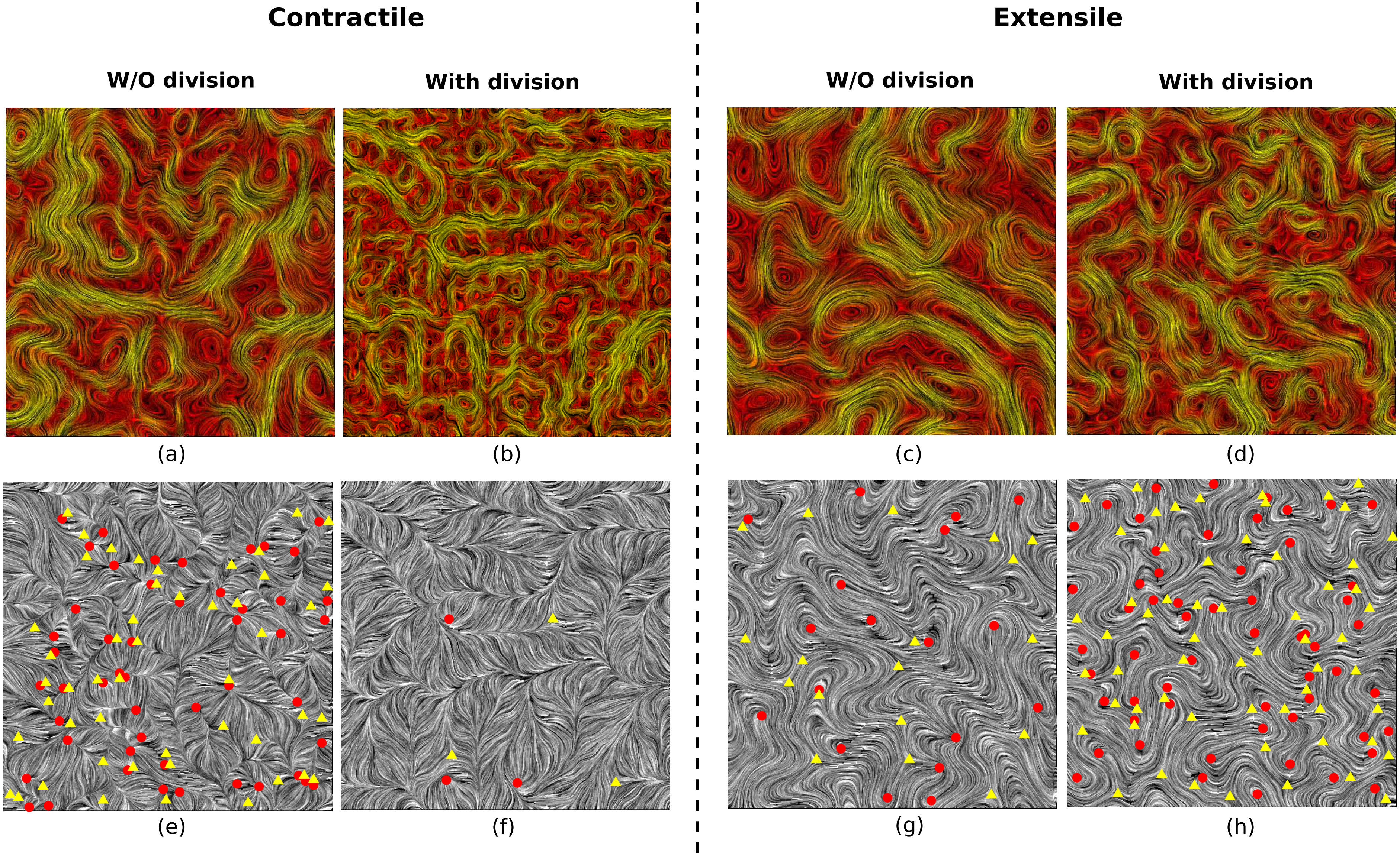
Cell division

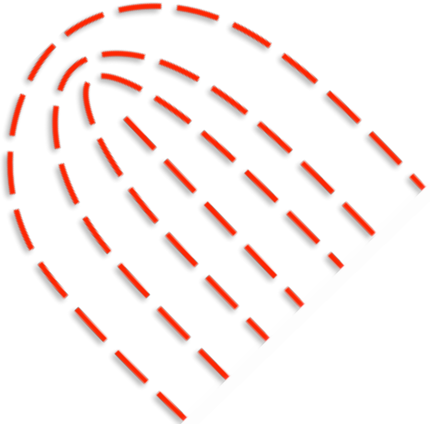




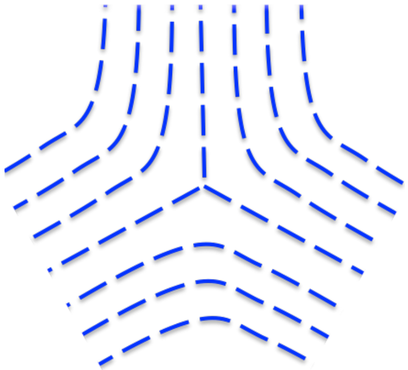
(more division events)

2. Division acts as extensile stress

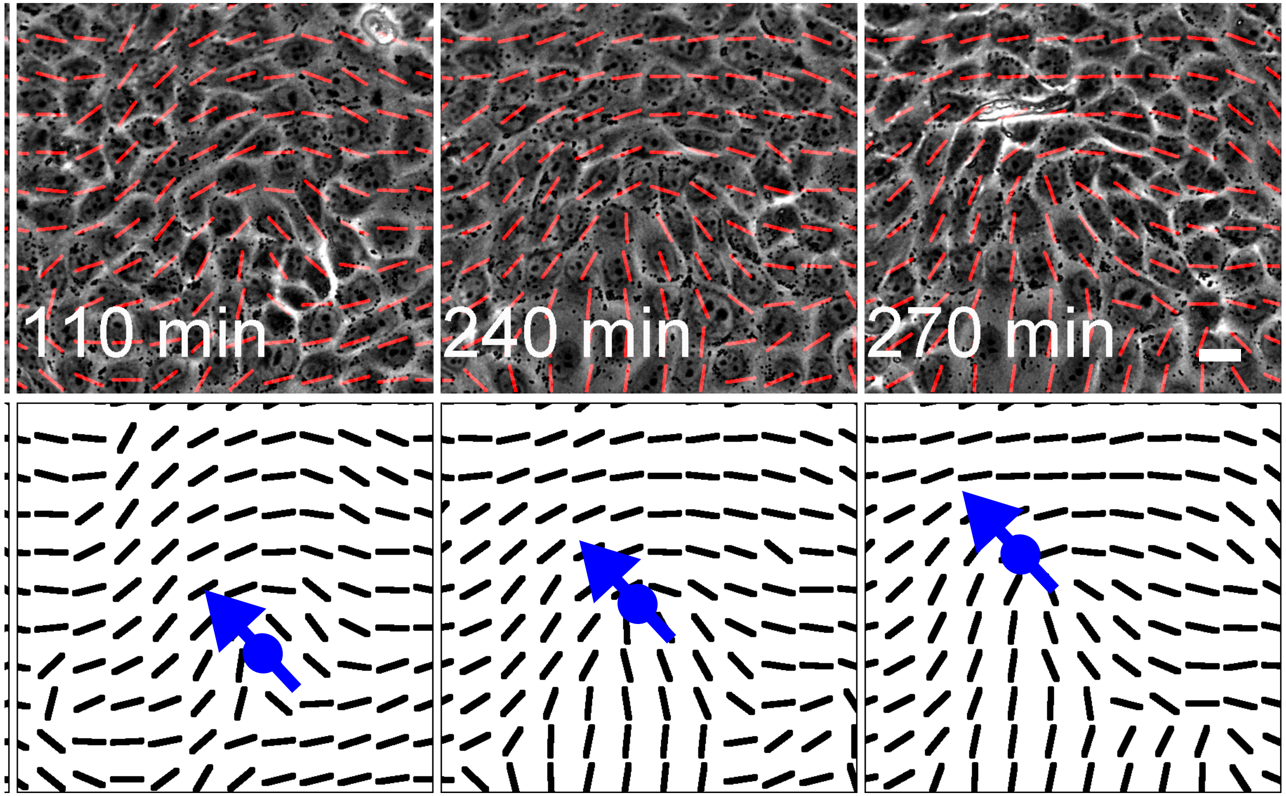




+1/2



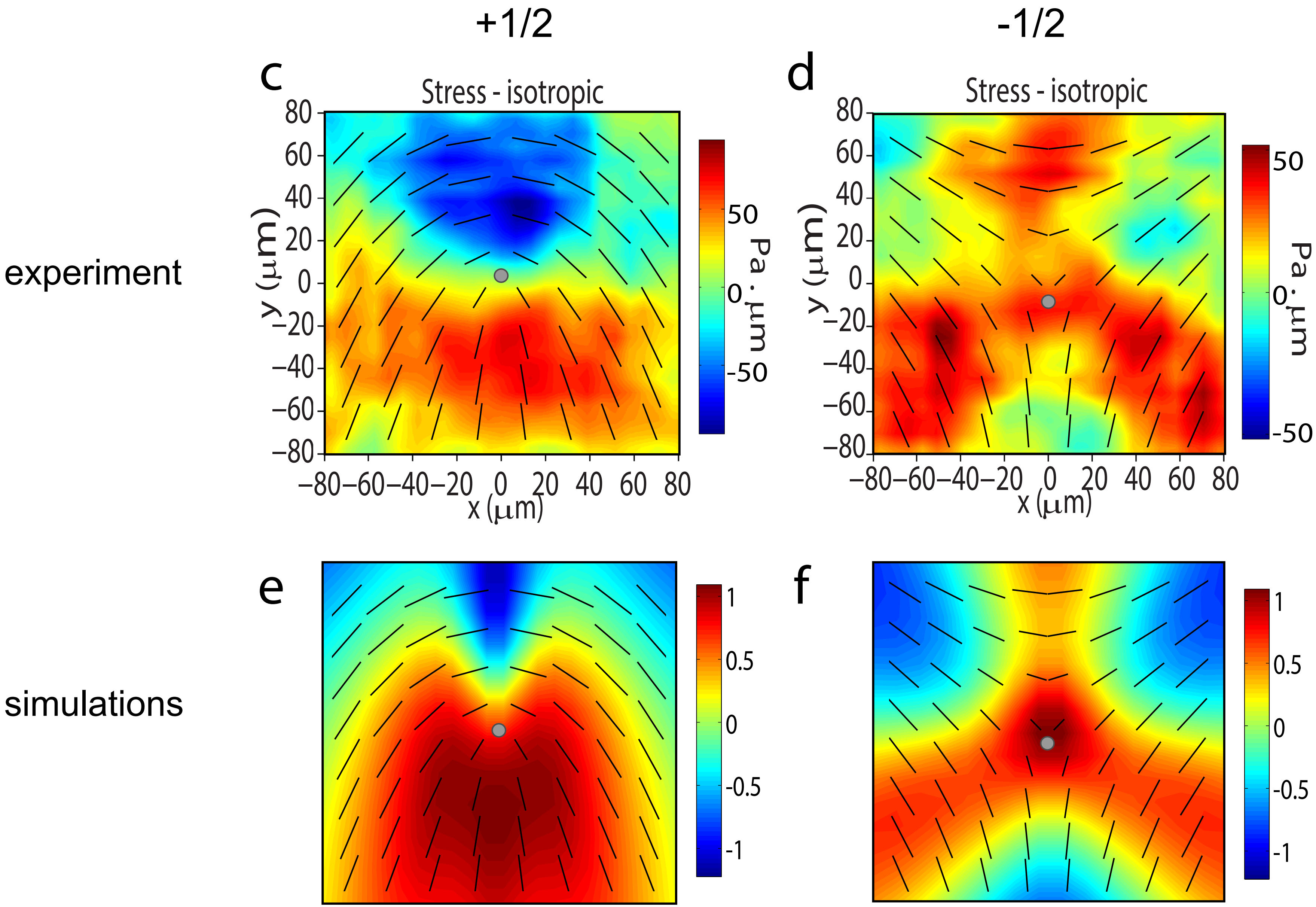
-1/2

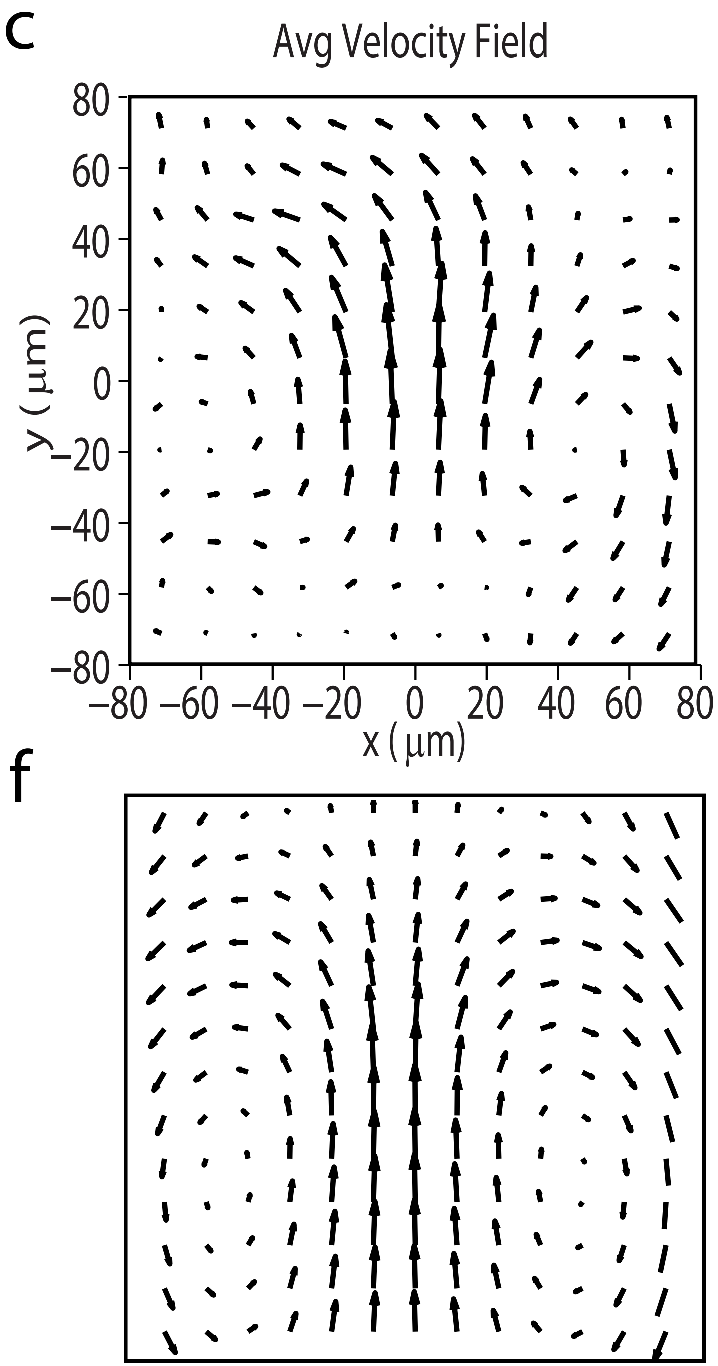


Motile +1/2 defect in a layer of MDCK cells

Thuan Beng Saw, Vincent Nier,
Philippe Marcq, Benoit Ladoux

Isotropic stress around a topological defect

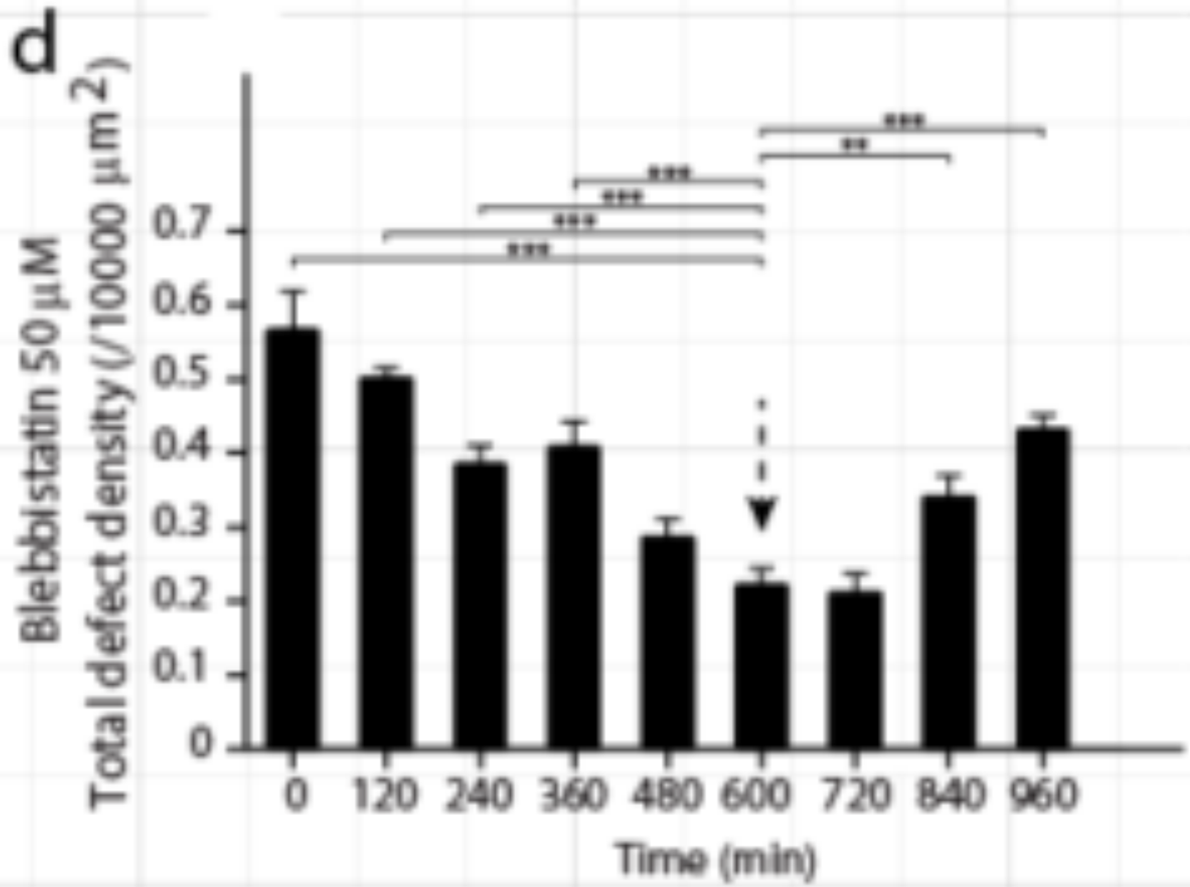




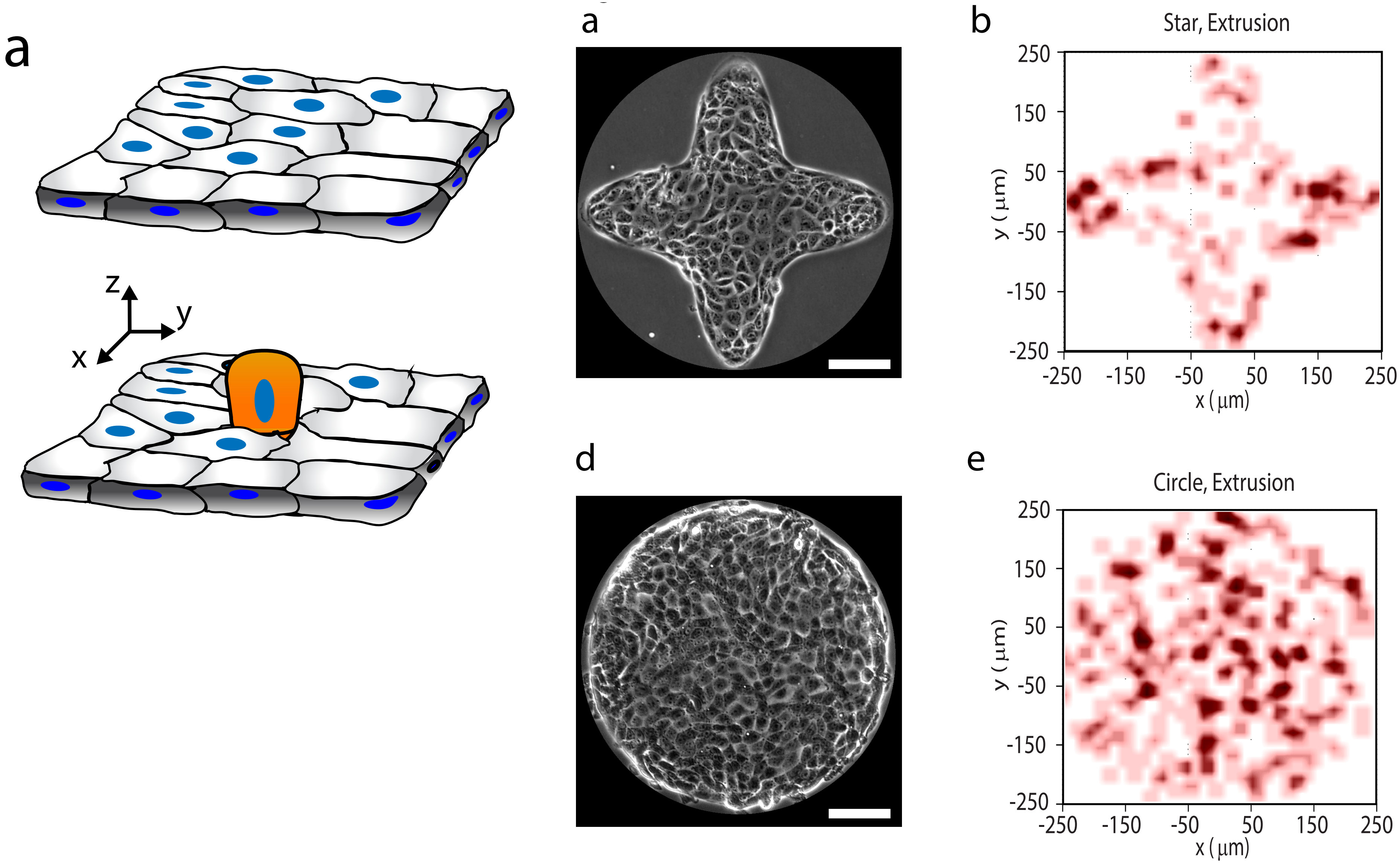
Flow field around +1/2 defect

Top: experiment

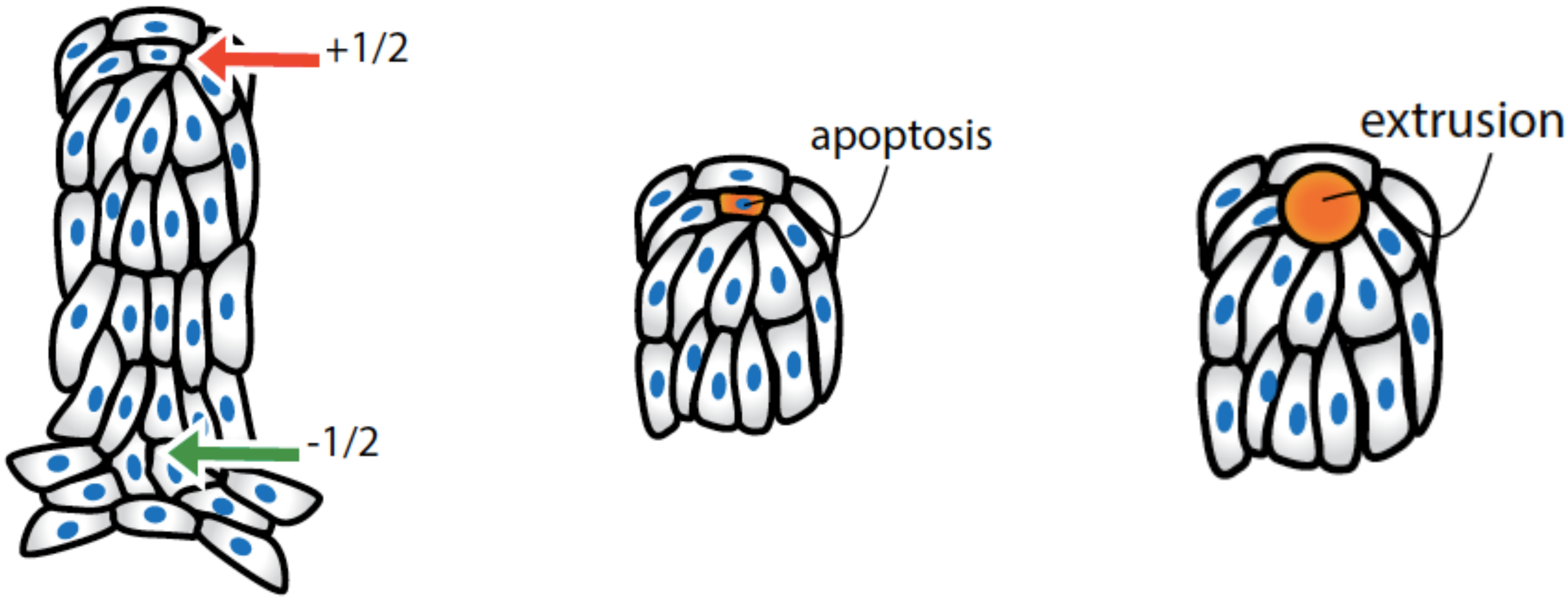
Bottom: simulations


d
Blebbistatin 50 µM
Total defect density (/10000 µm 2)
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0
120
240
360
480
600
720
840
960
Time (min)
***
**
***
***
***
***

Extrusion of dead cells – correlated to topological defects



Dead cells are ejected at topological defects



1.
Cell movements generate +1/2, -1/2 defect pair.

2.
+1/2 defect compresses cells, triggers apoptosis.

3.
Apoptotic extrusion at +1/2 defect core.

Confinement by walls can lead to regular vortex lattices in active systems & topological microfluidics

The transition to active turbulence in a channel is in the directed percolation universality class

Cell layers act as active nematics, the topological defects are linked to cell death

Topological defects in epithelia govern the extrusion of dead cells,
T. Beng Saw, A. Doostmohammadi, J.M. Yeomans, B. Ladoux et al, Nature 544, 212 (2017)

Dancing disclinations in confined active nematics, Tyler N. Shendruk, Amin Doostmohammadi, Kristian Thijssen and Julia M. Yeomans Soft Matter, online

Stabilzation of active matter by flow-vortex lattices and defect ordering, Amin Doostmohammadi, Michael Adamer, Sumesh Thampi and Julia M Yeomans, Nature Comms **7** 10557 (2016)

Onset of meso-scale turbulence in active nematics, Amin Doostmohammadi, Tyler Shendruk, Kristian Thijssen, Julia M Yeomans, Nature Comms, in press