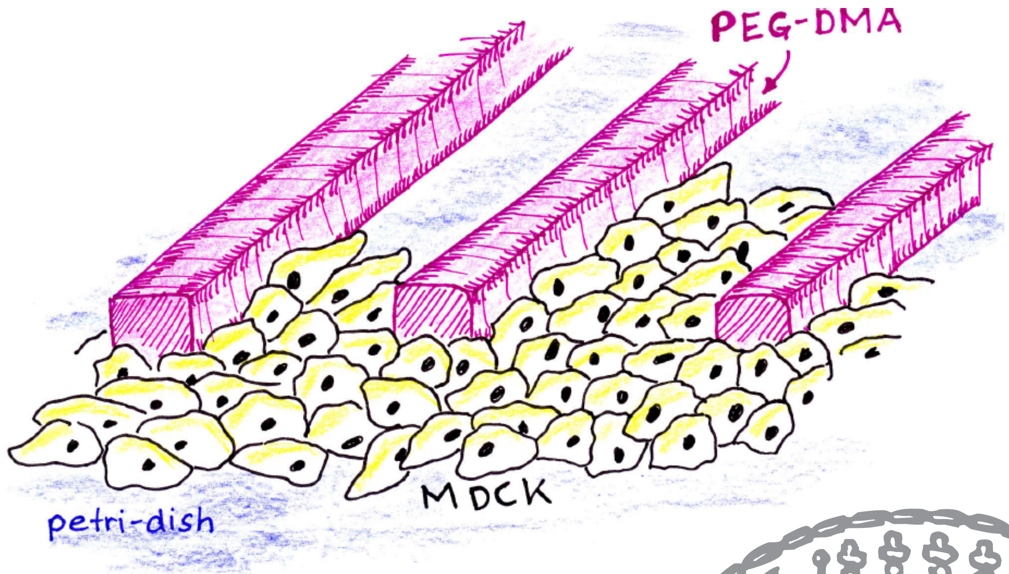
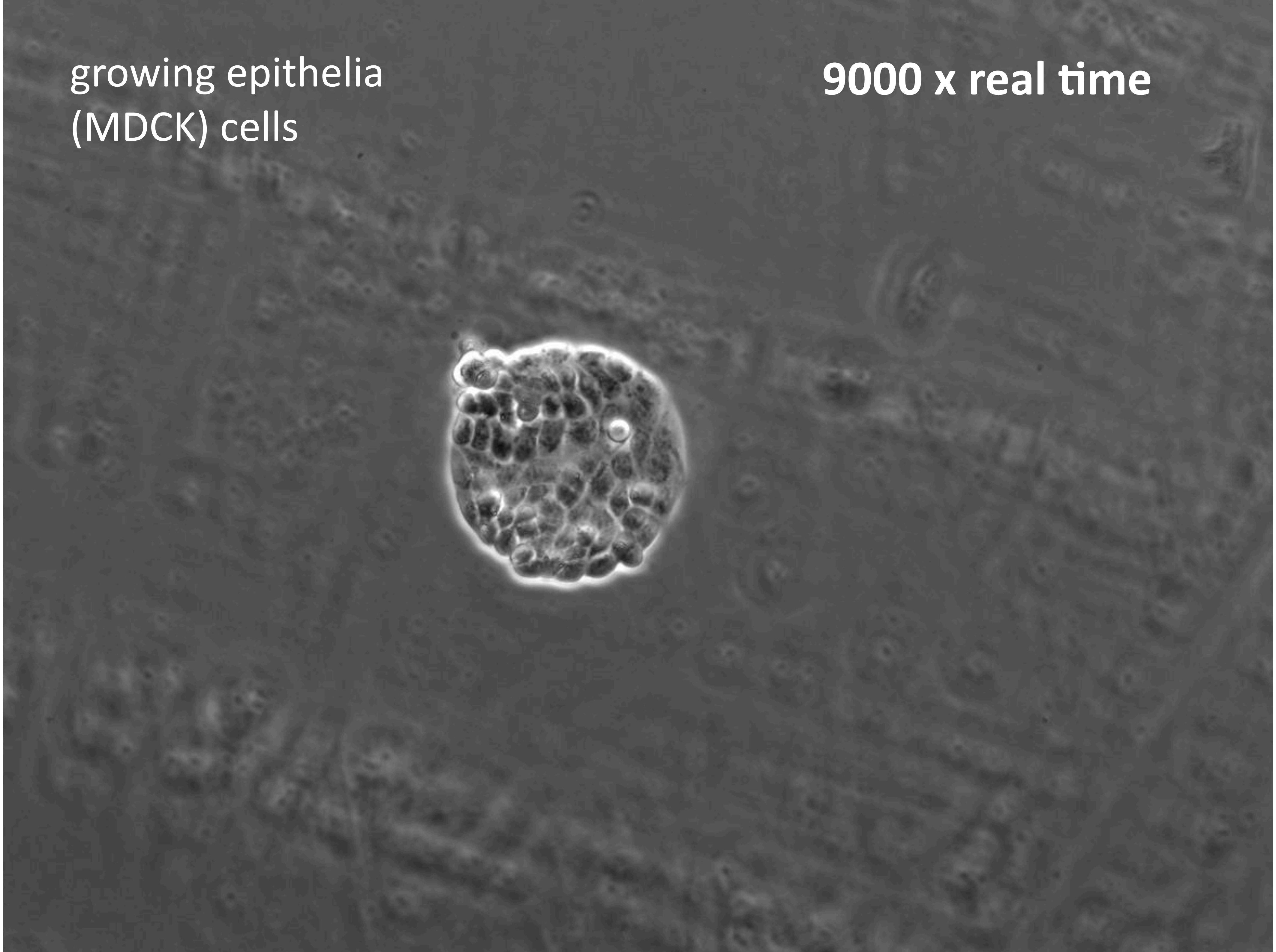
Cell migration on microstructured surfaces:
- from single cell to collective behavior

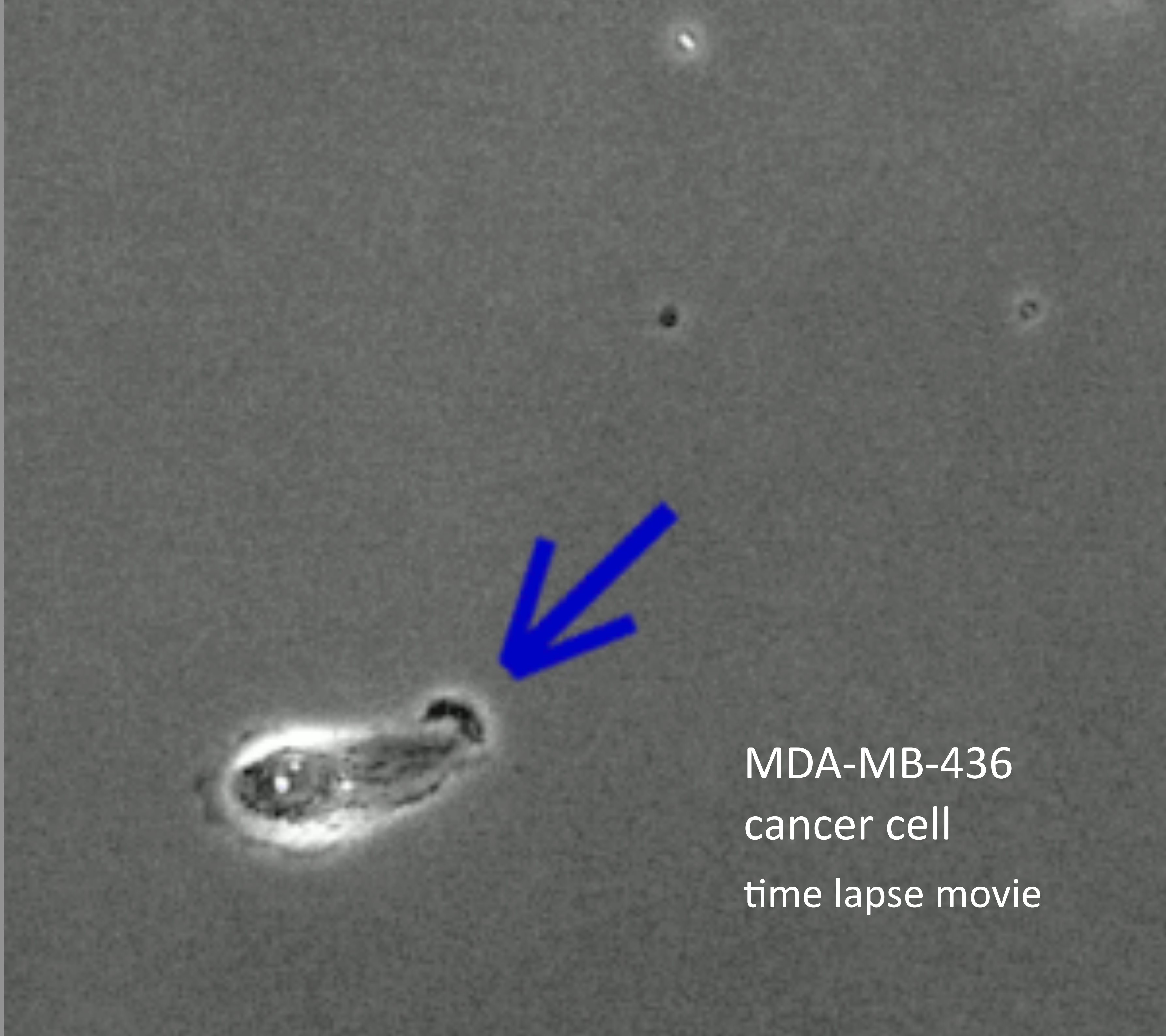
Joachim Rädler

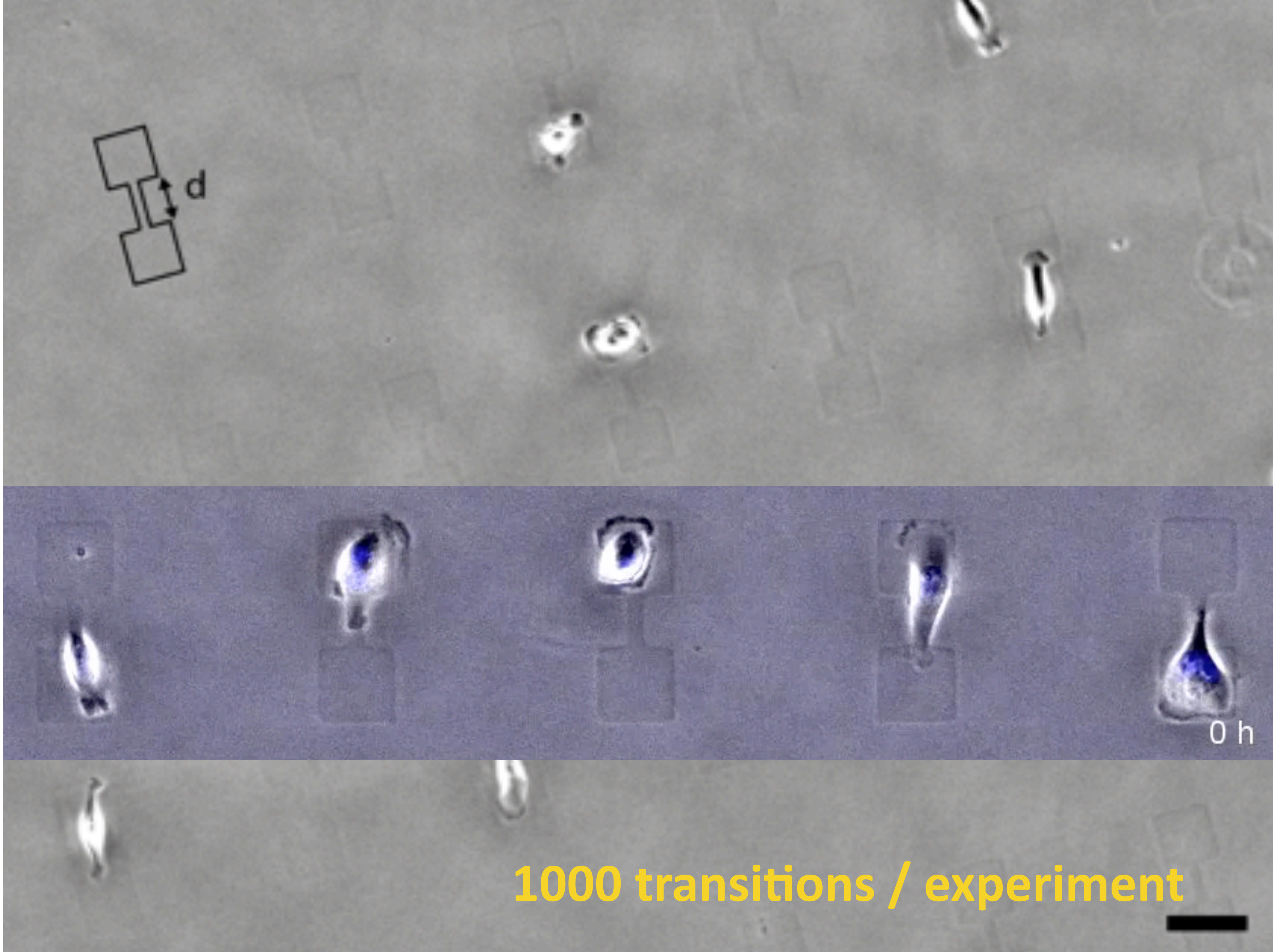
soft condensed matter group
physics faculty, LMU, Munich
Center for NanoScience (CeNS)



ASC school on the Physics of Life, 9th Oct. 2019

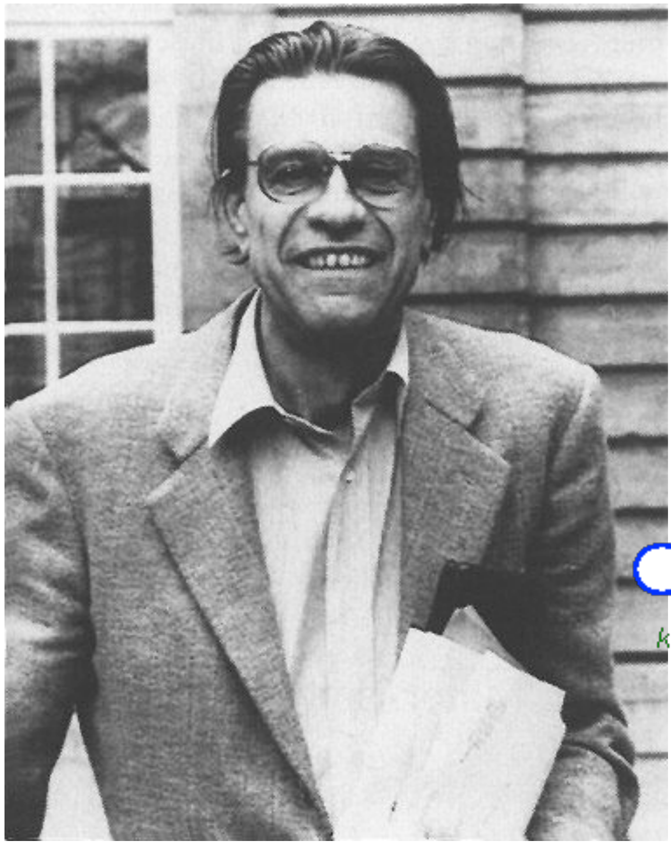

growing epithelia (MDCK) cells
9000 x real time

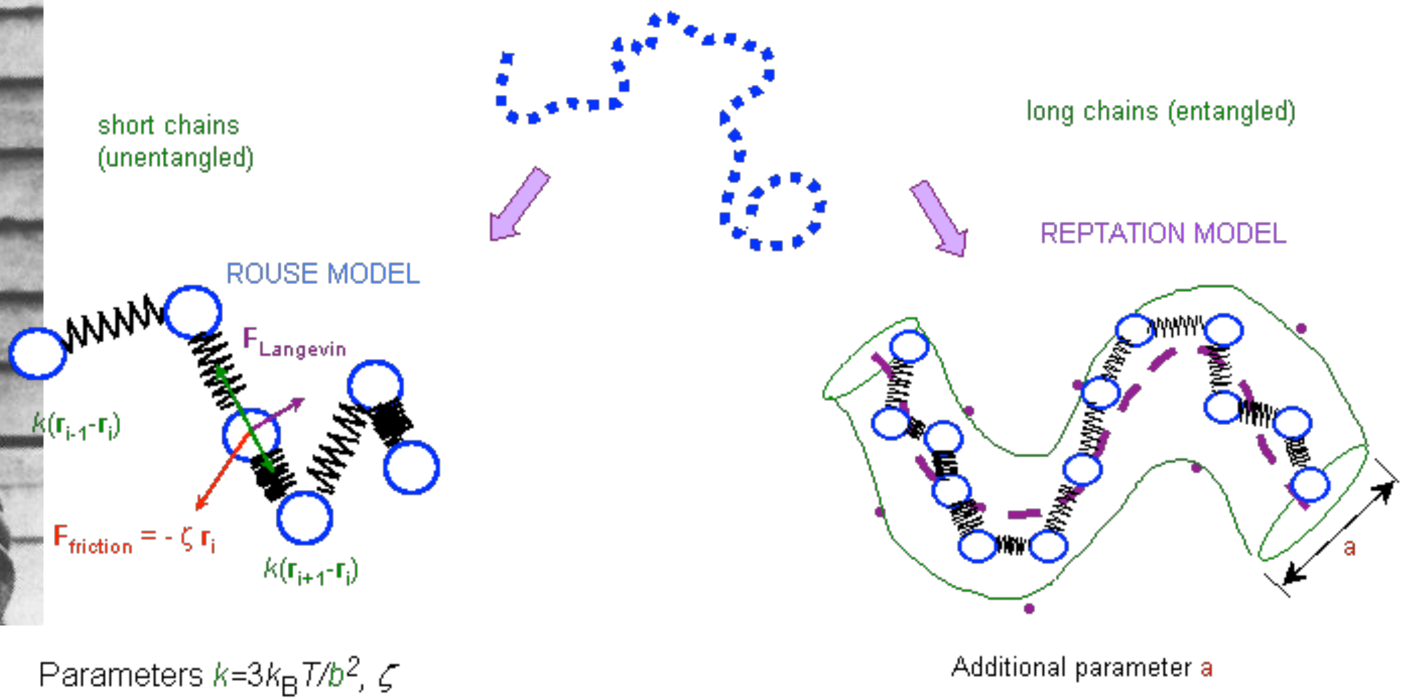

MDA-MB-436
cancer cell
time lapse movie


d
0 h
1000 transitions / experiment

Pierre-Gilles de Gennes

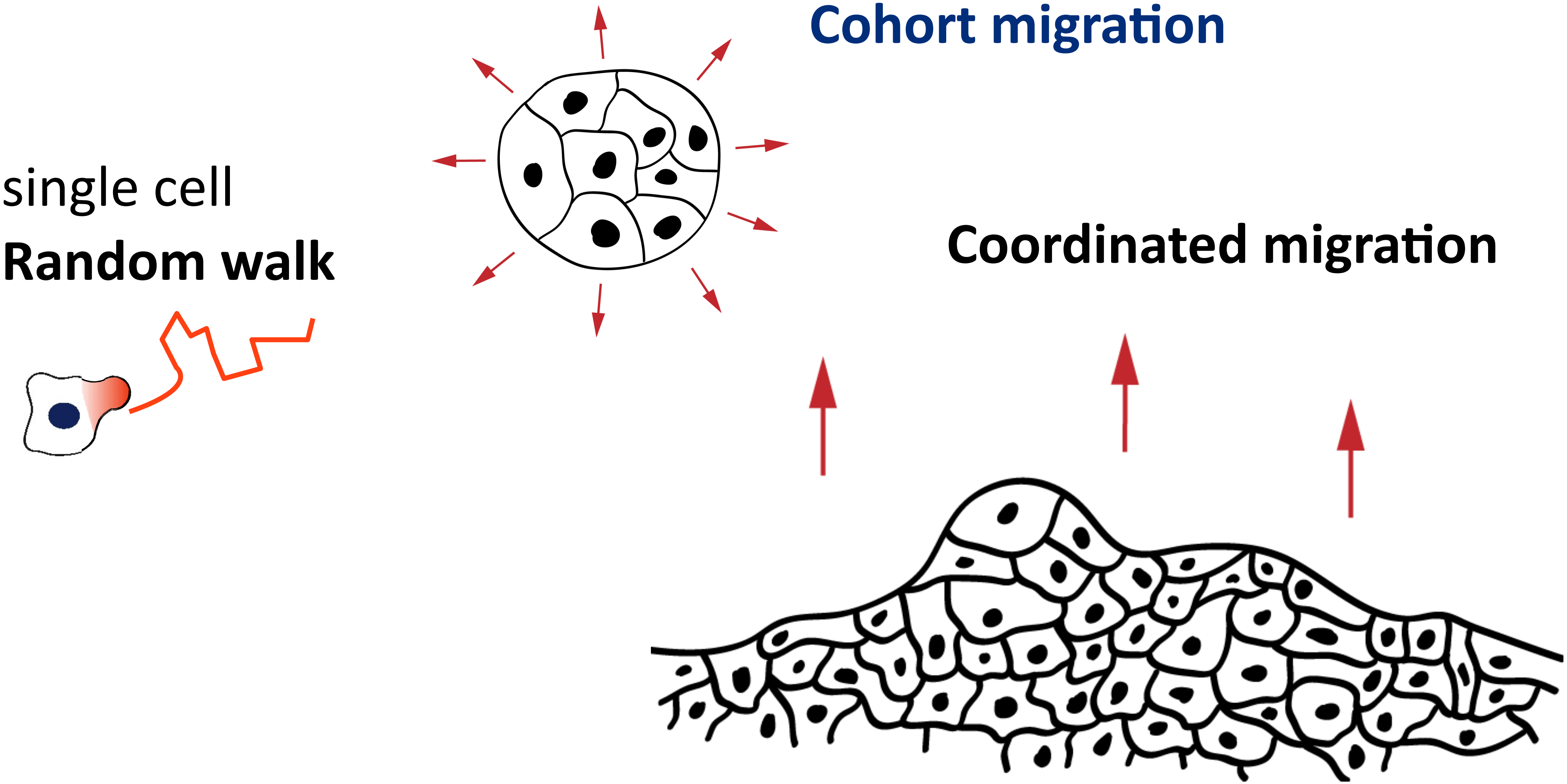
Soft Matter



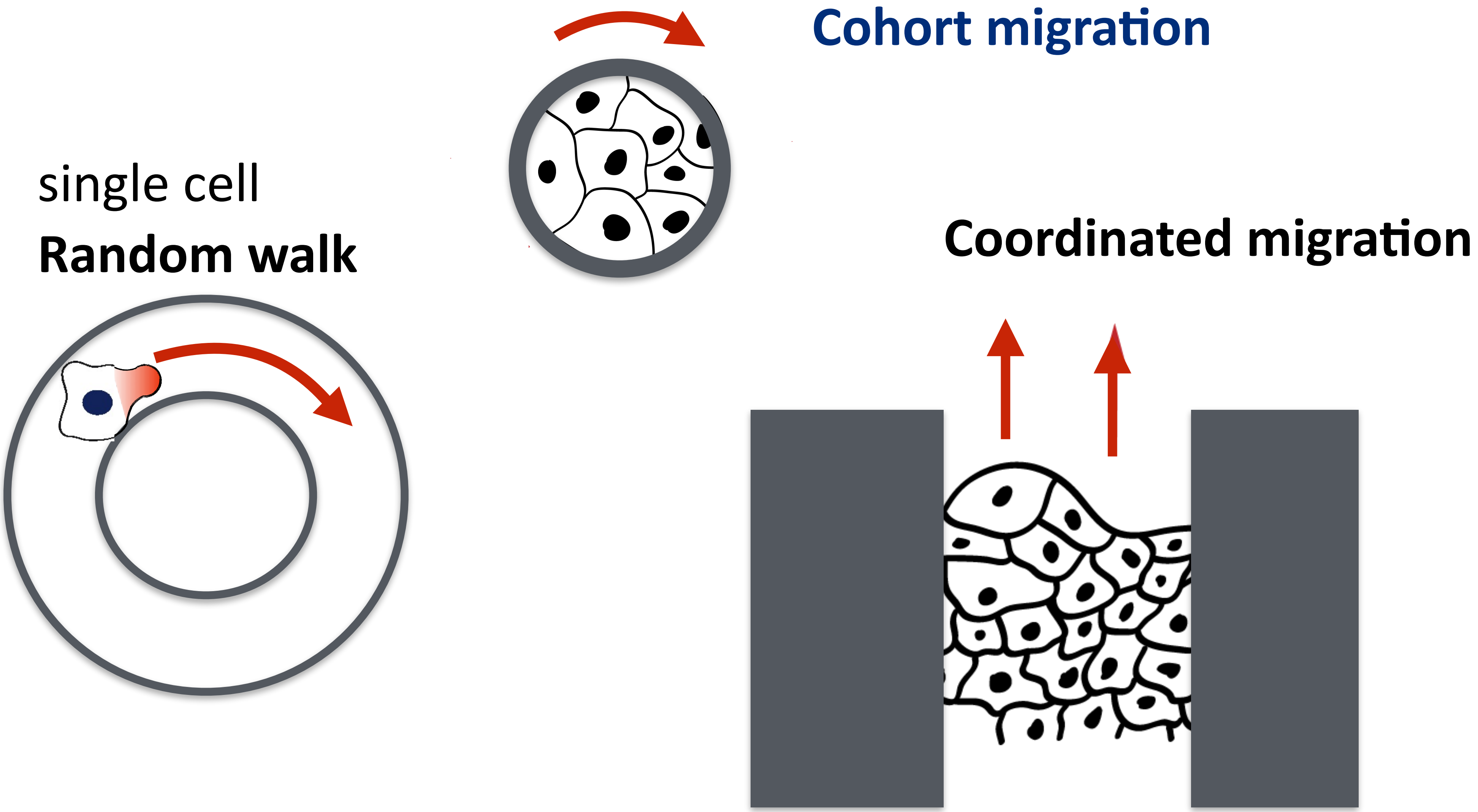


The Nobel Prize in Physics 1991 was awarded to Pierre-Gilles de Gennes *"for discovering that methods developed for studying order phenomena in simple systems can be generalized to more complex forms of matter, in particular to liquid crystals and polymers"*.

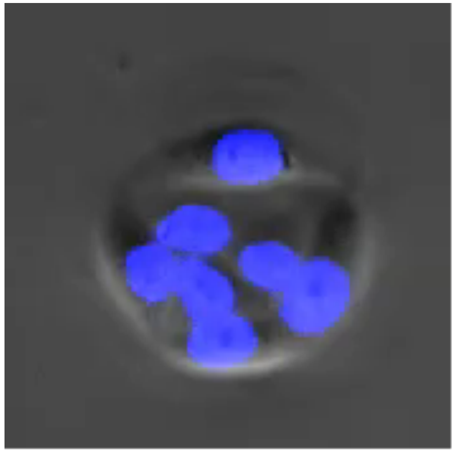
From Single Cell to Collective Cell Migration

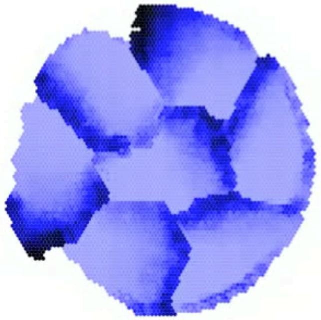


From Single Cell to Collective Cell Migration



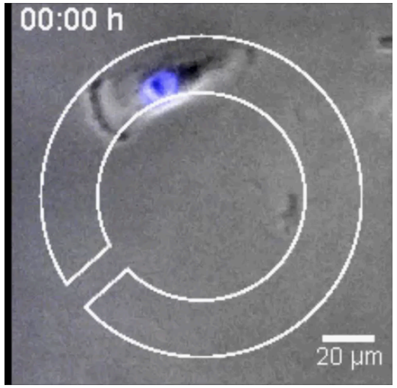
Migratory phenotypes on artificial micro-pattern



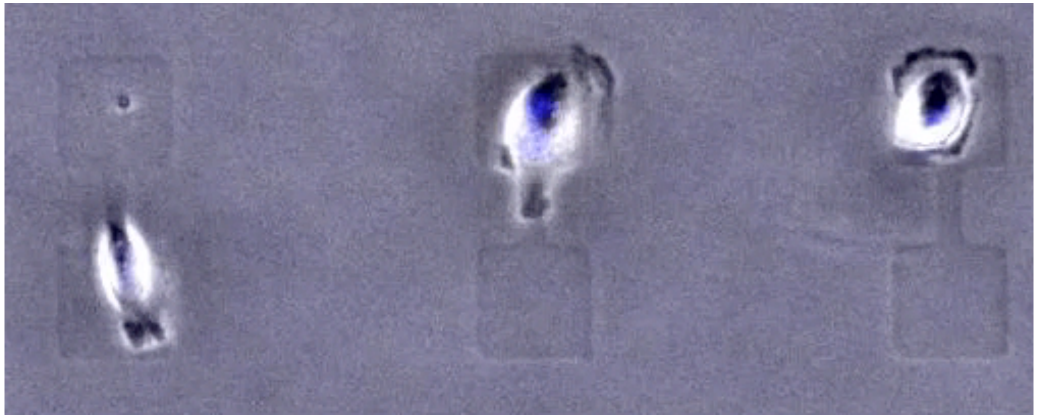


Felix Segerer
Alicia Piera

collaborators:
Erwin Frey
Florian Thüroff
Andriy Goychuk



Christoph Schreiber
Sophia Schaffer
Fang Zhou



collaborators:
Ernst Wagner
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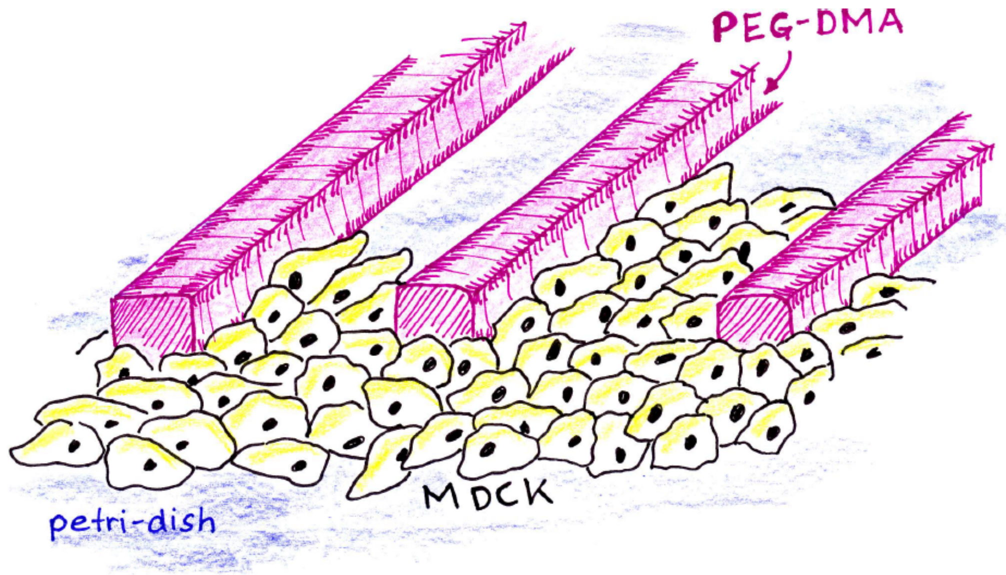
Alexandra Fink
Peter Röttgermann
Christoph Schreiber

collaborators:
Chase Broedersz
David Brückner

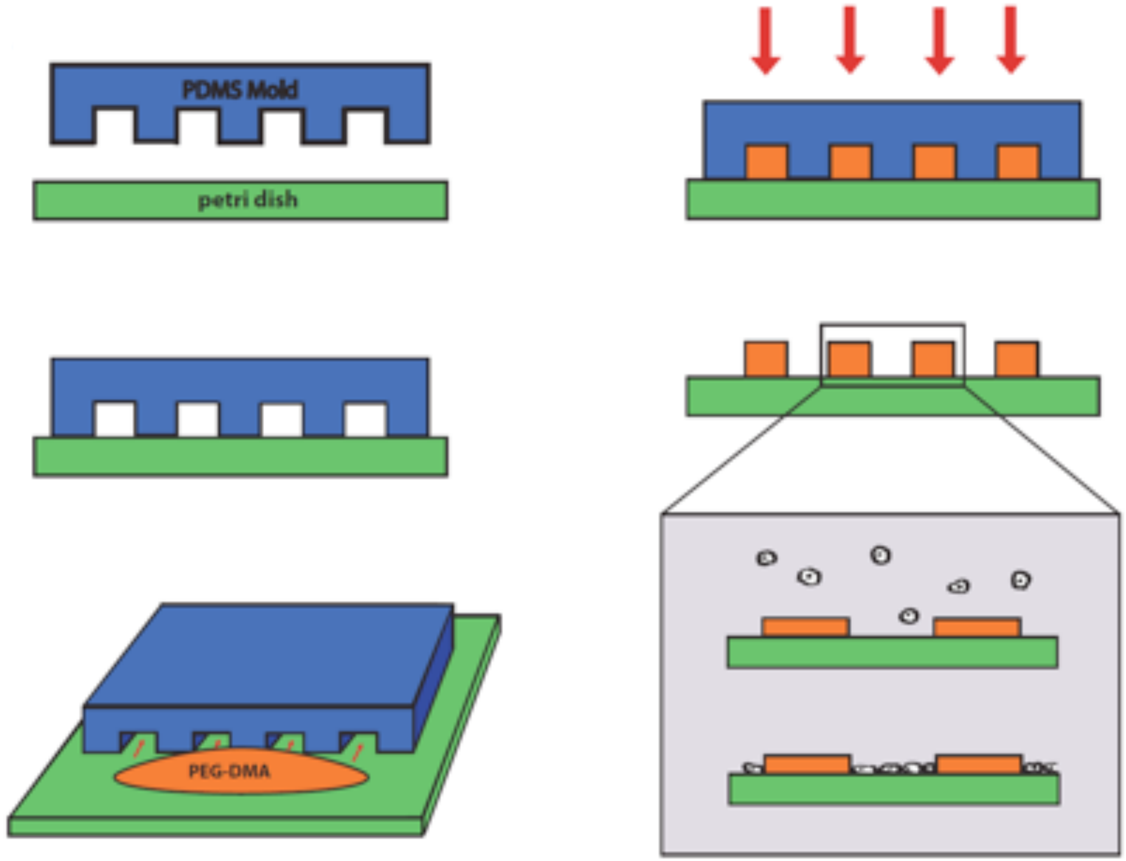
Flow and diffusion in channel-guided cell migration



Anna-Kristina Marel, Matthias Zorn, Christoph Klingner,
Roland Wedlich-Söldner, Erwin Frey, Joachim O. Rädler

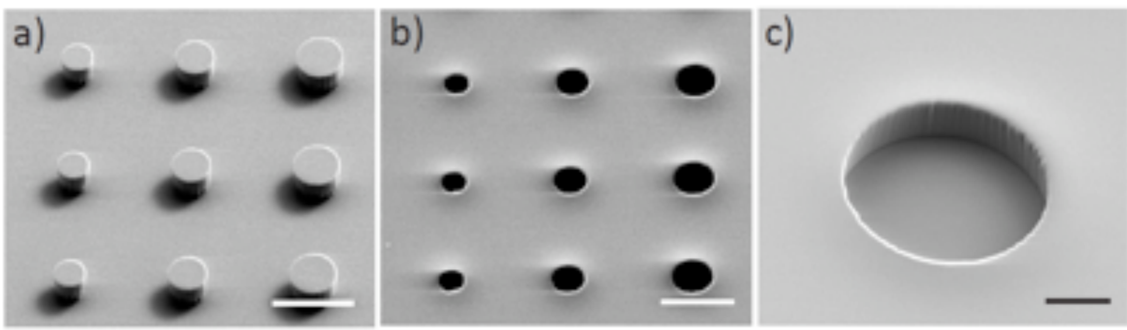
Biophysical Journal vol.107(5) 1054 (2014)

Microenvironments for cell migration



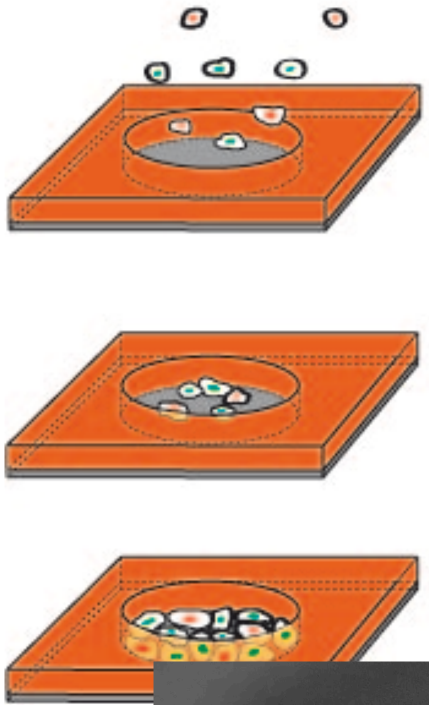
capillary-force lithography under polydimethylsiloxane (PDMS) stamps

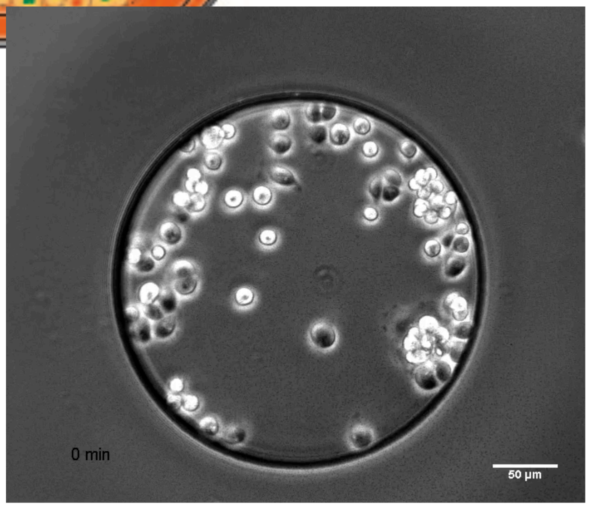
poly(ethylene glycol) dimethacrylate (PEGDMA)

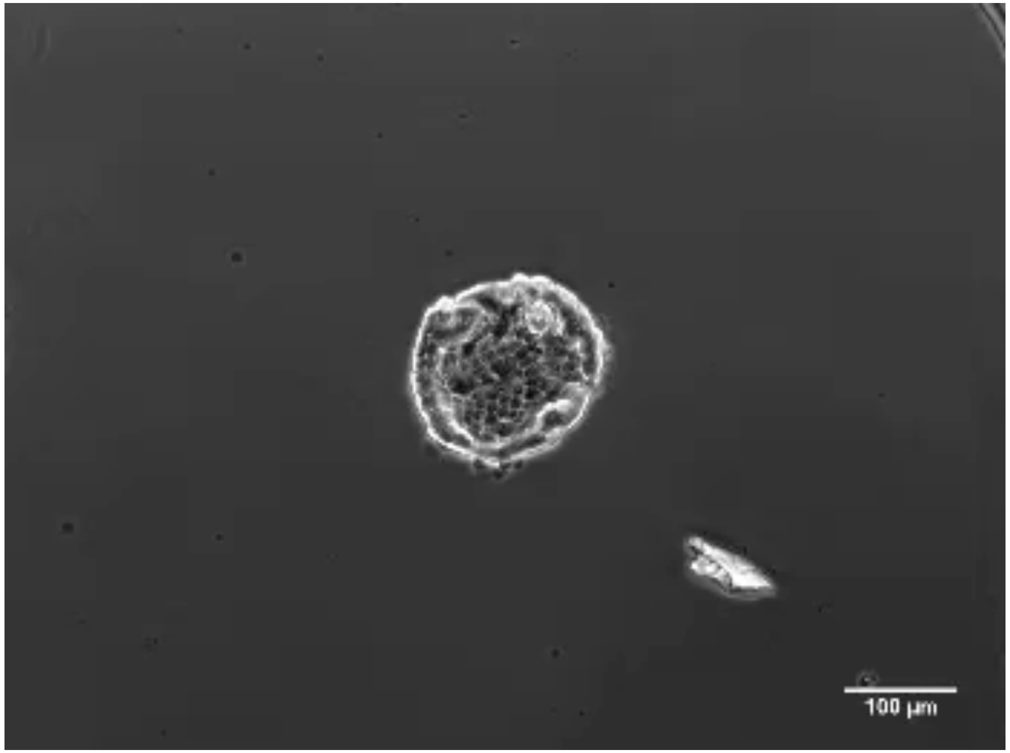


hydrogel microwell arrays

Cell Proliferation & Collective migration

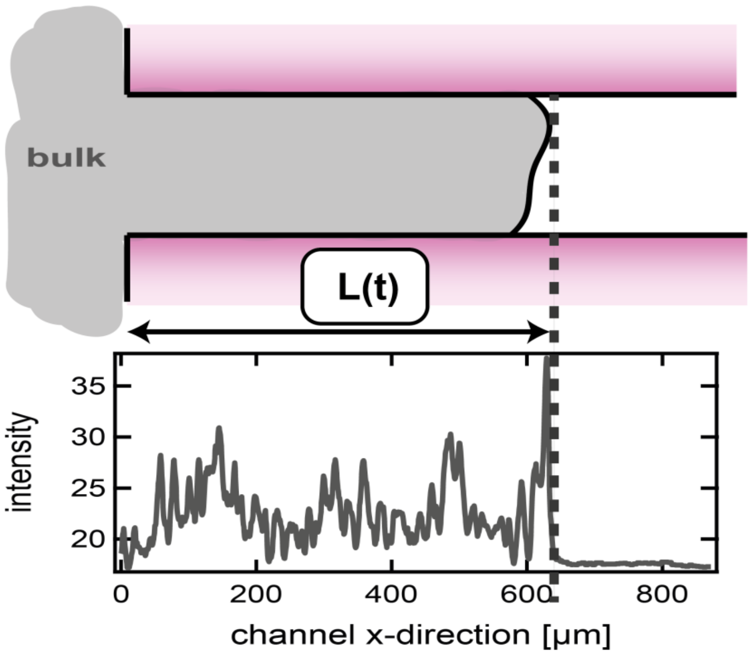


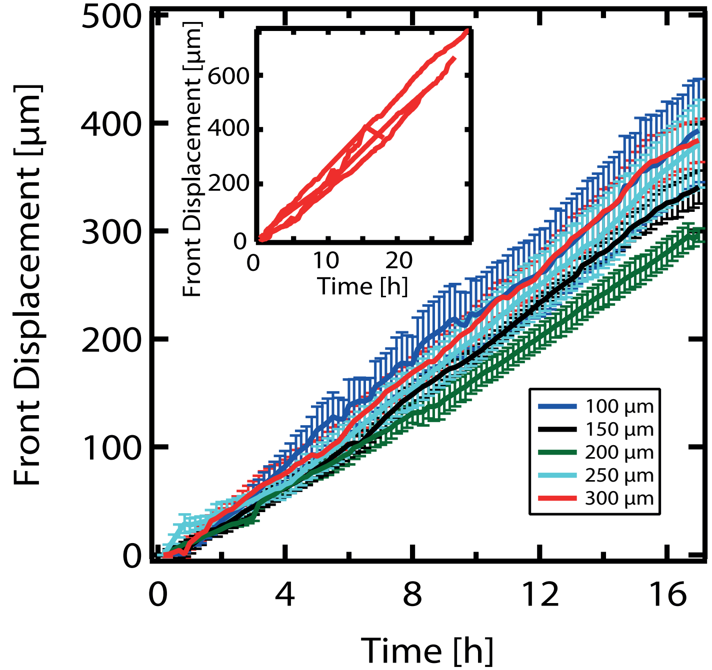


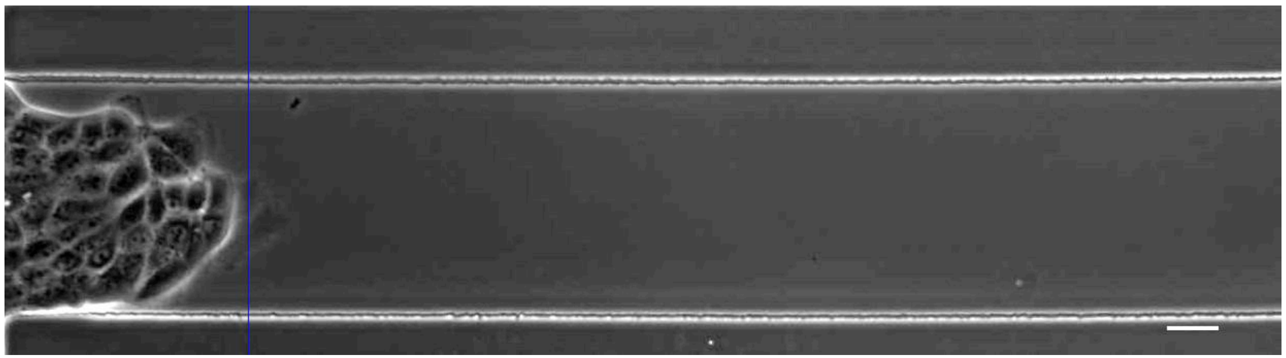


Madin-Darby canine kidney (MDCK) cells

The velocity of cell invasion







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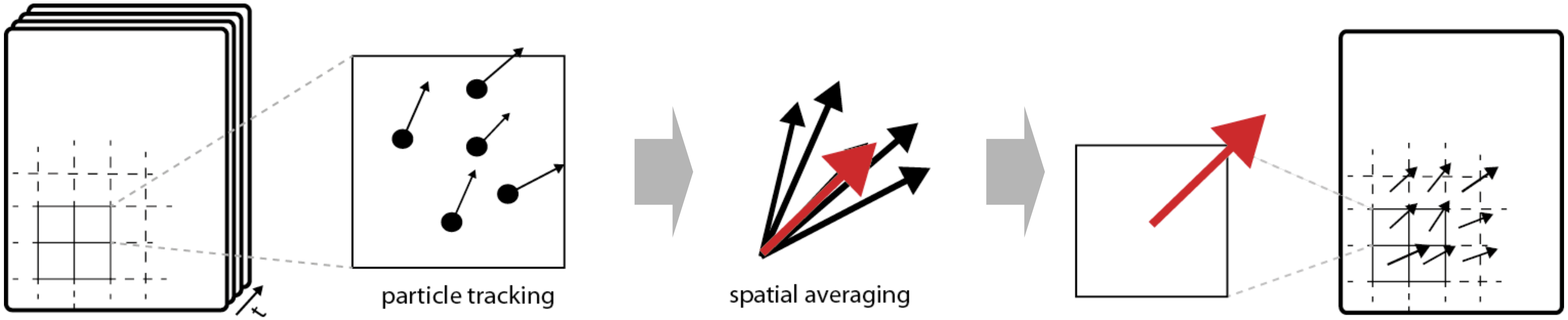
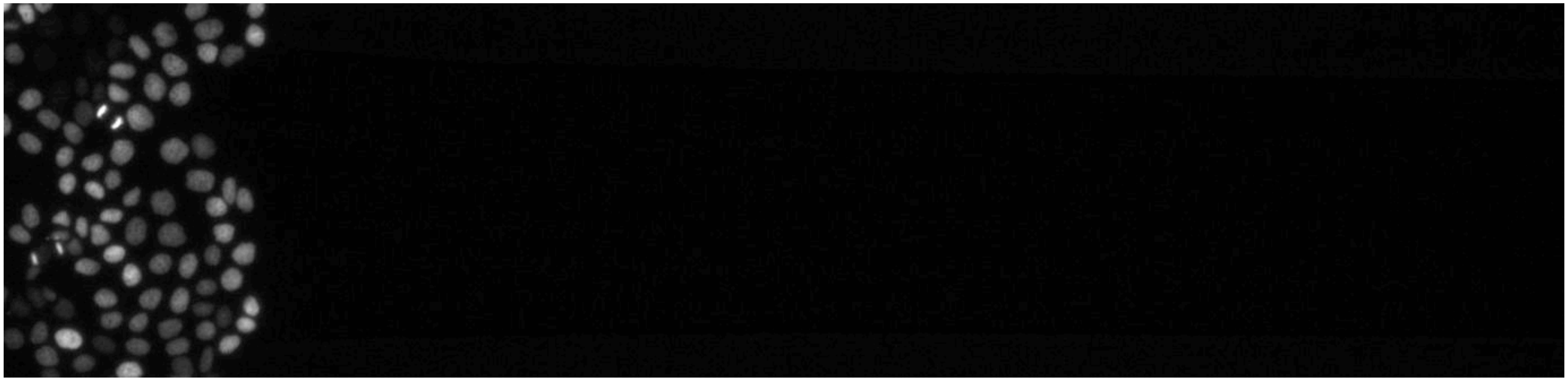
Particle image velocimetry yields flow field



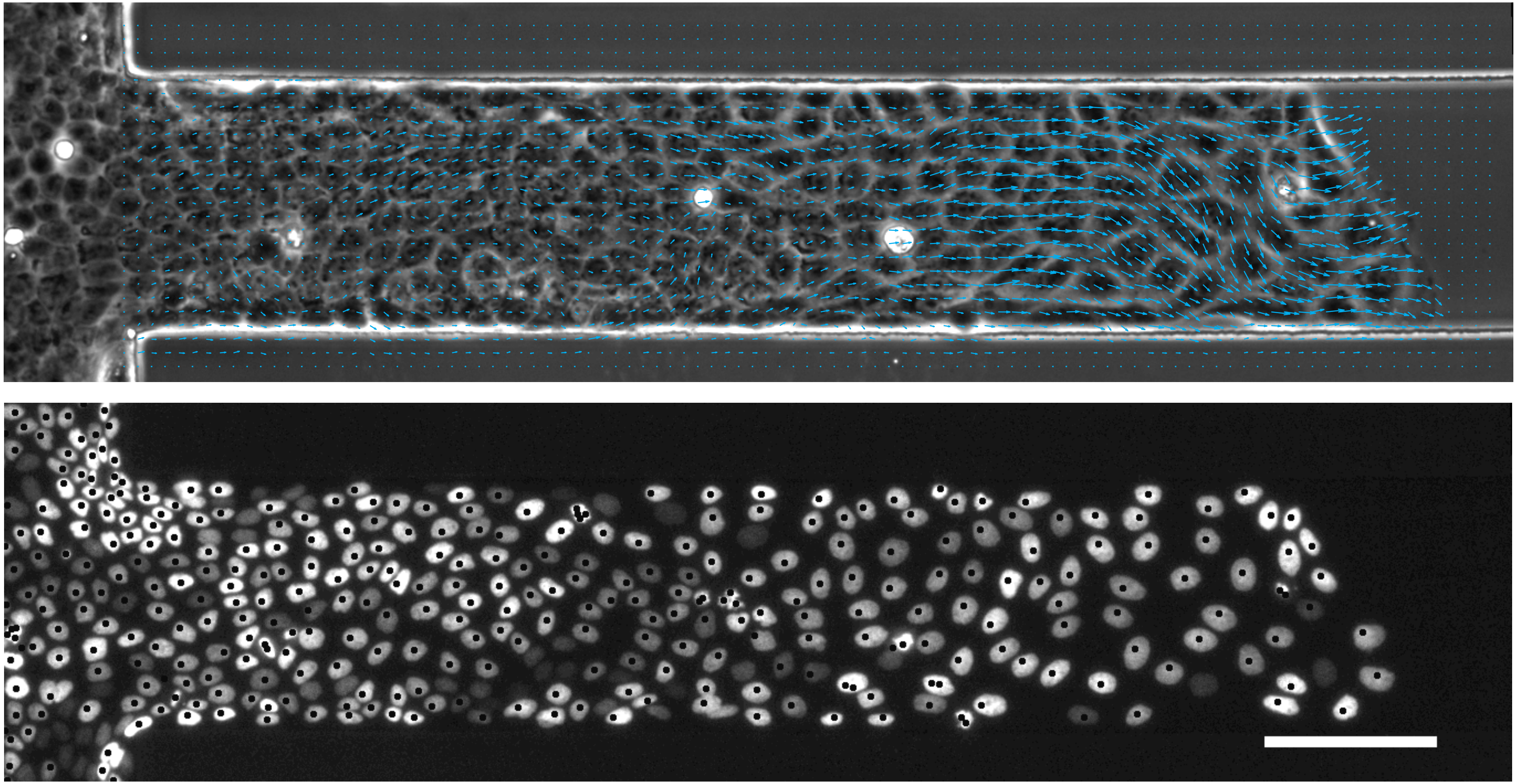
Fluorescent nuclei yield single cell trajectories

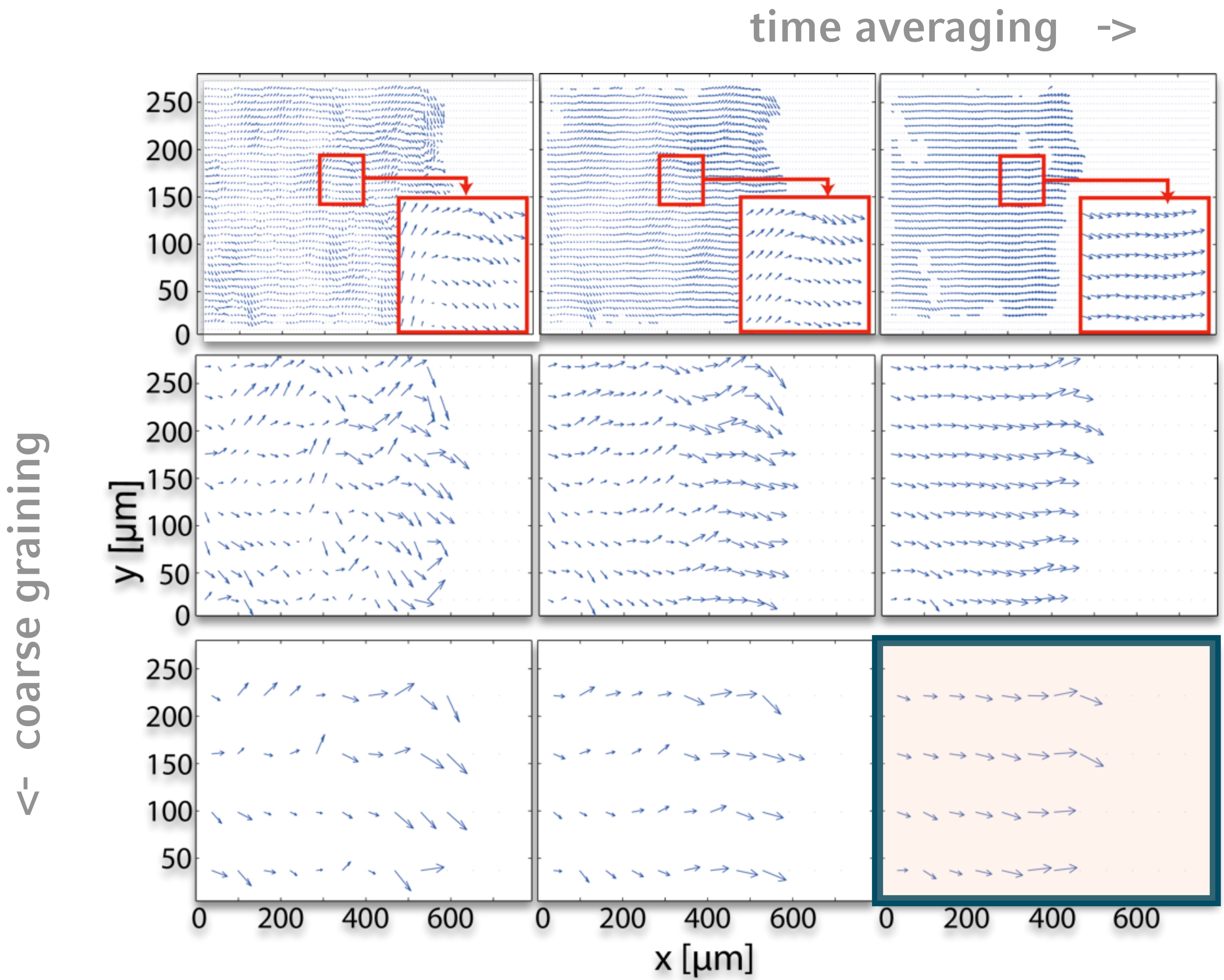
Alternating phase contrast / fluorescence time-lapse microscopy



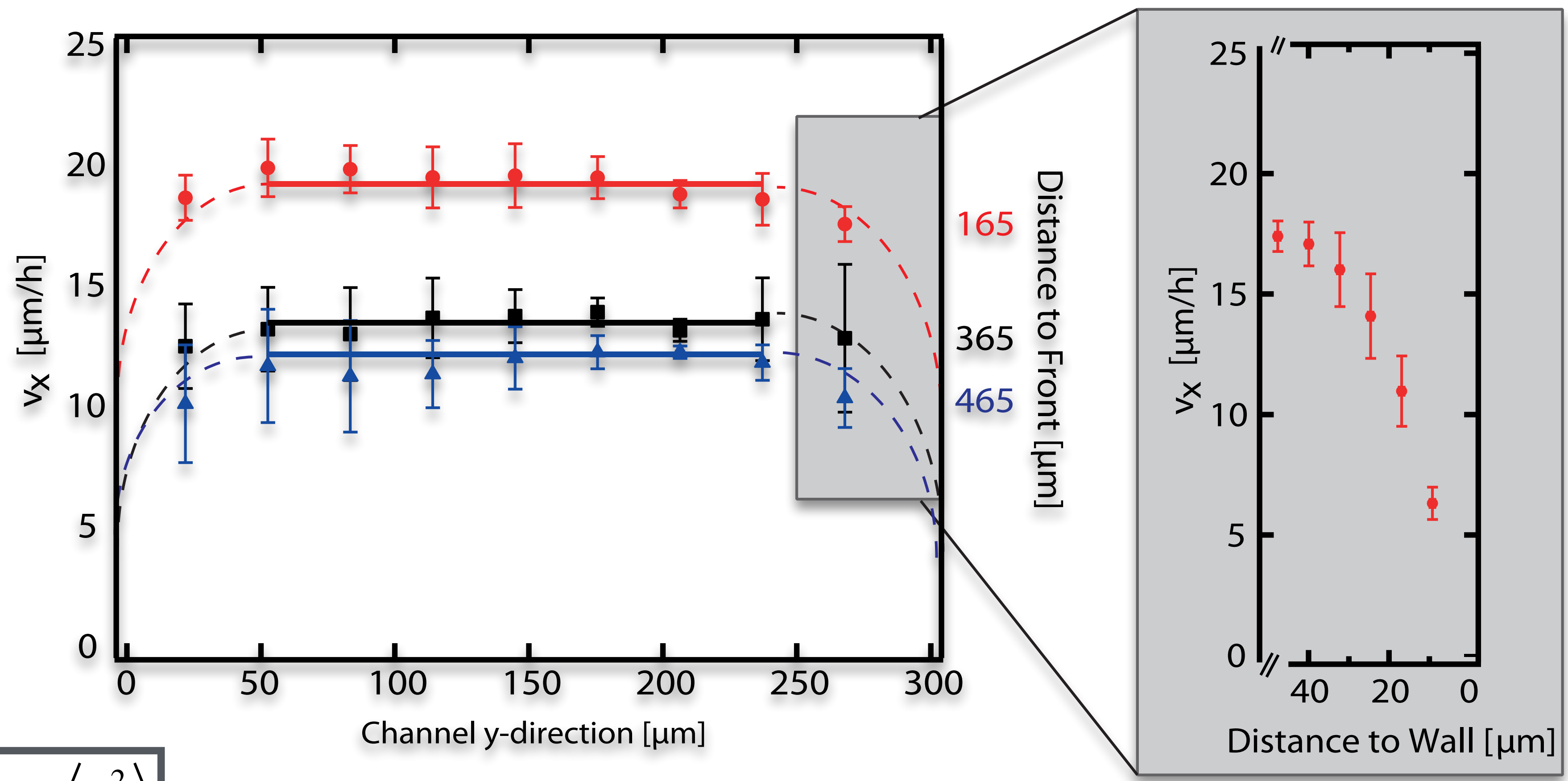
Reconstructing cell-flow in 2-dimensional channels

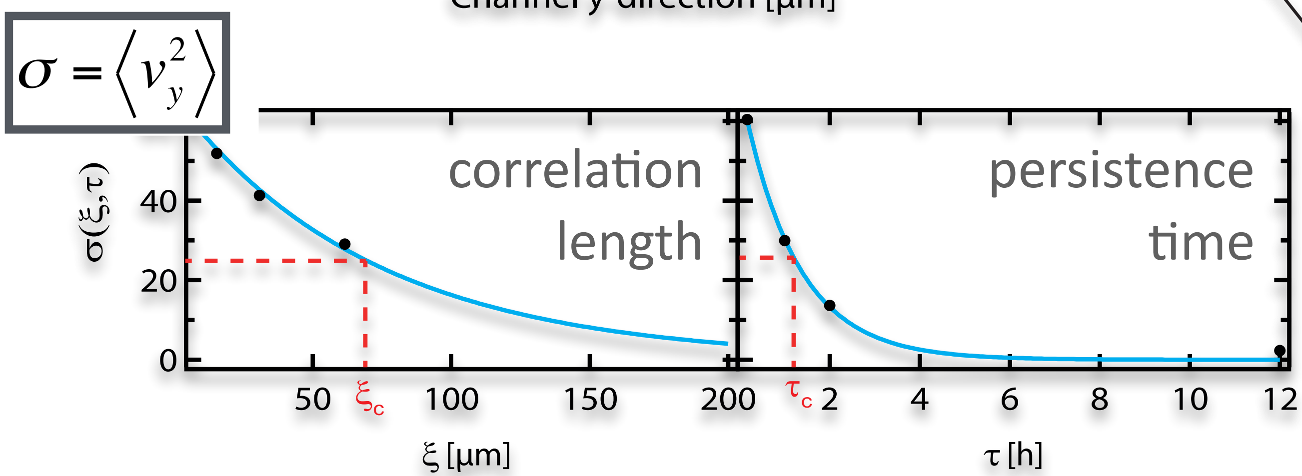
Alternating phase contrast / fluorescence time-lapse microscopy




time averaging ->
<- coarse graining
y [µm]
x [µm]
0
50
100
150
200
250
0
200
400
600

Cell flow field shows plug-flow like profile

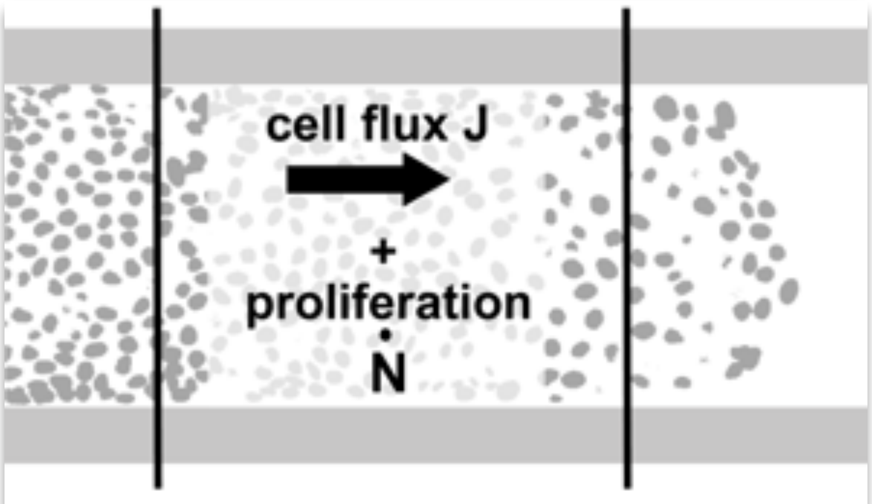


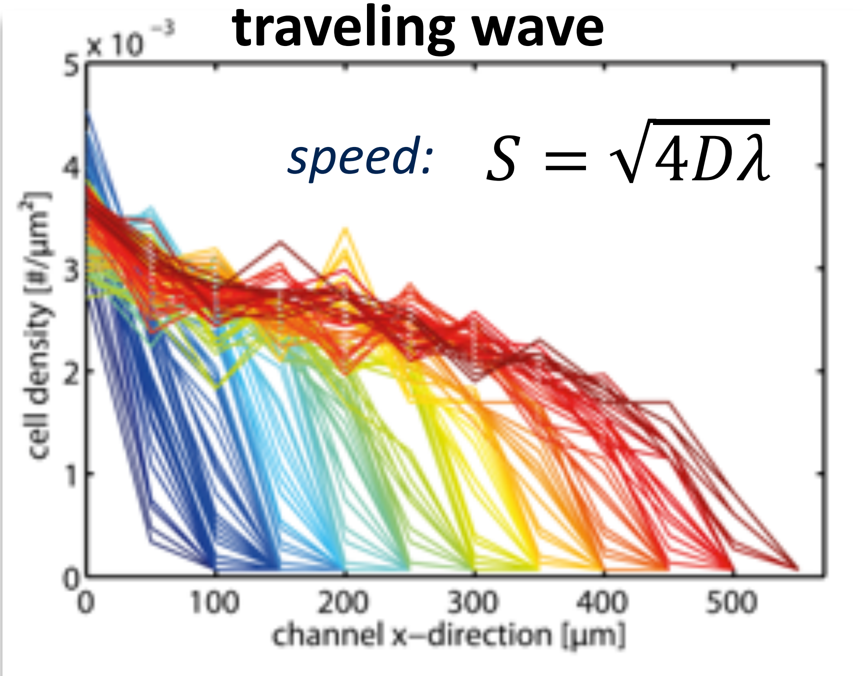


$\xi \approx 70\ \mu m$

$\tau \approx 1{,}2\ h$

Mathematical model of cell density profile





$$J = -D_c \frac{dc}{dx}$$

„Ficks Law"

cell flux proportional to cell density gradient

D_c: generalized transport coefficient

$$\dot{N} = N_0 e^{\lambda t}$$

„cell proliferation"

cells number grows exponentially

$$\frac{\partial c}{\partial t} = D\nabla^2 c + \lambda c\left(1 - \frac{c}{K}\right)$$

Fisher-Kolmogorov Eq.

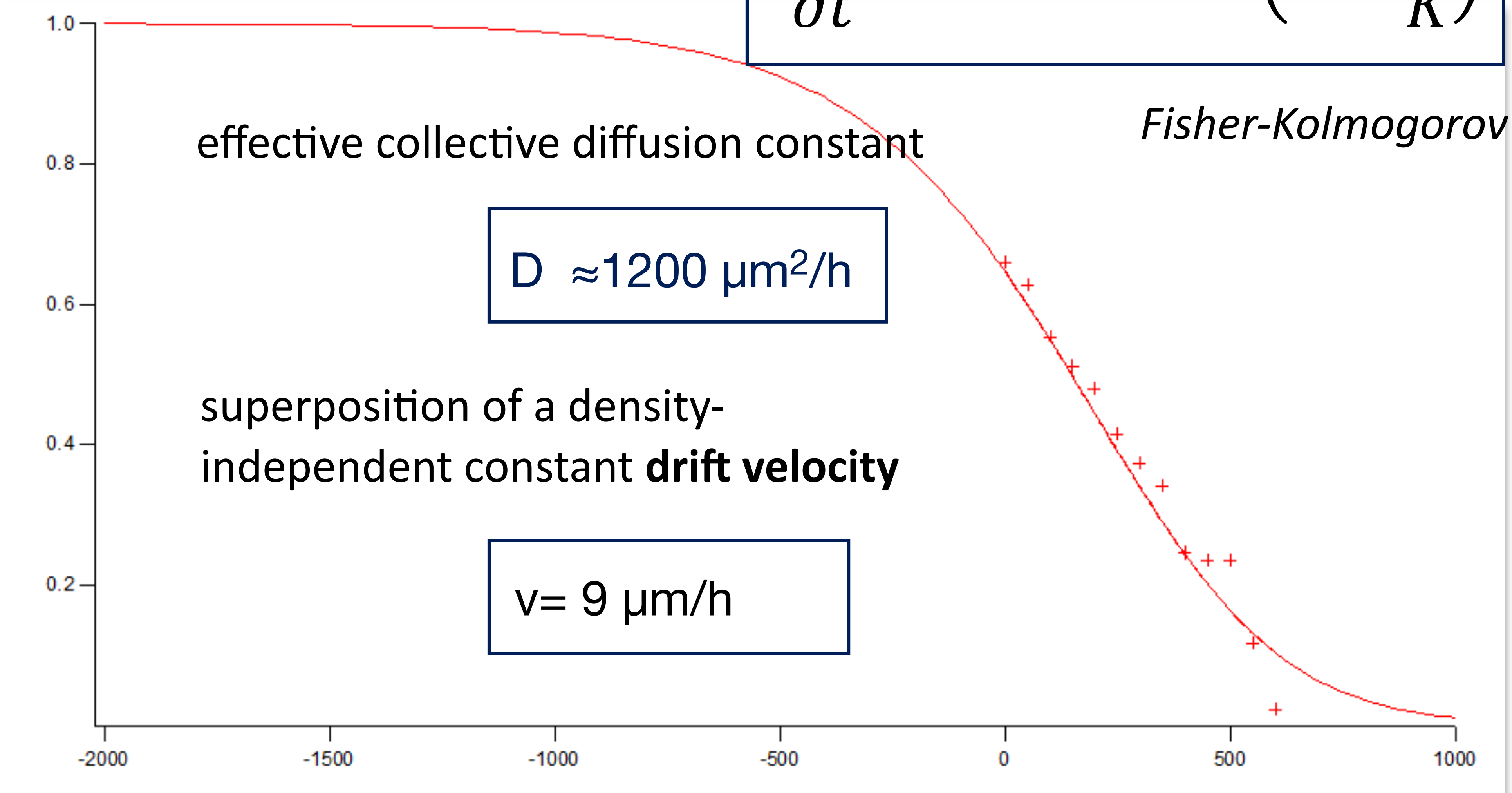
includes logistic growth with capacity K

Proliferation & Diffusion: Emergence of traveling waves

$$\frac{\partial c}{\partial t} = D\nabla^2 c + \lambda c \left(1 - \frac{c}{K}\right)$$

Fisher-Kolmogorov

Stationary shape



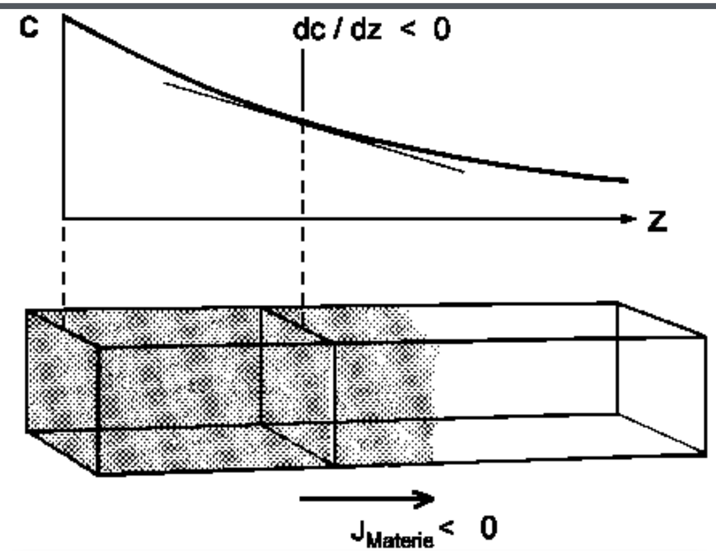
effective collective diffusion constant

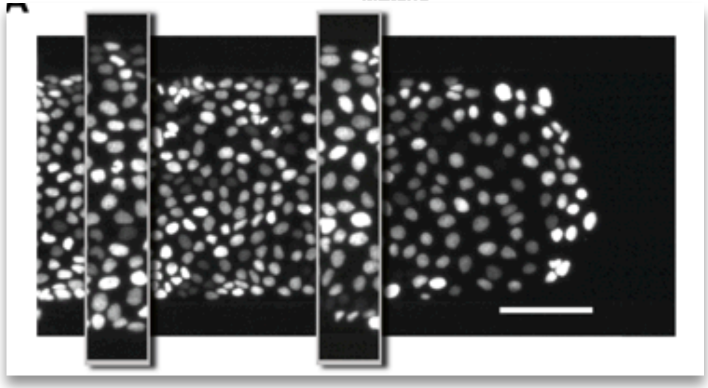
D ≈1200 μm²/h

superposition of a density-independent constant **drift velocity**

v= 9 μm/h

Collective vs. Self Diffusion





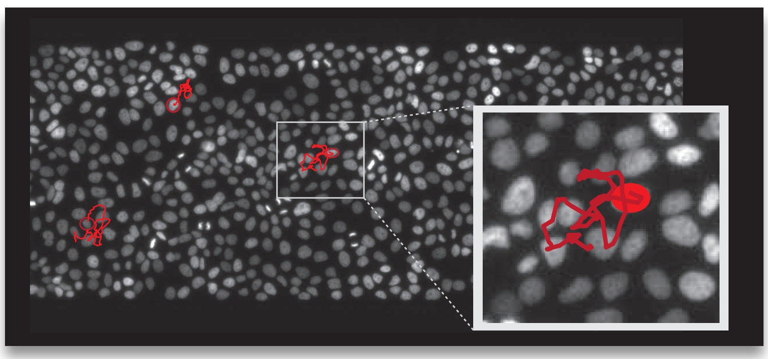
$$J = -D_c \frac{dc}{dx} + J_0$$

cell flow proportional to cell density gradient

$D_C \approx \xi^2 / 4\tau$

$D_C \approx 1200\ \mu m^2/h$

Collective diffusion is determined
by the correlation length ξ and time τ



$$\langle x^2 \rangle = 4Dt$$

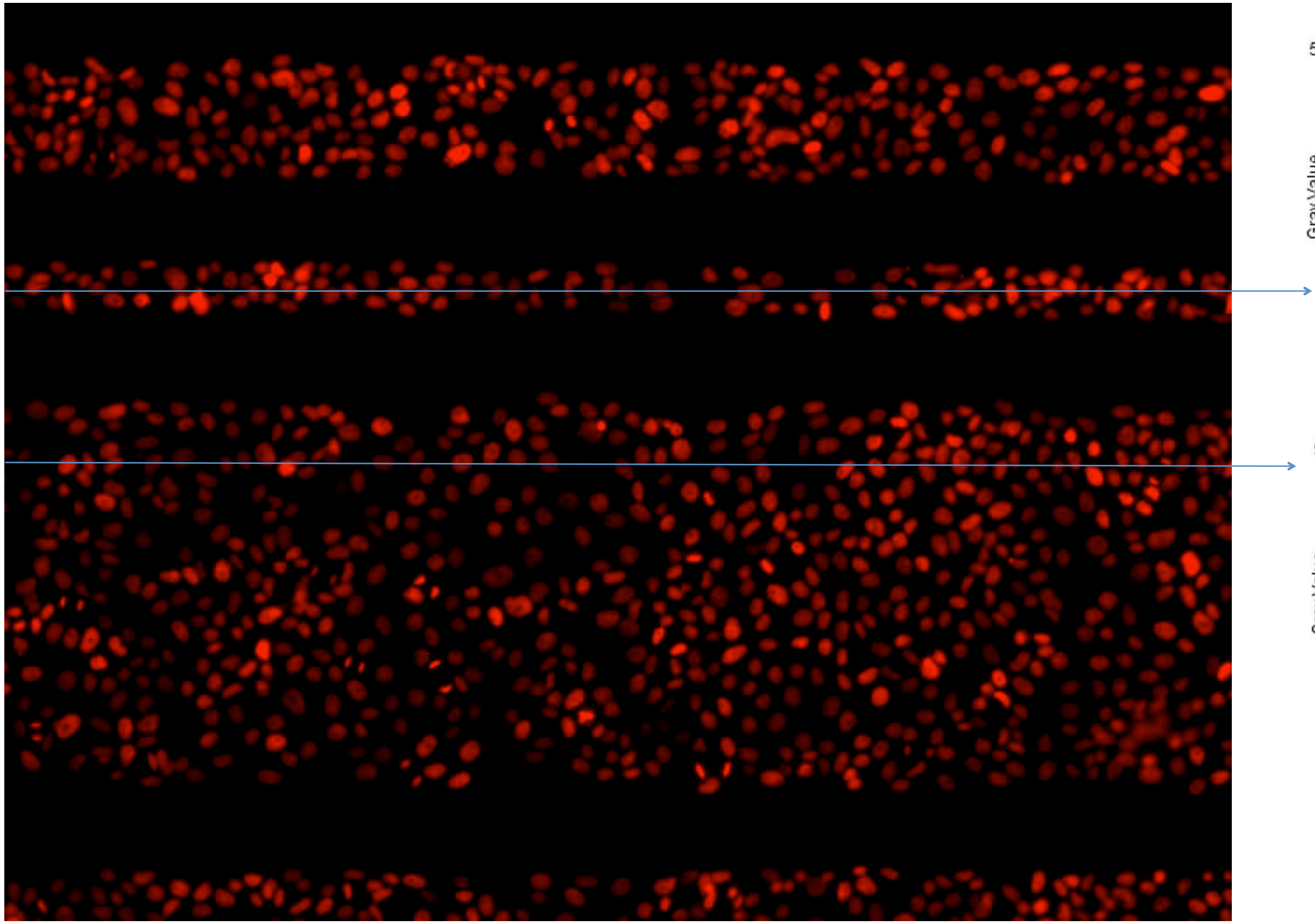
the mean squared displacement (MSD)
grows linear with time

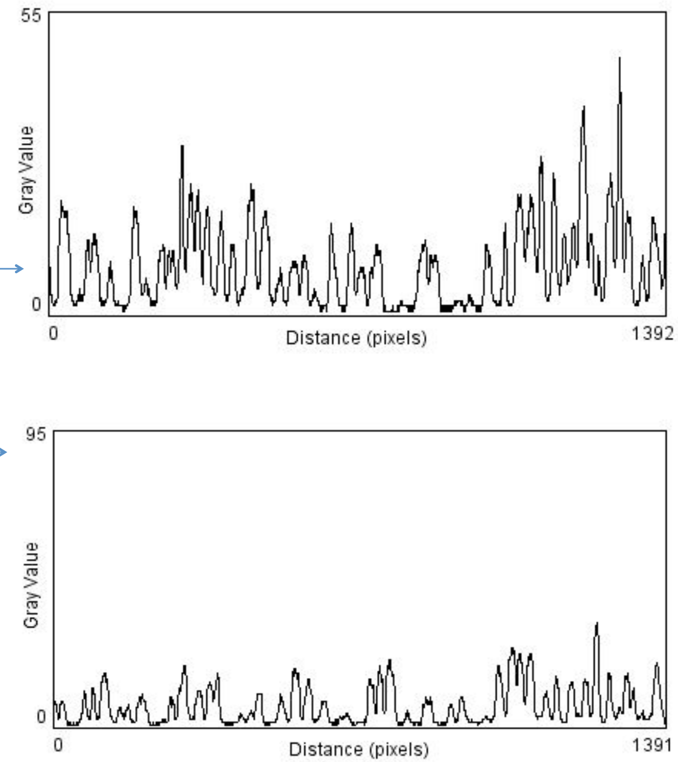
$D_S \approx 20\ \mu m^2/h$

Collective migration stochastic: „collective bursts“

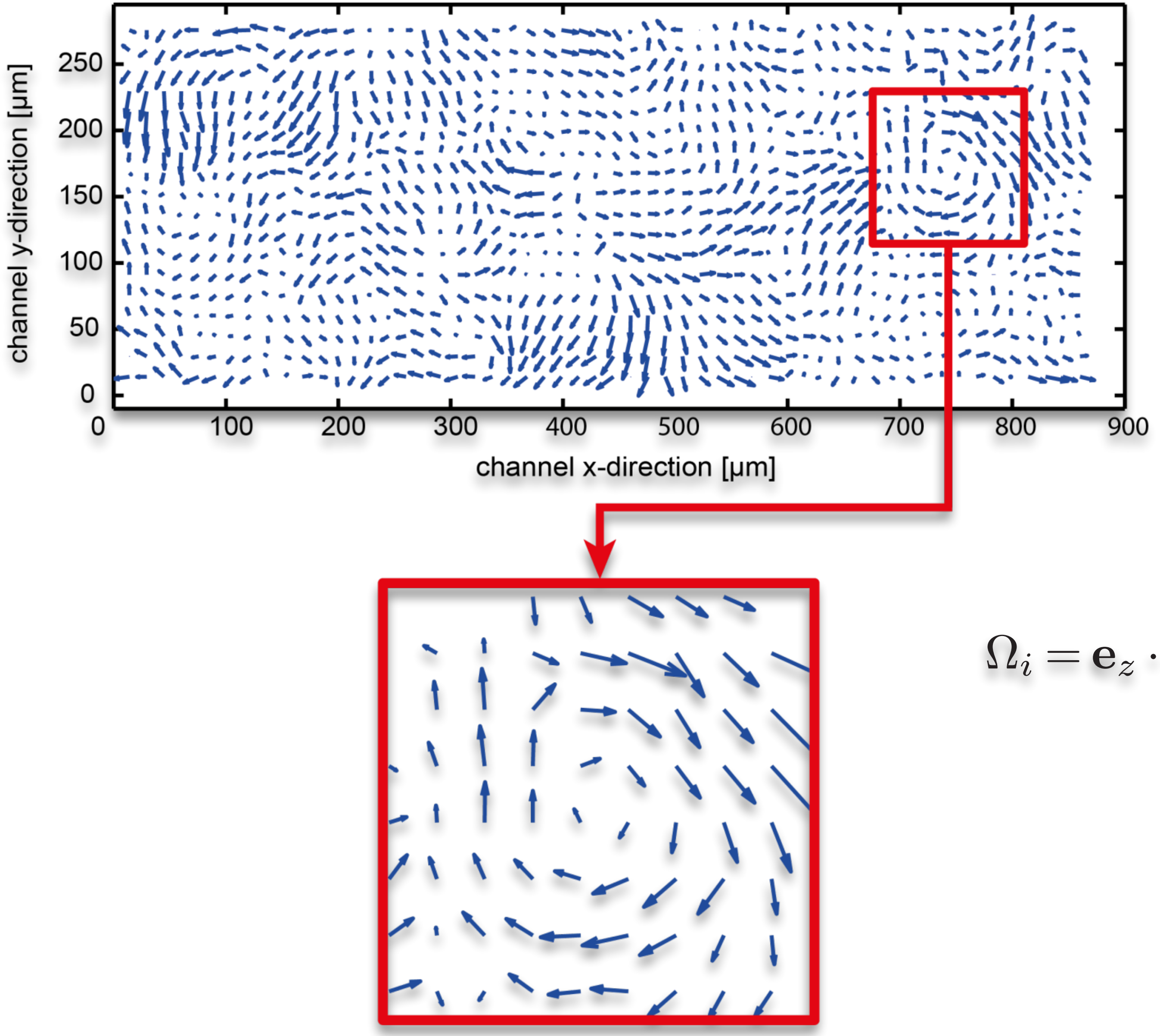
stochastic collective displacements
equilibrate cell density

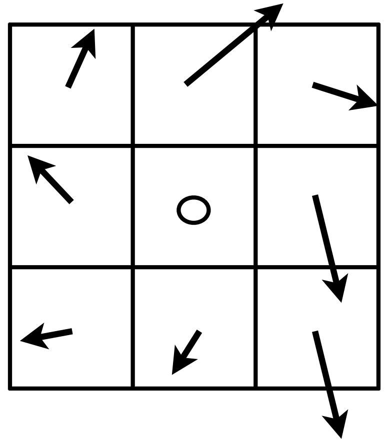
$$D_C \approx \xi^2 / 4\tau$$





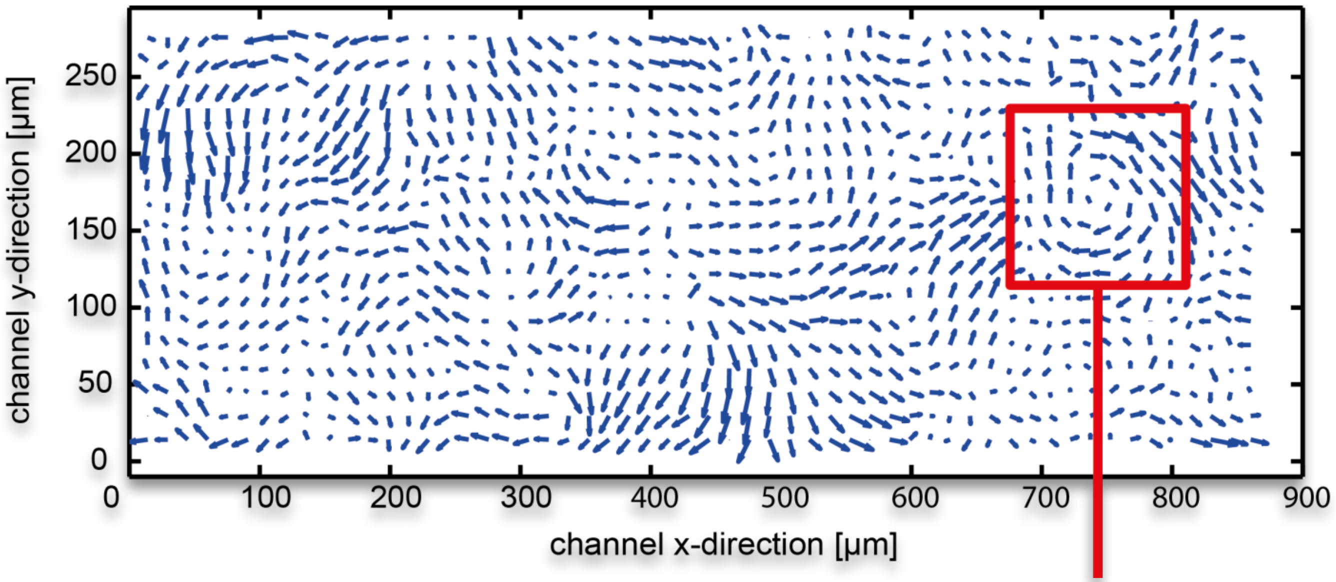
Swirls in collective flow

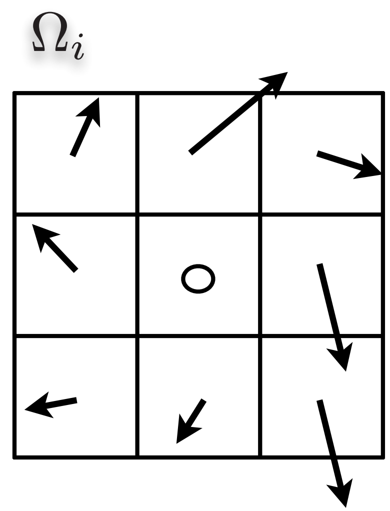




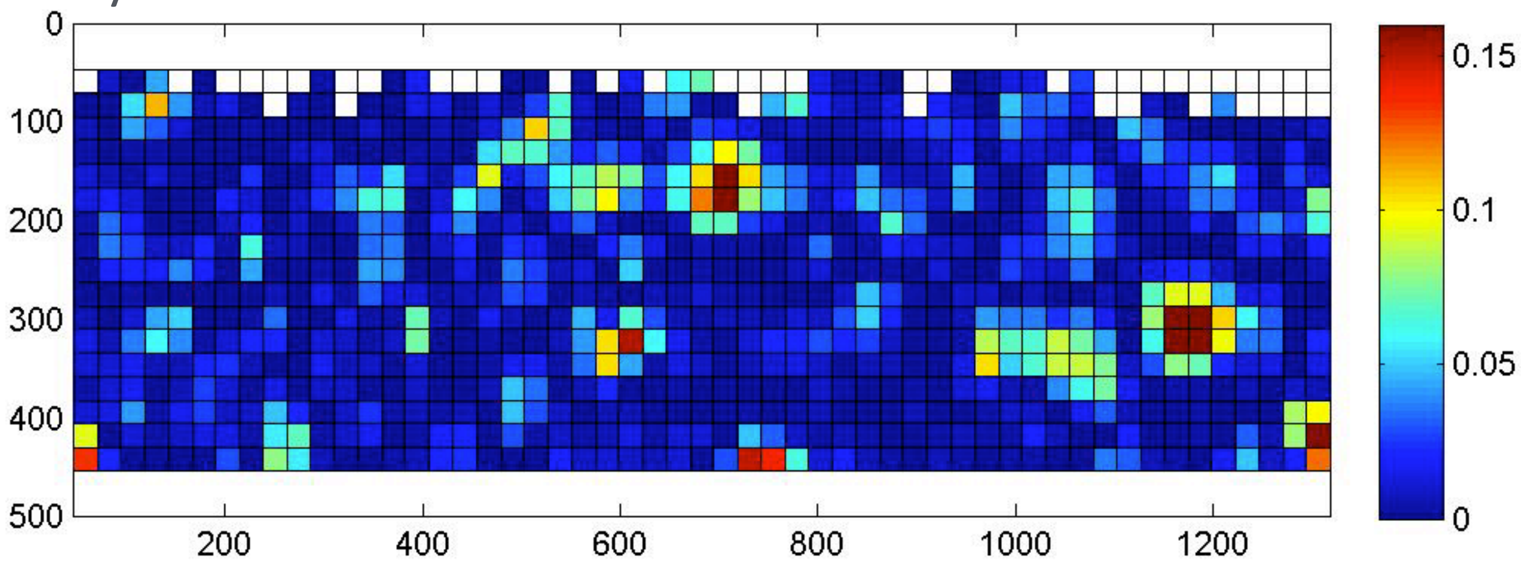
$$\Omega_i = \mathbf{e}_z \cdot (\mathbf{curl}\,\mathbf{v})_i = \frac{1}{nn_i} \sum_{j=1}^{nn_i} c_{i,j}\,.$$

Swirls in collective flow



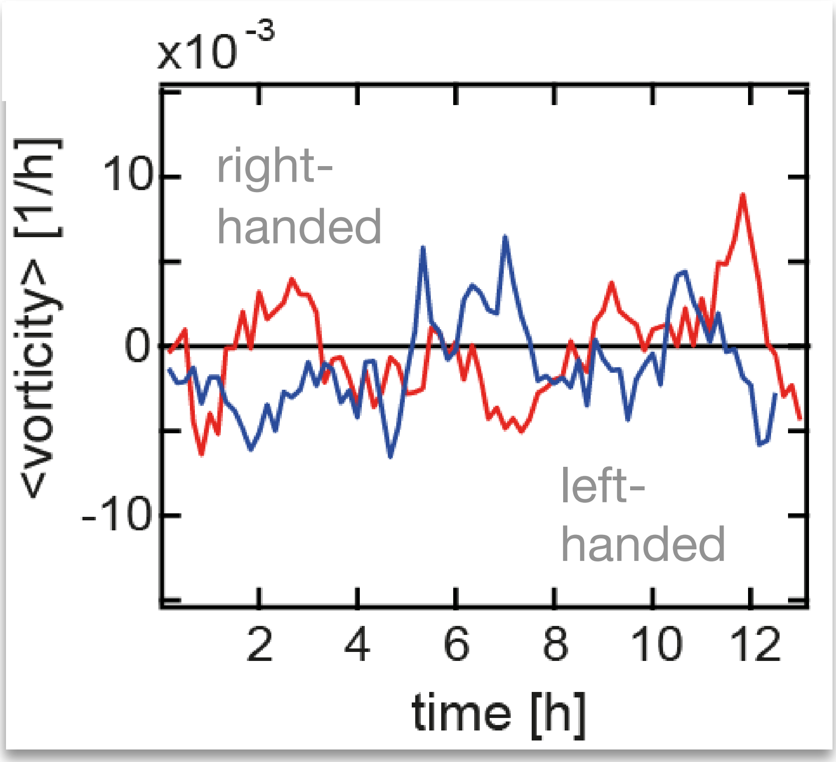


confluent layer of MDCK cells



Strength and Life Time of Vortices

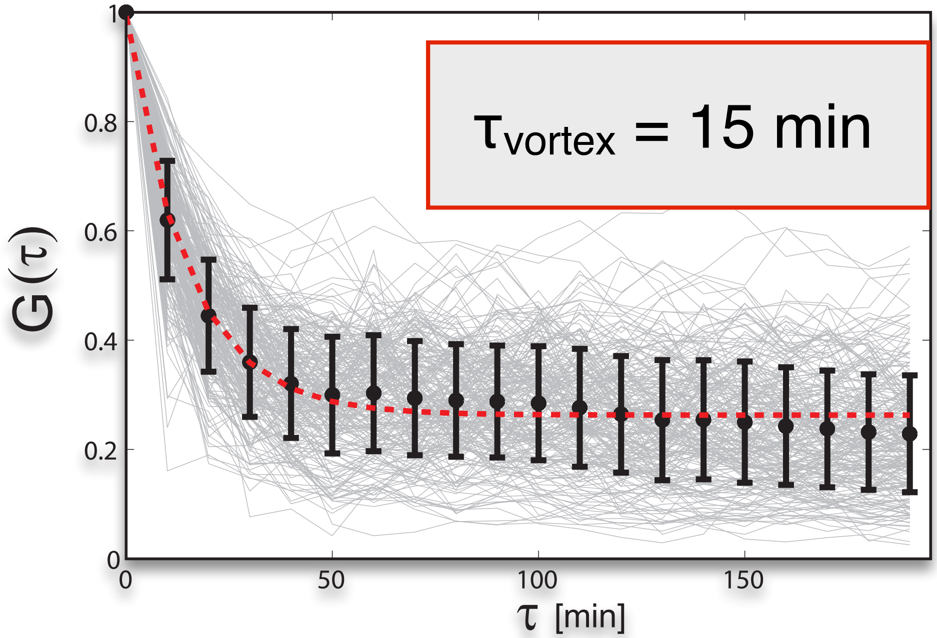
time course of vorticity Ω_i



no chirality in spontaneous vortices

time correlation of vorticity strength $\langle \Omega^2 \rangle$

$$G(\tau) = \frac{\langle \Omega^2(t) \rangle \cdot \langle \Omega^2(t+\tau) \rangle}{\Omega(t)^4}$$

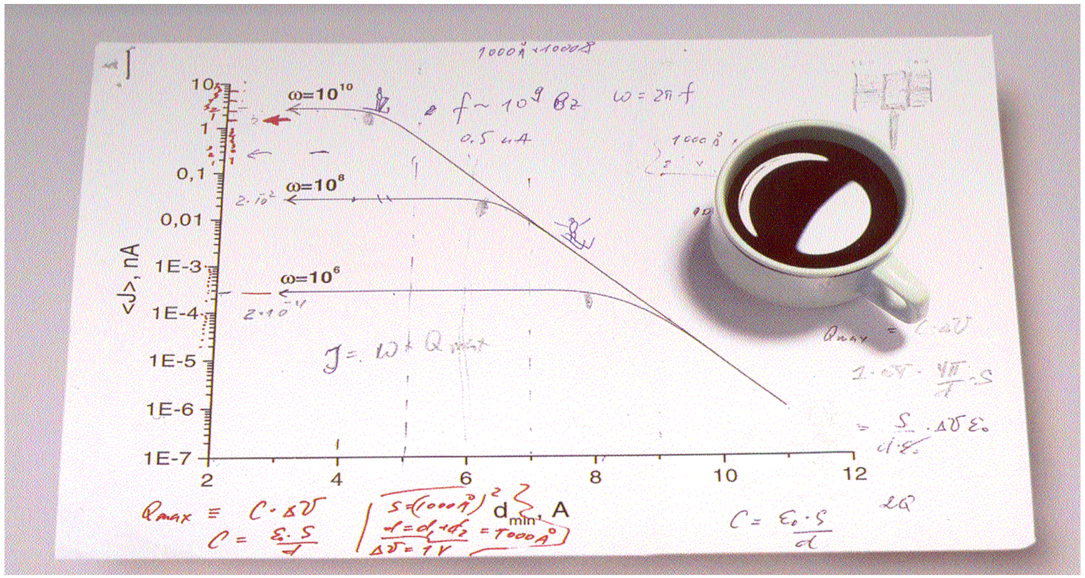


vortices are short-lived !

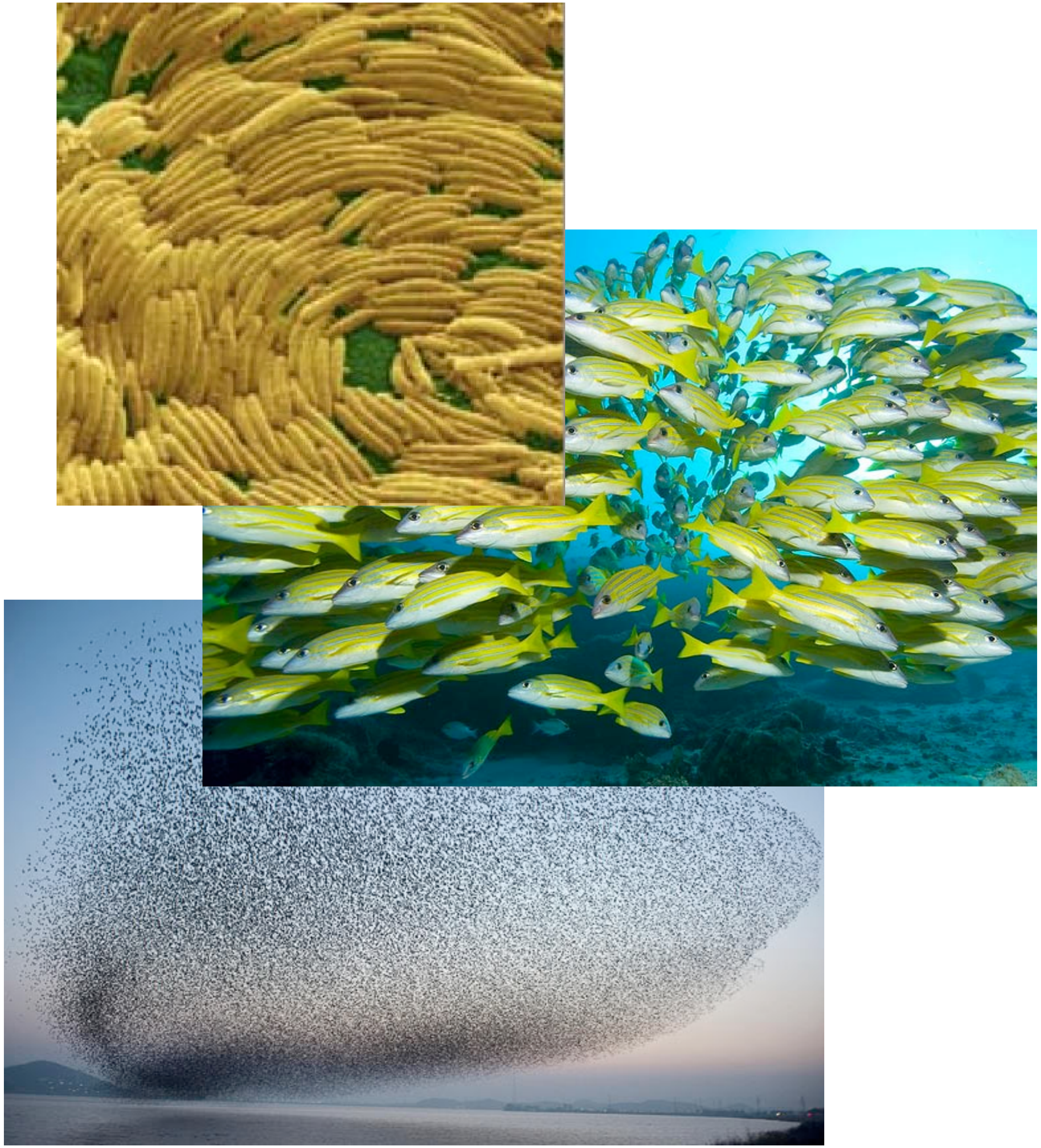
Biophysical Journal vol.107(5) 1054 (2014)

Modelling Collective Motion - Active Matter

- particle based models (Viszek type)
  - dissipative particle dynamics (DPD)
- cellular Potts models (CPM)
- phase field models (PFM)

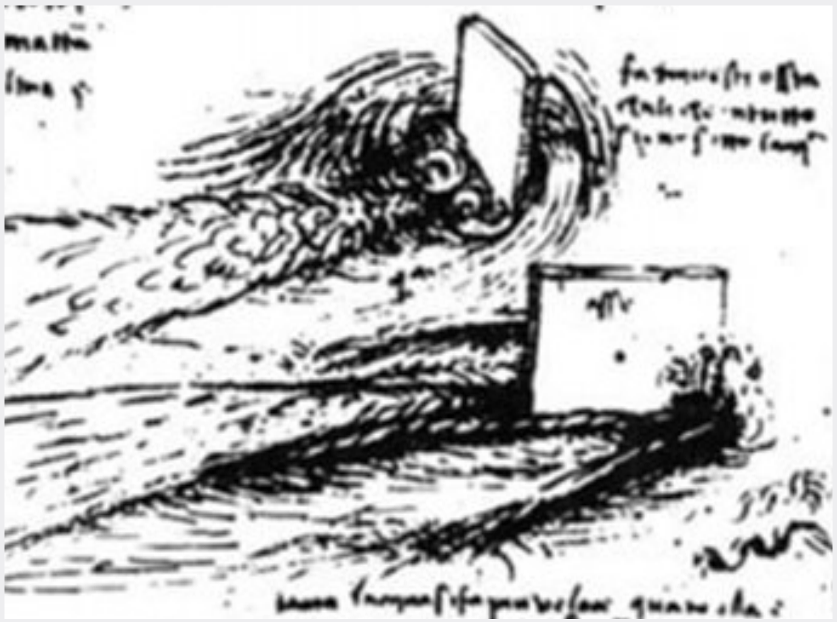


Active Matter: an ensemble of self-propelled units

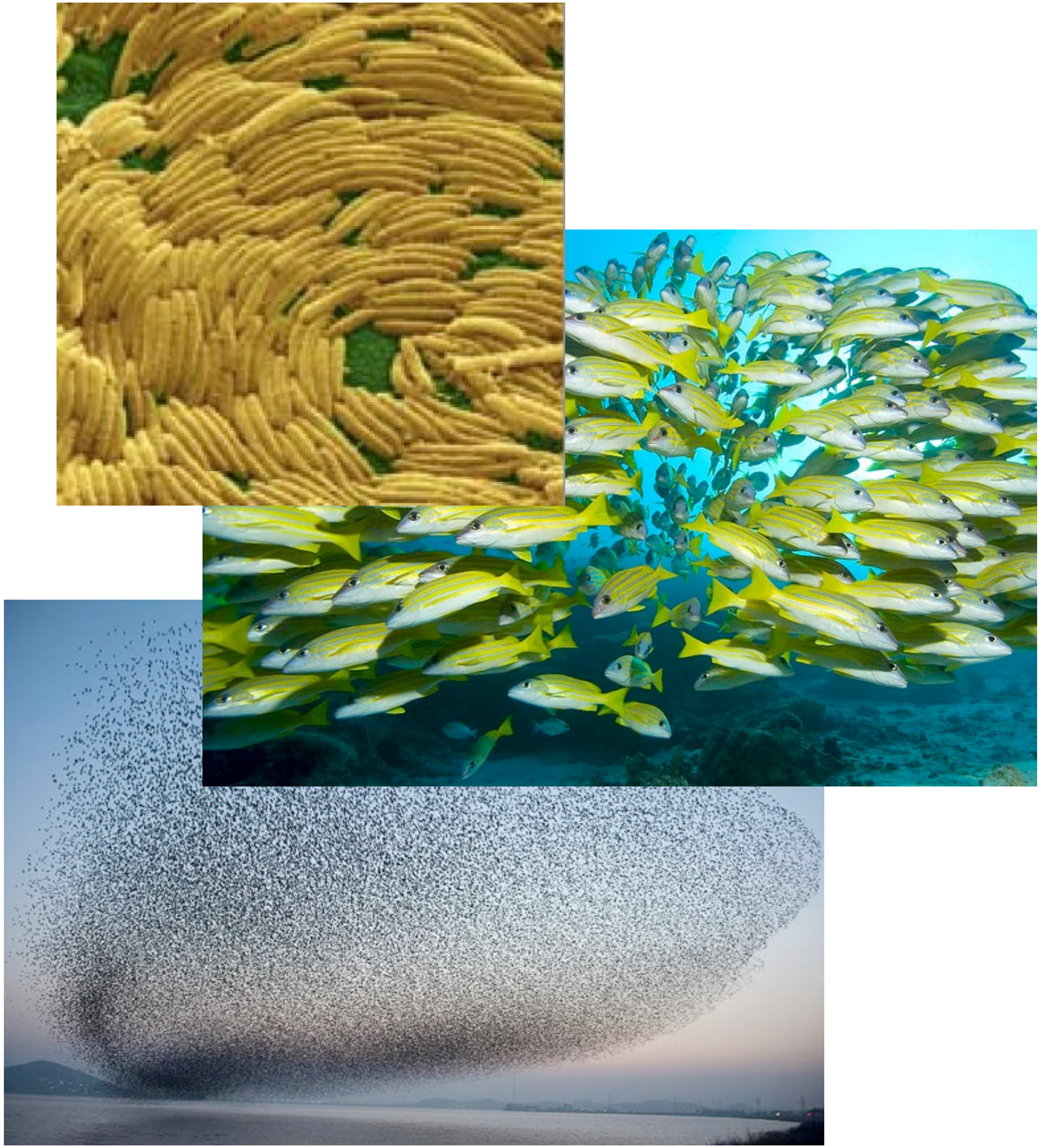


Observe the fish in the water
and you will understand
the birds in the air

Leonardo da Vinci



Active Matter: an ensemble of self-propelled units



collective behavior:
things move together

emergent phenomena:
e.g. pattern formation
order-disorder transitions

Active Matter:

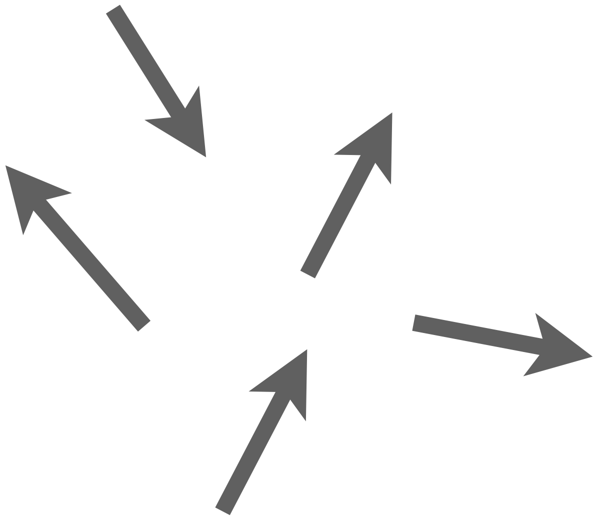
non-equilibrium system

non-linear dynamics

„active noise" = eff. temp.

T. Vicsek & Anna Zafeiris
cond-mat-stat-mech arXiv 2012

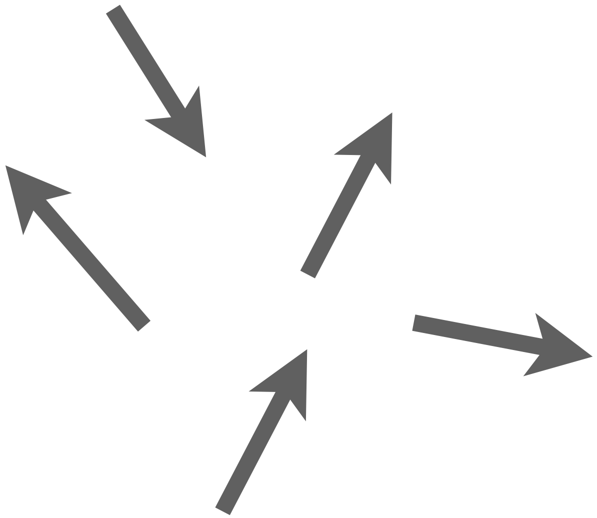
Collective Behavior in Active Soft Matter



(SPP Model)

$$\mathbf{x}_i(t+1) = \mathbf{x}_i(t) + \mathbf{v}_i(t)\Delta t\,.$$

The Viscek Model of Self-Propelled Particles



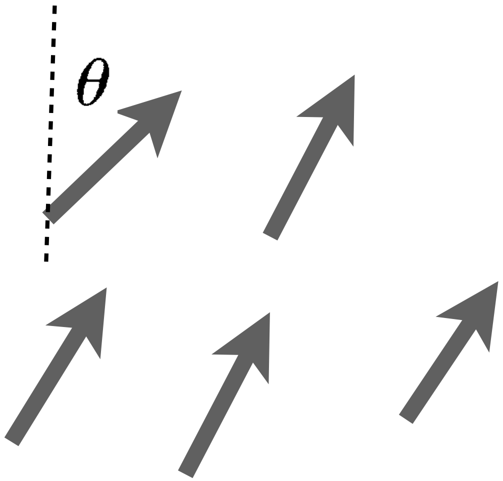
$$\mathbf{x}_i(t+1) = \mathbf{x}_i(t) + \mathbf{v}_i(t)\Delta t \,.$$

disorder - order transition

average direction of motion within radius r

random perturbation

$$\theta(t+1) = \langle \theta(t) \rangle_r + \Delta\theta \,,$$

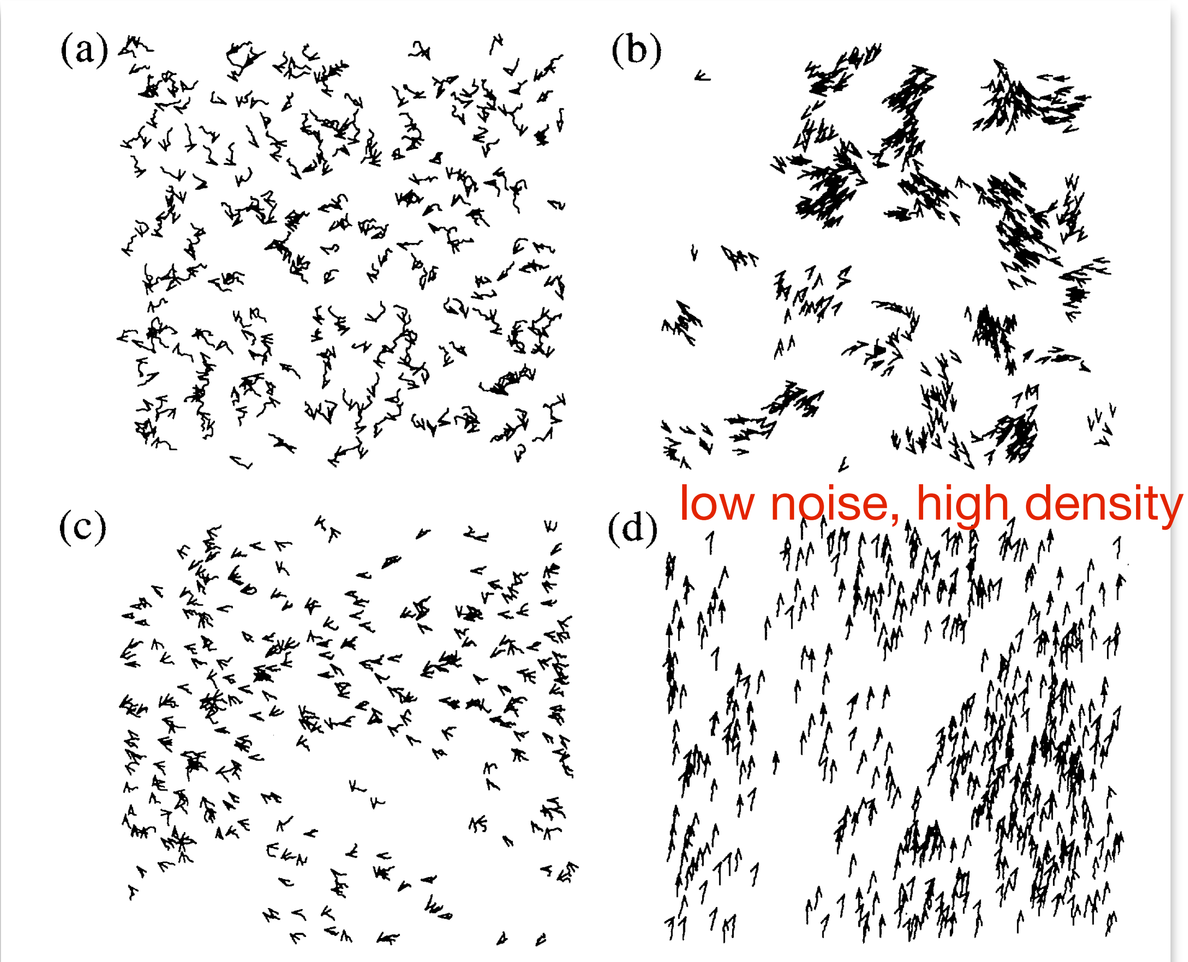


The Viscek Model of Self-Propelled Particles

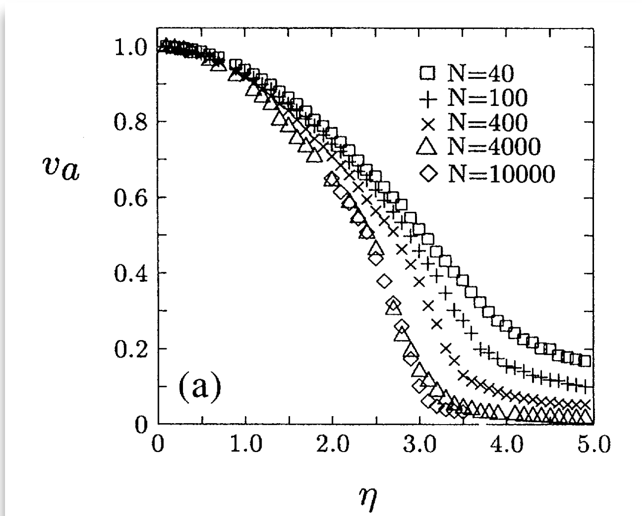
VOLUME 75, NUMBER 6 PHYSICAL REVIEW LETTERS 7 AUGUST 1995

Novel Type of Phase Transition in a System of Self-Driven Particles

Tamás Vicsek,[1,2] András Czirók,[1] Eshel Ben-Jacob,[3] Inon Cohen,[3] and Ofer Shochet[3]

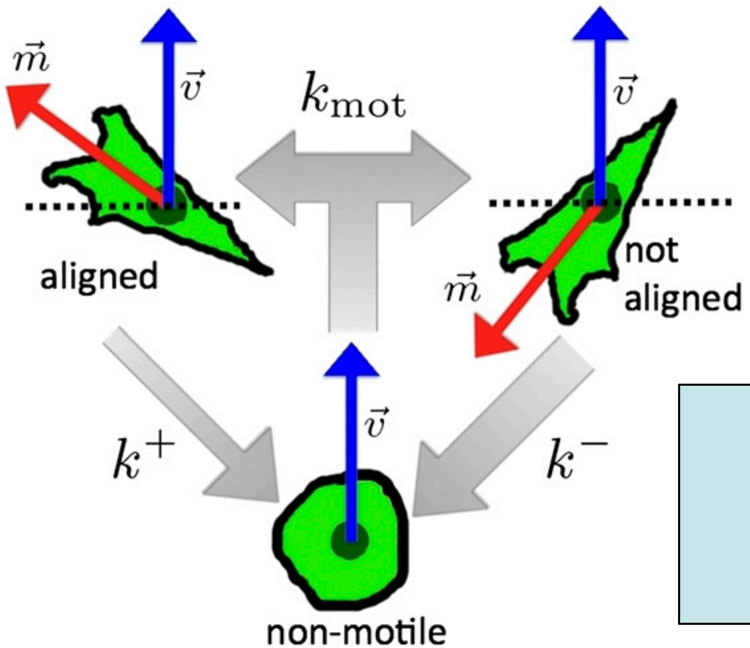


kinetic second order phase transition into long-ranged order with spontaneously selected direction



Alignment of cellular motility forces with tissue flow as a mechanism for efficient wound healing

Markus Basan[a], Jens Elgeti[b], Edouard Hannezo[c], Wouter-Jan Rappel[a], and Herbert Levine[d,1]



Dissipative particle dynamics (DPD)

- locally conserves momentum
- models friction and fluctuations

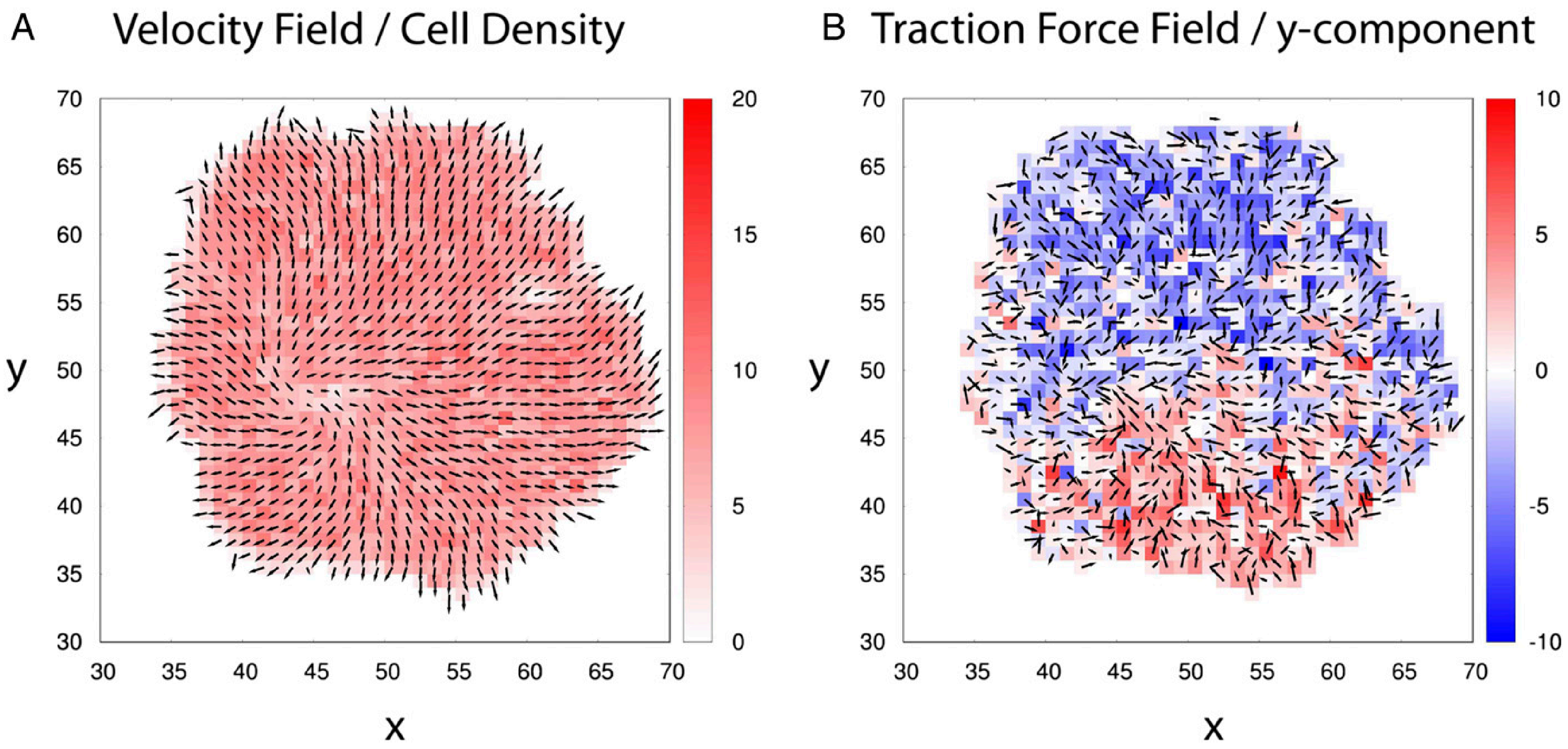
$$\frac{dp}{dt} = \vec{m} + \vec{F}_{\mathrm{exp}} + \vec{F}_{\mathrm{int}} + \vec{F}_{\mathrm{B}} + \sum_{r \le R_{\mathrm{CC}}} \left(\vec{F}_{\mathrm{rep/ad}} + \vec{F}_{\mathrm{df}} + \vec{\eta} \right)$$

m: motility force

.. we propose that the motility forces of cells in the tissue tend to align with the flow …

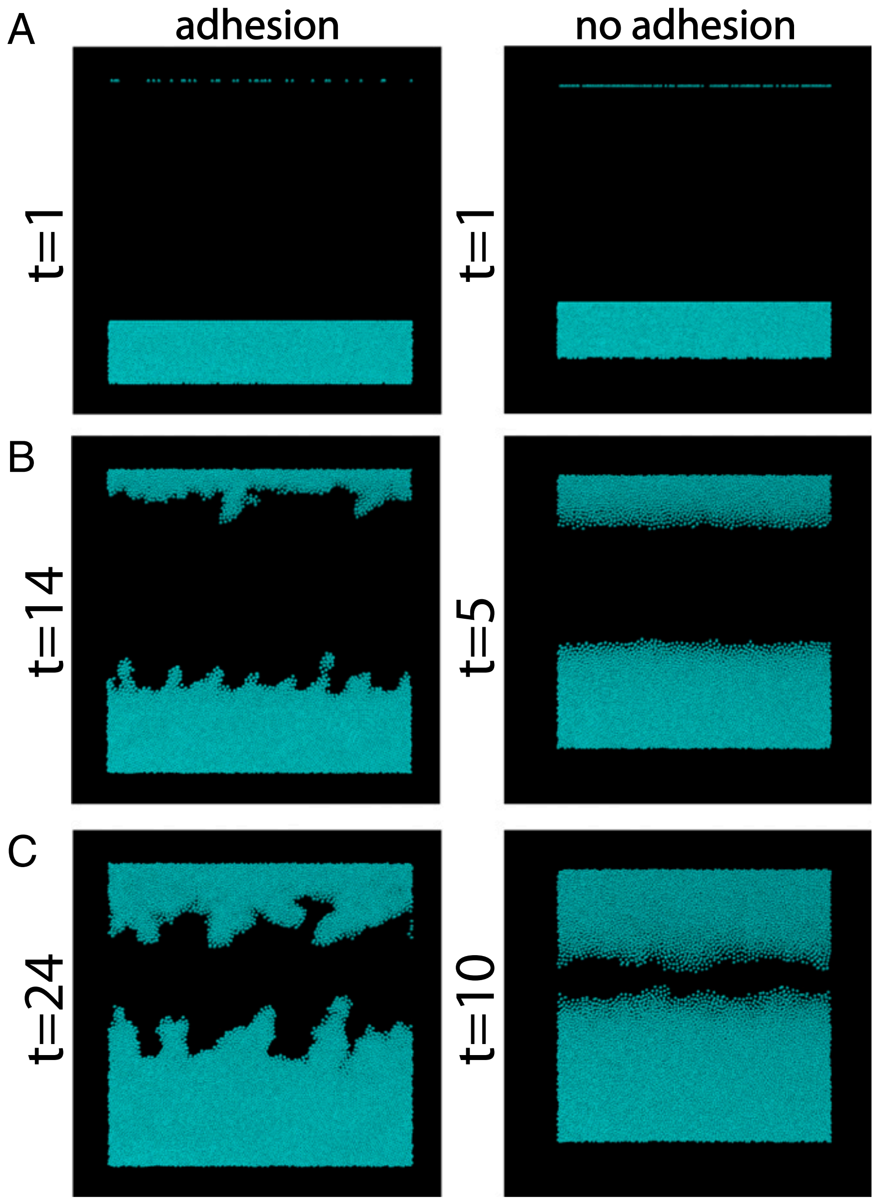
2452–2459 | PNAS | **February 12, 2013** | vol. 110 | no. 7

DPD reproduces tension in expanding cell sheets



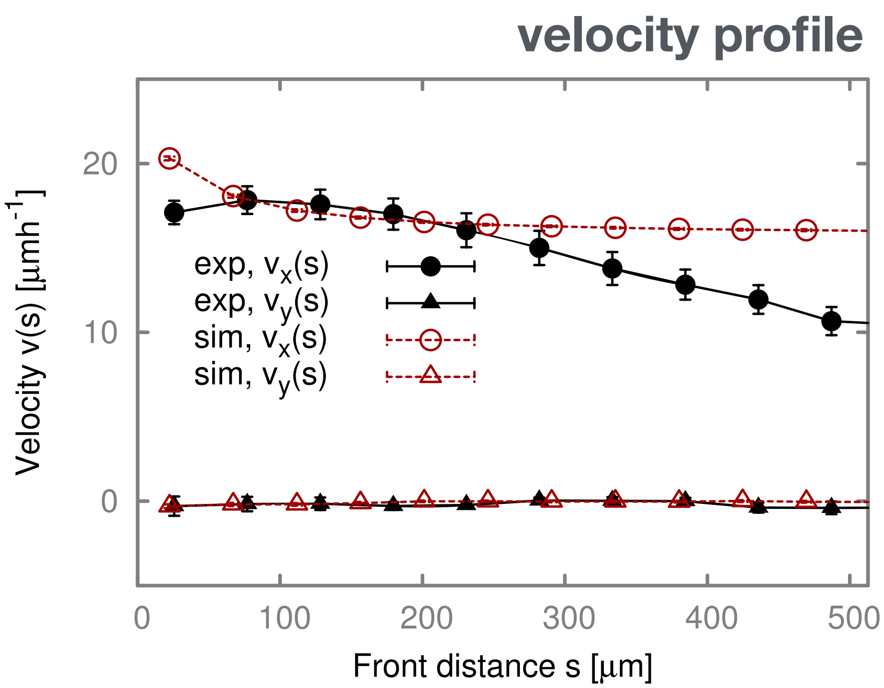
2452–2459 | PNAS | **February 12, 2013** | vol. 110 | no. 7

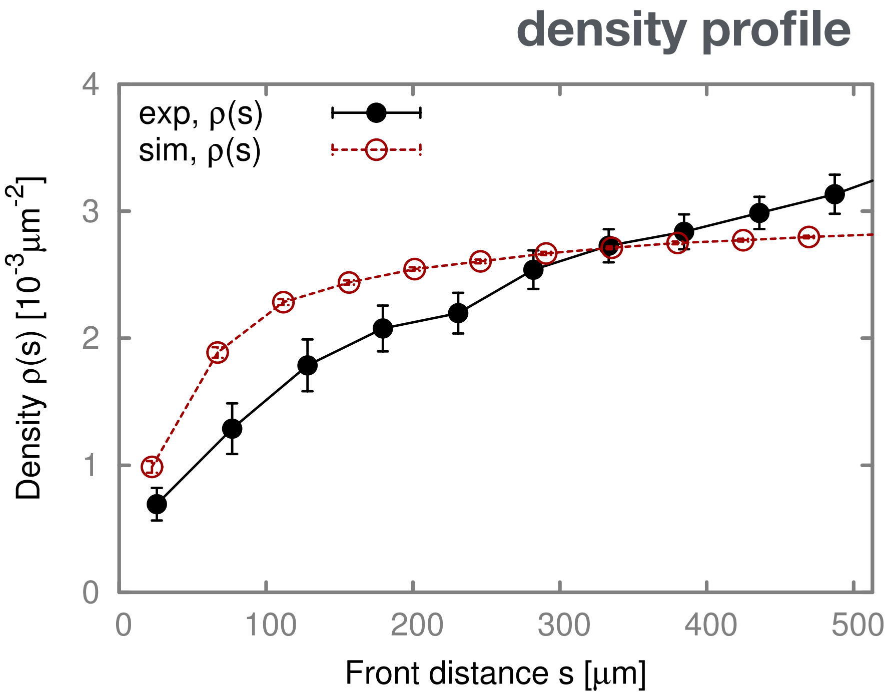
DPD reproduce finger formation at invading fronts

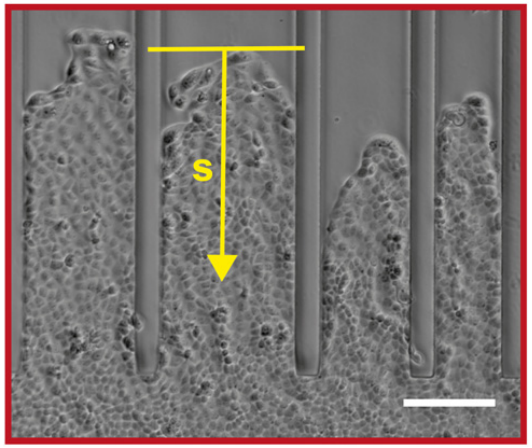


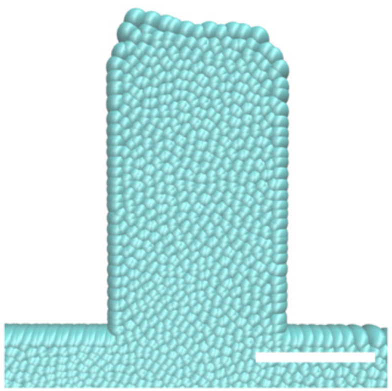
2452–2459 | PNAS | **February 12, 2013** | vol. 110 | no. 7

DPD modeling of channel flow





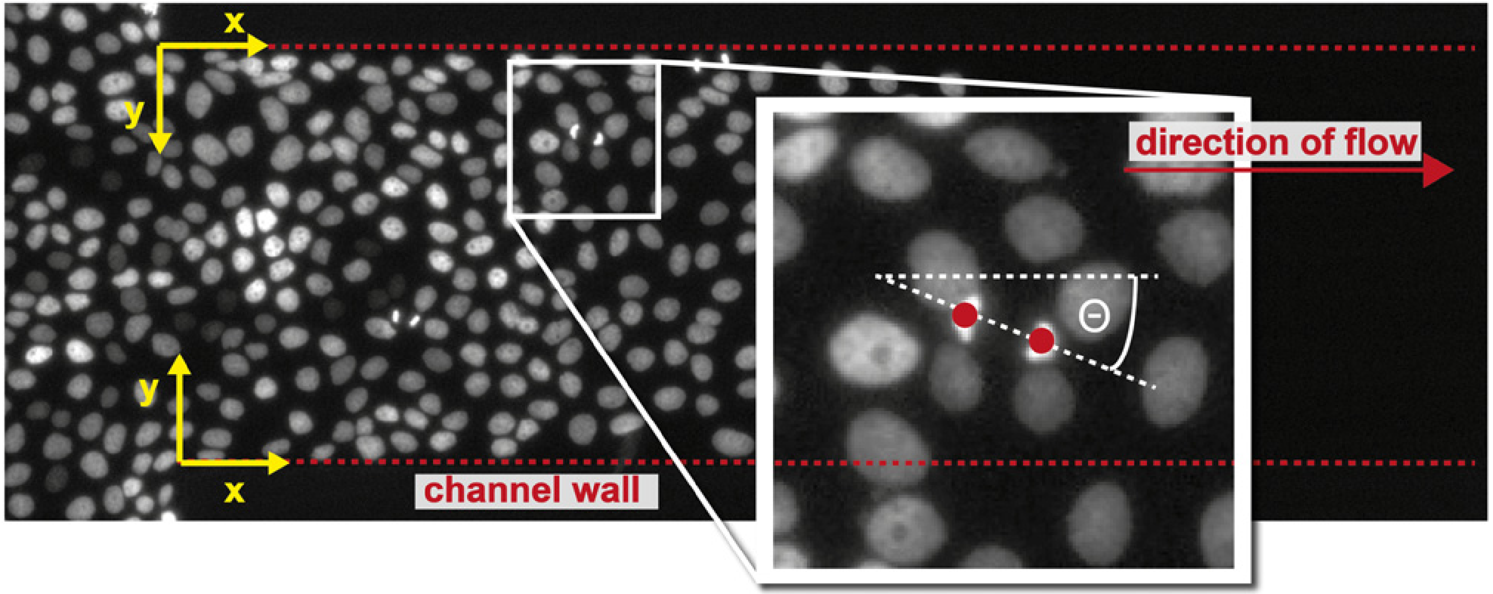


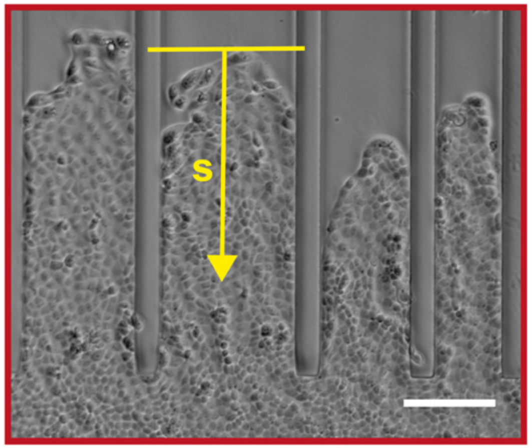


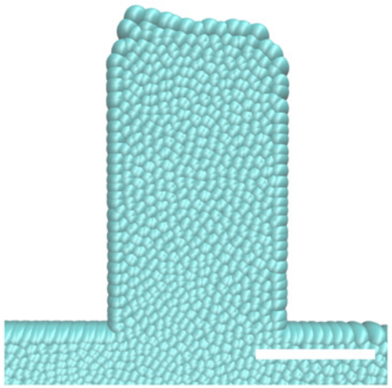
A. Marel, N. Podewitz, M. Zorn, J. Rädler and Jens Elgeti

New Journal of Physics 16 (2014)

Alignment of cell division axes in directed migration



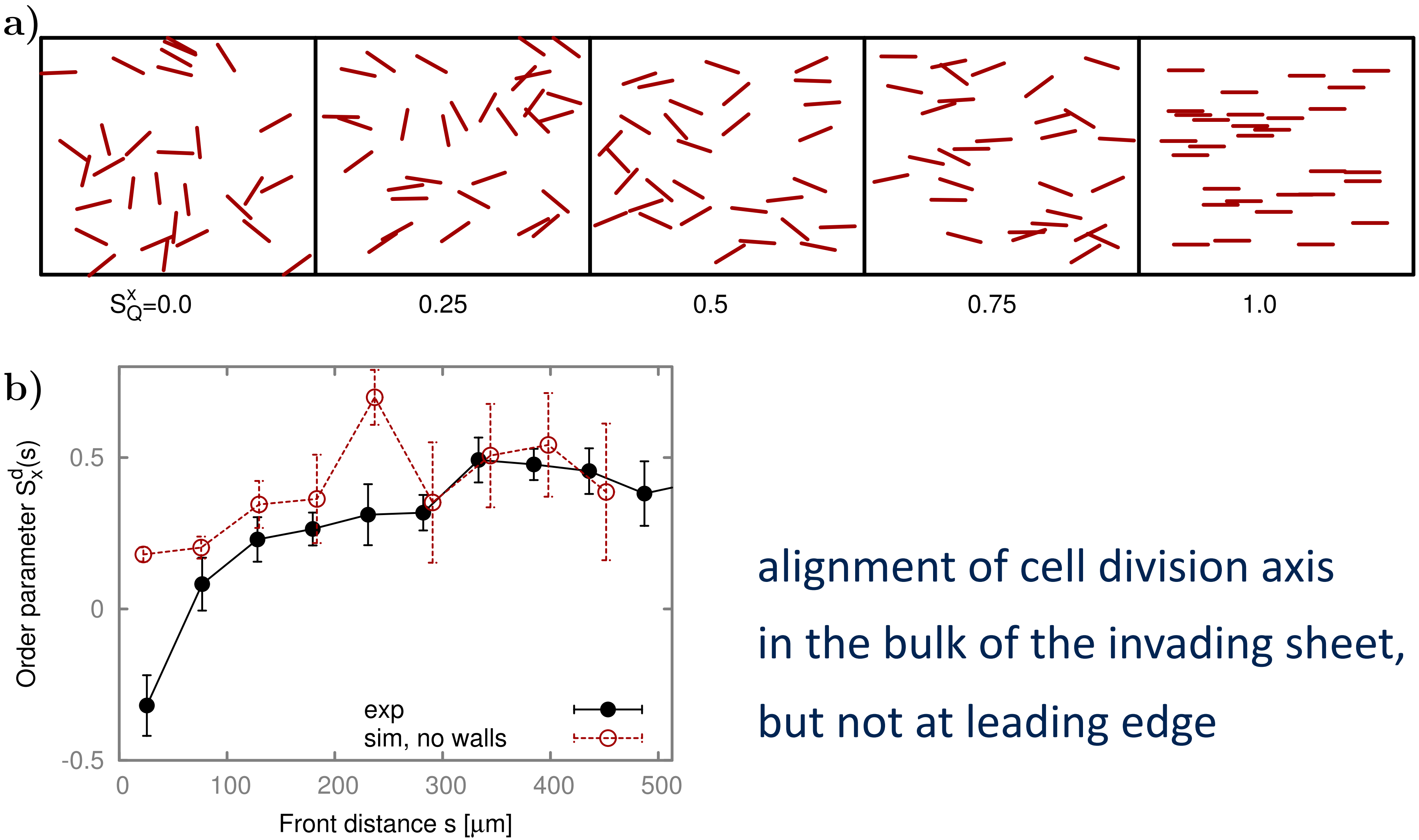




A. Marel, N. Podewitz, M. Zorn,
J. Rädler and Jens Elgeti

New Journal of Physics 16 (2014)

Alignment of cell division axes in directed migration



alignment of cell division axis

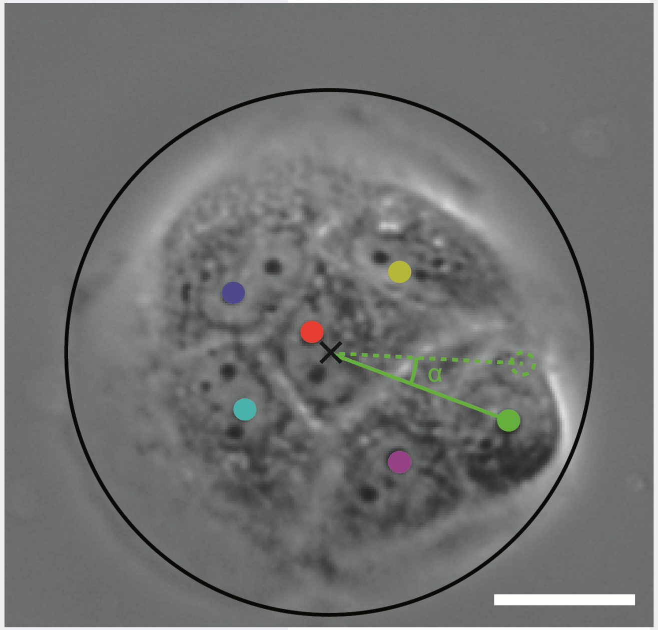
in the bulk of the invading sheet,

but not at leading edge

Marel et al. New Journal of Physics 16 (2014) 115005

Emergence and Persistence of Collective Cell Migration on Small Circular Micropatterns

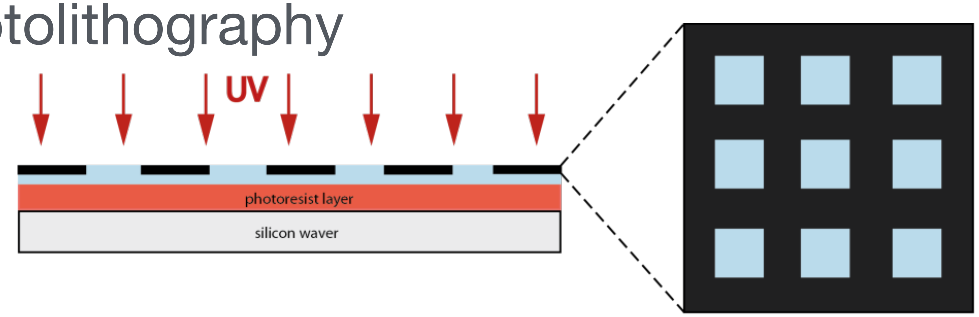
- small system size
- defined boundary conditions



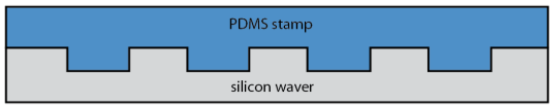
F. Segerer, F. Thüroff, A. Piera Alberola E. Frey and J.O. Rädler, PRL 114, 228102 (2015)

Plasma - Induced Patterning

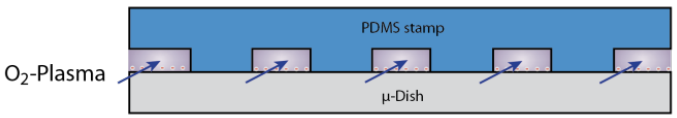
1) Photolithography



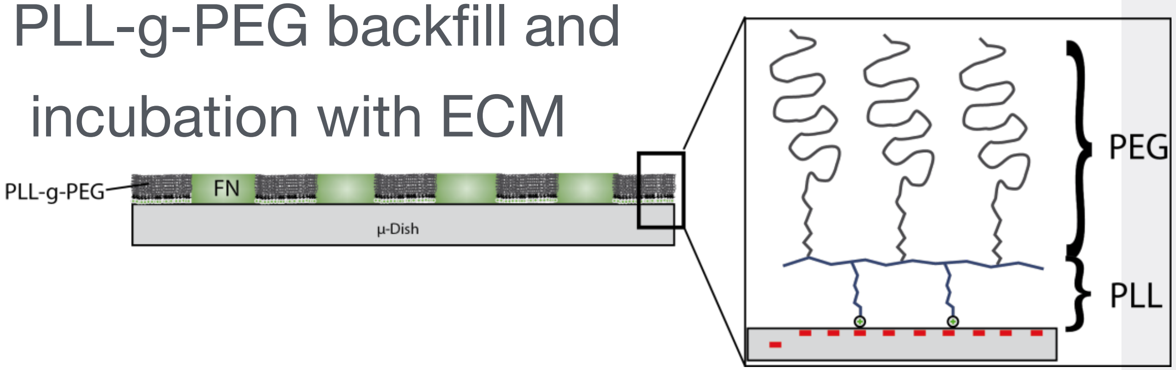
2) PDMS stamp on substrate

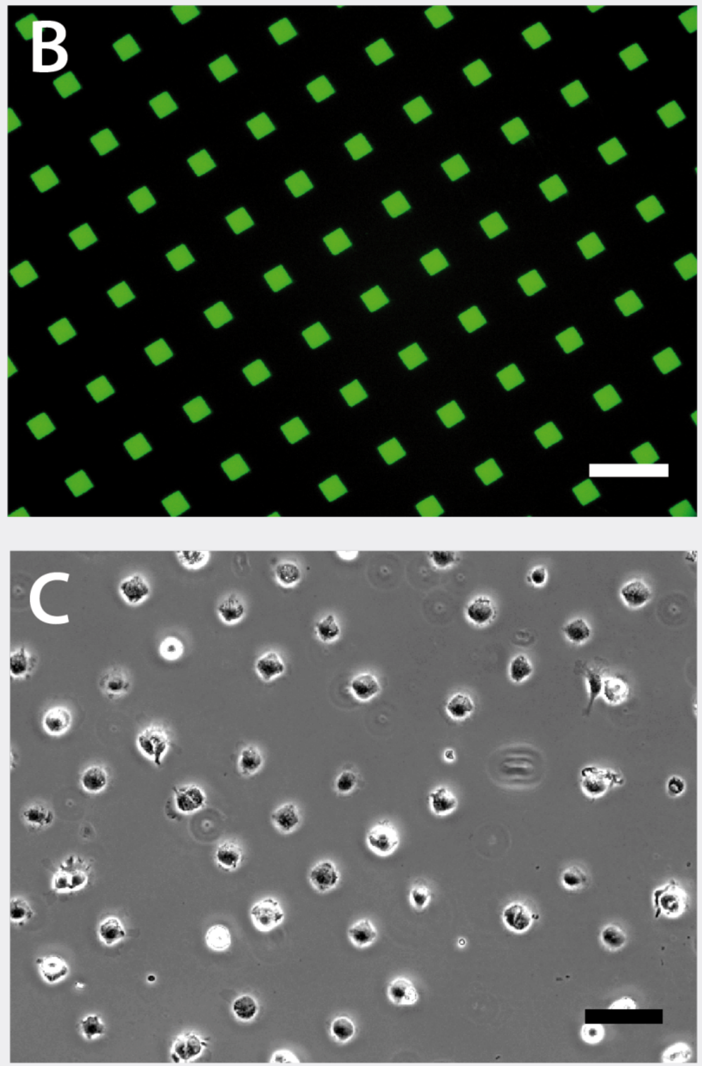


3) Plasma-induced patterning



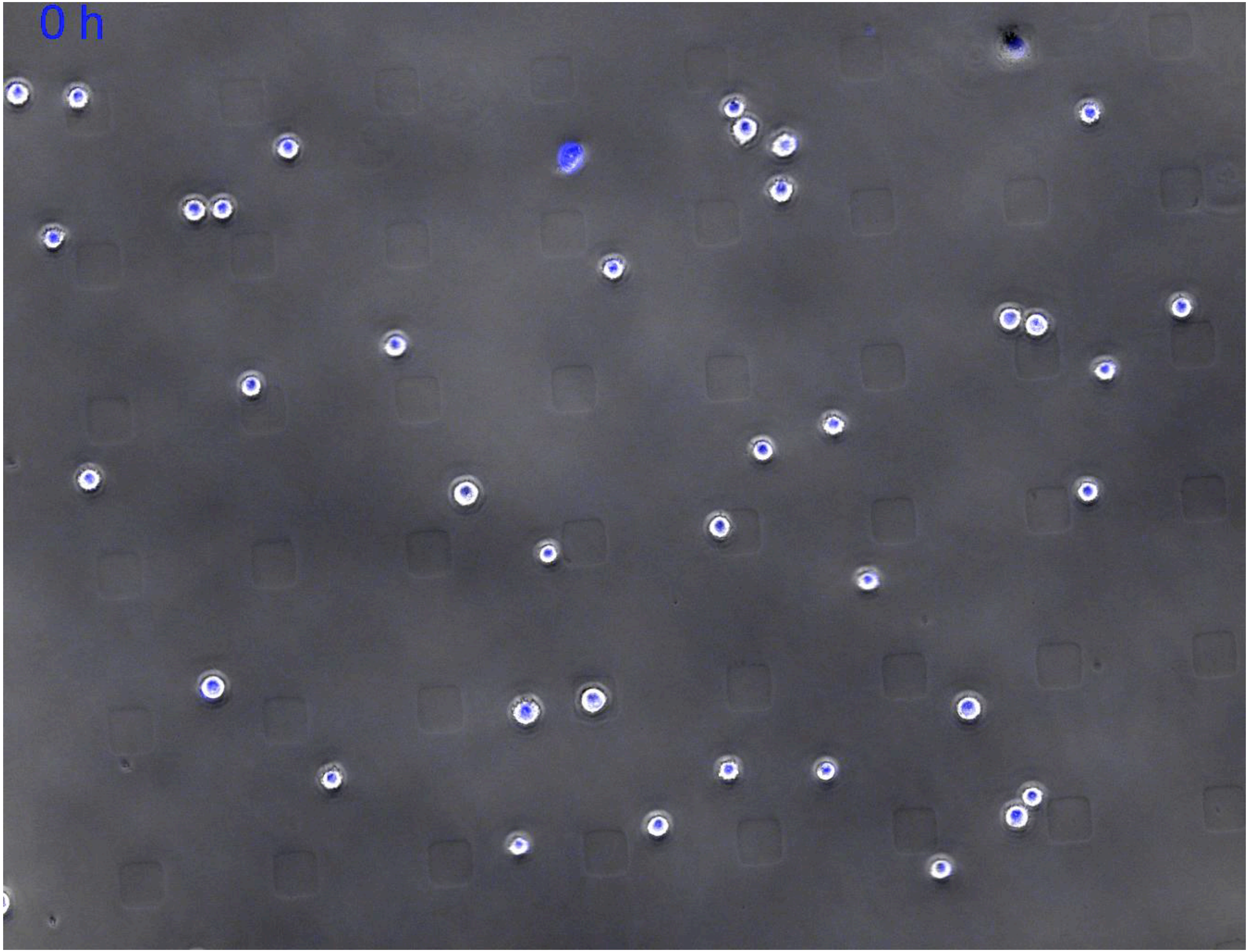
4) PLL-g-PEG backfill and incubation with ECM





Peter Röttgermann, Soft Matter (2014)

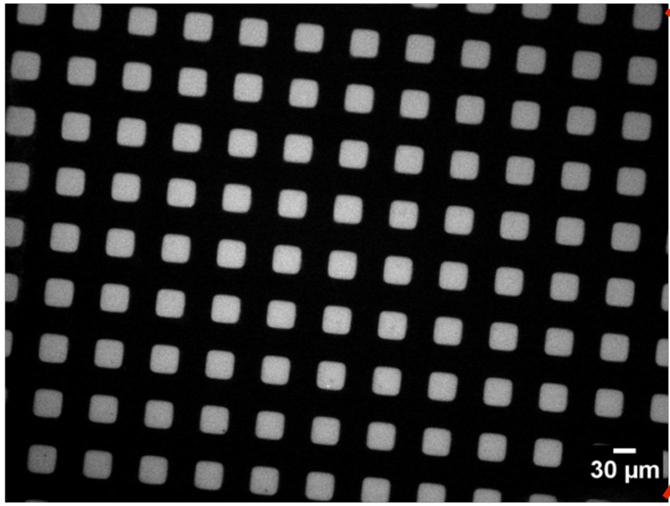
F. Segerer, P. Röttgermann, S. Schuster, A Alberola, S. Zahler, and J Rädler. Biointerphases 11(1) (2016) 011005.

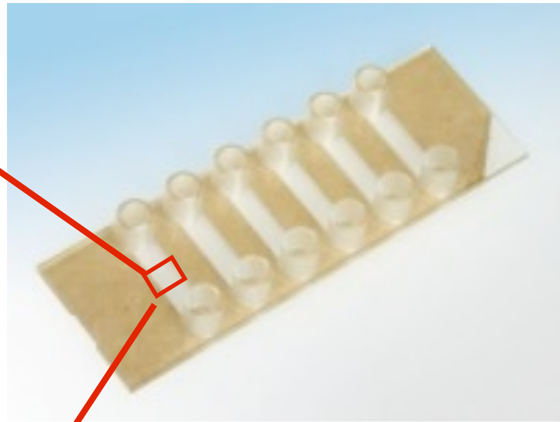


Peter Röttgermann, Soft Matter (2014)

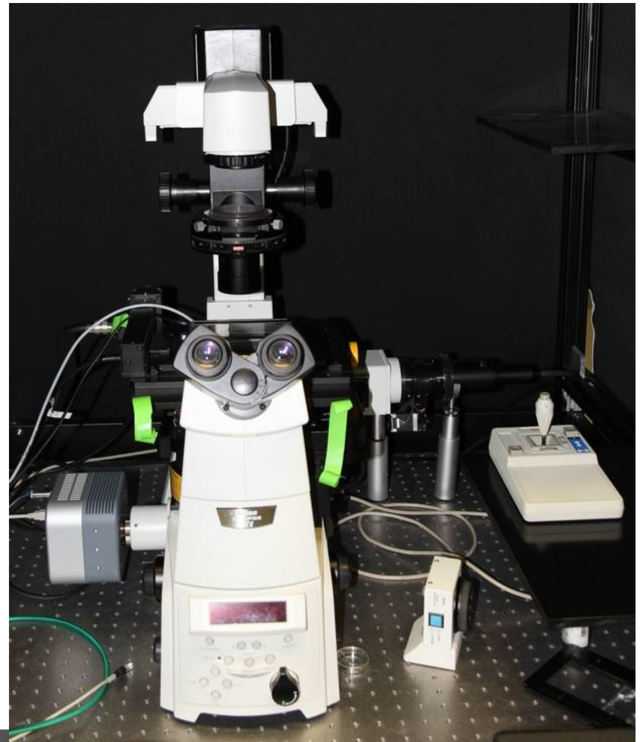
Live Cell Imaging on Single Cell Arrays

structured substrates





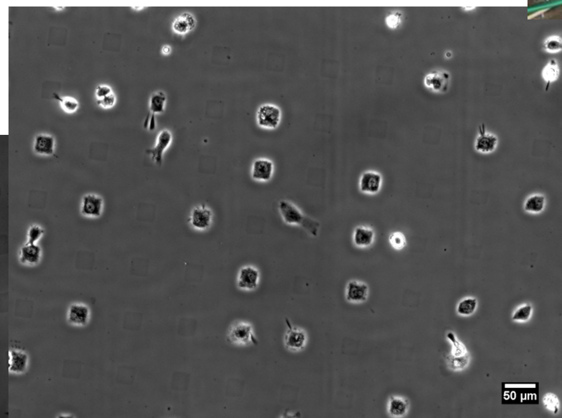
channel - chambers

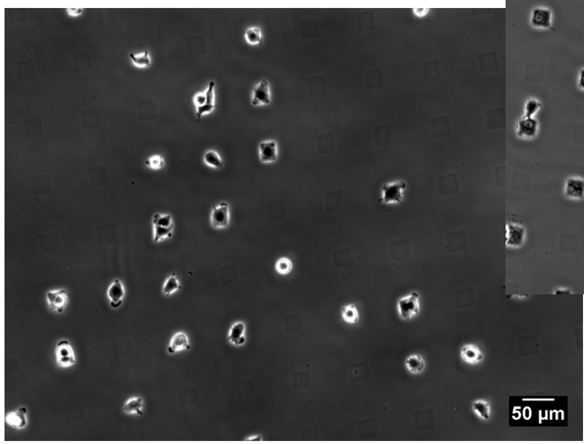


Cells are seeded out & settle

-> transfection

automated
time-lapse movie
acquisition
scanning

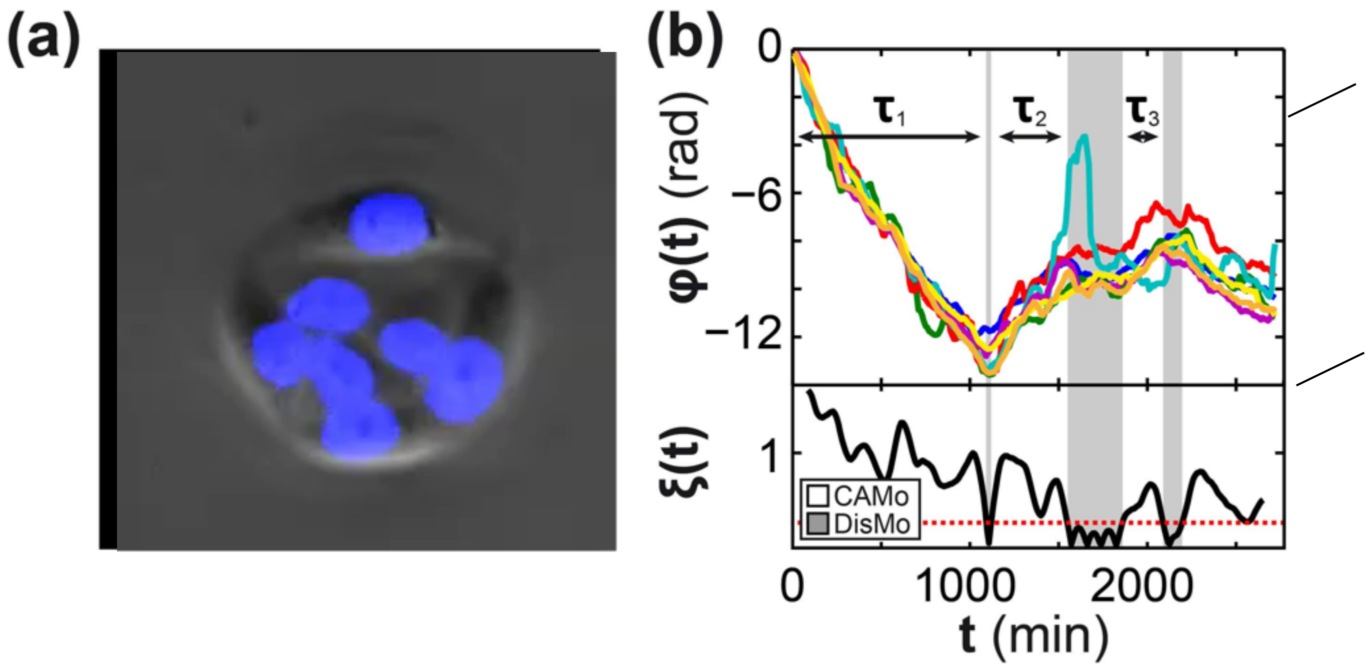




Huh7

A549 cells

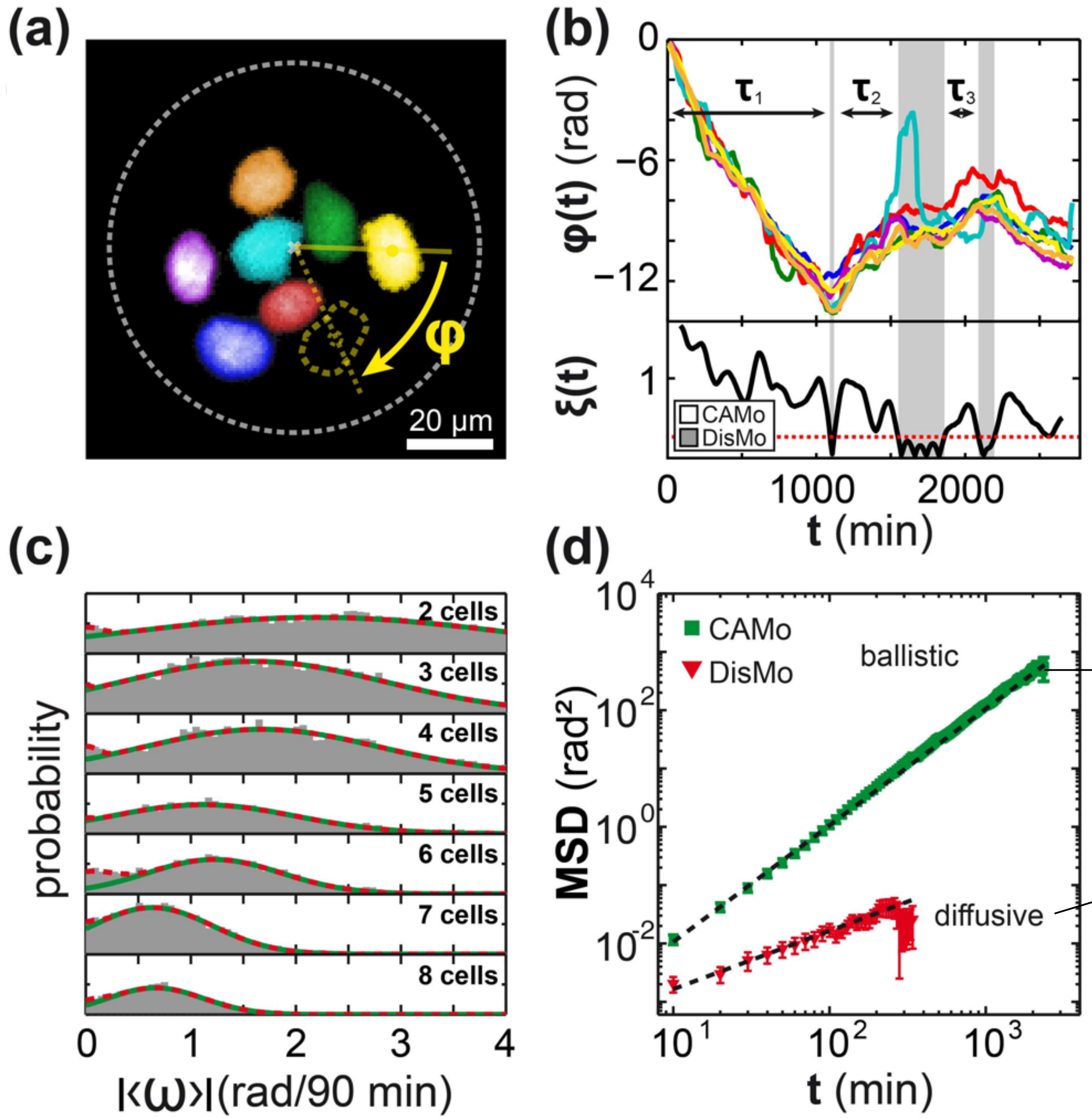
States of Coherent Angular Motion (CAMo)



Individual angular traces

F. Segerer, F. Thüroff, A. Piera Alberola E. Frey and J.O. Rädler, PRL 114, 228102 (2015)

States of Coherent Angular Motion (CAMo)

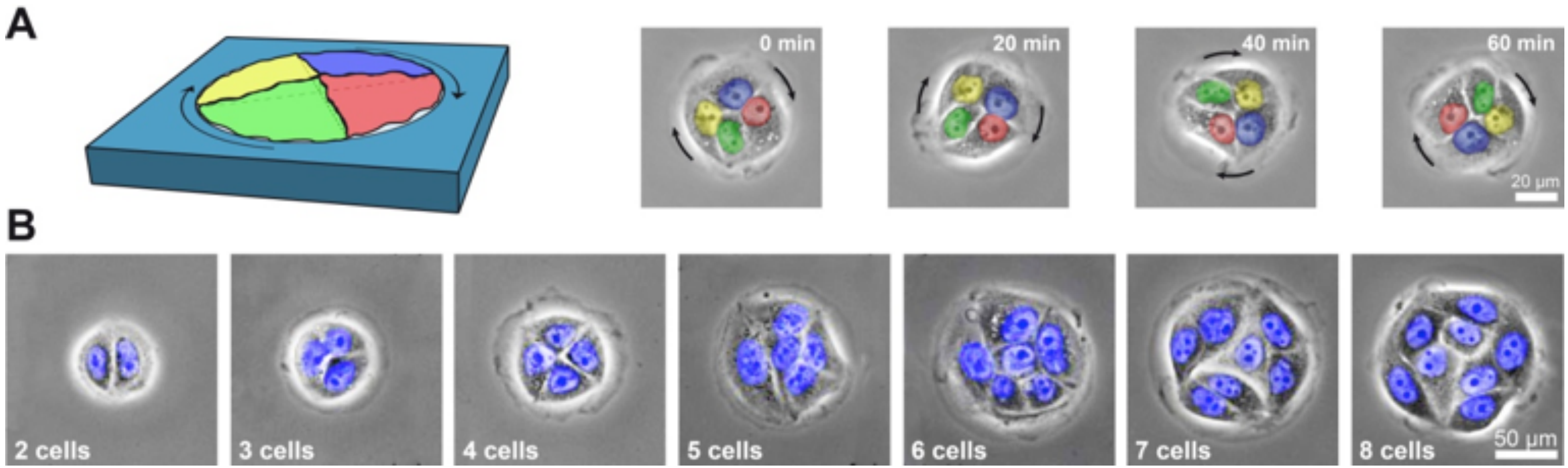


Individual angular traces

coherent state

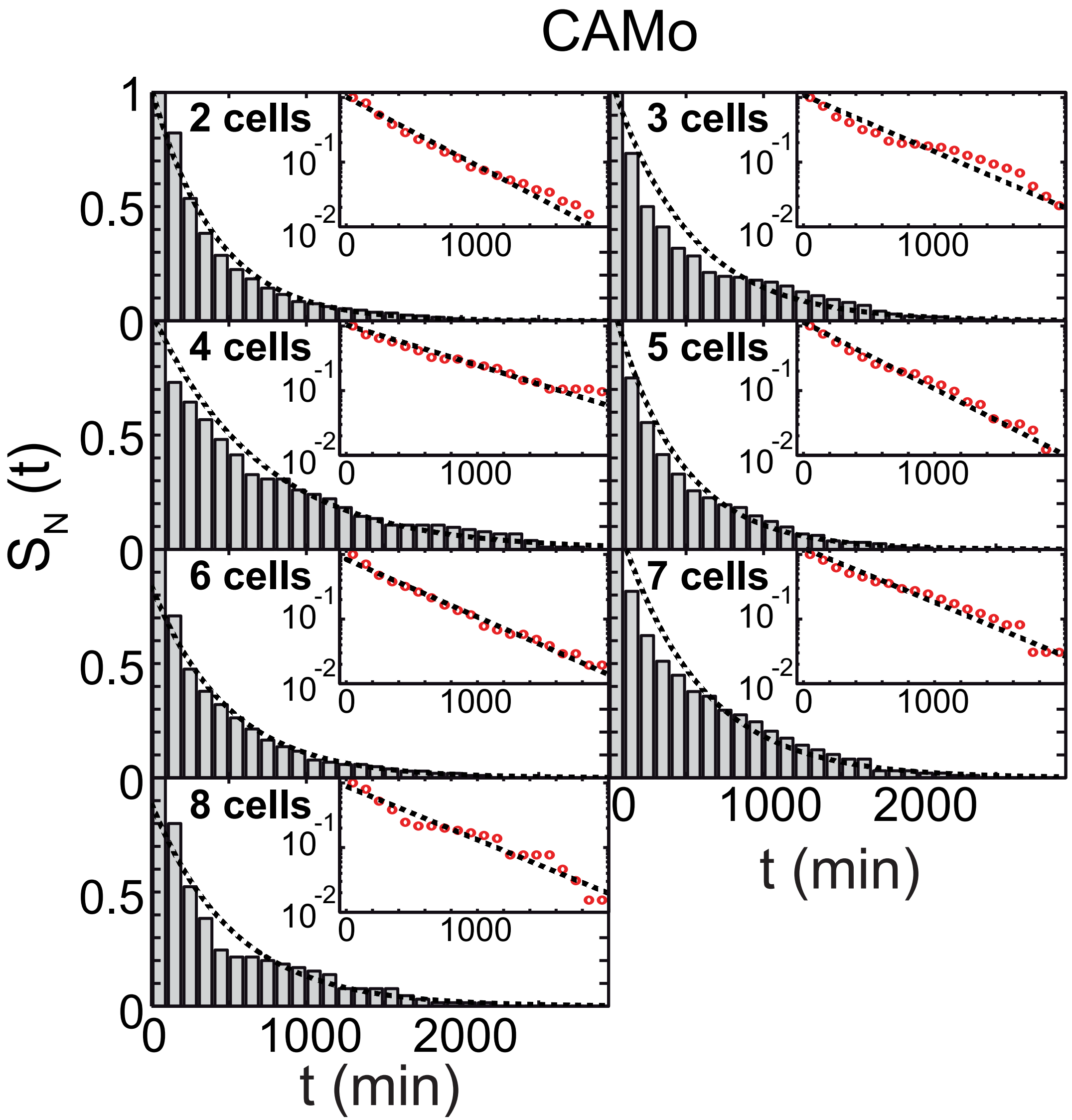
disordered state

Collective migration as a function of system size



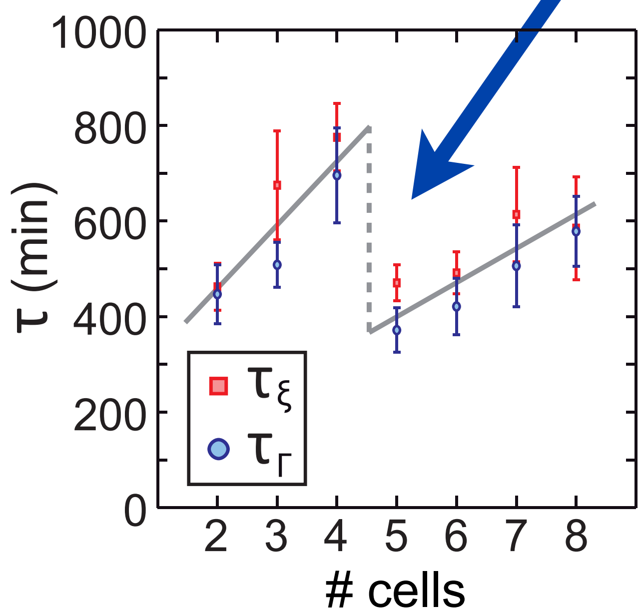
F. Segerer, F. Thüroff, A. Piera Alberola E. Frey and J.O. Rädler, PRL 114, 228102 (2015)

The migration „states“ exhibit a defined life time



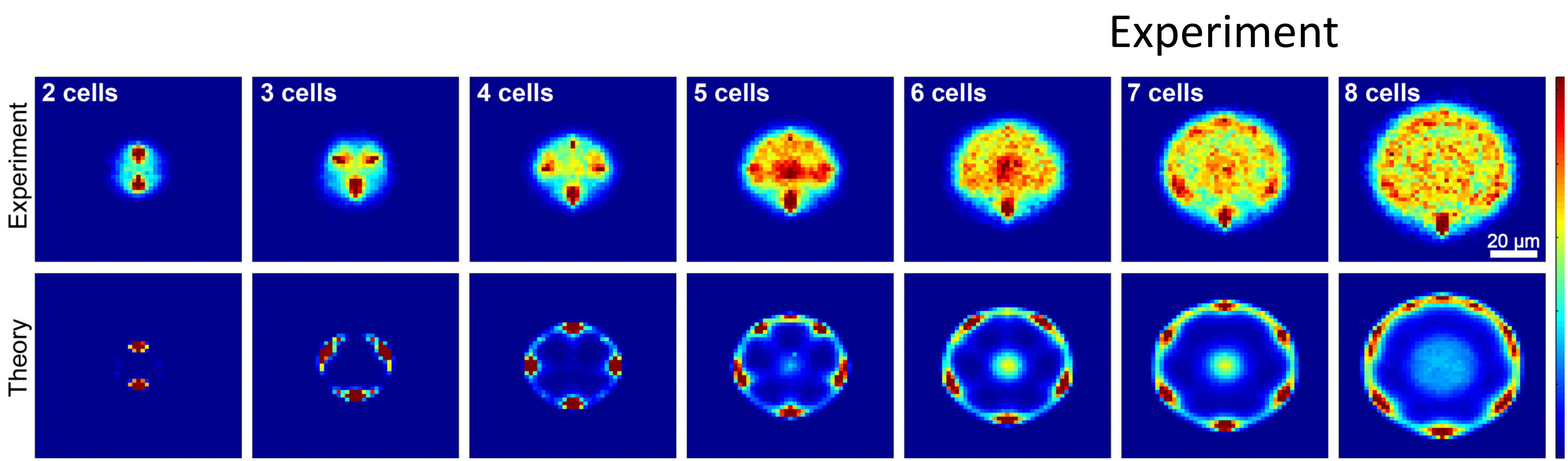
persistence time grows as a function of system size (i.e. number of cells)

discontinuity

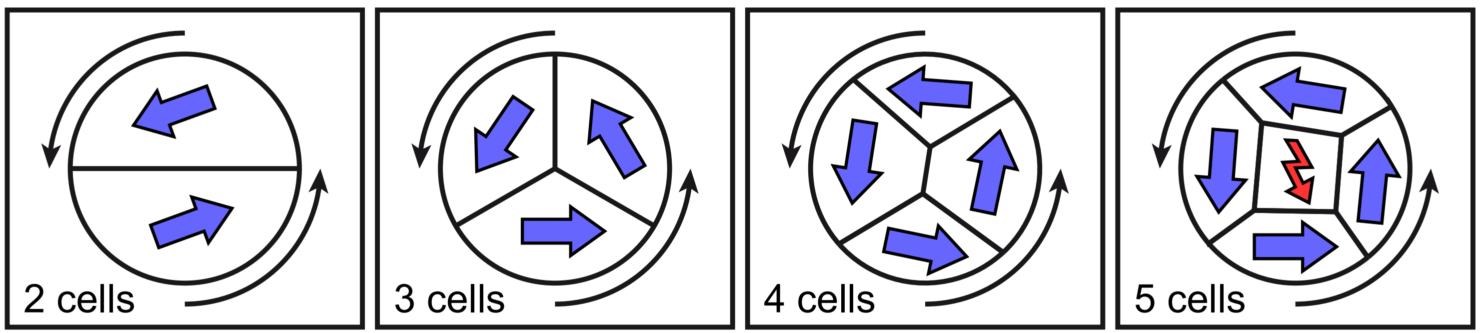


F. Segerer, F. Thüroff, A. Piera Alberola E. Frey and J.O. Rädler, PRL 114, 228102 (2015)

Average spatial correlation on the circle

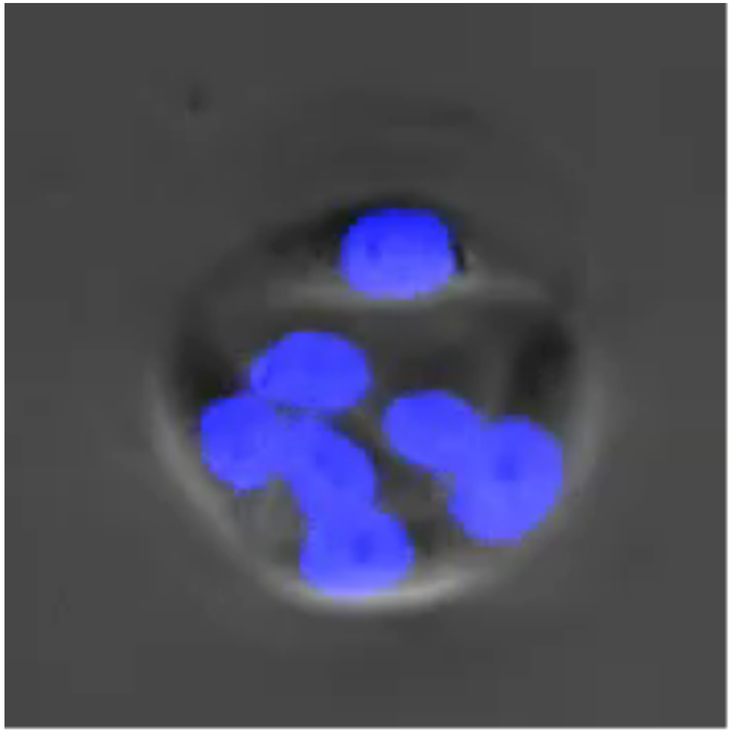


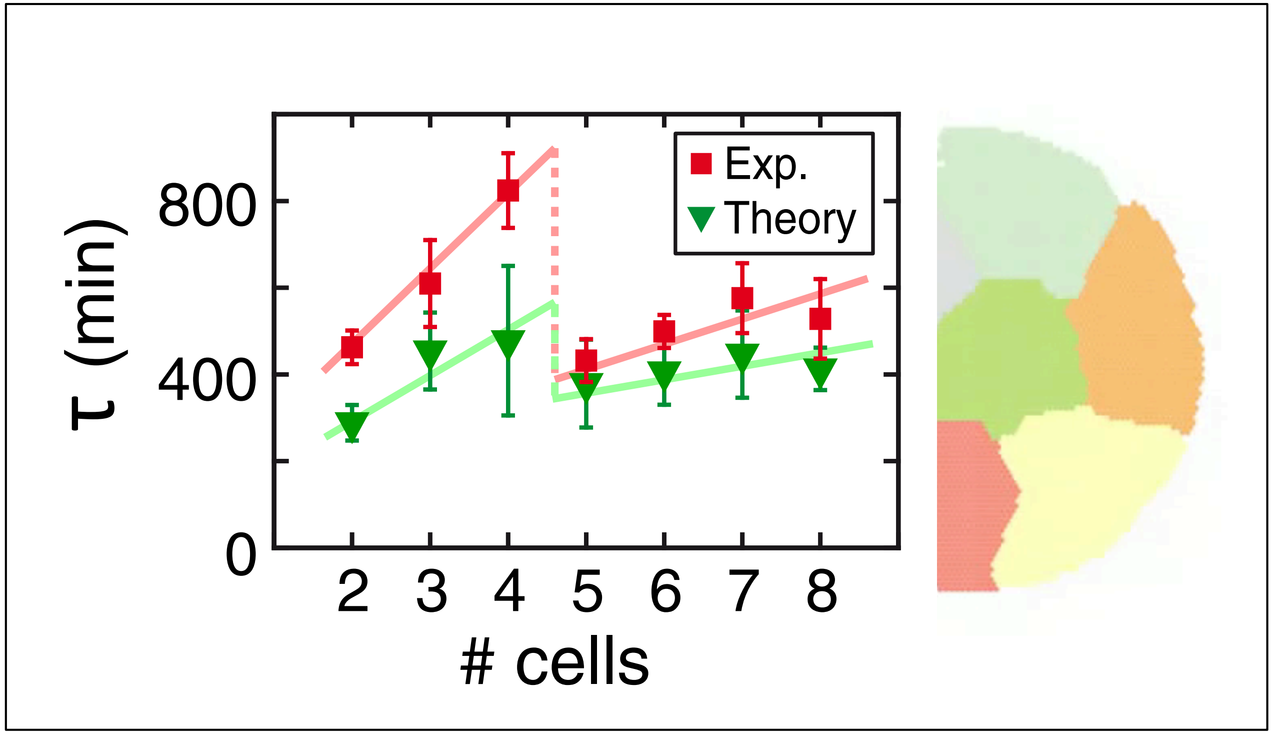
Simulation



center cell impedes polarization: „frustrated state“

Experiment vs. computer simulation



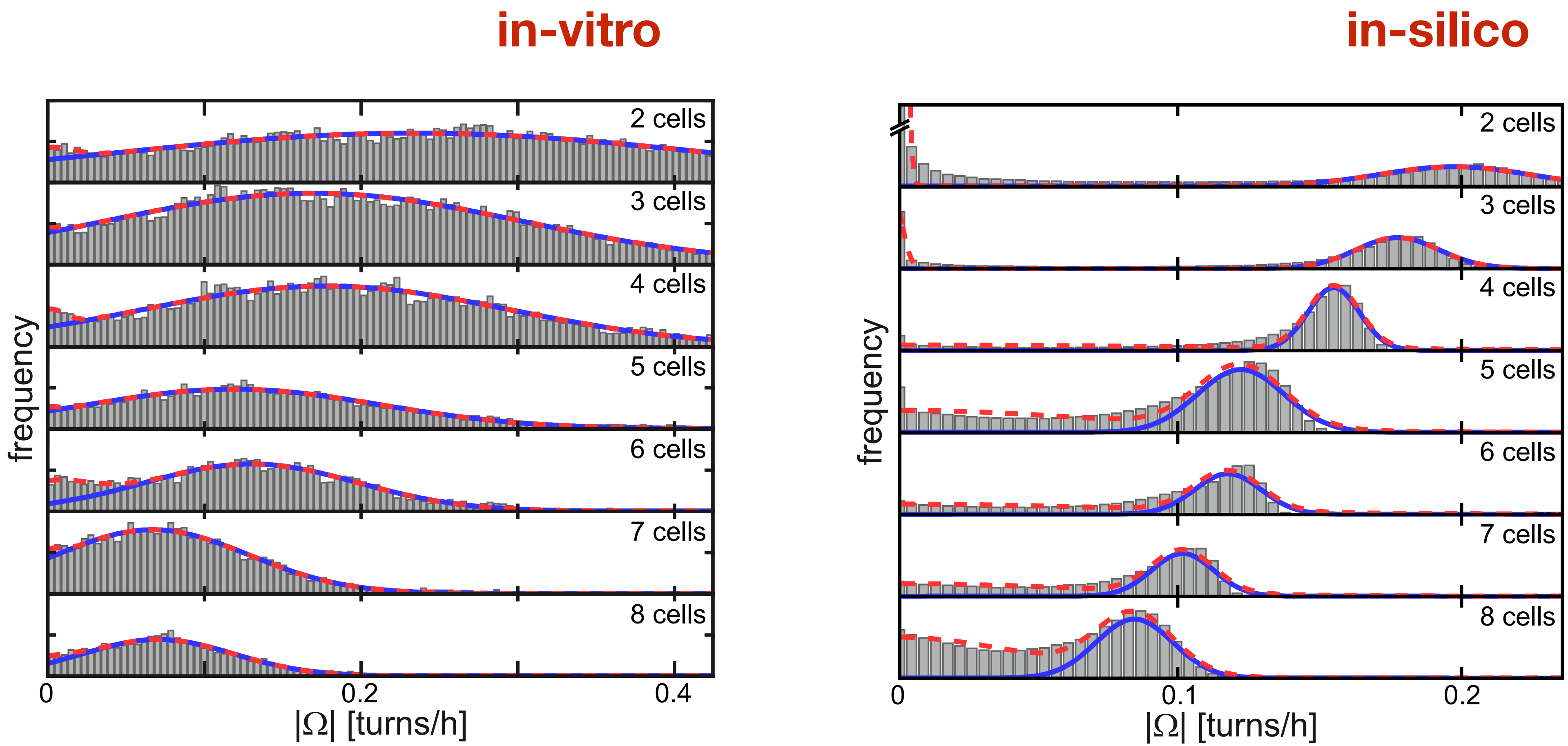


experiment
(F. Segerer)

cellular automata model
including scalar polarization field
(F. Thüroff, E. Frey)

F. Segerer, F. Thüroff, A. Piera Alberola E. Frey and J.O. Rädler, PRL 114, 228102 (2015)

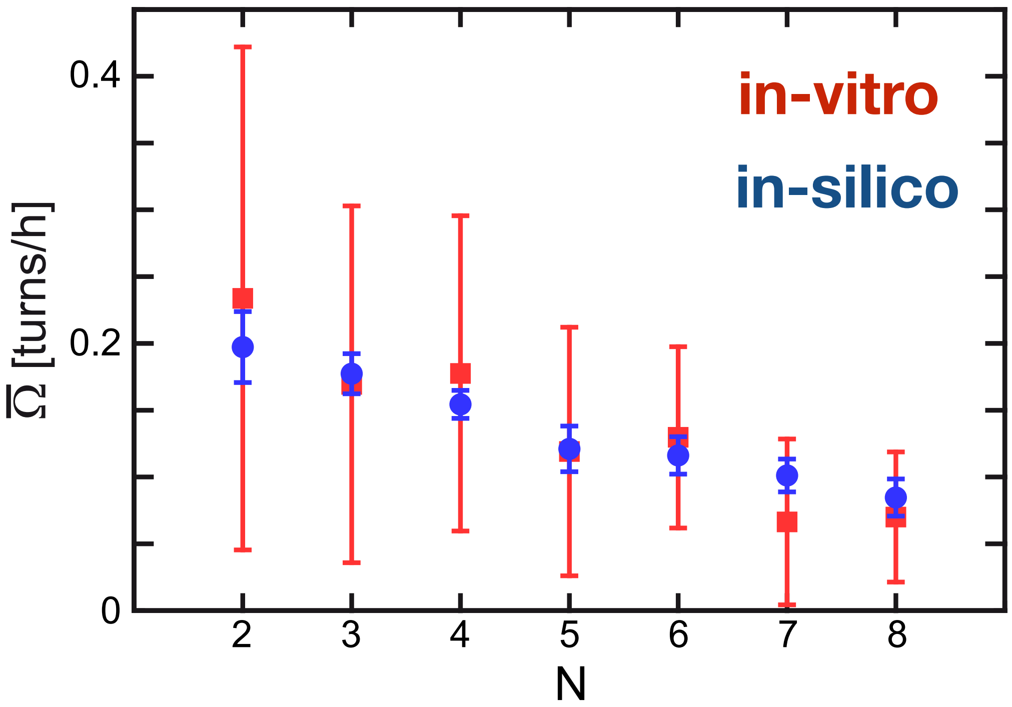
Angular velocity distribution

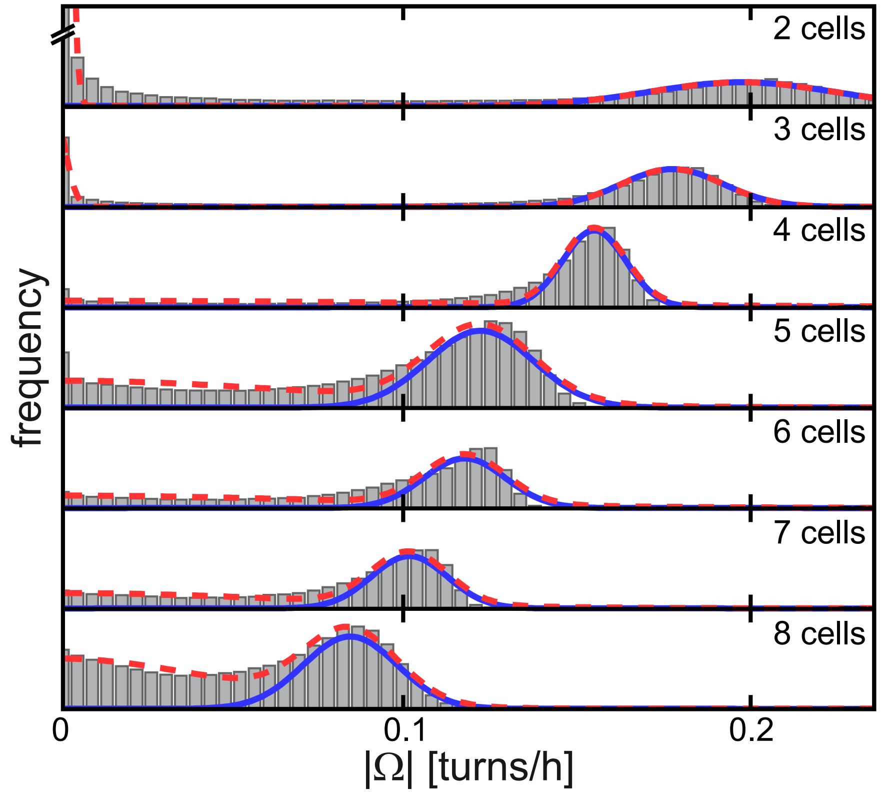


F. Segerer, F. Thüroff, A. Piera Alberola E. Frey and J.O. Rädler, PRL 114, 228102 (2015)

Survival frequency of coherent and disordered state

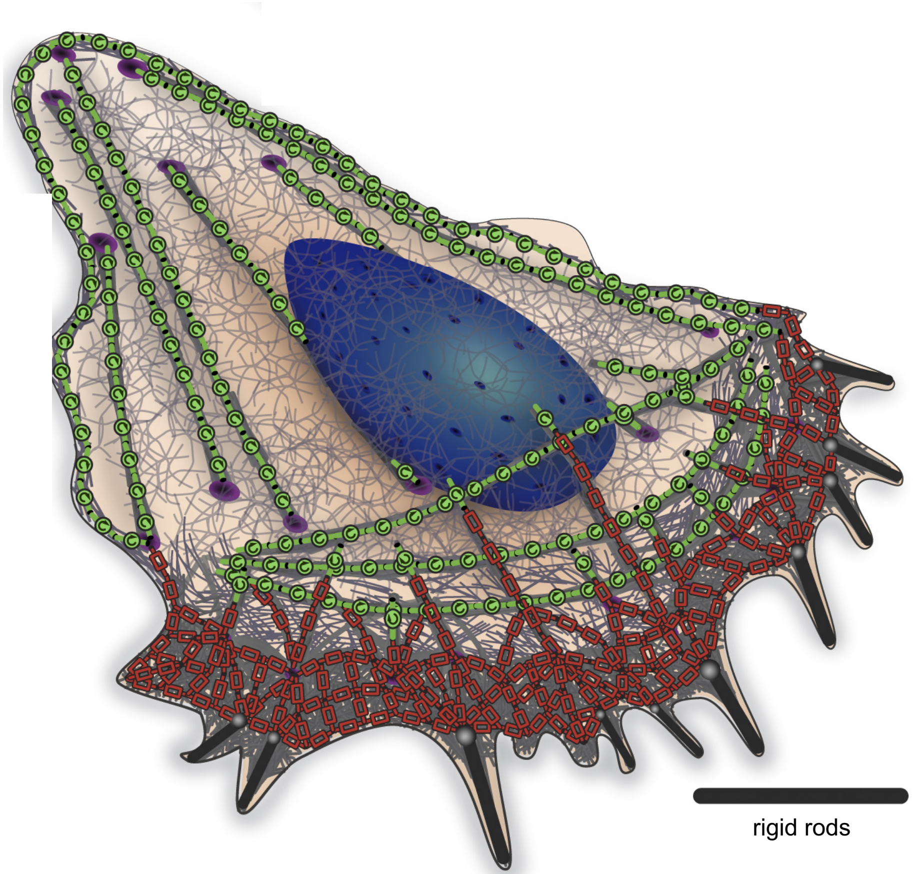
velocity peak positions





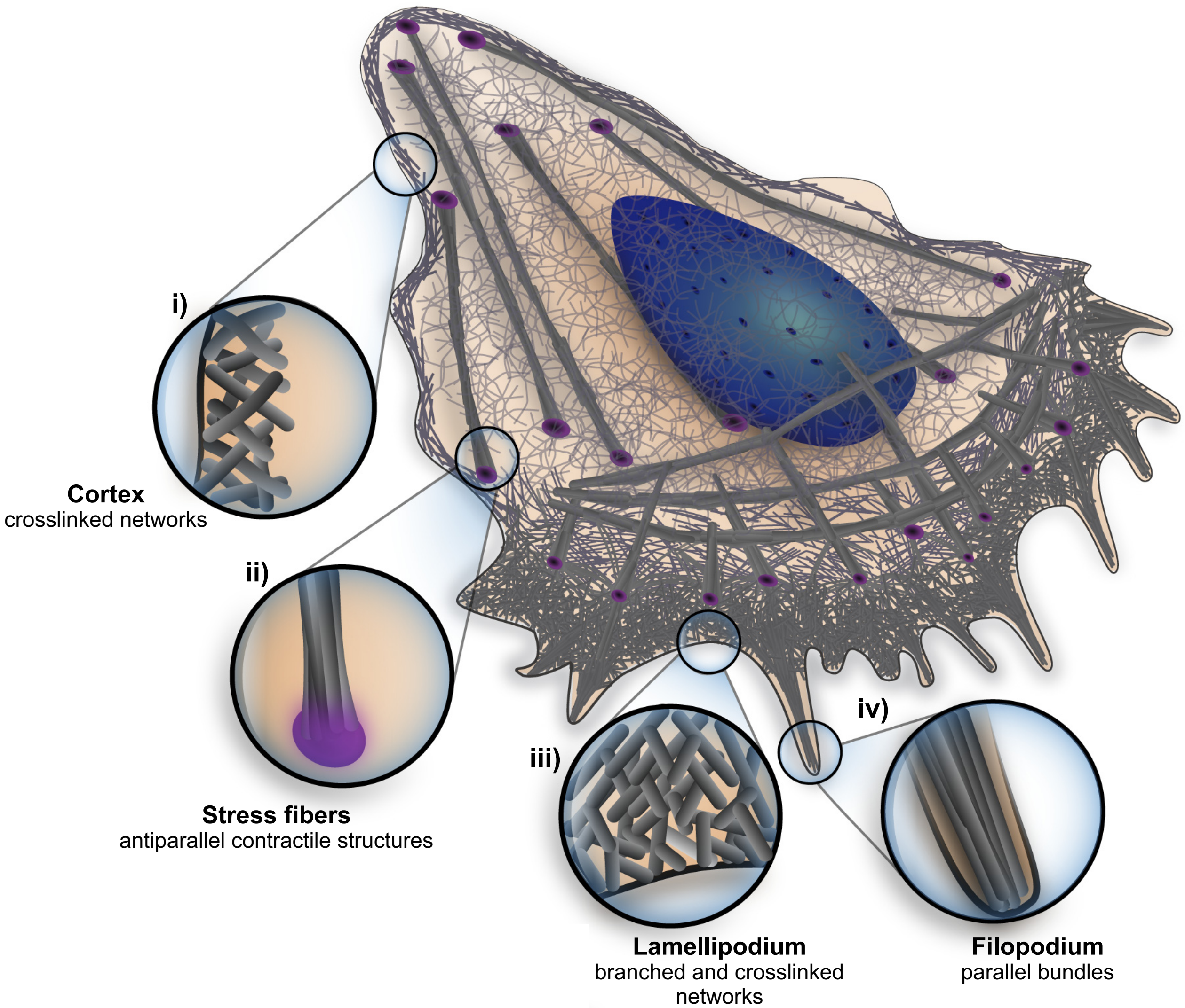
F. Segerer, F. Thüroff, A. Piera Alberola E. Frey and J.O. Rädler, PRL 114, 228102 (2015)

ACTIN DYNAMICS, ARCHITECTURE, AND MECHANICS IN CELL MOTILITY



Blanchoin et al., Physiol Rev VOL 94, 2014

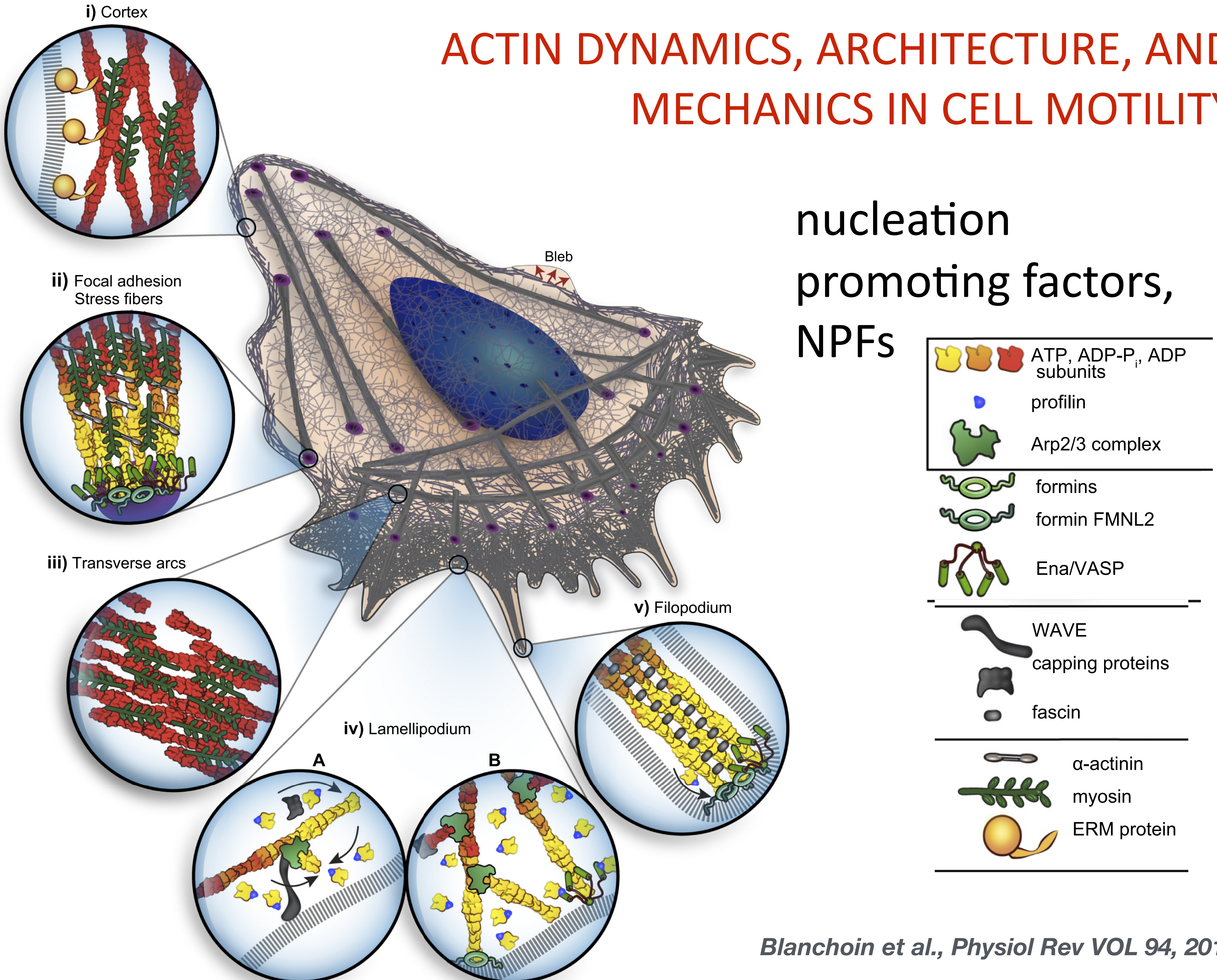
ACTIN DYNAMICS, ARCHITECTURE, AND MECHANICS IN CELL MOTILITY



Blanchoin et al., Physiol Rev VOL 94, 2014

ACTIN DYNAMICS, ARCHITECTURE, AND MECHANICS IN CELL MOTILITY

nucleation promoting factors, NPFs

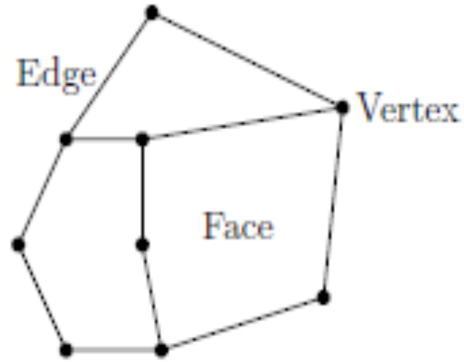


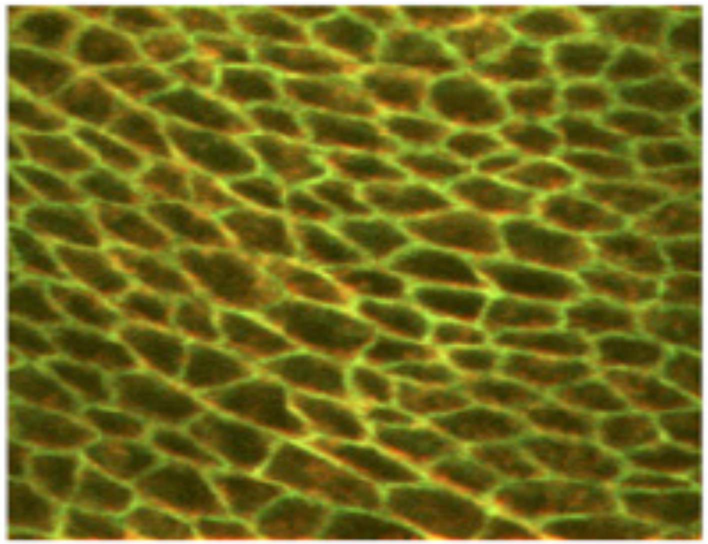
Blanchoin et al., Physiol Rev VOL 94, 2014

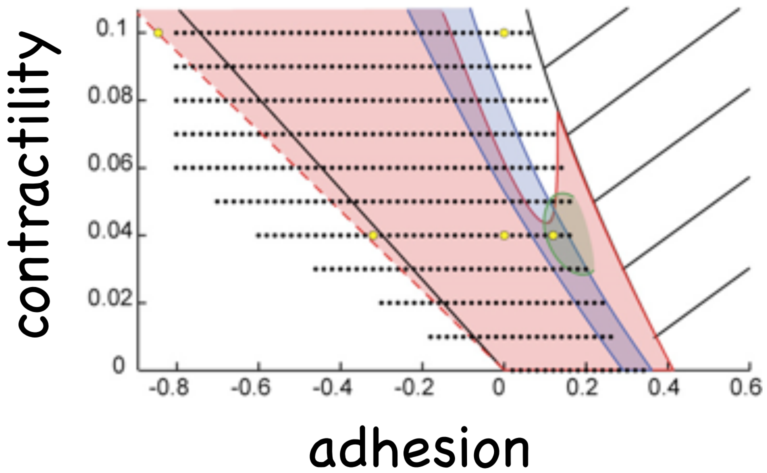
Cell shape in monolayers

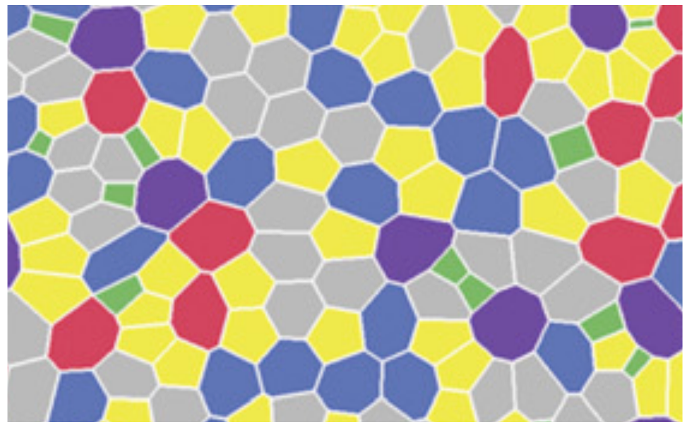
The Influence of Cell Mechanics, Cell-Cell Interactions, and Proliferation on Epithelial Packing

Reza Farhadifar,[1,3] Jens-Christian Röper,[2,3]
Benoit Aigouy,[2] Suzanne Eaton,[2,*]
and Frank Jülicher[1,*]



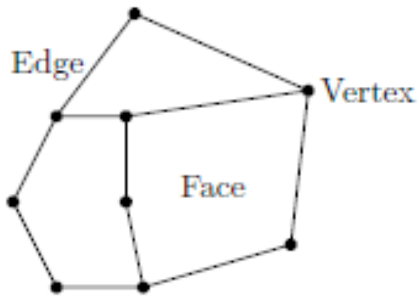


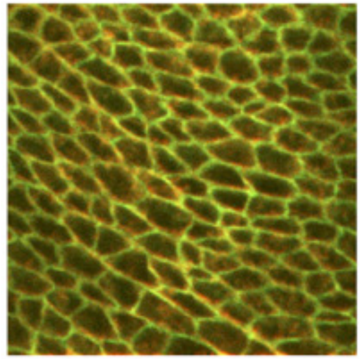




Farhadifar et al. (2007) Curr. Biol.

Vertex models and cell mechanics





Effective elastic energy

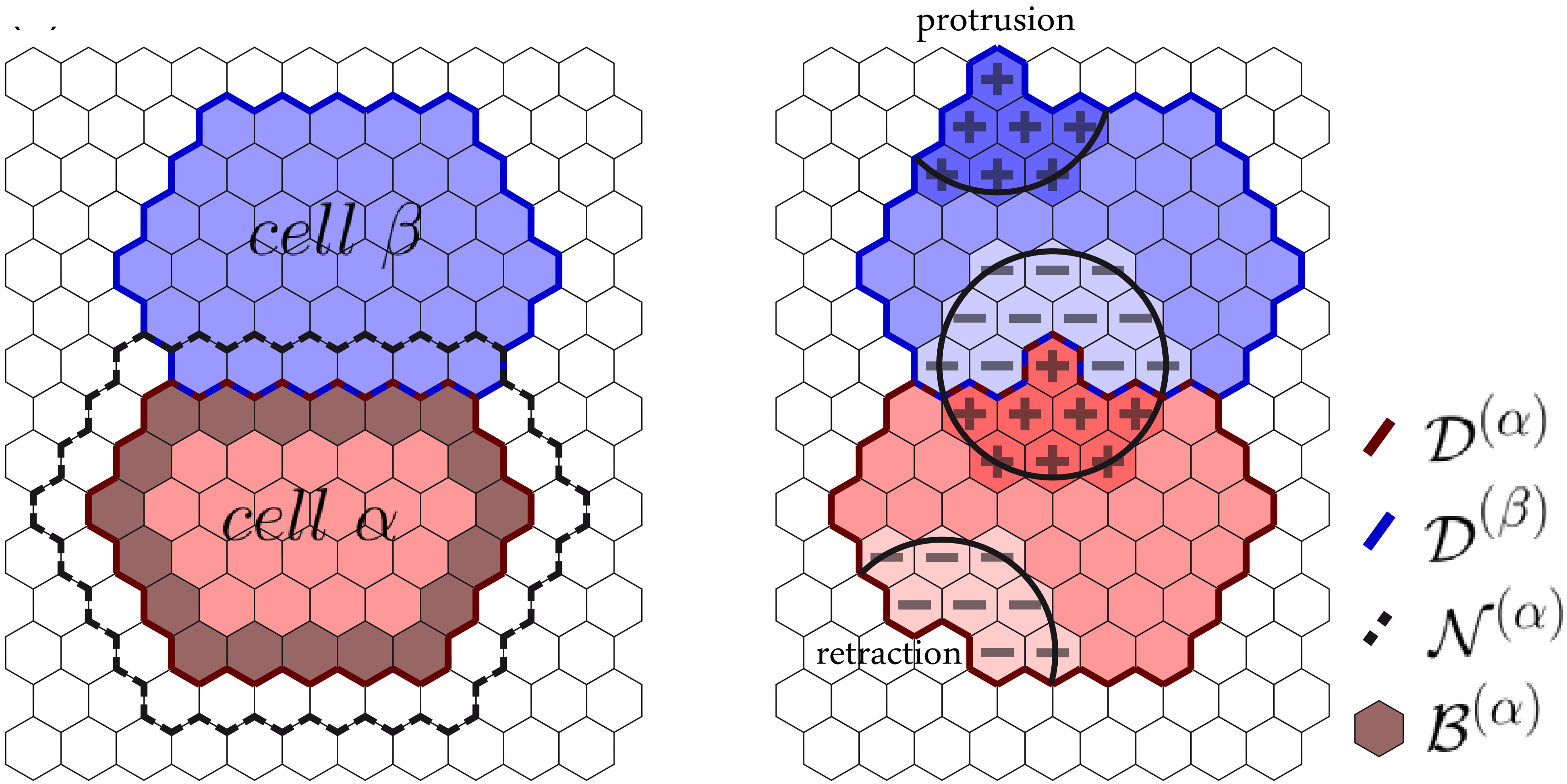
$$E(R_i) = \sum_{\alpha} \frac{K_\alpha}{2}(A_\alpha - A_\alpha^{(0)})^2 + \sum_{<i,j>} \Lambda_{ij} l_{ij} + \sum_{\alpha} \frac{\Gamma_\alpha}{2} L_\alpha^2$$

Area elasticity (cell height and volume)

Line tension (cell-cell adhesion)

Contractility (mechanics of the actin-myosin ring)

Agent based Modeling (Potts Modell)



cell represented as a set of pixels

based on the original Potts model by
F. Graner and J. A. Glazier, Phys. Rev. Lett. 69, 2013 (1992).

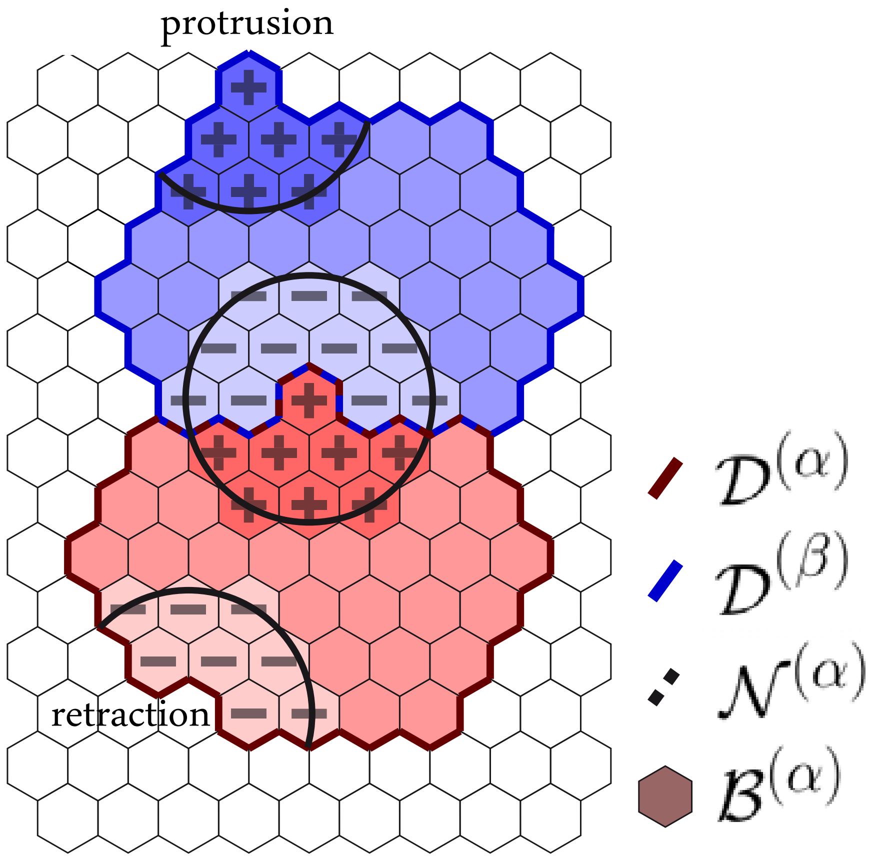
Thüroff, Goychuk, Reiter & Frey (2019) bioRxiv

Agent based Modeling (Potts Modell)

- protrusion and retraction events copy events with probability:

$$p(\mathcal{T}) = \min\{1,\, e^{-\Delta\mathcal{H}}\}$$

$$\mathcal{H} = \mathcal{H}_{\mathrm{cont}} + \mathcal{H}_{\mathrm{adh}} + \mathcal{H}_{\mathrm{cyto}}$$



Thüroff, Goychuk, Reiter & Frey (2019) bioRxiv

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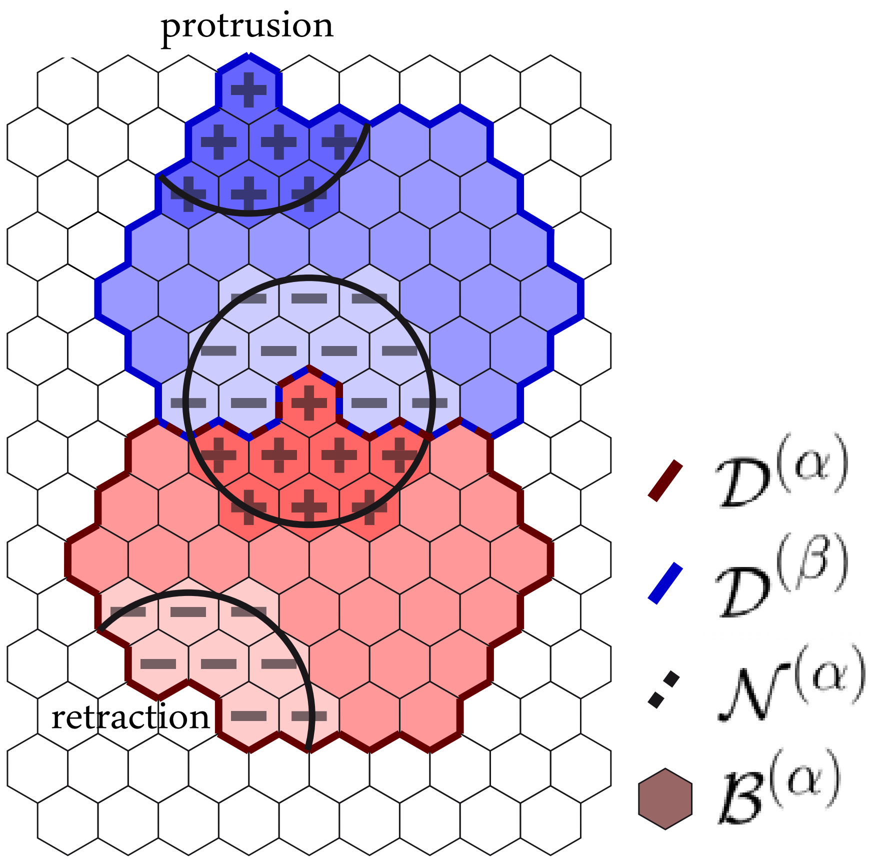


- cell contractility (Hcont),

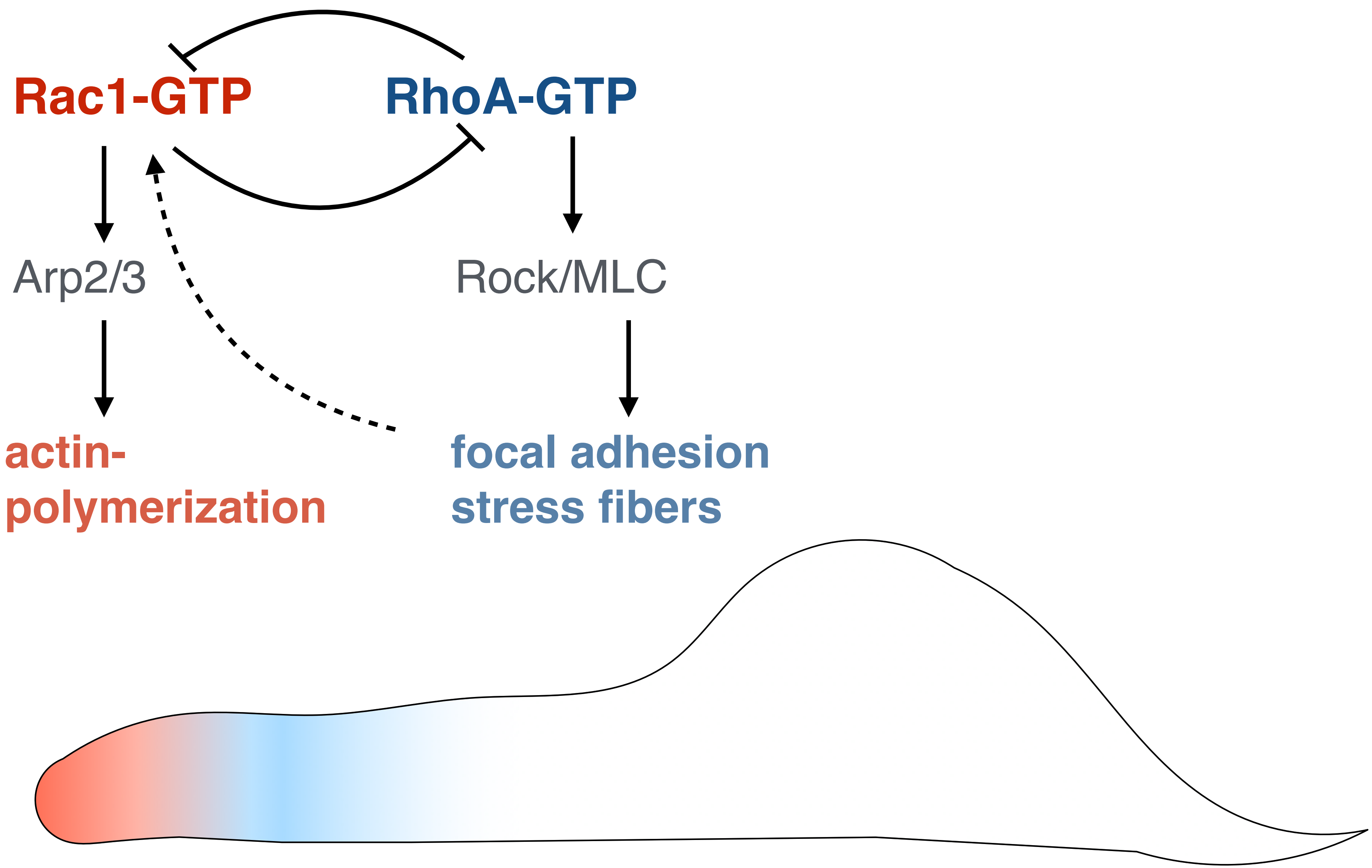
$$\mathcal{H}_{\text{cont}} = m\, P_\alpha^2(t) + a\, A_\alpha^2(t)$$

stiffness parameters for the perimeter $P\alpha(t)$ and the area $A\alpha(t)$

- cell-cell adhesion (H_{adh})
- cytoskeletal remodeling (H_{cyto})

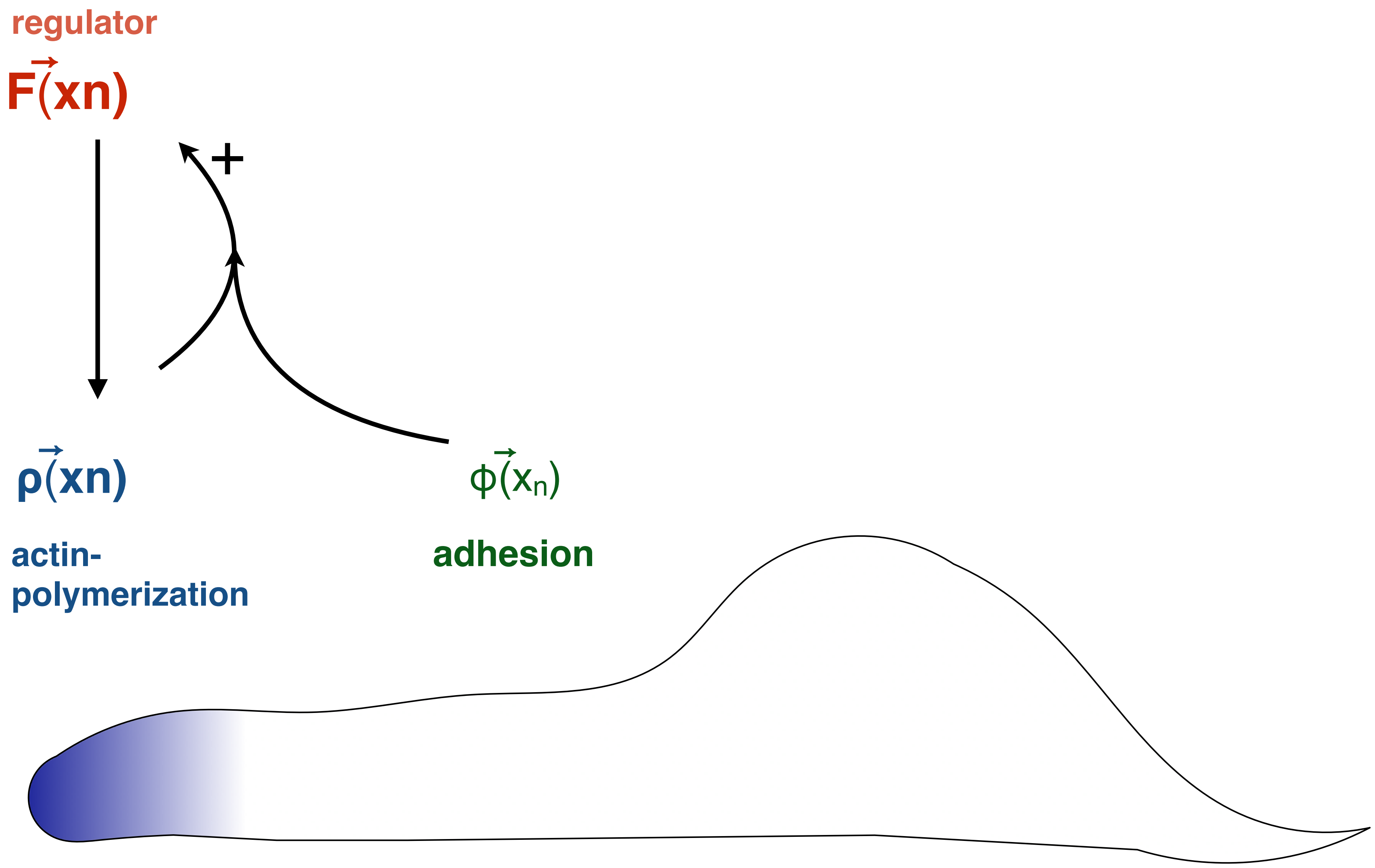
Thüroff, Goychuk, Reiter & Frey (2019) bioRxiv

Rho GTPases and cell polarity: biochemical view



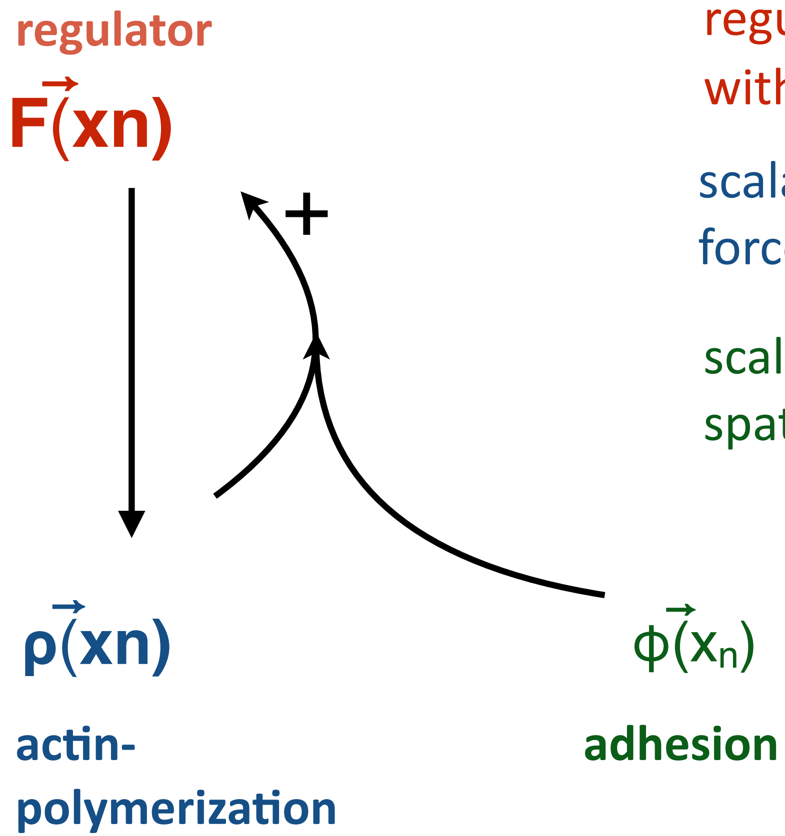
Thüroff, Goychuk, Reiter & Frey (2019) bioRxiv

Rho GTPases and cell polarity in CPM model



Thüroff, Goychuk, Reiter & Frey (2019) bioRxiv

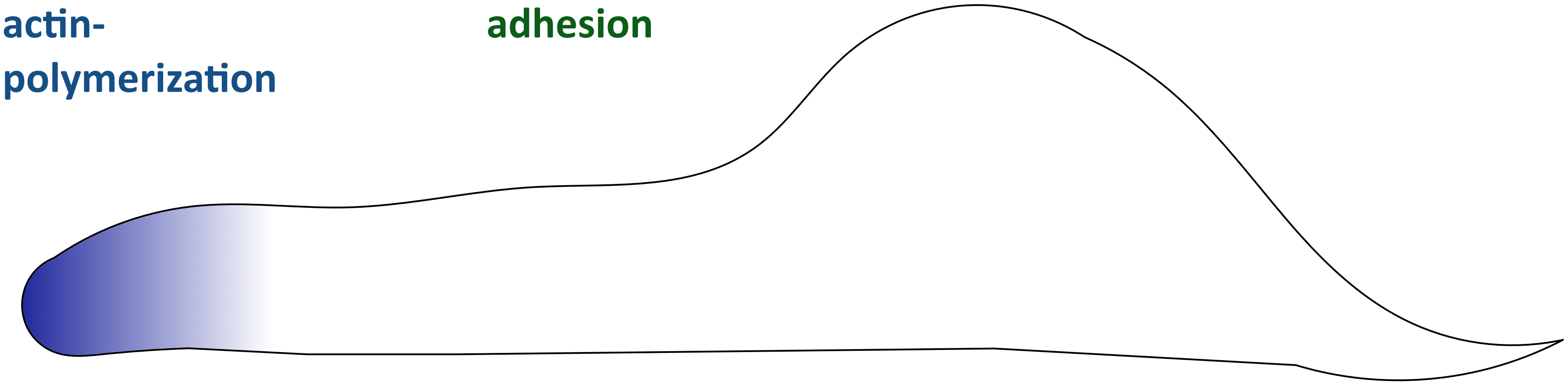
Rho GTPases and cell polarity in CPM model



regulatory factors $\vec{F}(xn)$ used to update $\vec{\rho}(x_n)$ with a radius R

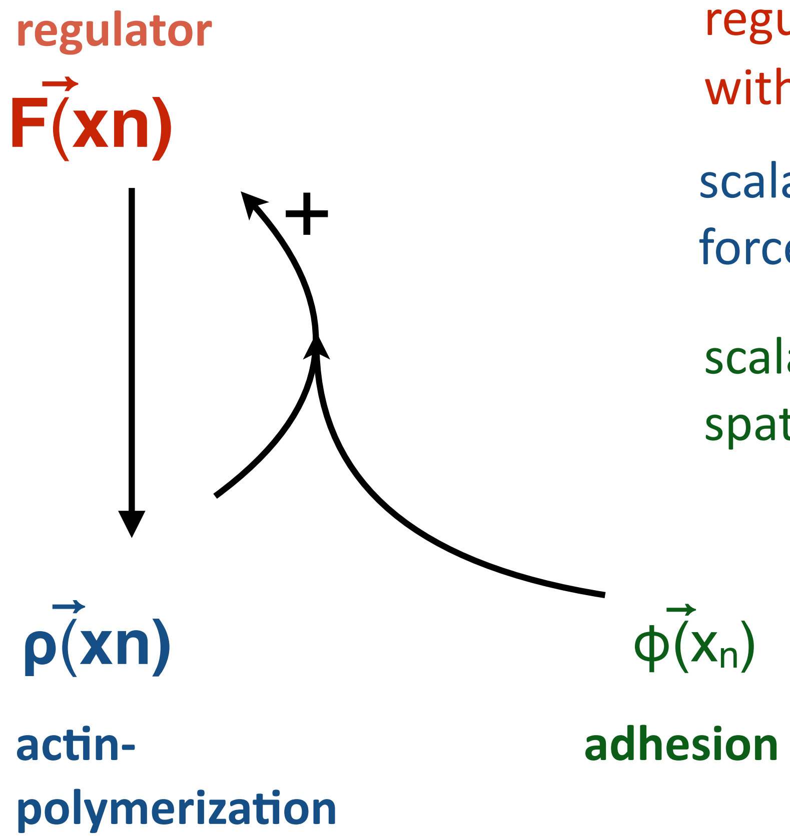
scalar field $\vec{\rho}(x_n)$ represents overall density of force-generating cytoskeletal structures (Actin)

scalar field variable $\vec{\phi}(x_n)$ accounts for spatial variations of substrate



Thüroff, Goychuk, Reiter & Frey (2019) bioRxiv

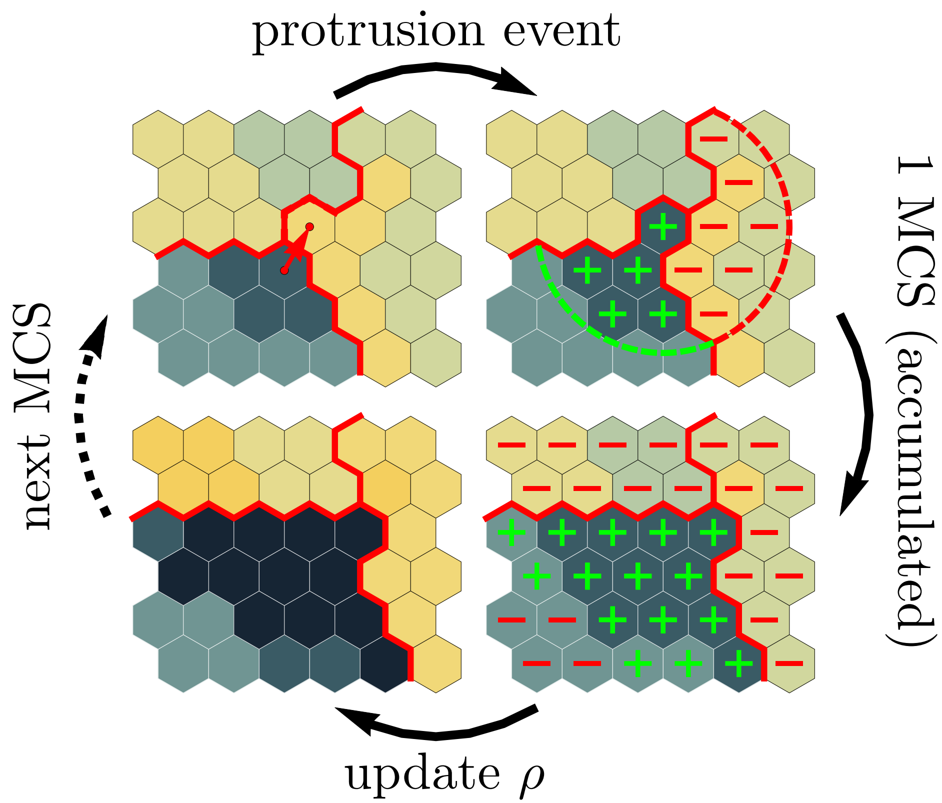
Monte-Carlo scheme for protrusions events



regulatory factors $\vec{F}(xn)$ used to update $\rho(\vec{x}_n)$ with a radius R

scalar field $\rho(\vec{x}_n)$ represents overall density of force-generating cytoskeletal structures (Actin)

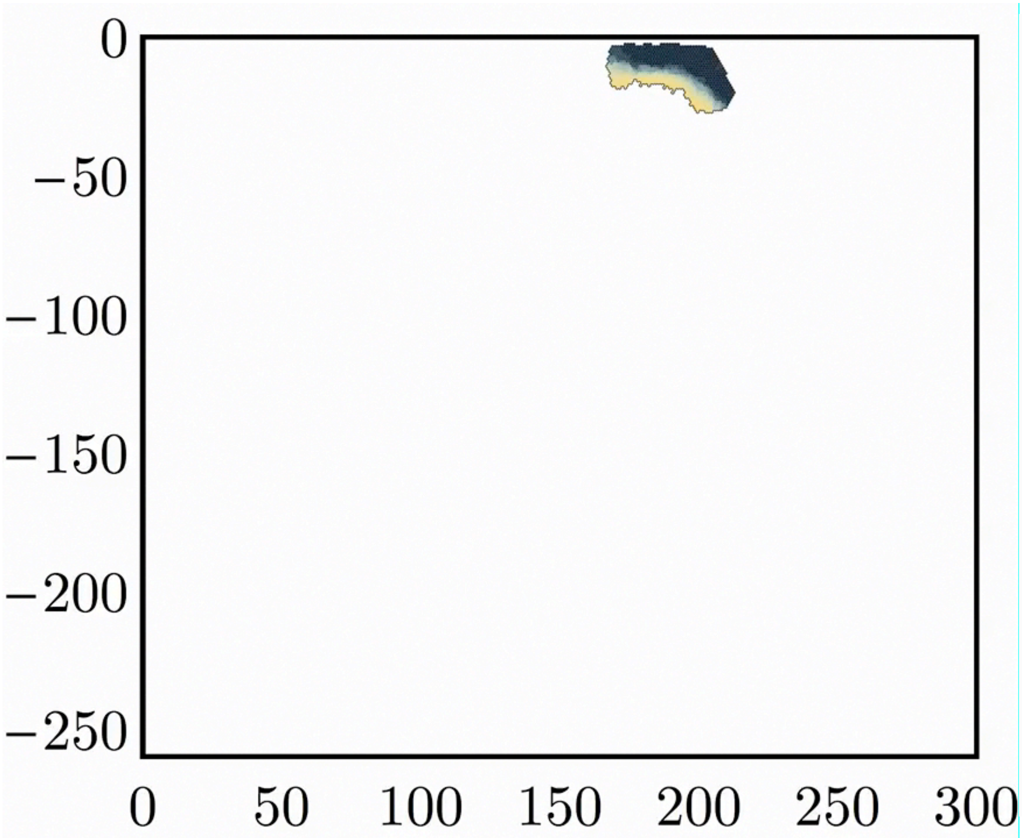
scalar field variable $\phi(\vec{x}_n)$ accounts for spatial variations of substrate

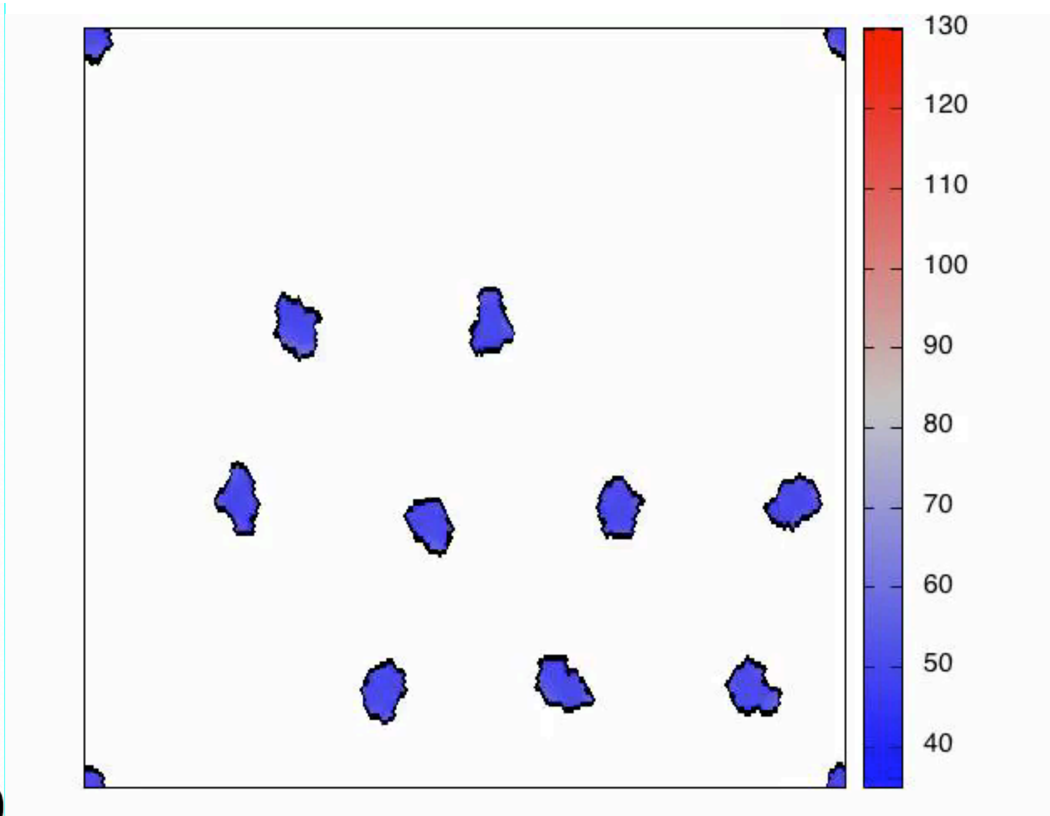


$$\mathcal{H}_{\text{cyto}} = \rho_\beta(\mathbf{x}_t, t) - \rho_\alpha(\mathbf{x}_s, t)$$

energy gain or loss for elementary protrusion event

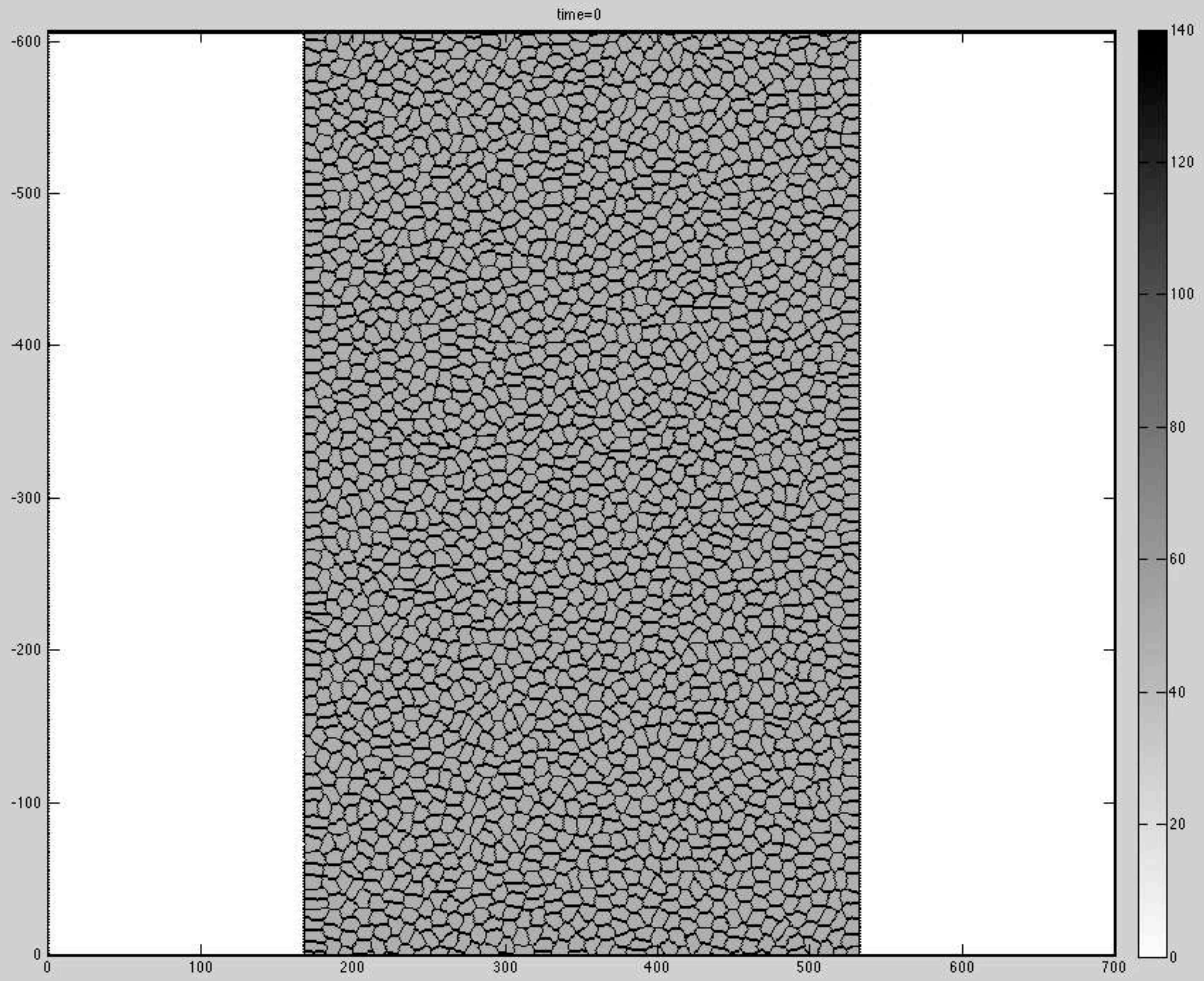
From single cell migration to collective dynamics





Thüroff, Goychuk, Reiter & Frey (2019) bioRxiv

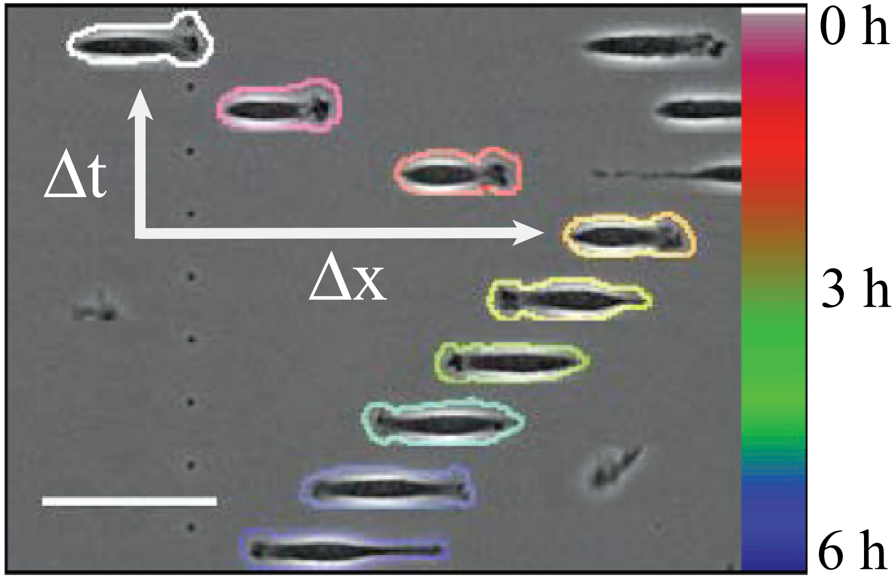
Tissue level - dynamics



Thüroff, Goychuk, Reiter & Frey (2019) bioRxiv

Micropattern as standardized platforms:

„The first world cell race"



persistent random walk analysis:

mean-squared displacement (MSD)

$$\langle \delta(\tau)^2 \rangle = 2 t_p v^2 (\tau - t_p (1 - \exp(-\tau / t_p)))$$

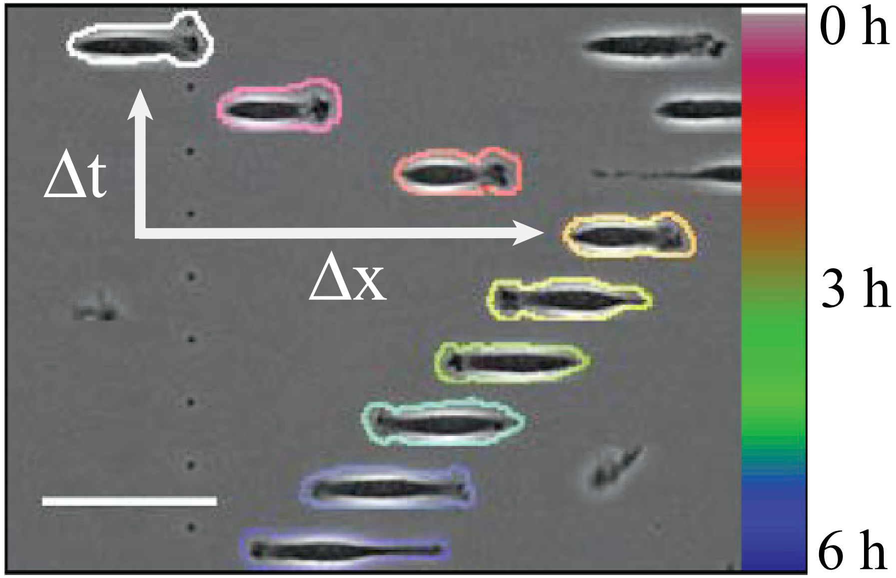
characteristic speed: *v* (describes deterministic motion)

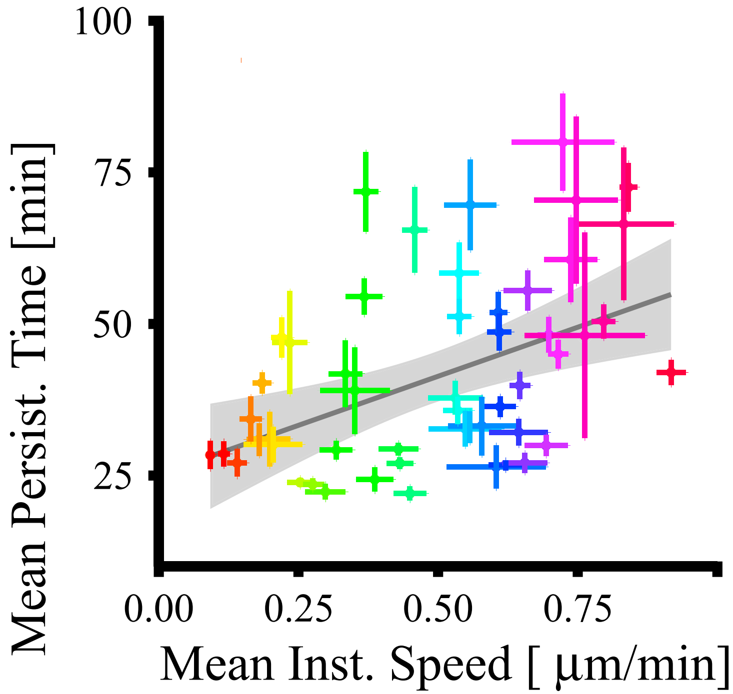
persistence time: t_p (describes randomness, noise)

Maiuri, P. et al. (2012). Curr. Biol. *22*, R673–R675.
Maiuri et al., 2015, Cell 161, 374–386

Micropattern as standardized platforms:

„The first world cell race“



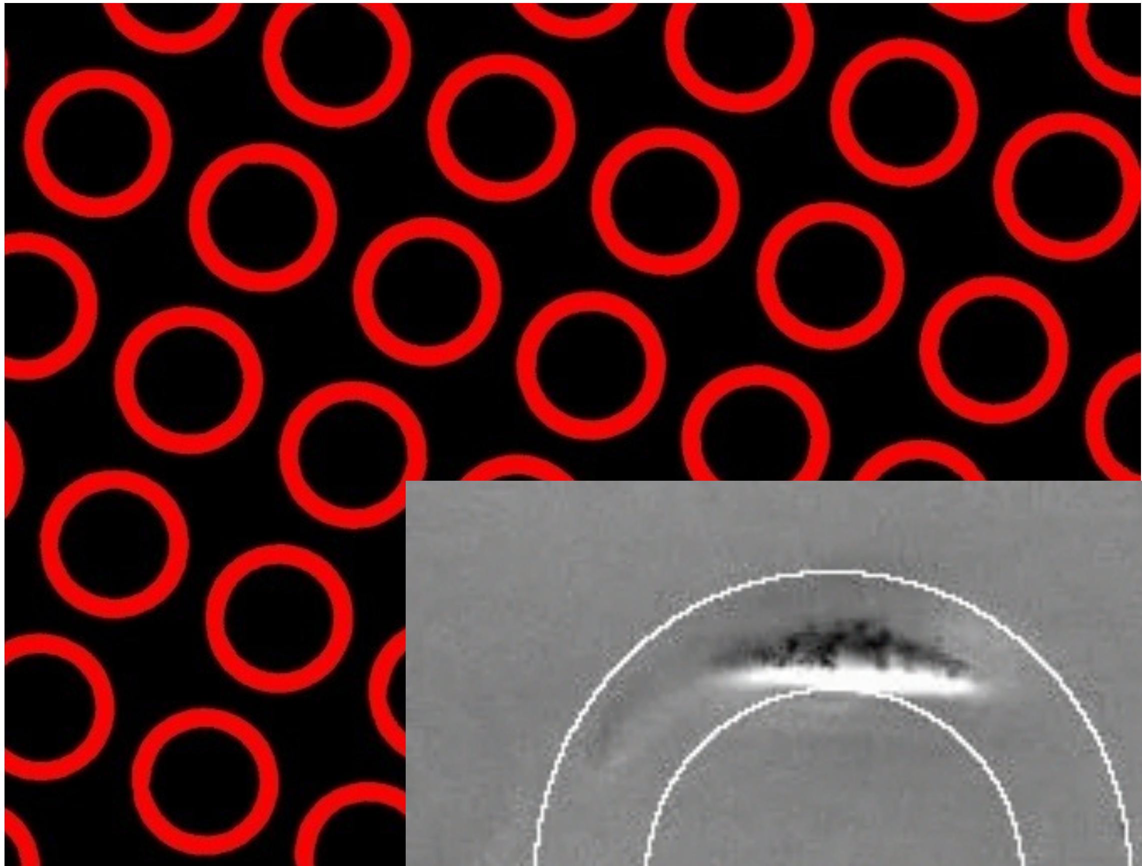


universal scaling
cell speed and cell persistence

$$\tau \propto e^{\lambda \cdot \mathcal{V}}$$

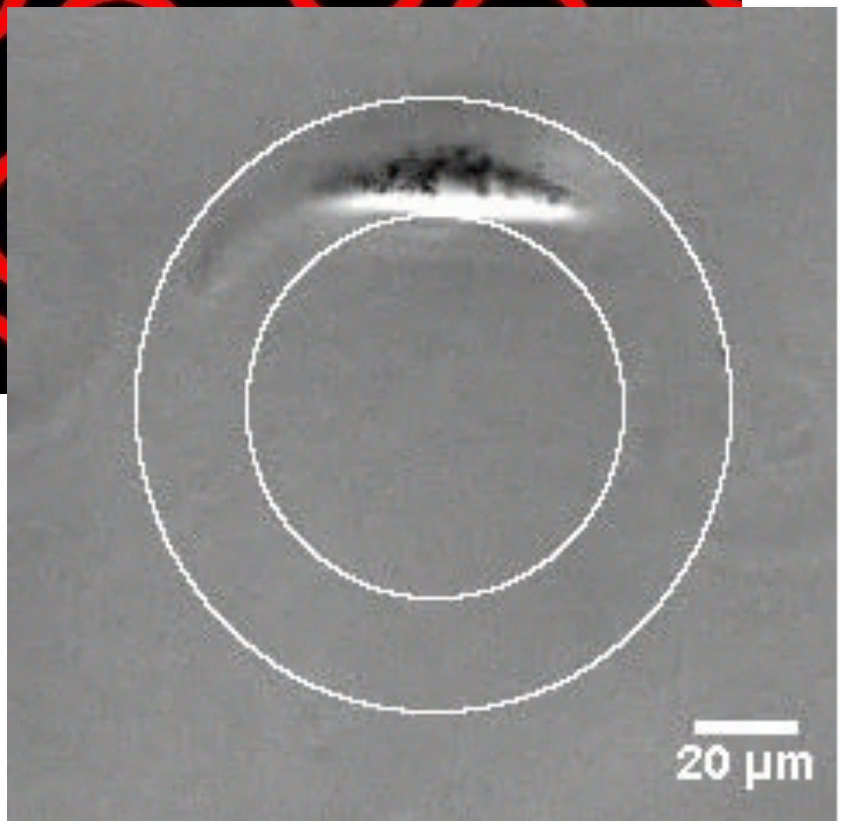
Maiuri, P. et al. (2012). Curr. Biol. *22*, R673–R675.
Maiuri et al., 2015, Cell 161, 374–386

Single cell migration on ring shaped structures



fibronectin coated
ring pattern (µCP)
in PEG-PLL

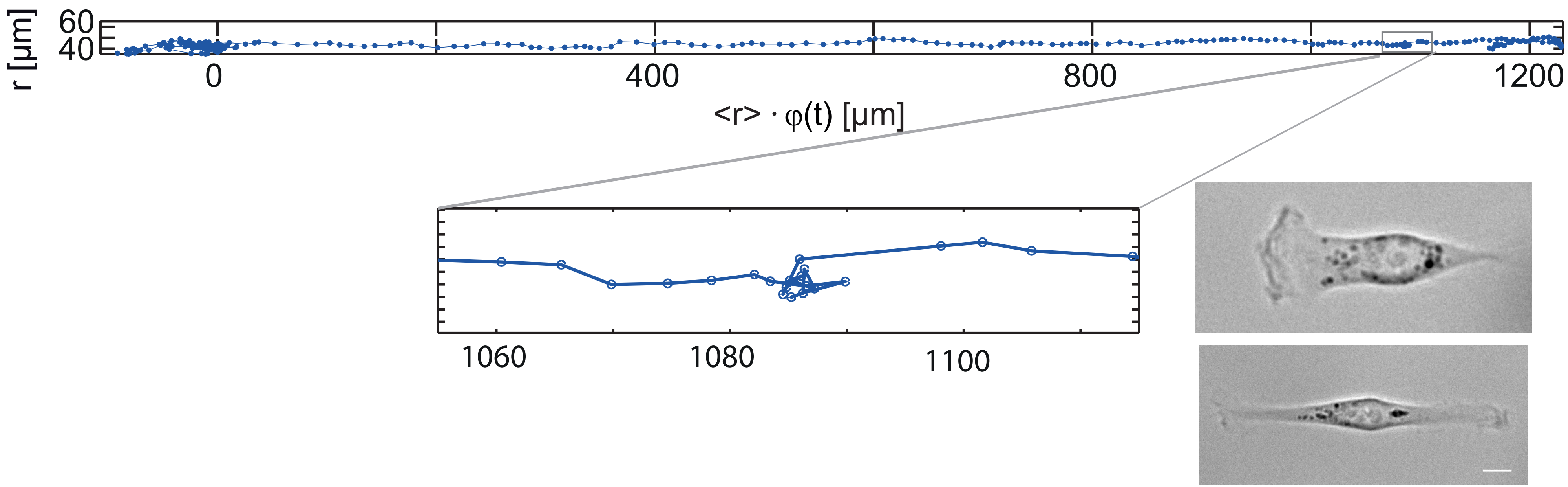
radius 50 µm / width 20 µm



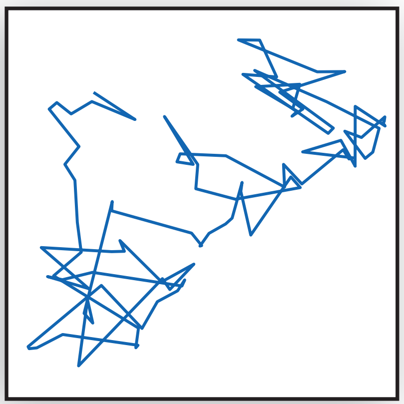
breast cancer
cell line
MDA-MB-436

Chr Schreiber, F.J. Segerer, E.Wagner, A. Roidl & J.Rädler
Sci Reports 6 (2016): 26858.

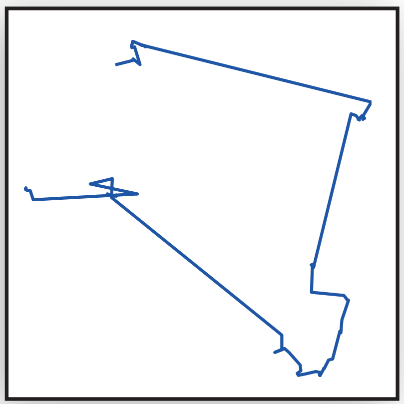
Choice of migration models



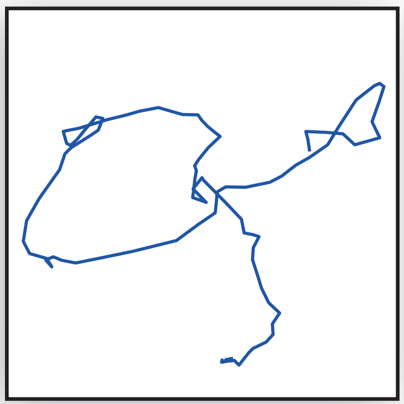
Random walk



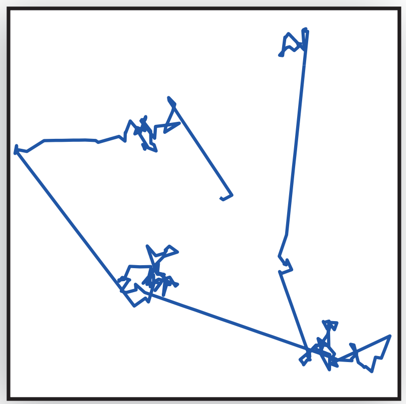
Lévy walk



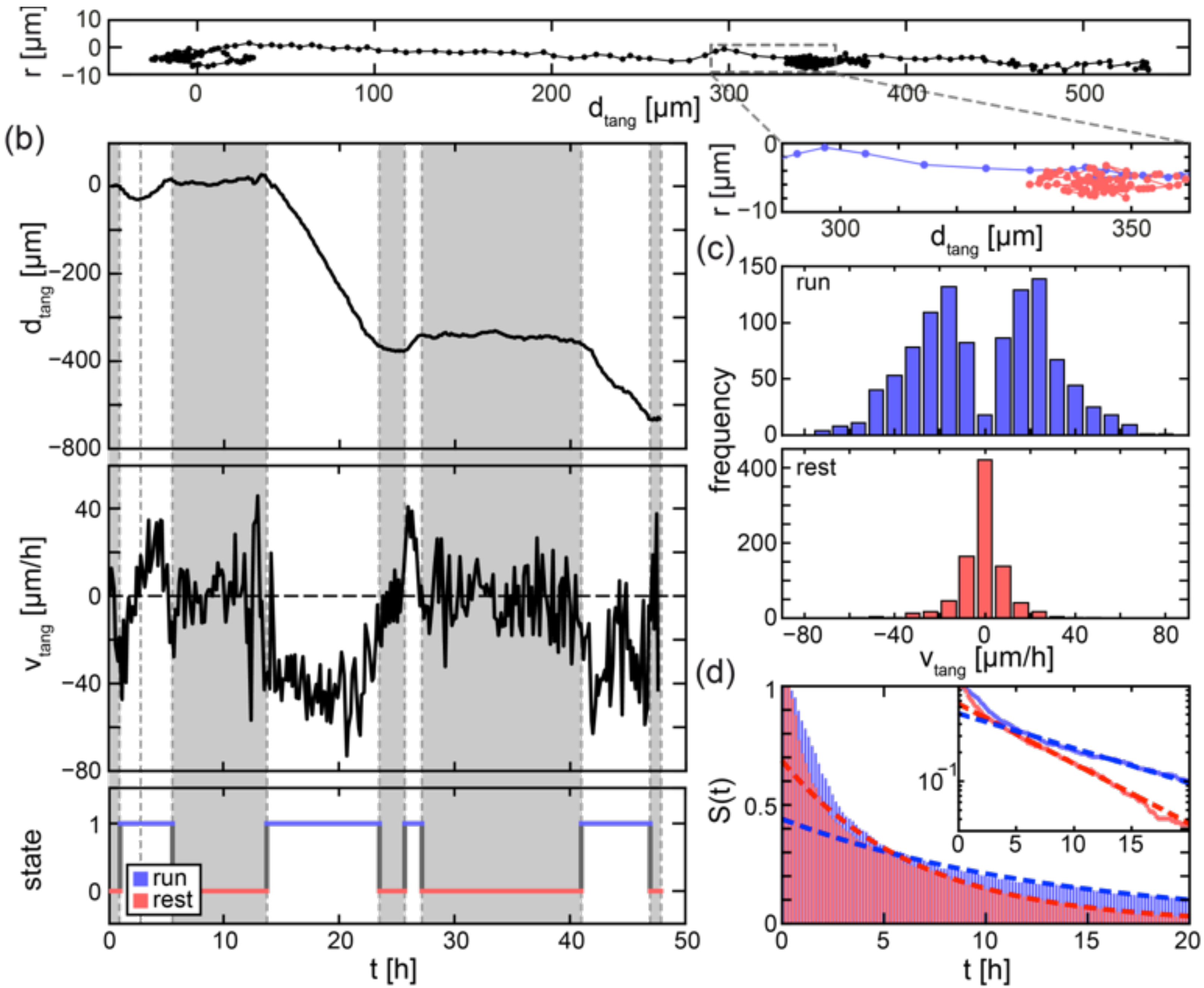
Persistent random walk



Two state motion



Two-state migration model

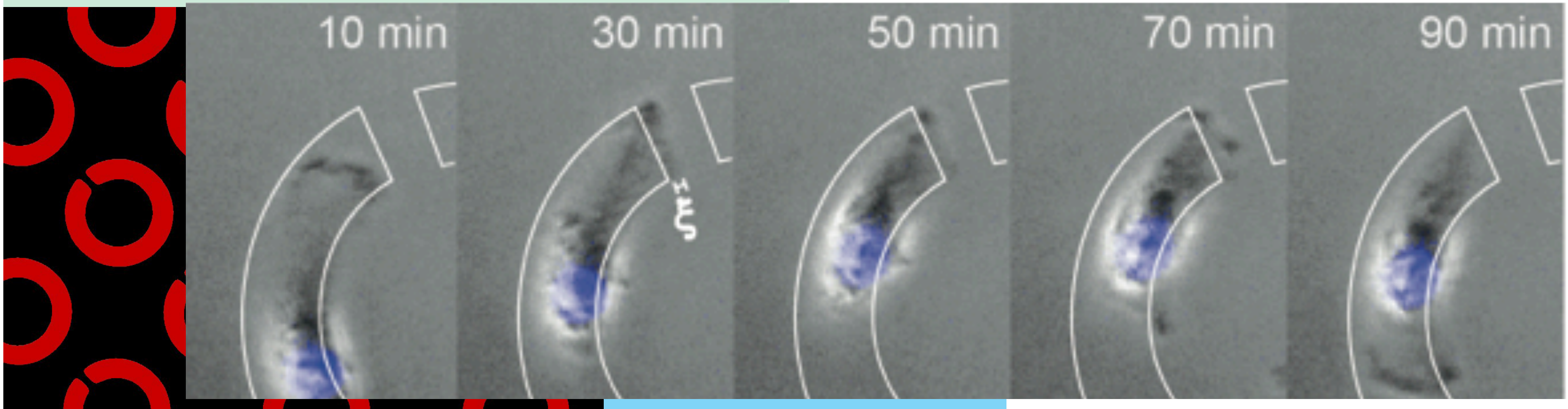


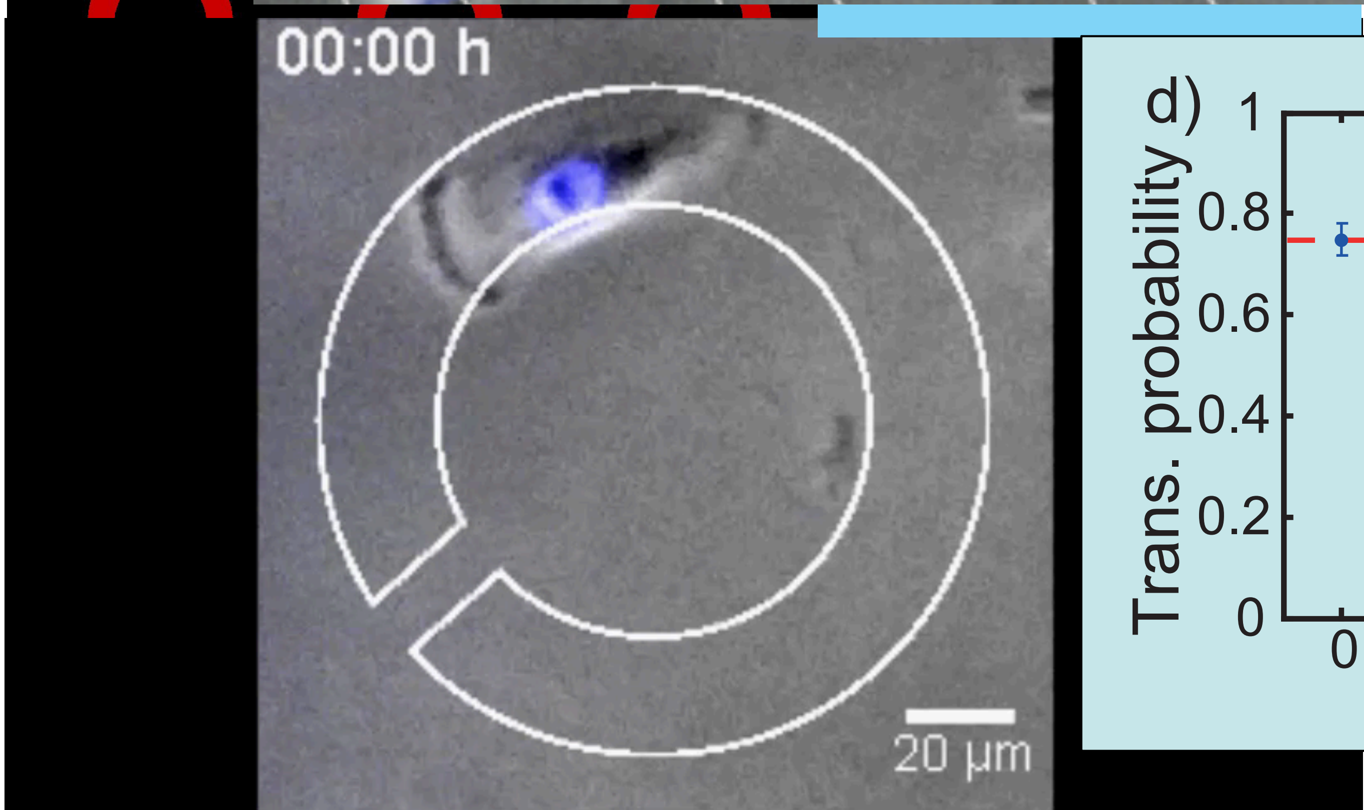
runs

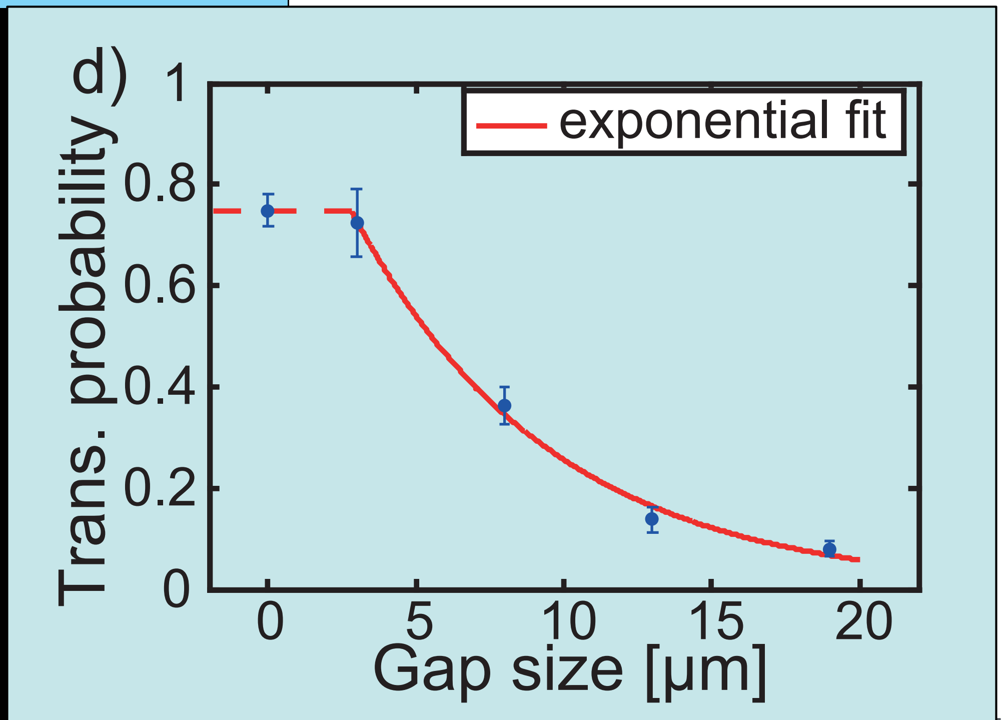
rests

exponential time distribution

Transit probability at chemical barriers

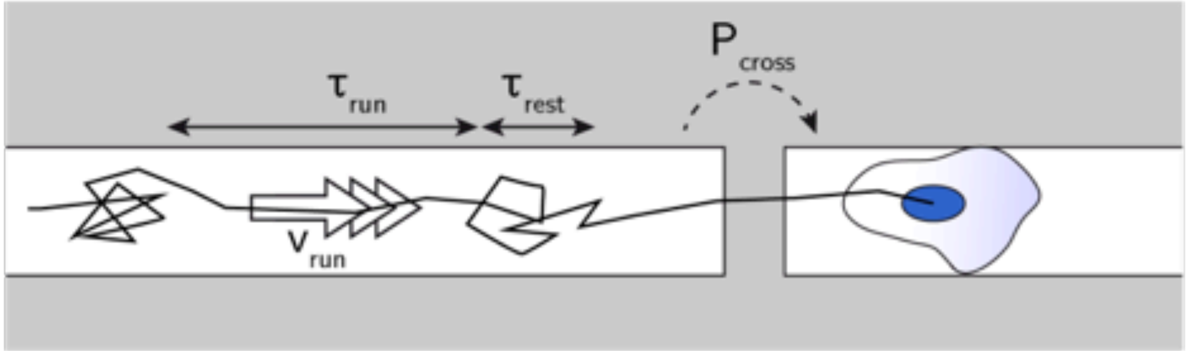






C. Schreiber et al. Sci Reports (2015)

Multiparameter motility phenotyping

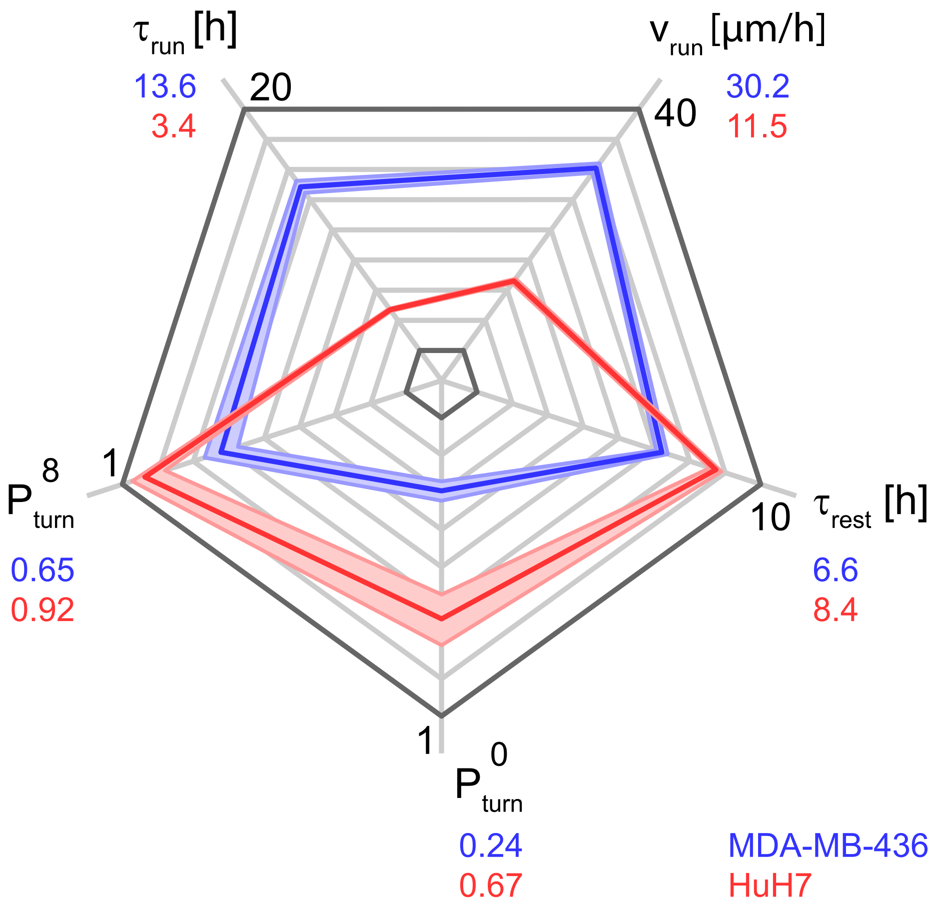


run persistence time, τ_{run};
rest persistence time, τ_{rest};
run velocity, v_{run};
reversal probability, $P_{turn}^{d_{gap}}$,

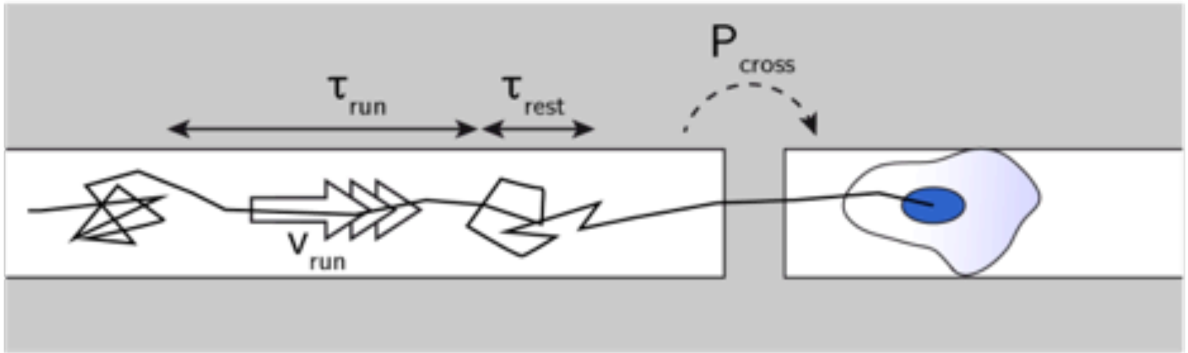
breast cancer cell line
MDA-MB-436
(mesenchymal phenotype)

Huh7 hepato cellular
carcinoma cells

cell lines cells differ
=> „migratory fingerprint“



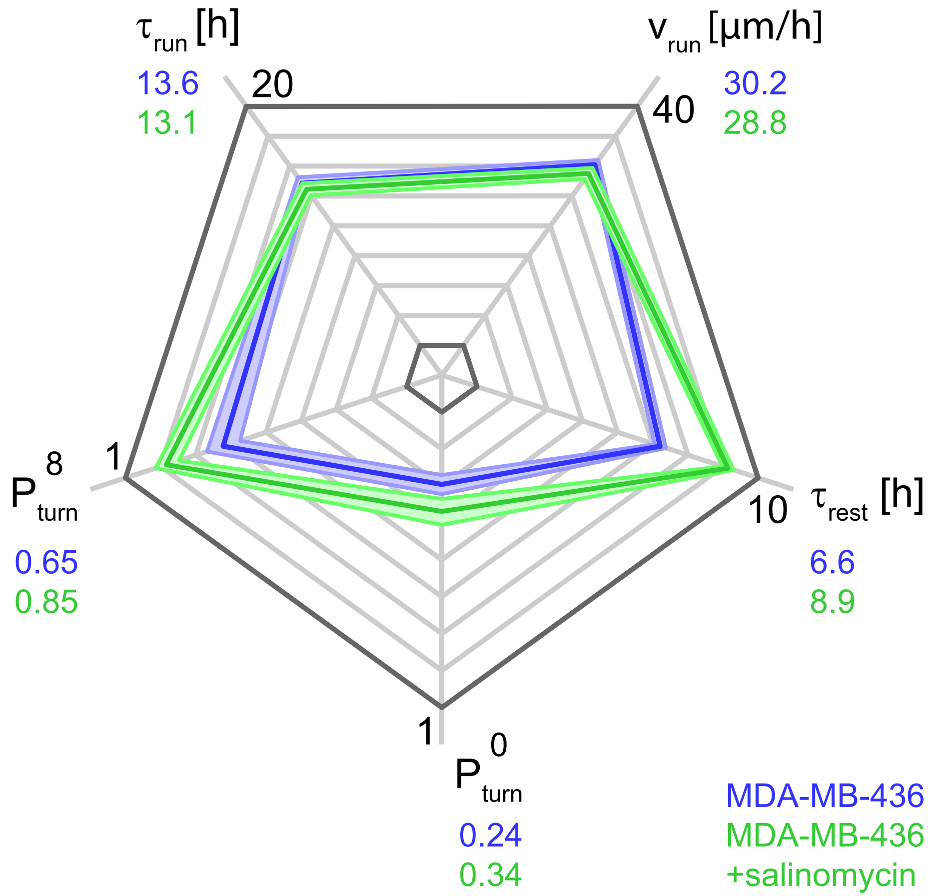
Multiparameter motility phenotyping



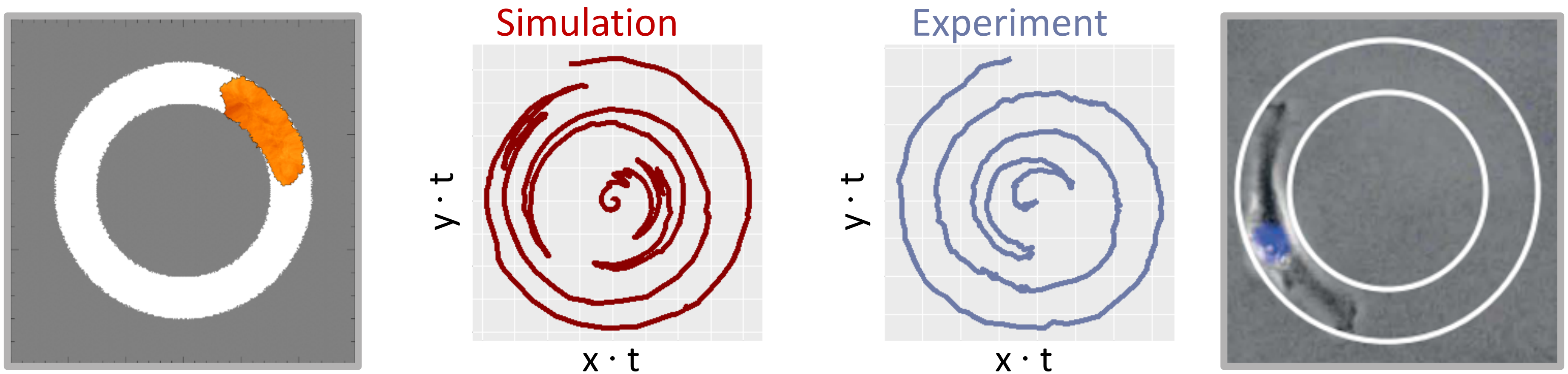
run persistence time, τ_{run};
rest persistence time, τ_{rest};
run velocity, v_{run};
reversal probability, $P^{d_{gap}}_{turn}$,

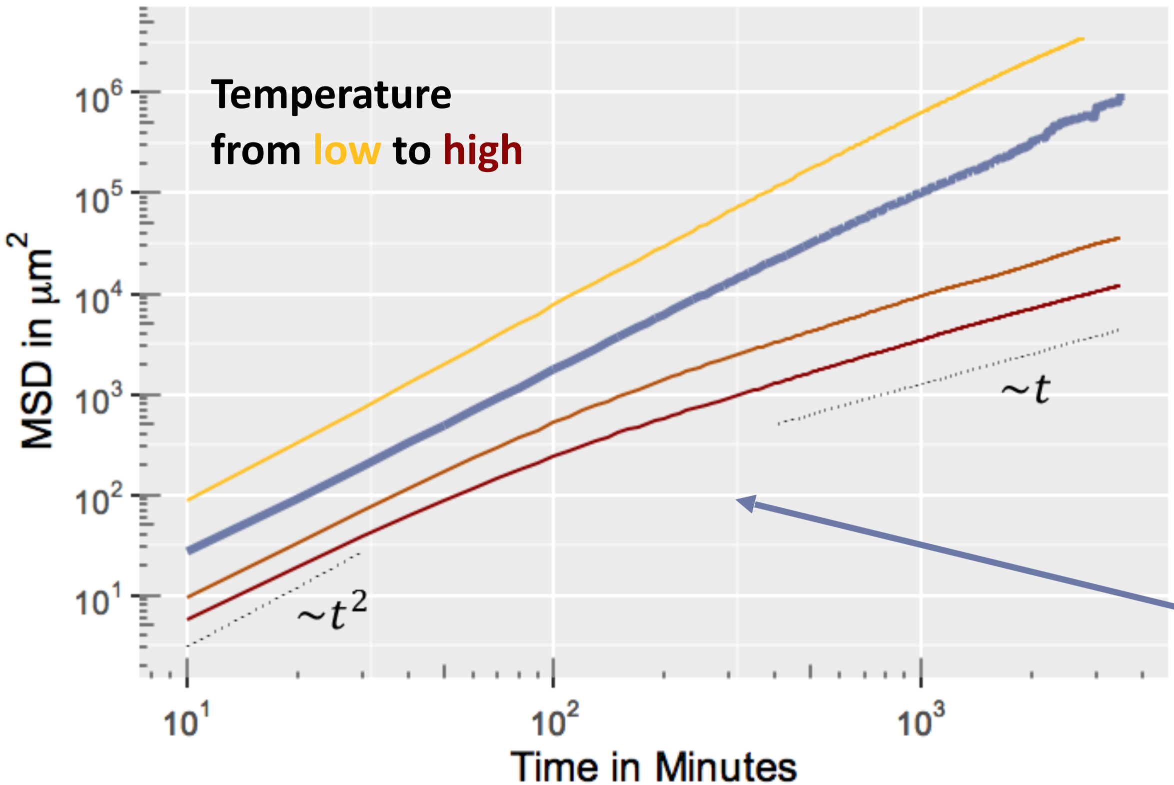
breast cancer cell line
MDA-MB-436
(mesenchymal phenotype)

Salinomycin affects
rest time and crossing probability,
but not velocity and run-times



Motility Parameters: Mean Square Displacement

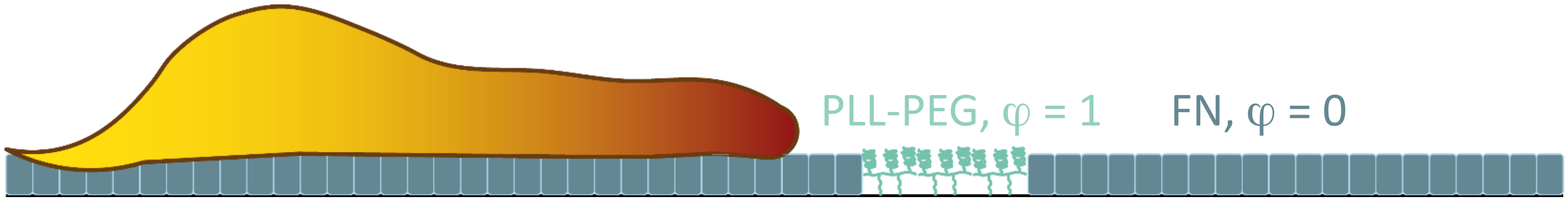


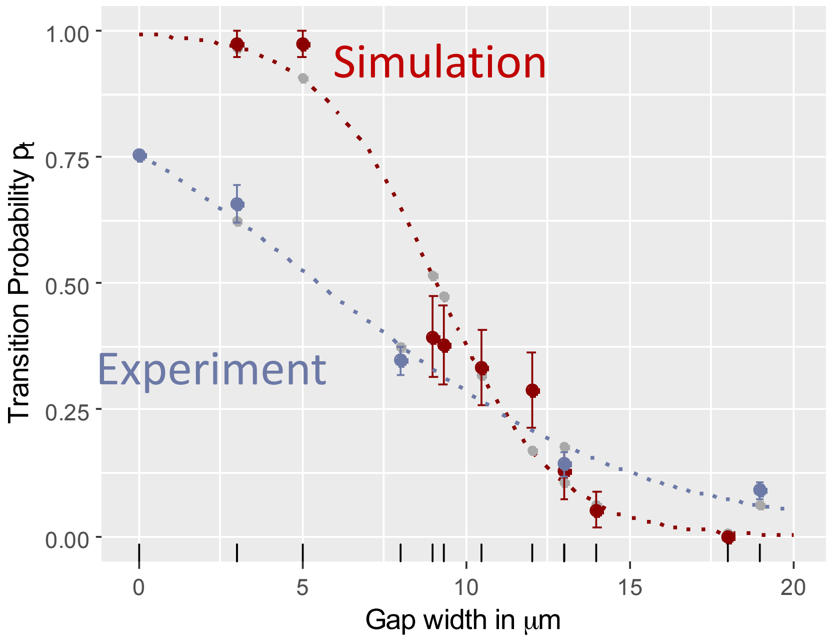


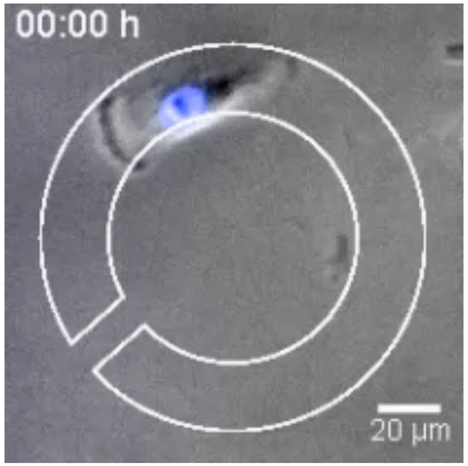
effective temperature changes migration from ballistic to persistent random walk

Persistent random walk: Exponential Crossover

Adhesion Parameters: Affinity barriers



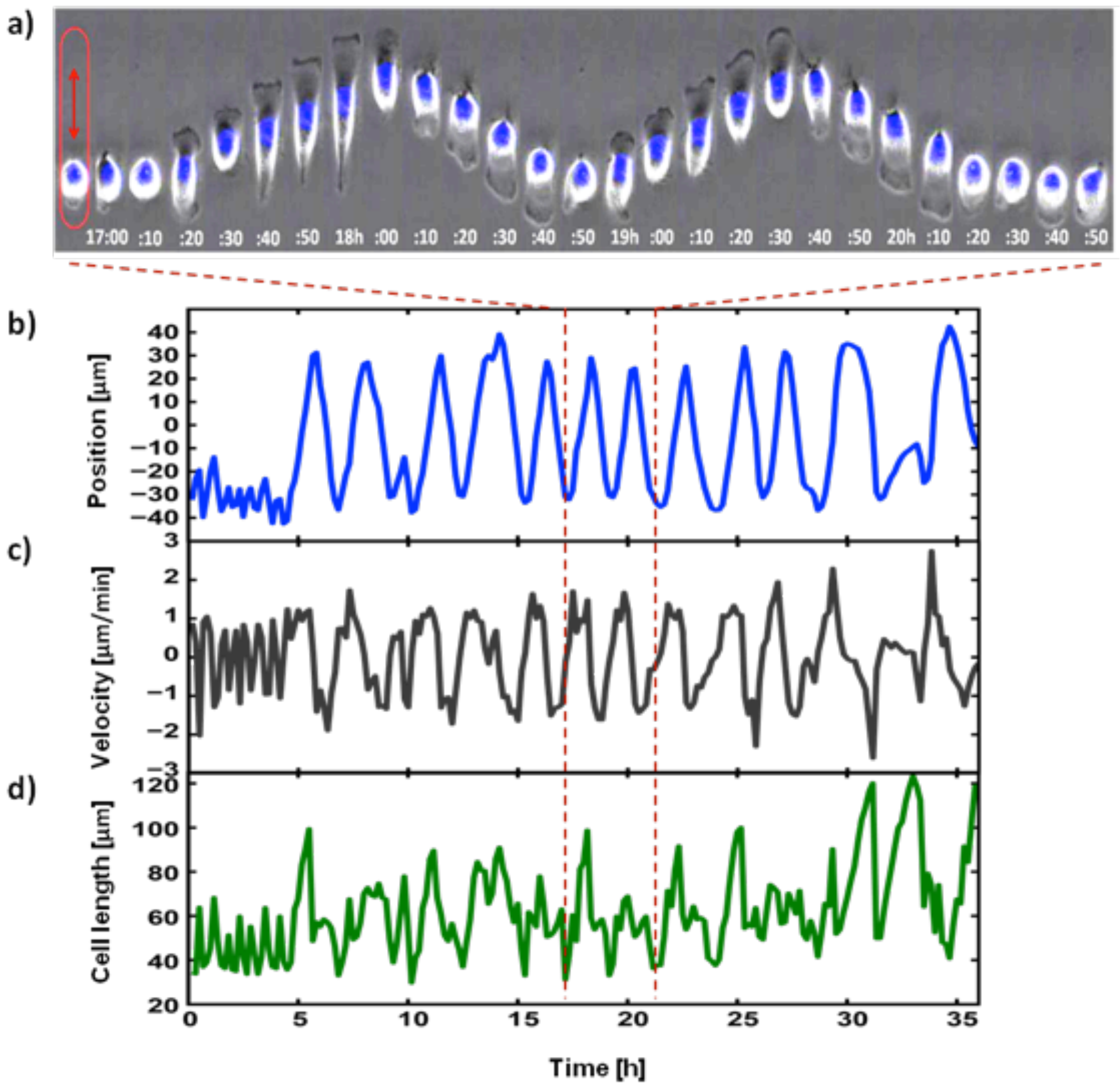


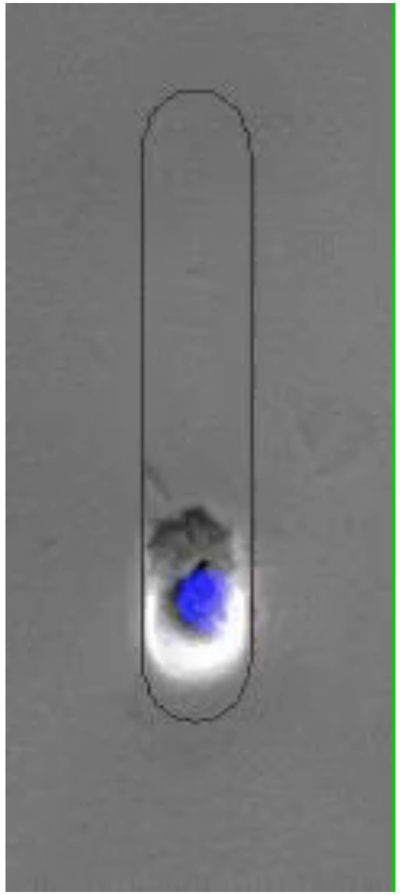


The PLL-PEG level φ describes the energy penalty for invading passivated grid sites.

The transition probability drops for increasing gap width.

Pol-to-pol migration in finite slits

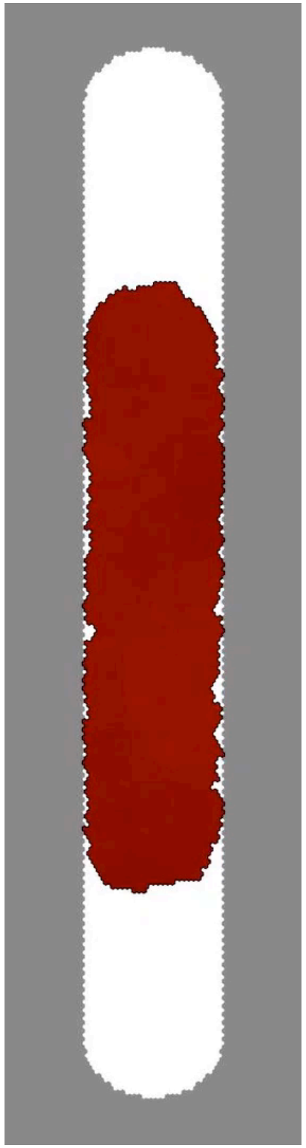


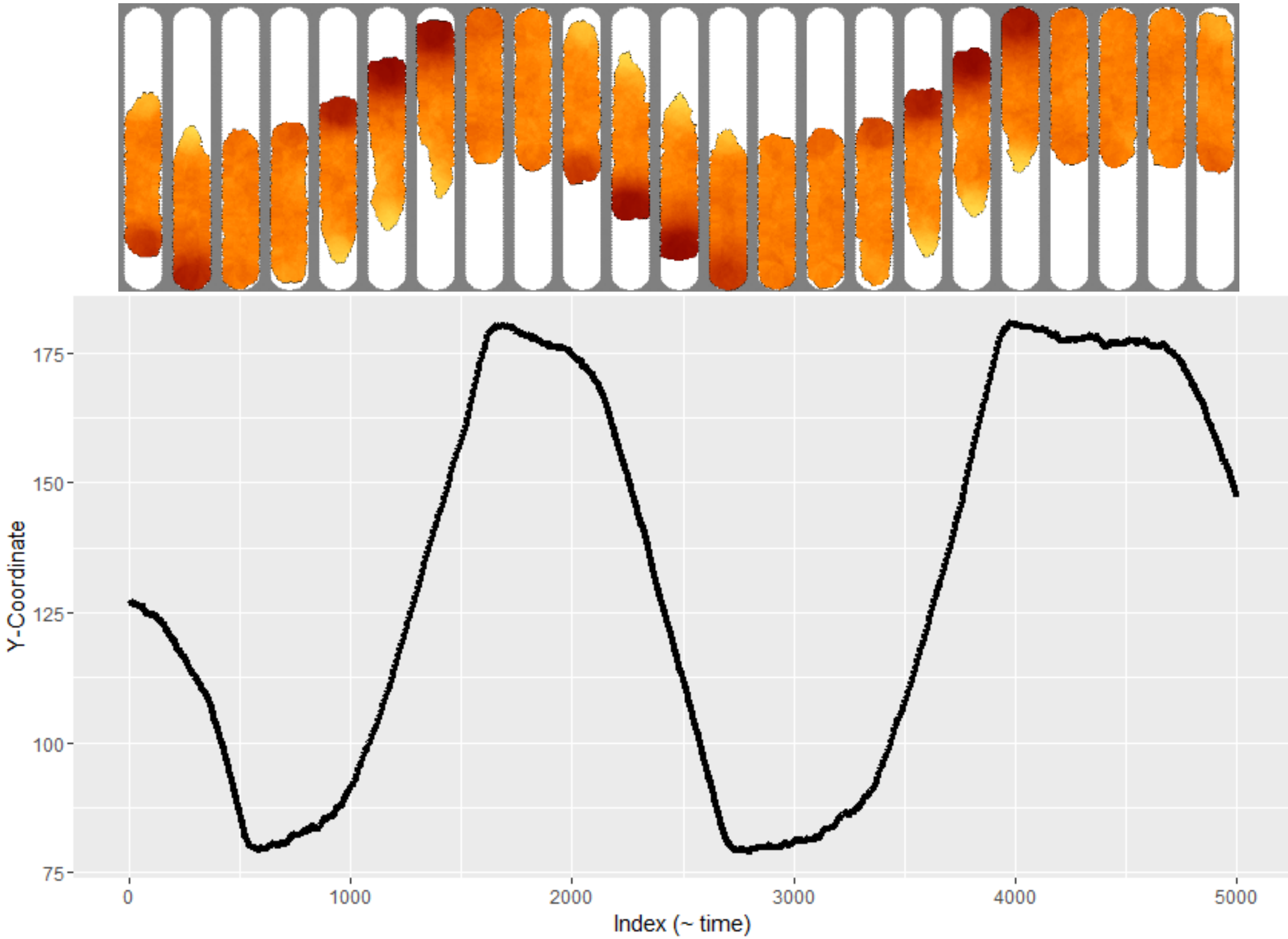


MDA-MB-231
human breast carcinoma

Fang Zhou

CPM simulation of pol-to-pol migration

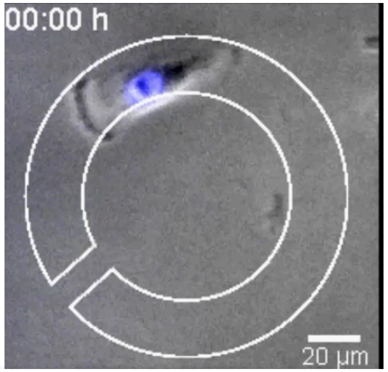




Sophia Schaffer / Andriy Goychuk

Single cell migration - spatiotemporal decisions

1D-Random walk
with barrier

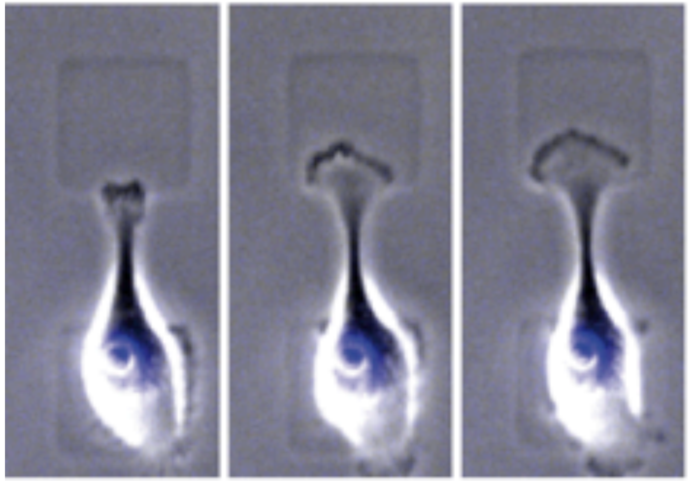


Christoph Schreiber
Sophia Schaffer
Fang Zhou

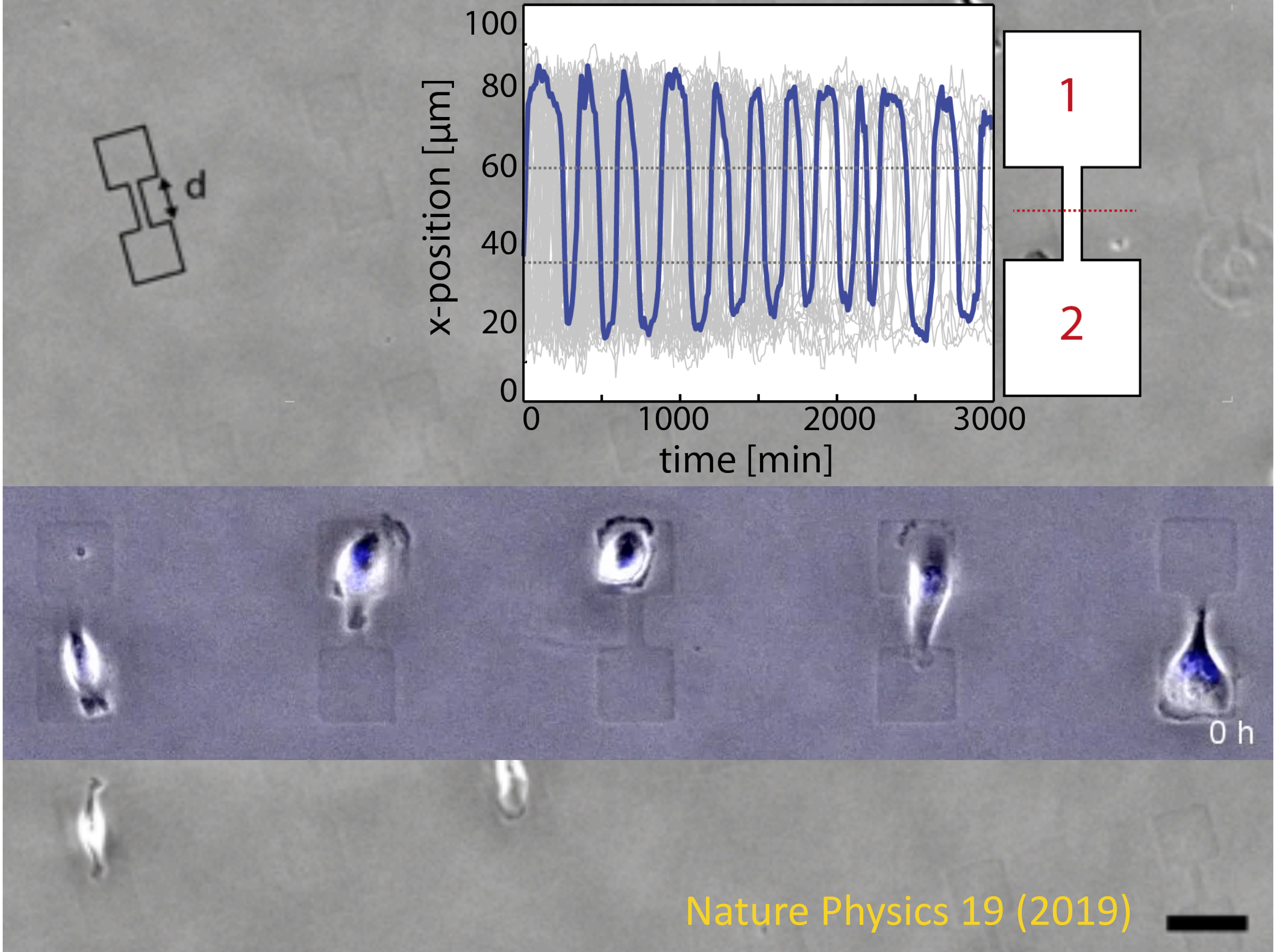
collaborators:
Ernst Wagner
Andreas Roidl
Erwin Frey
Florian Thürhoff
Andriy Goychuk

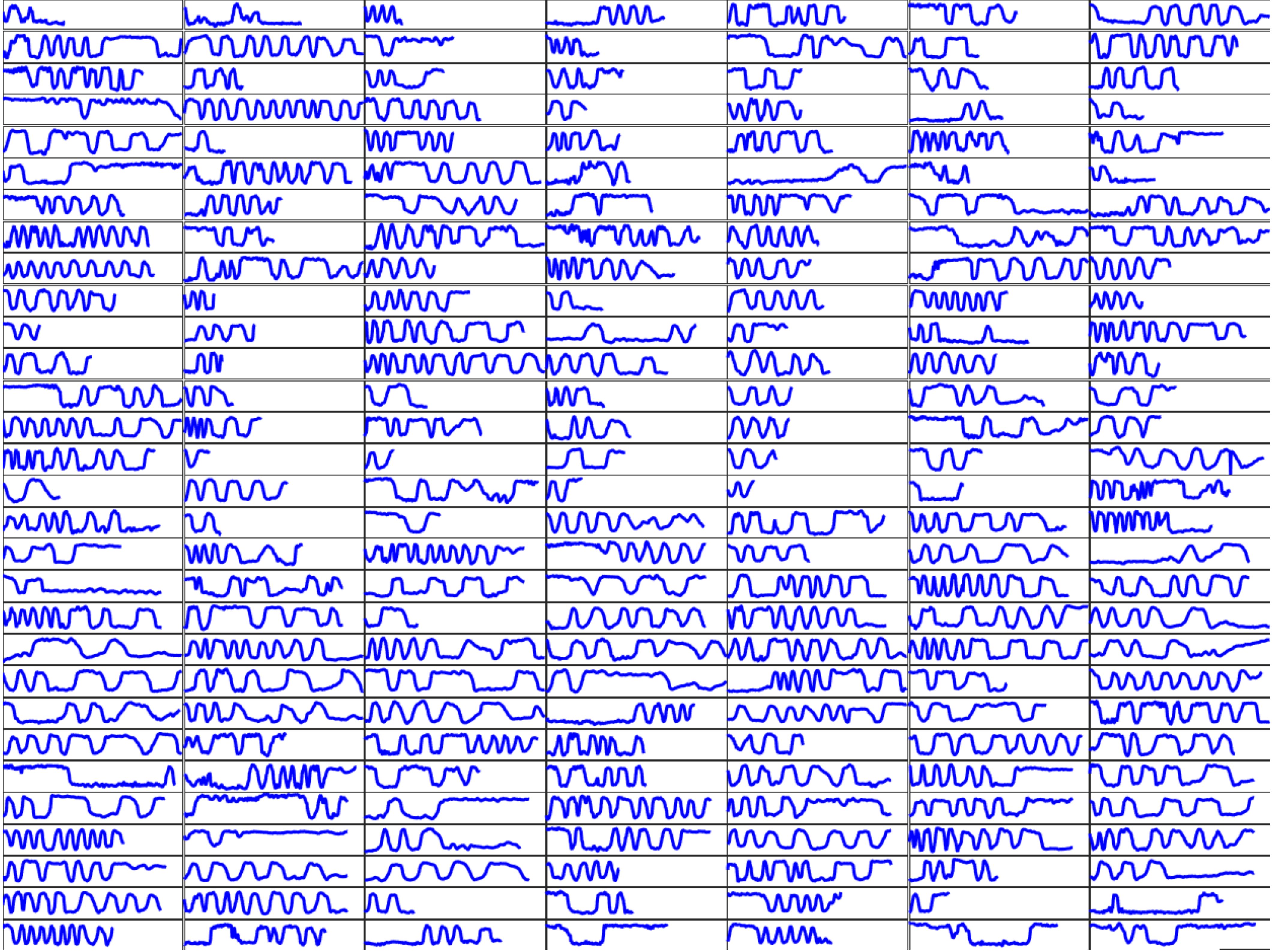
Two-State-System

Alexandra Fink
Peter Röttgermann
Christoph Schreiber

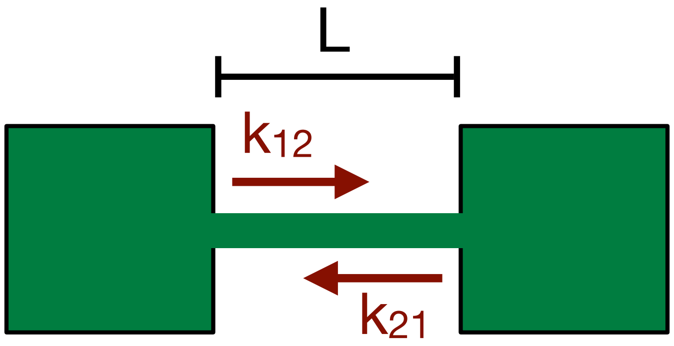


David Brückner & Chase Broedersz


d
100
80
60
40
20
0
x-position [µm]
0
1000
2000
3000
time [min]
1
2
0 h
Nature Physics 19 (2019)

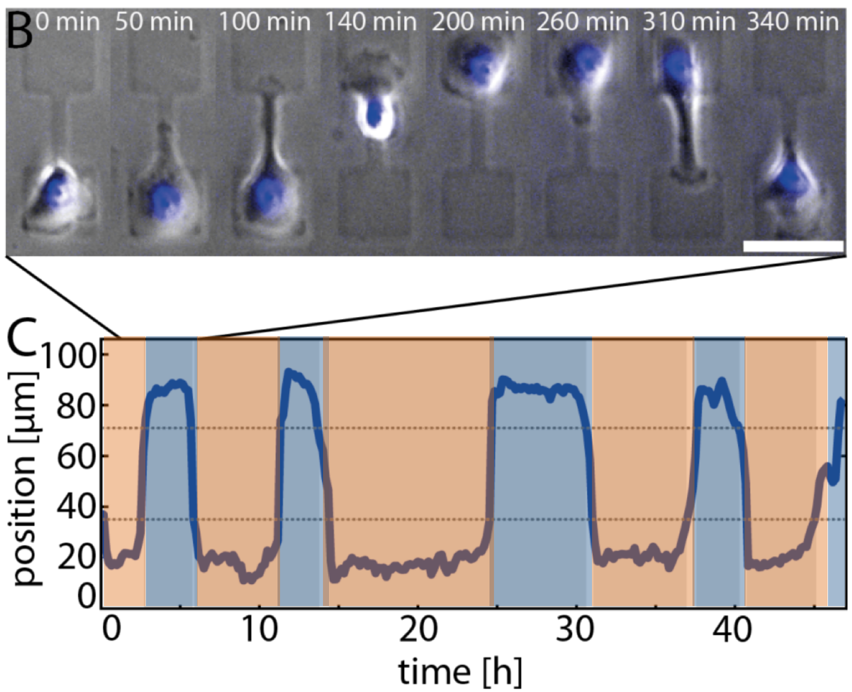


Cell migration in a two-state systems

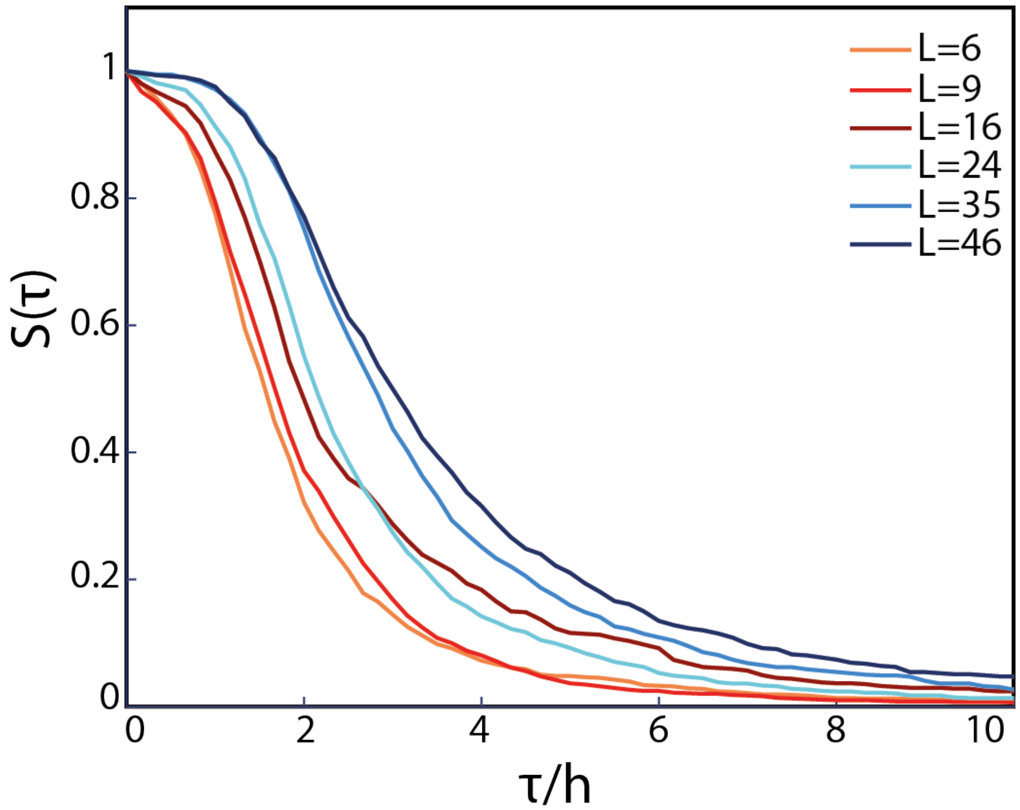


survival function for
various channel lengths

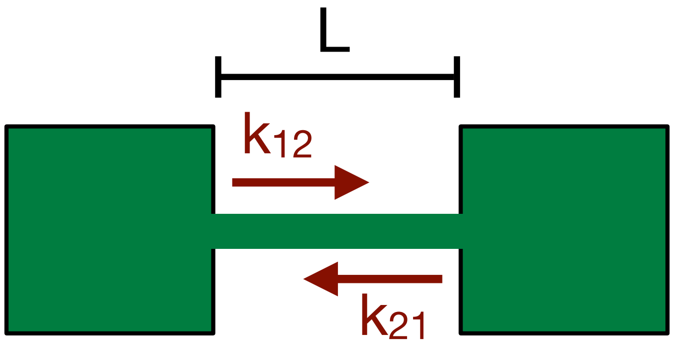
=> average escape times: $\langle\tau\rangle$ increases with channel length



MDA-MB-231 human breast carcinoma

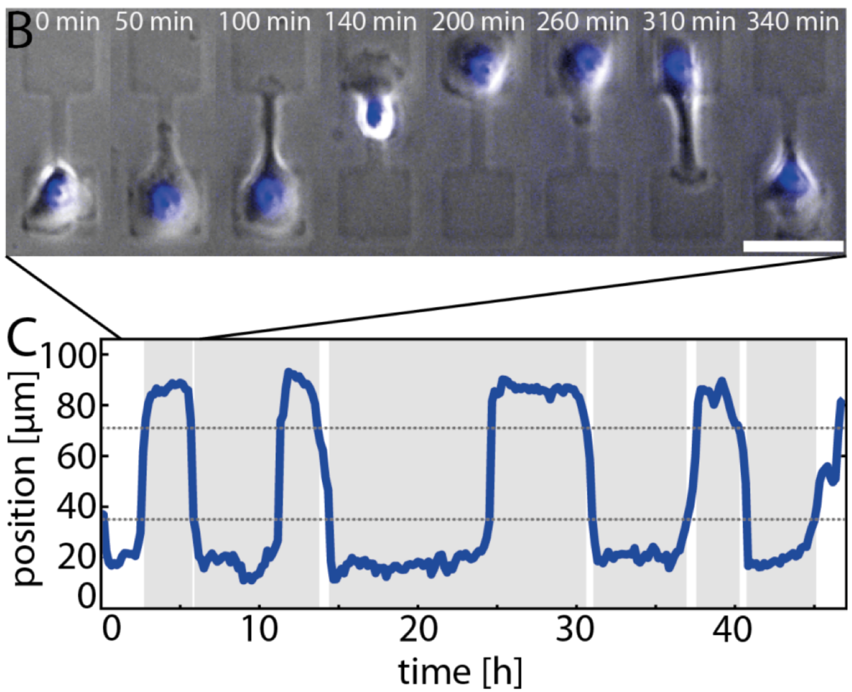


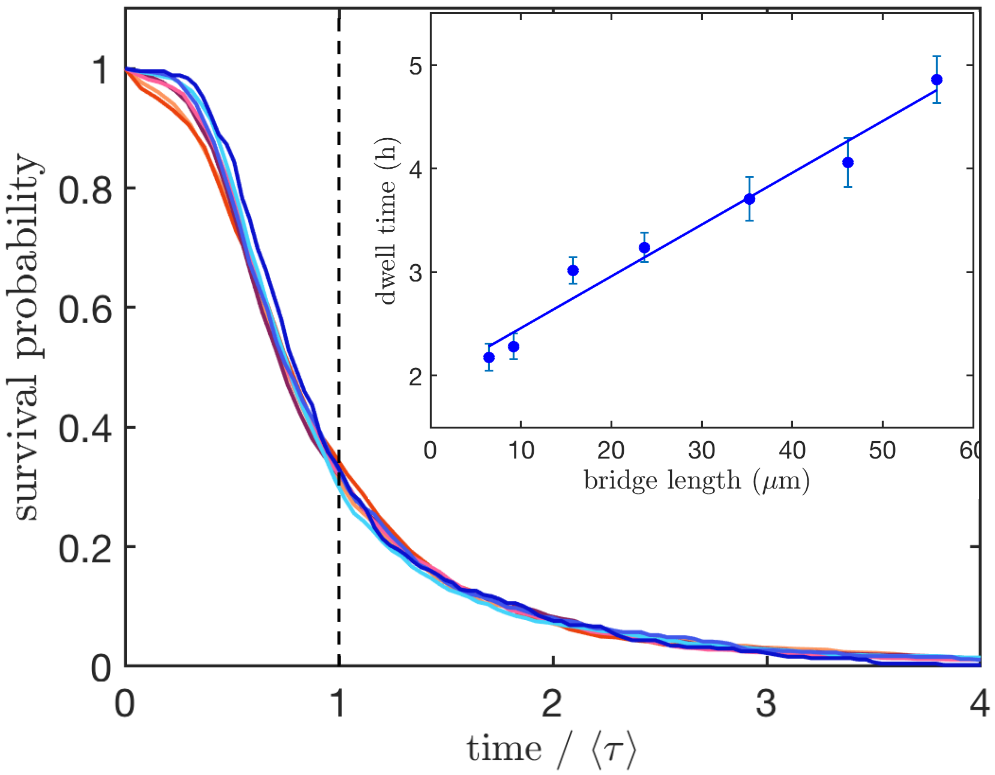
Cell migration in a two-state systems



normalized escape time distribution collapses on one master curve

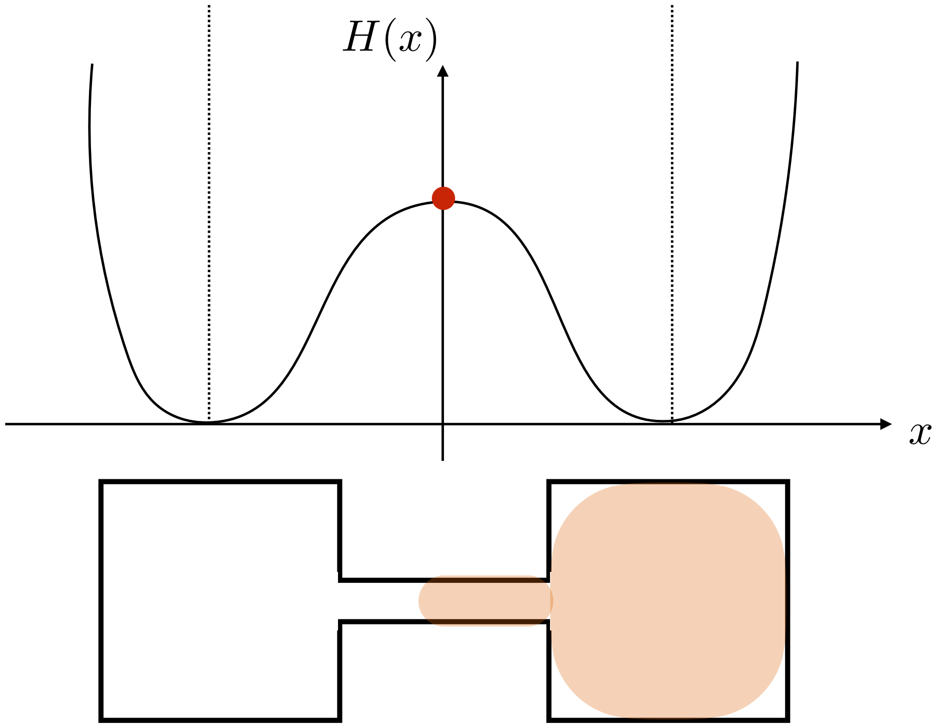
$$S(\tau) = f(\tau/\langle\tau\rangle)$$





MDA-MB-231 human breast carcinoma

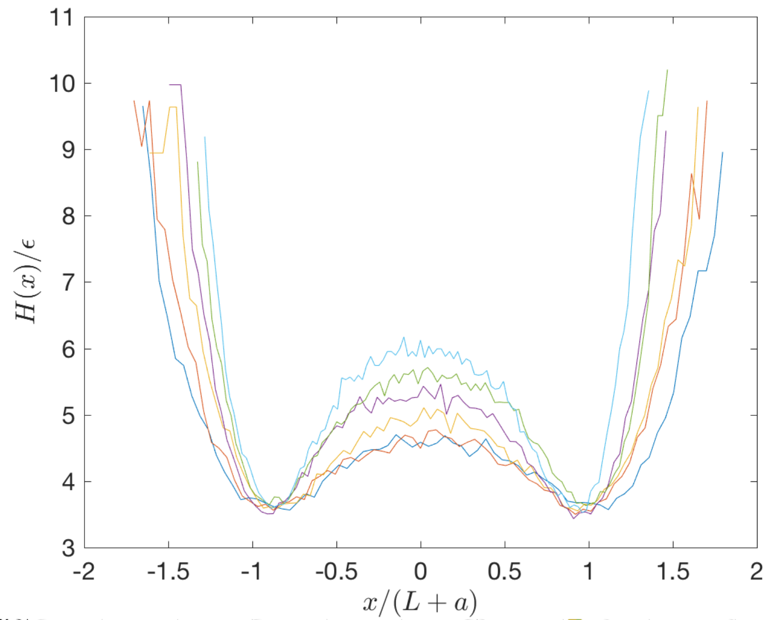
Theory of active matter systems

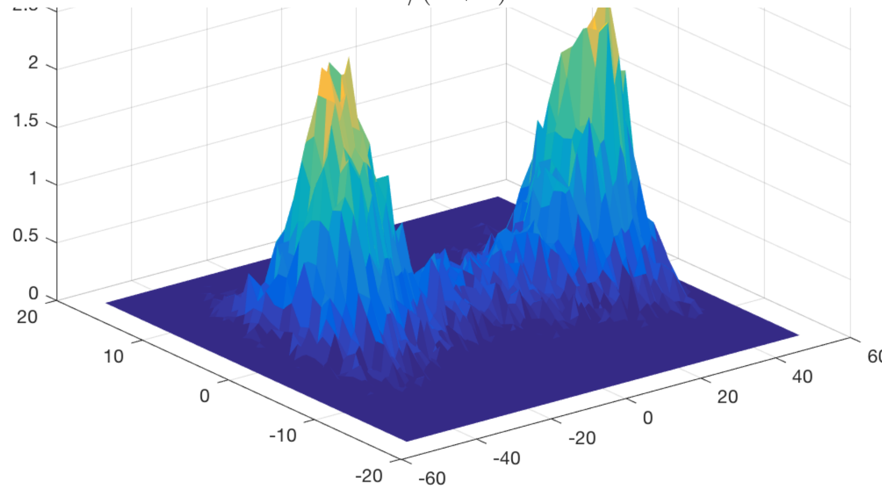


$$\dot{x} = -\partial_x H(x) + \epsilon\eta(t)$$

elastic energy — „active“ noise

deterministic — random



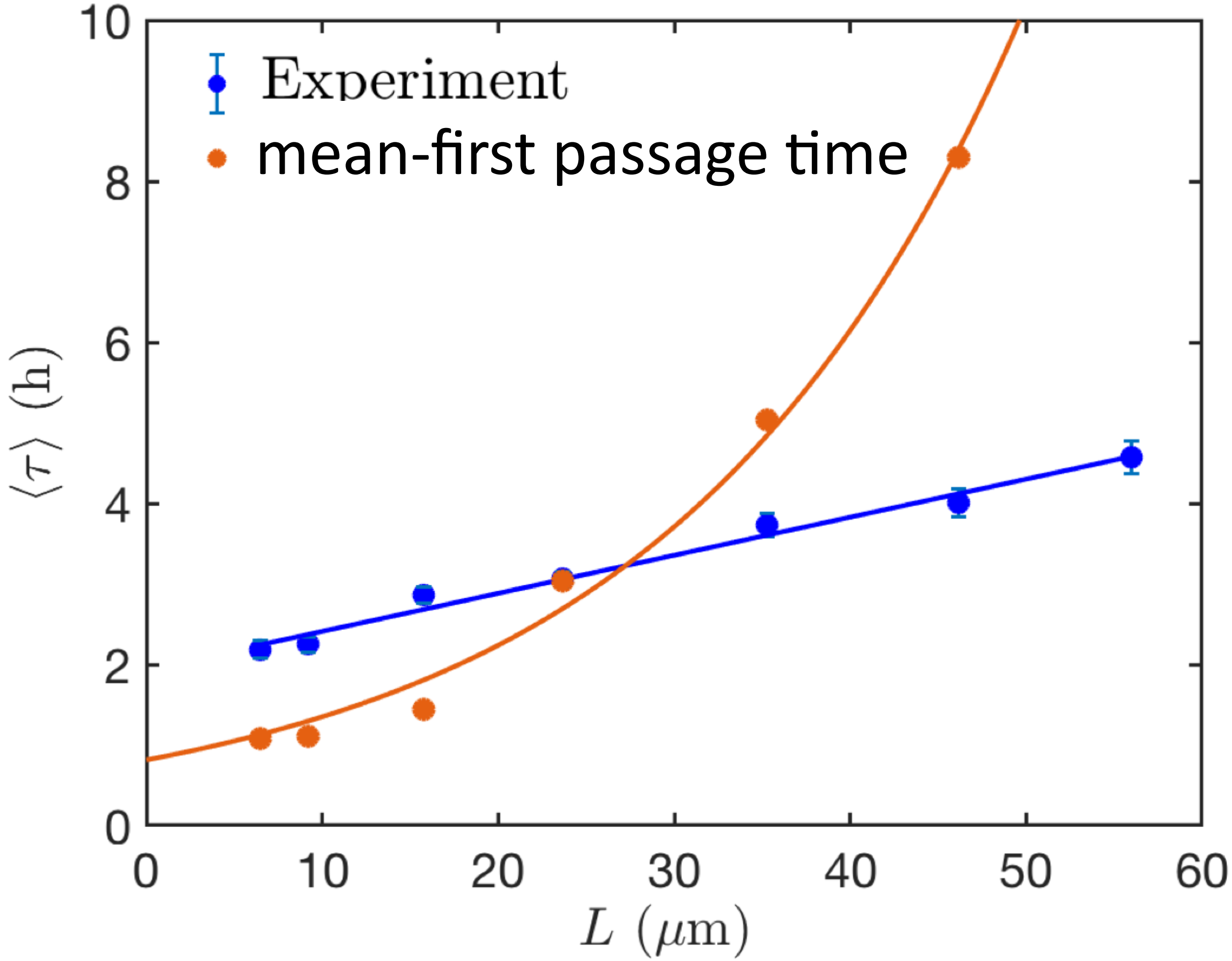


David Brückner / Chase Broedersz

Theory of active matter systems

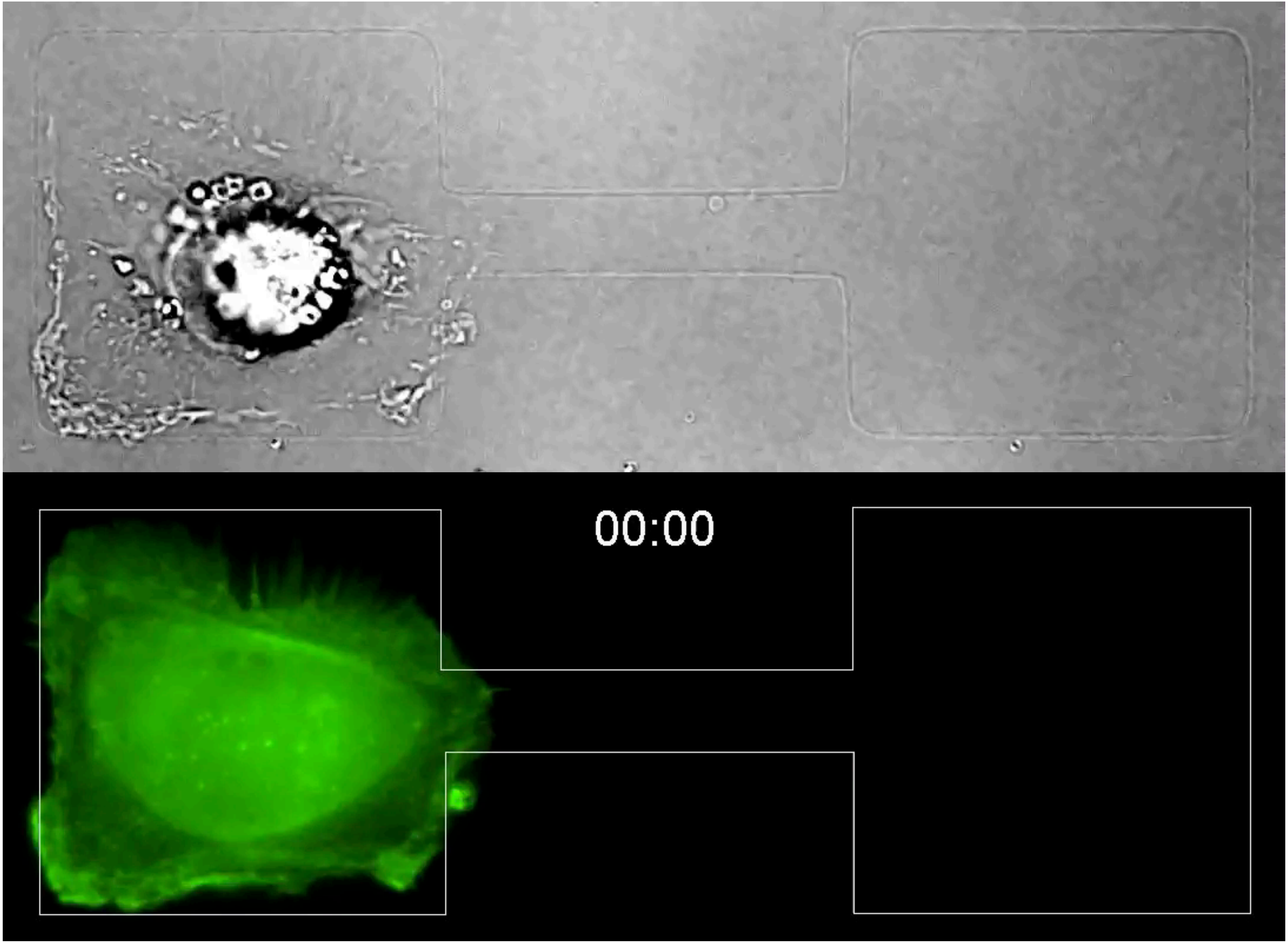
$$\langle \tau_L \rangle = \frac{1}{\sigma} \int_{x_0}^{x_r} \mathrm{d}y \exp\left(\frac{V_L(y)}{\sigma}\right) \int_{x_l}^{y} \mathrm{d}z \exp\left(-\frac{V_L(z)}{\sigma}\right)$$

Kramers expression for the transition rates



First order model fails to reproduce transition dynamics !

David Brückner / Chase Broedersz


00:00

Inferred equation of motion for confined cell migration

Ansatz $$\dot{v} = F(x,v) + \sigma(x,v)\eta(t)$$

second-order Langevin equation: acceleration = force + noise

$$\langle \eta(t)\eta(t')\rangle = \delta(t-t')$$

white noise conditon

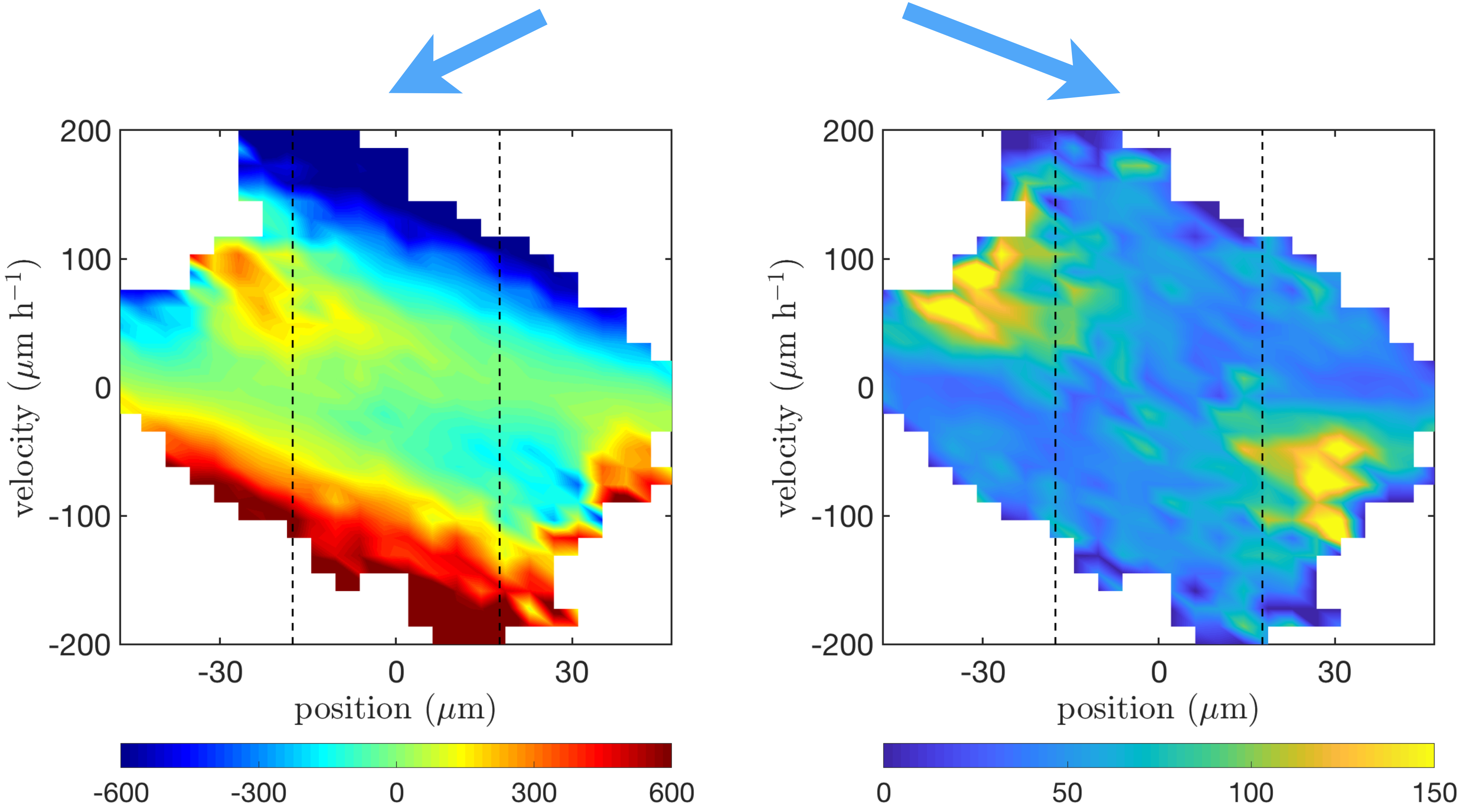
data-driven retrieval of force and noise field:

$$F(x,v) = \langle \dot{v} | x, v\rangle$$

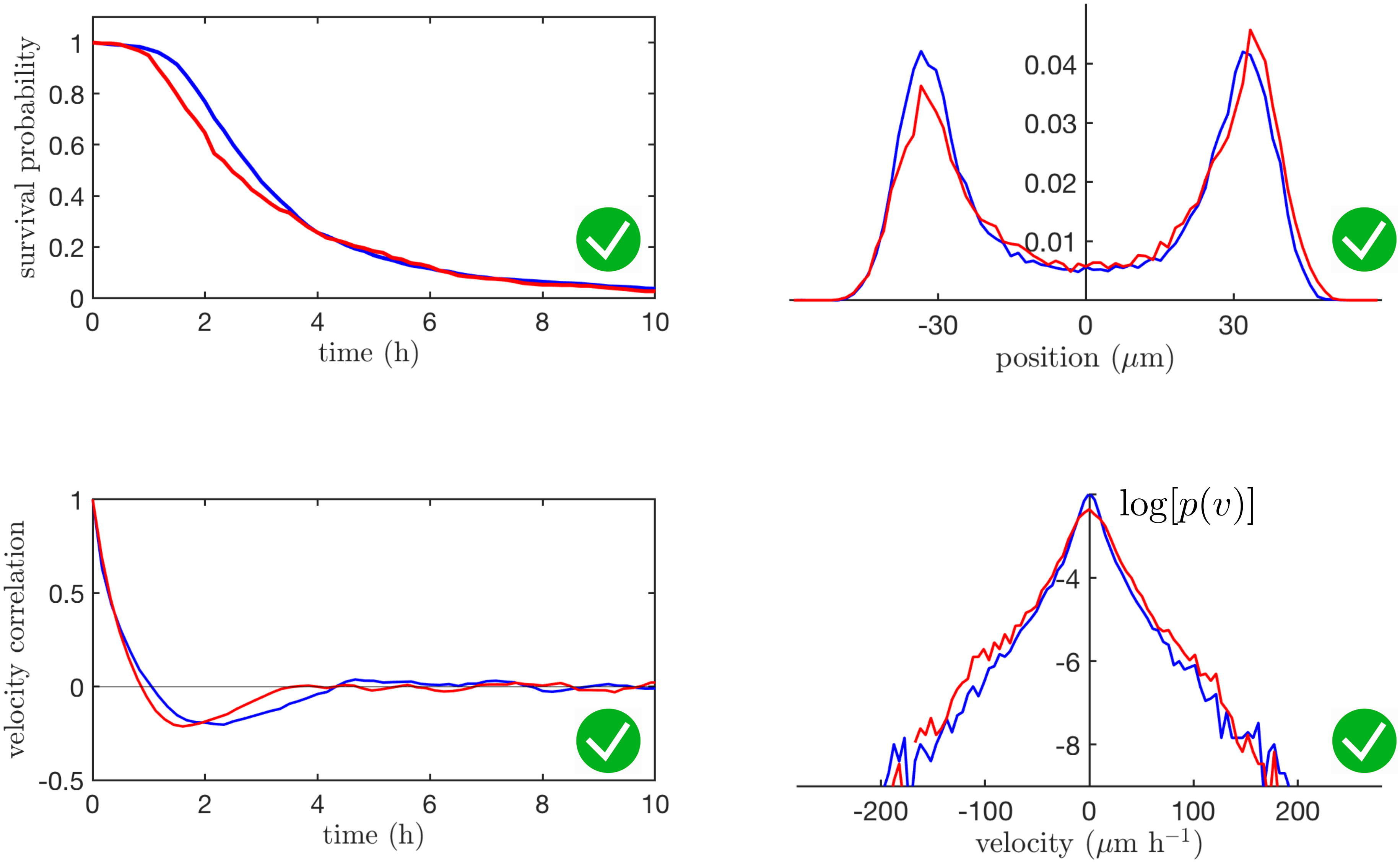
$$\sigma^2(x,v) = \Delta t \langle [\dot{v} - F(x,v)]^2 | x, v\rangle$$

Inferred equation of motion for confined cell migration

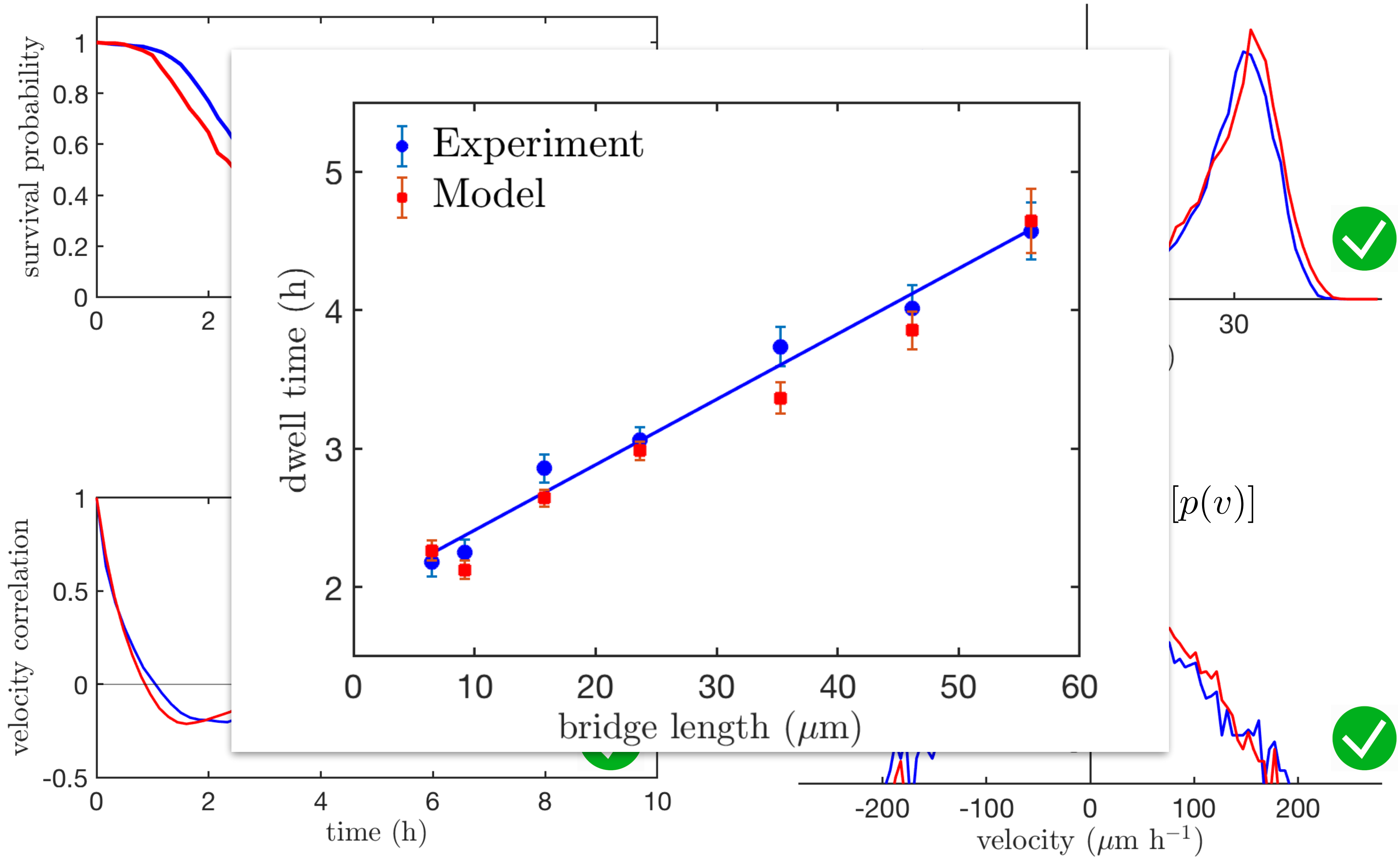
$$\frac{\mathrm{d}v}{\mathrm{d}t} = F(x, v) + \sigma^2(x, v)\eta(t)$$



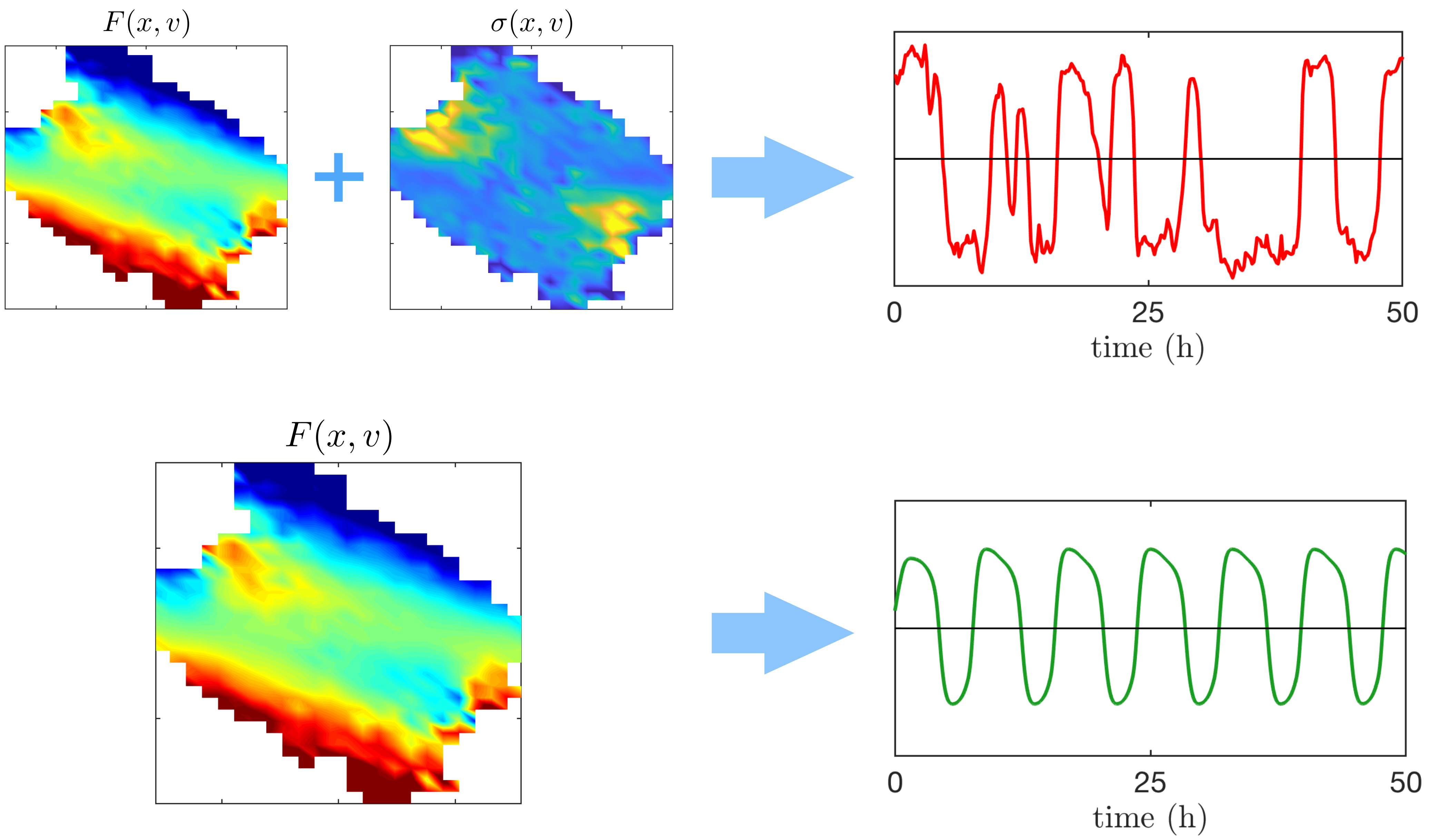
Model reproduces experimental dynamics



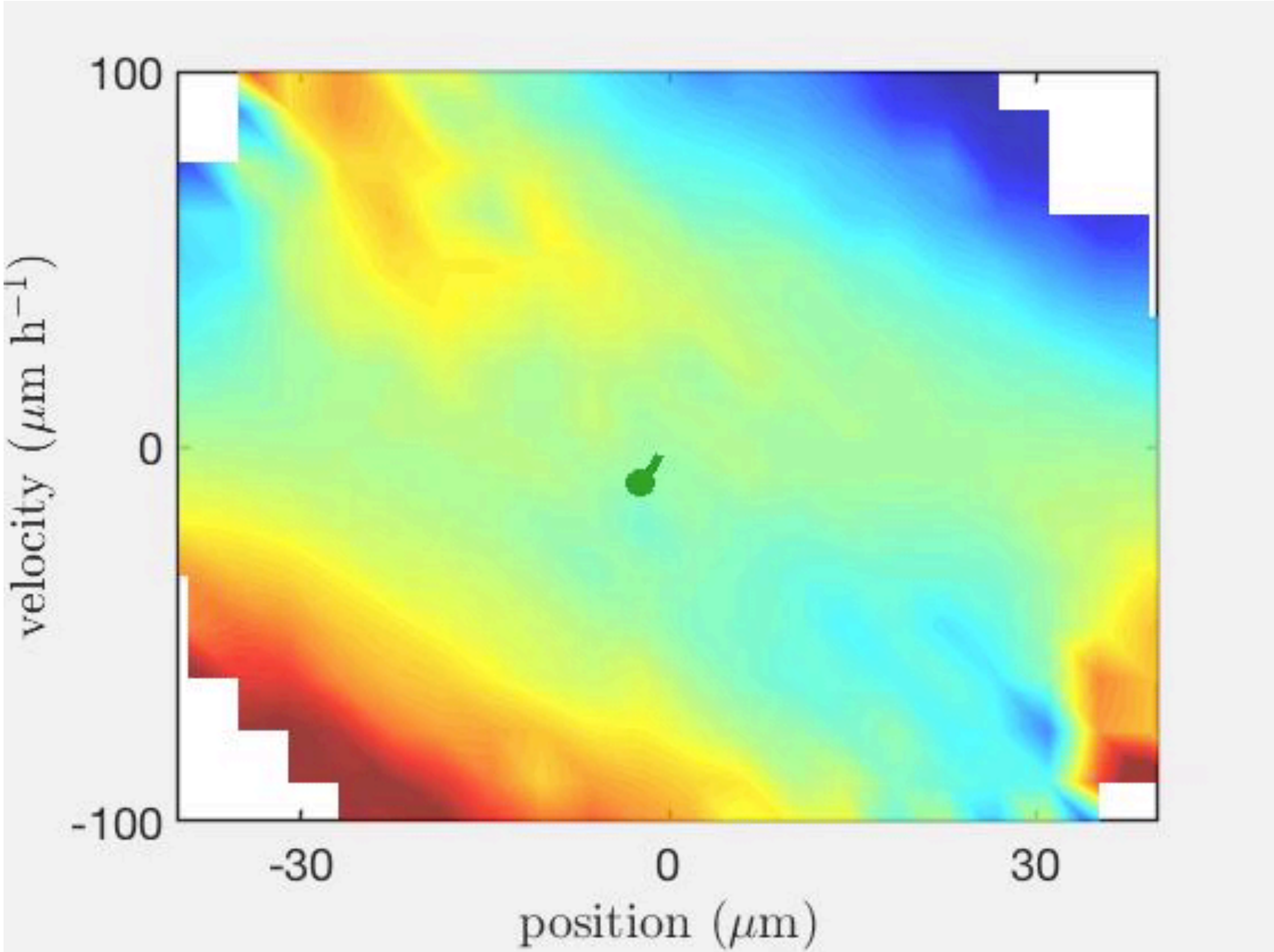
Model reproduces experimental dynamics



Deterministic component drives transitions

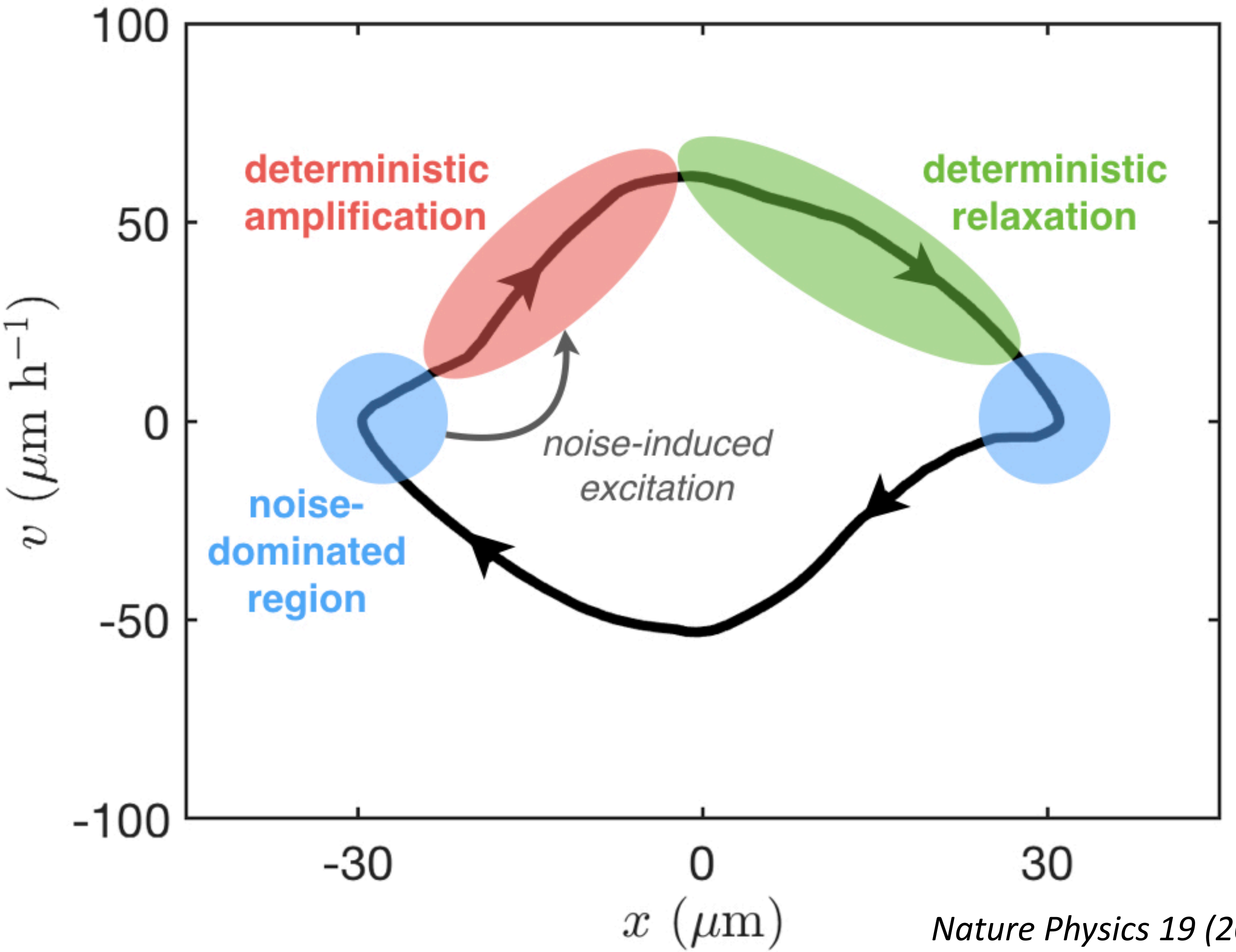


Deterministic dynamics exhibits a limit cycle



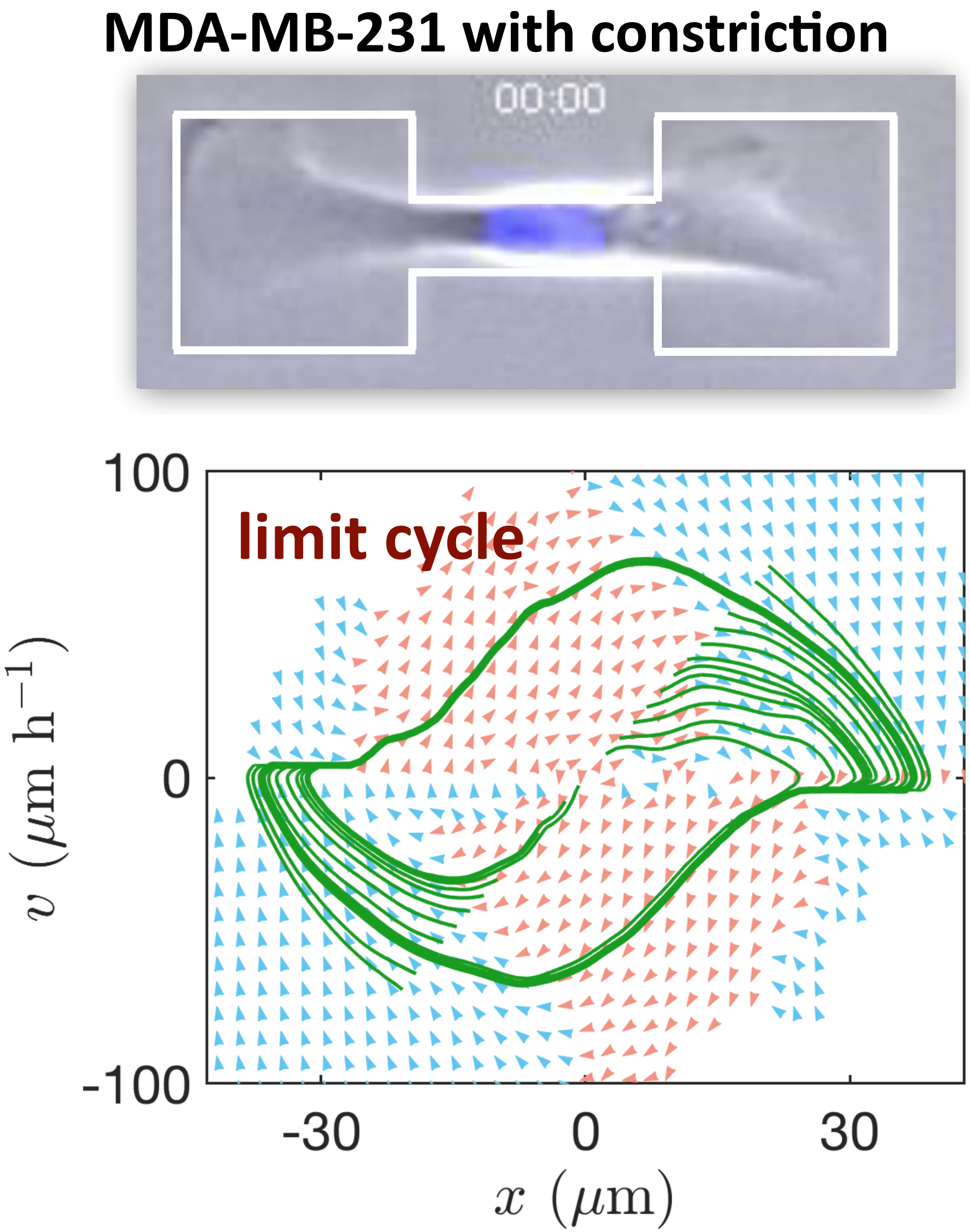
Nature Physics 19 (2019): 1592.

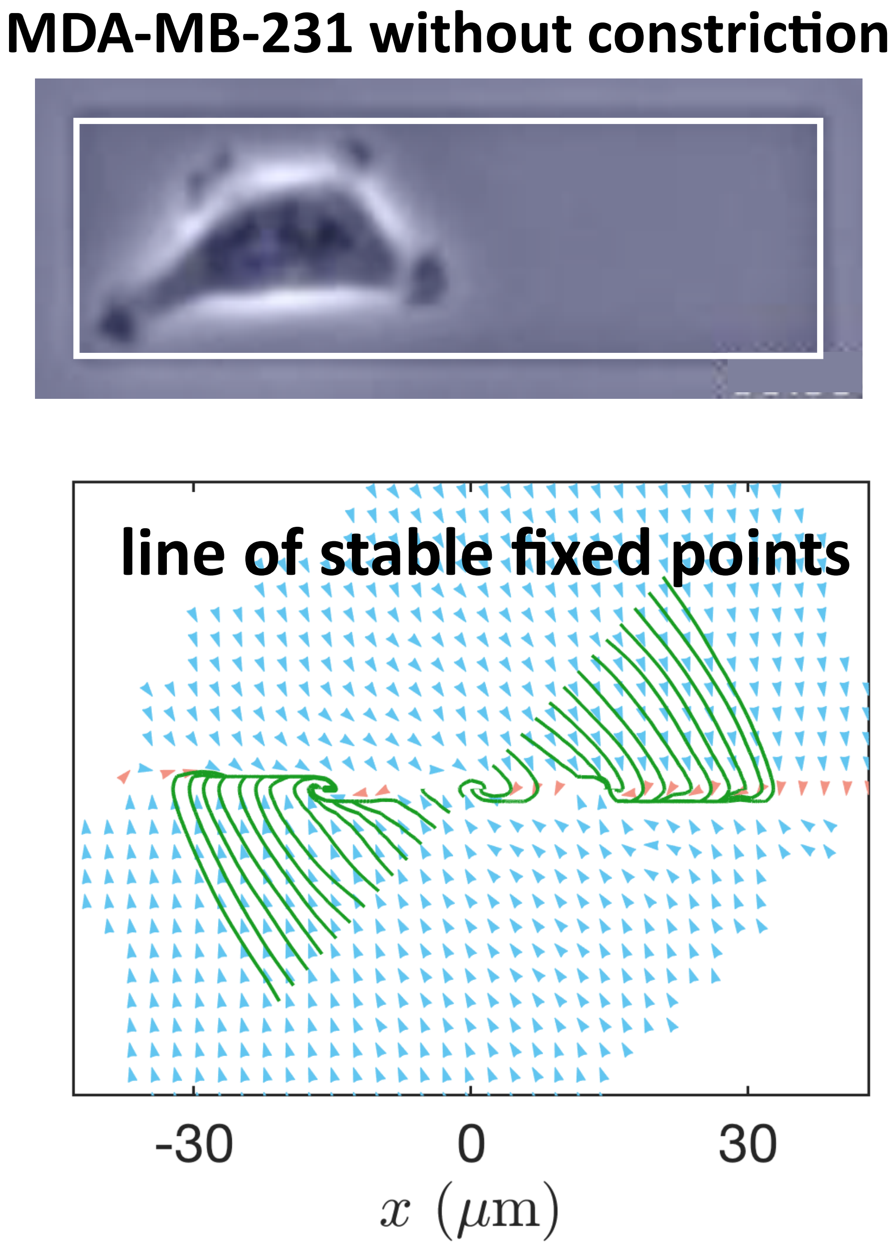
Noise induced excitations



Nature Physics 19 (2019): 1592.

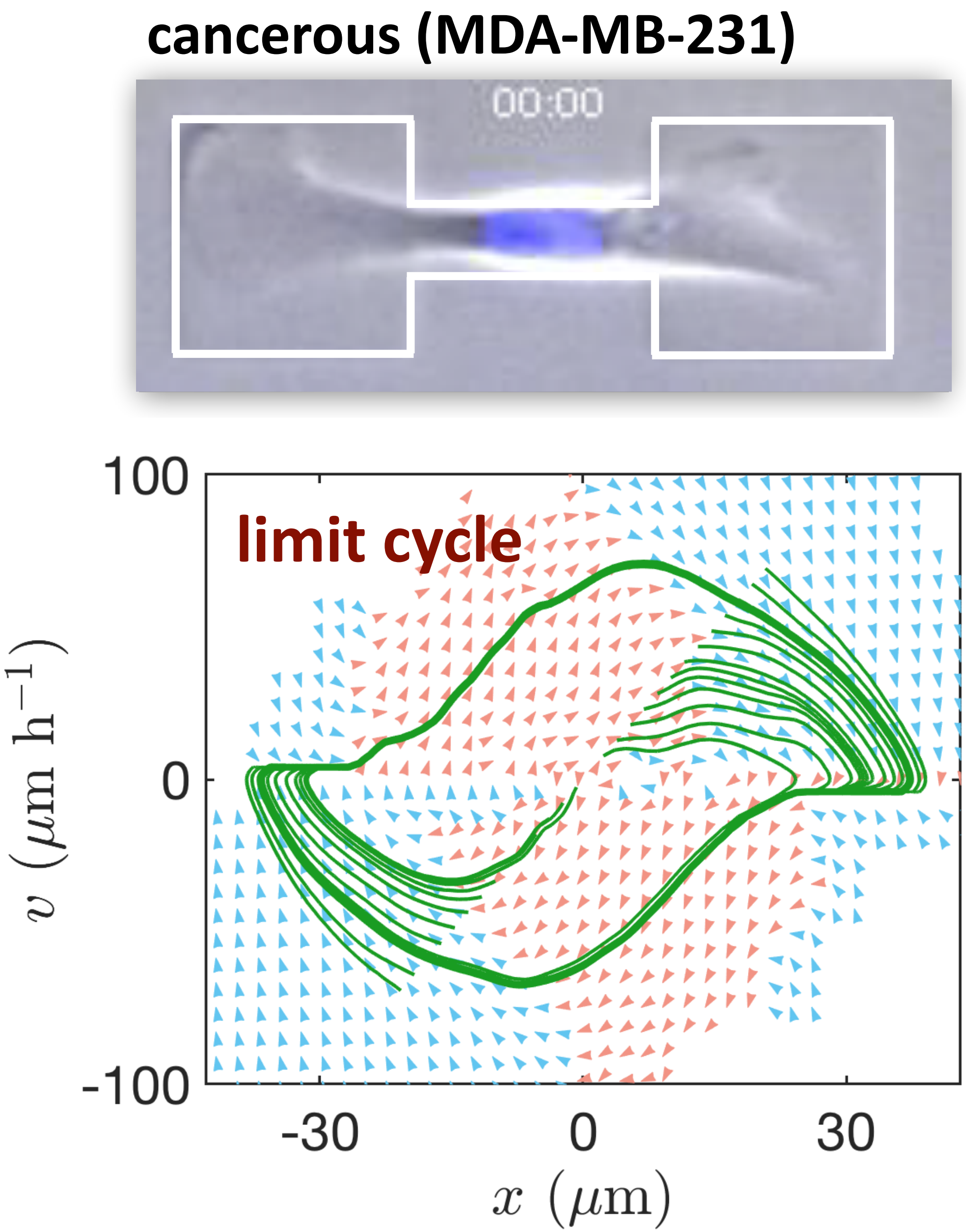
Narrow constrictions lead to speed amplification

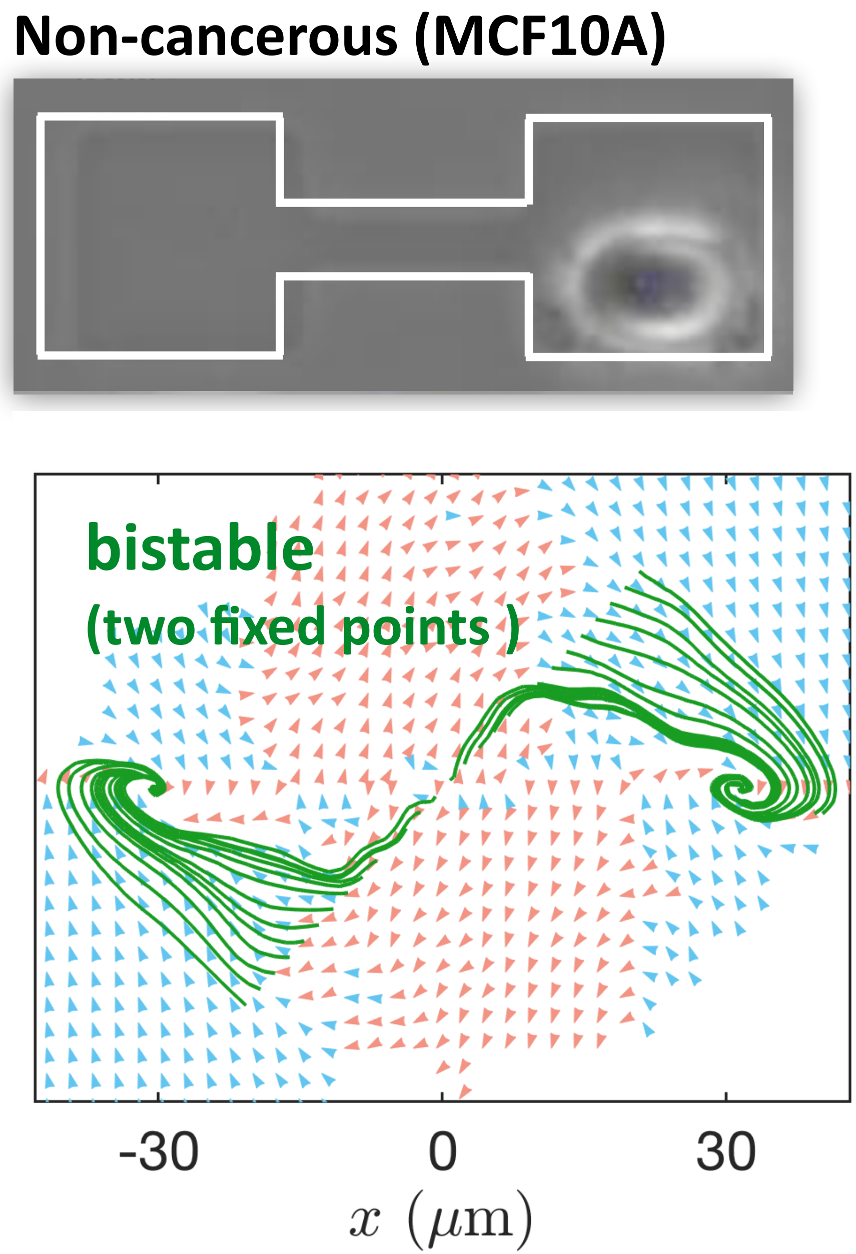




Nature Physics 19 (2019): 1592.

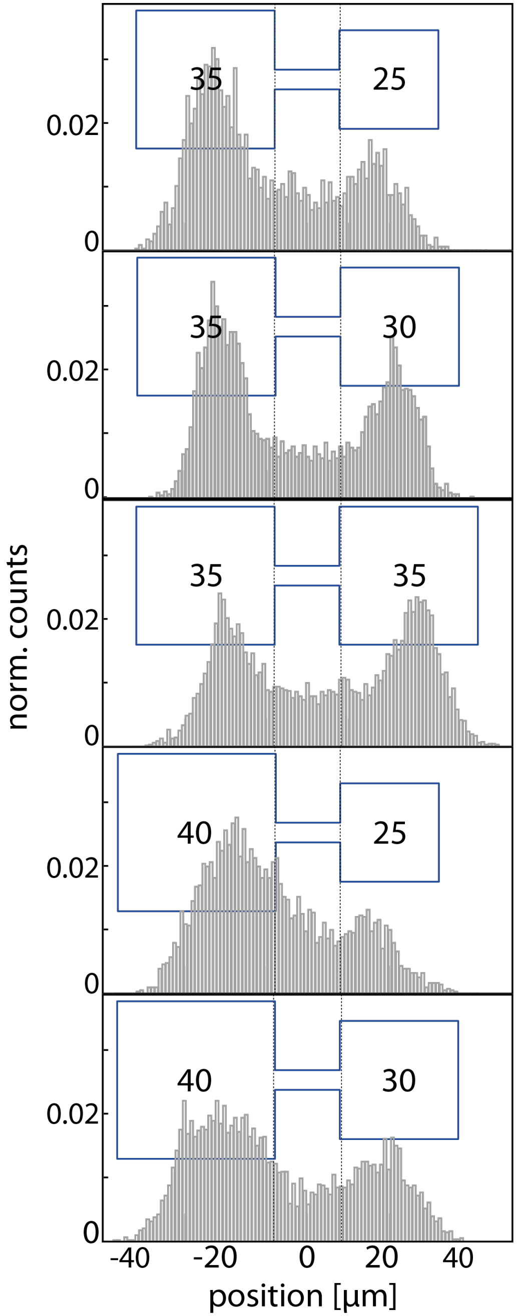
Method detects subtle differences between cells

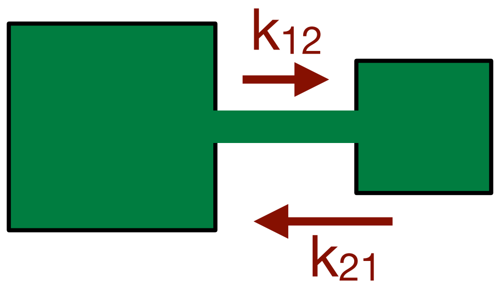


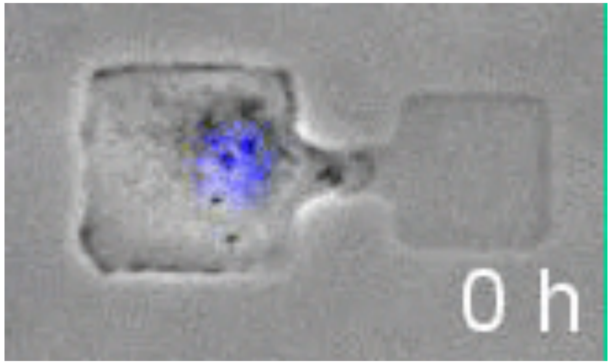


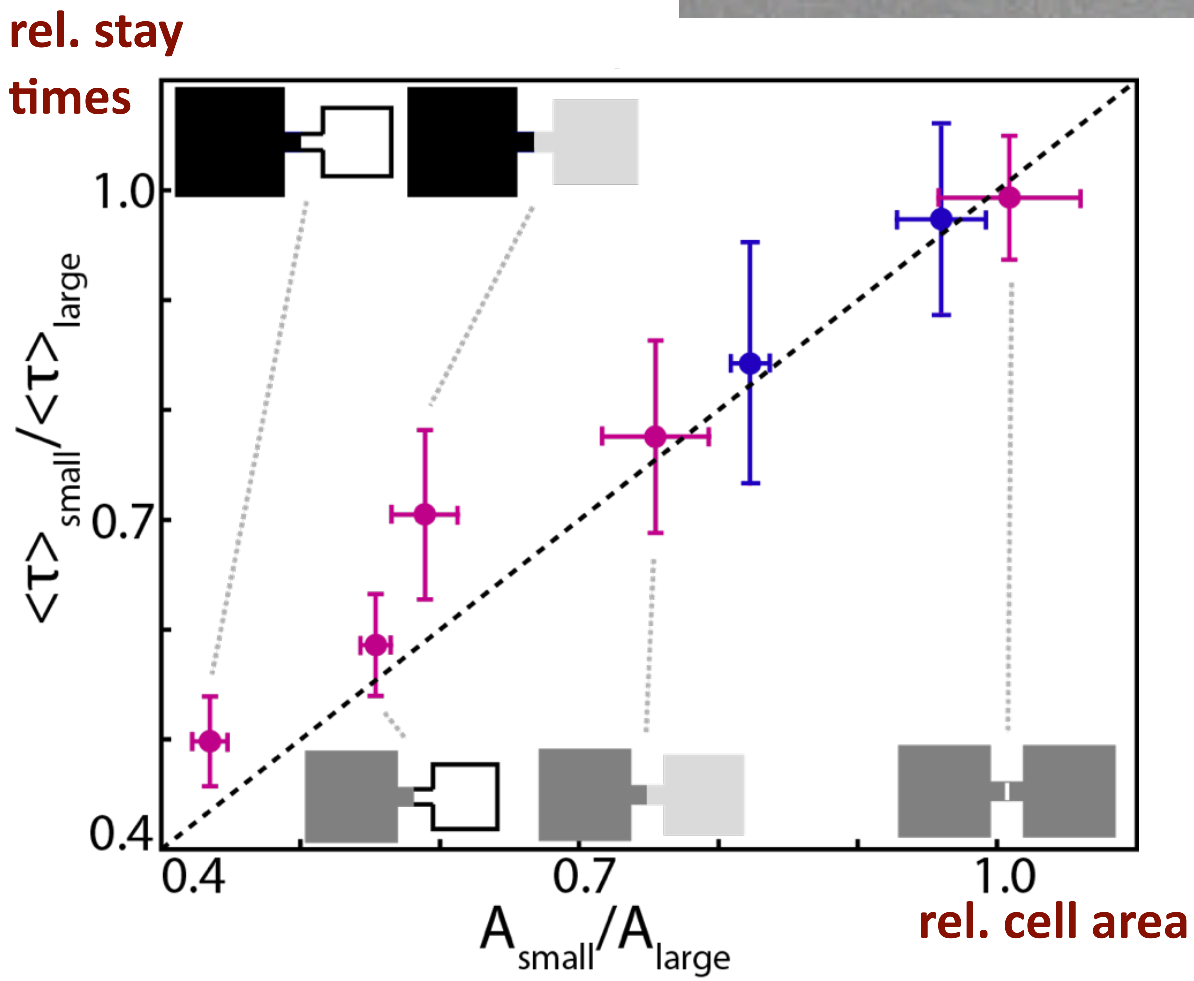
Nature Physics 19 (2019): 1592.

Two-state system with different areas

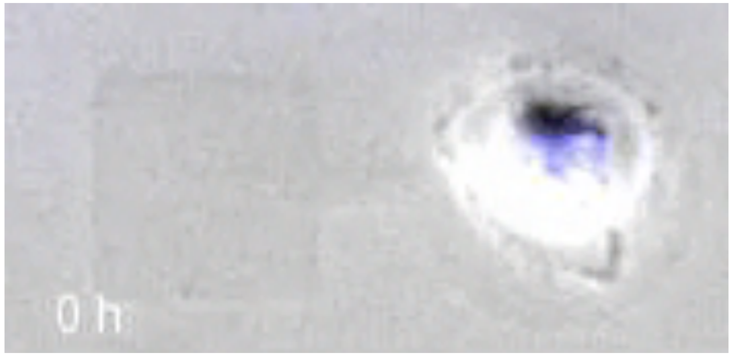




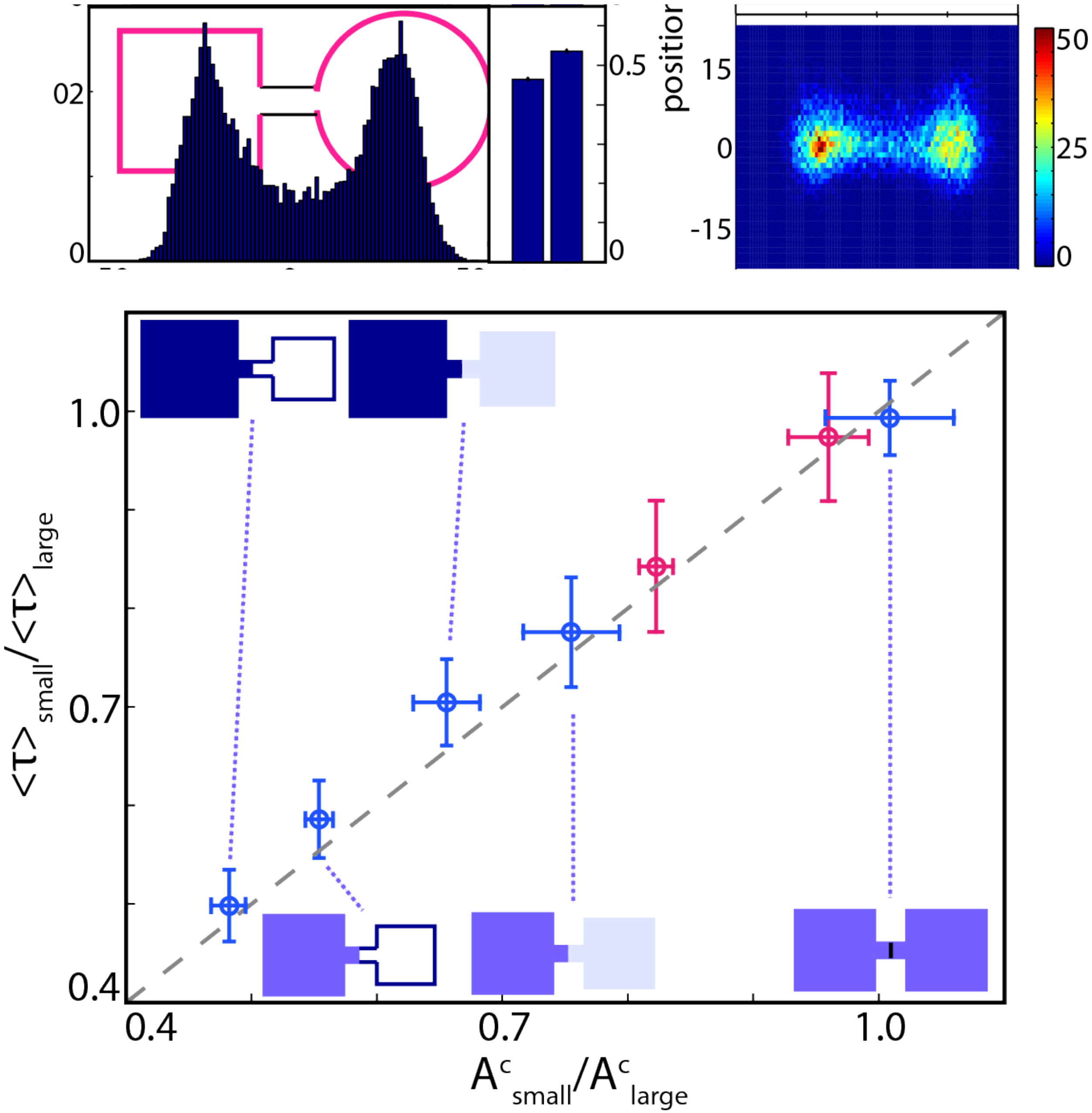




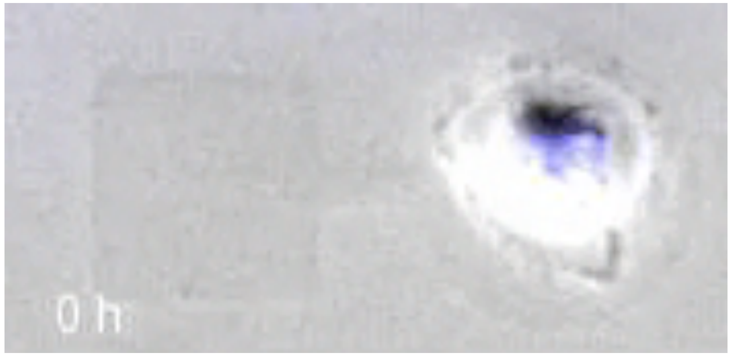
Pattern with different shapes



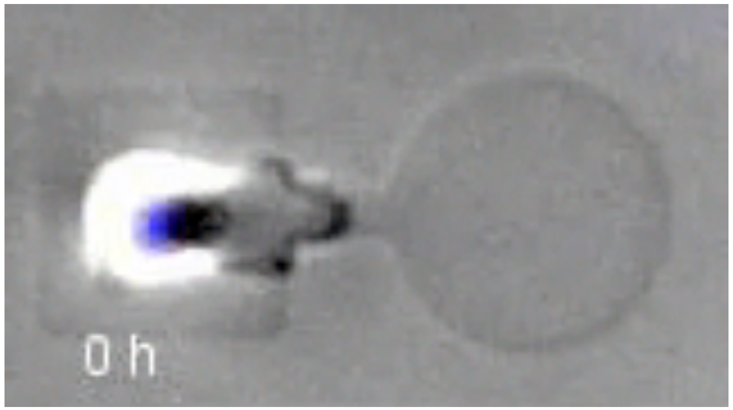
equal perimeter



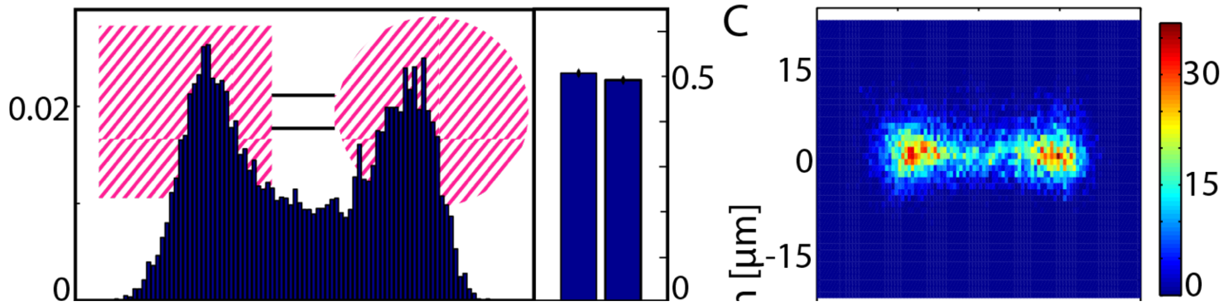
Pattern with different shapes

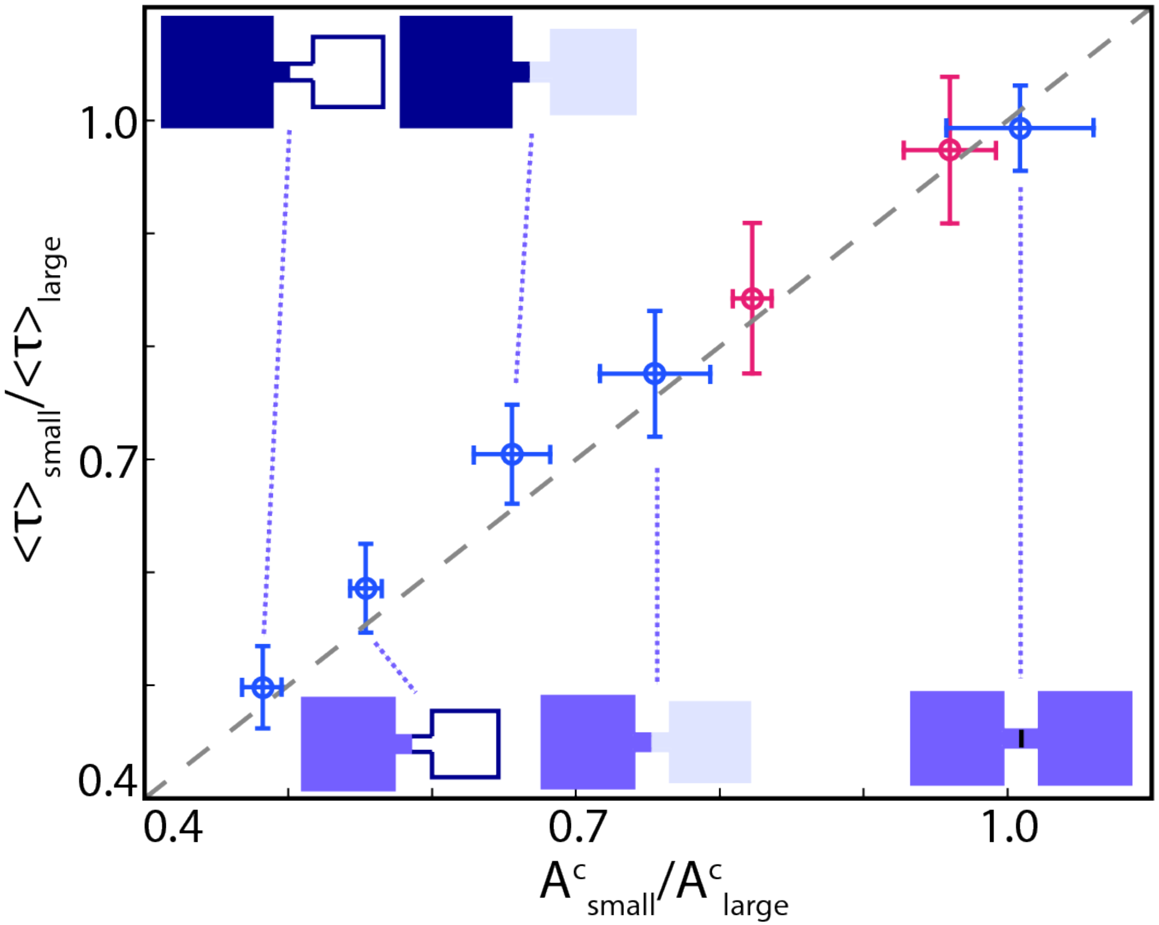


equal perimeter



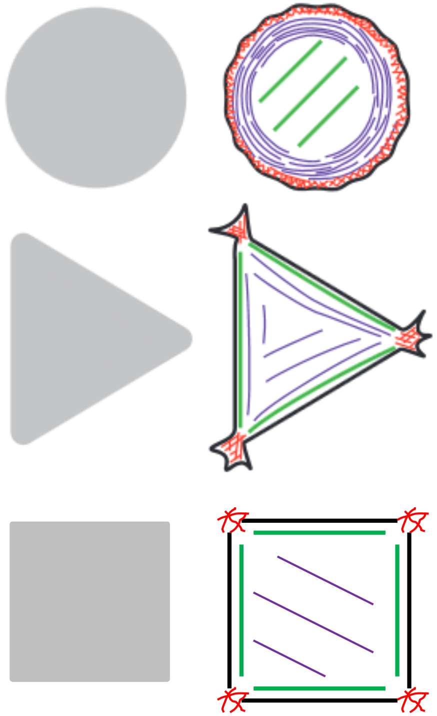
equal area





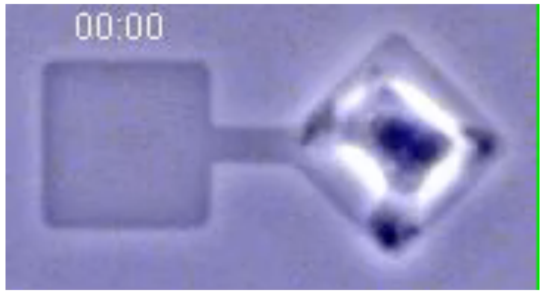
Anisotropic shapes affect transition rates

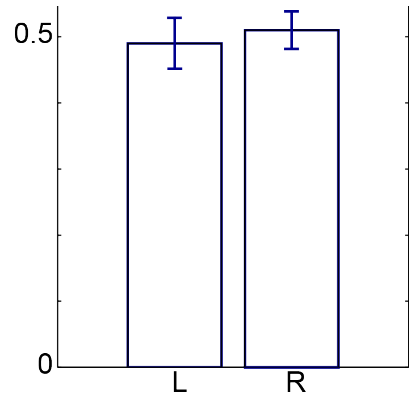
Static cell adhesion:



Théry, M., J Cell Sci 2010 123: 4201-4213

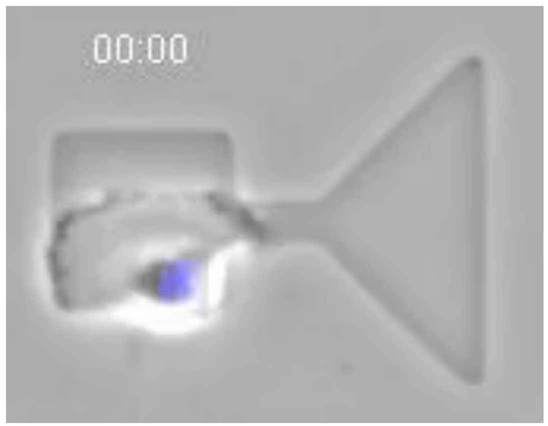
Dynamic system:

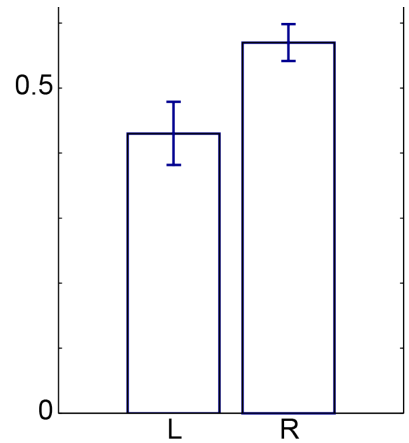




k_{LR}=0.43 h^{-1}

k_{RL}=0.41 h^{-1}

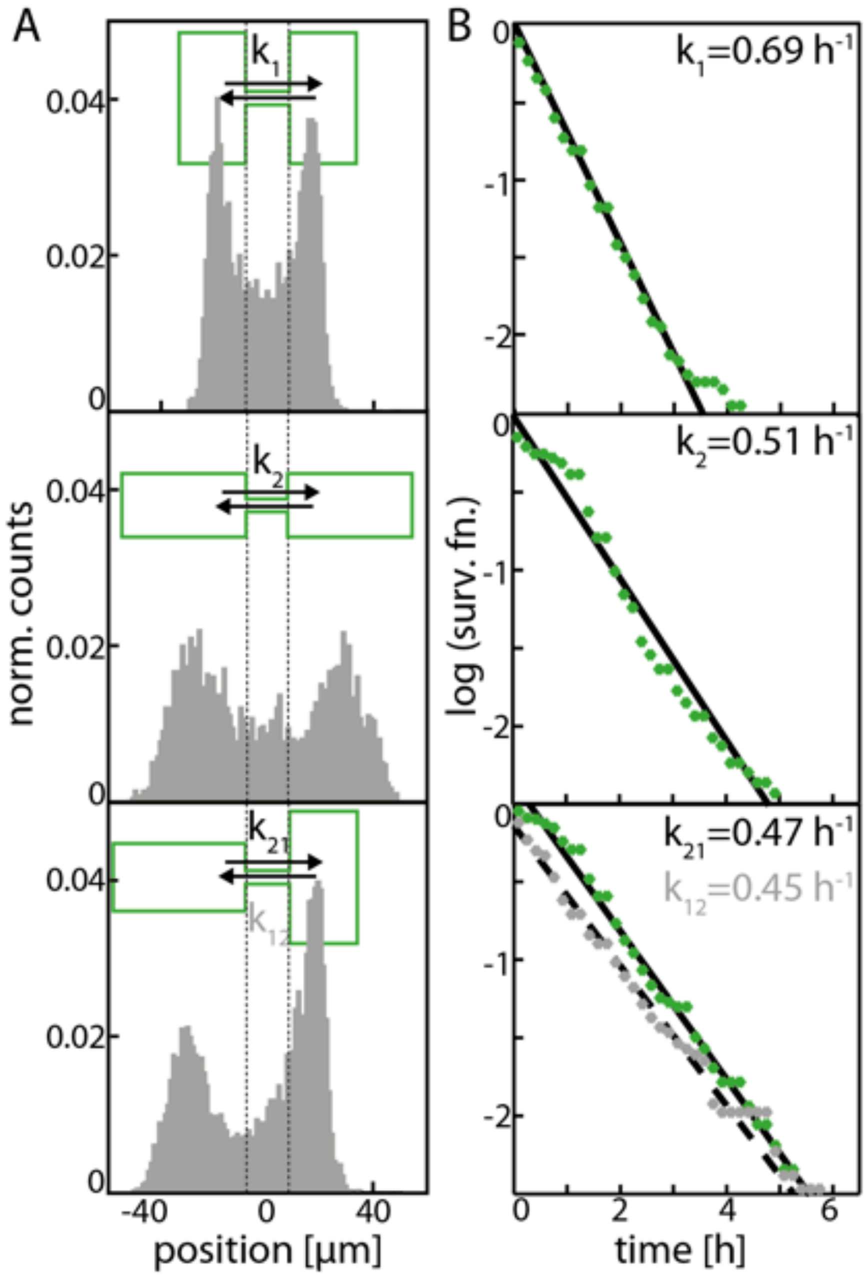


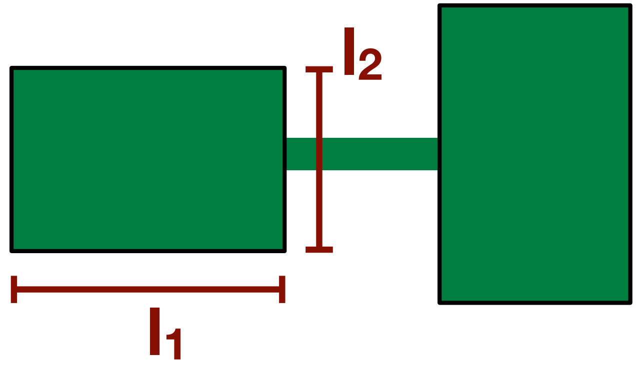


k_{LR}=0.41 h^{-1}

k_{RL}=0.29 h^{-1}

Orientation of cell polarization biases transition rates

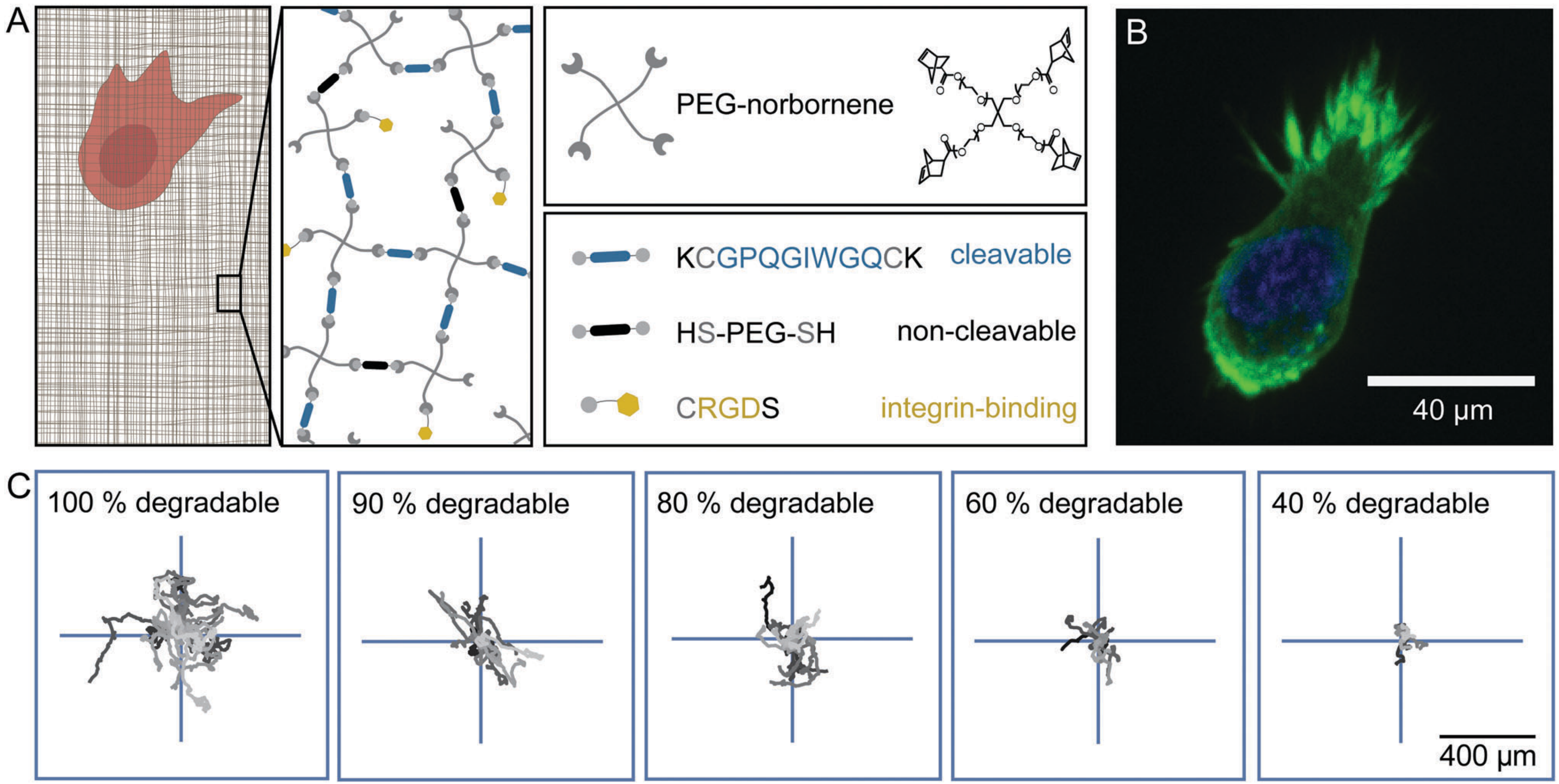




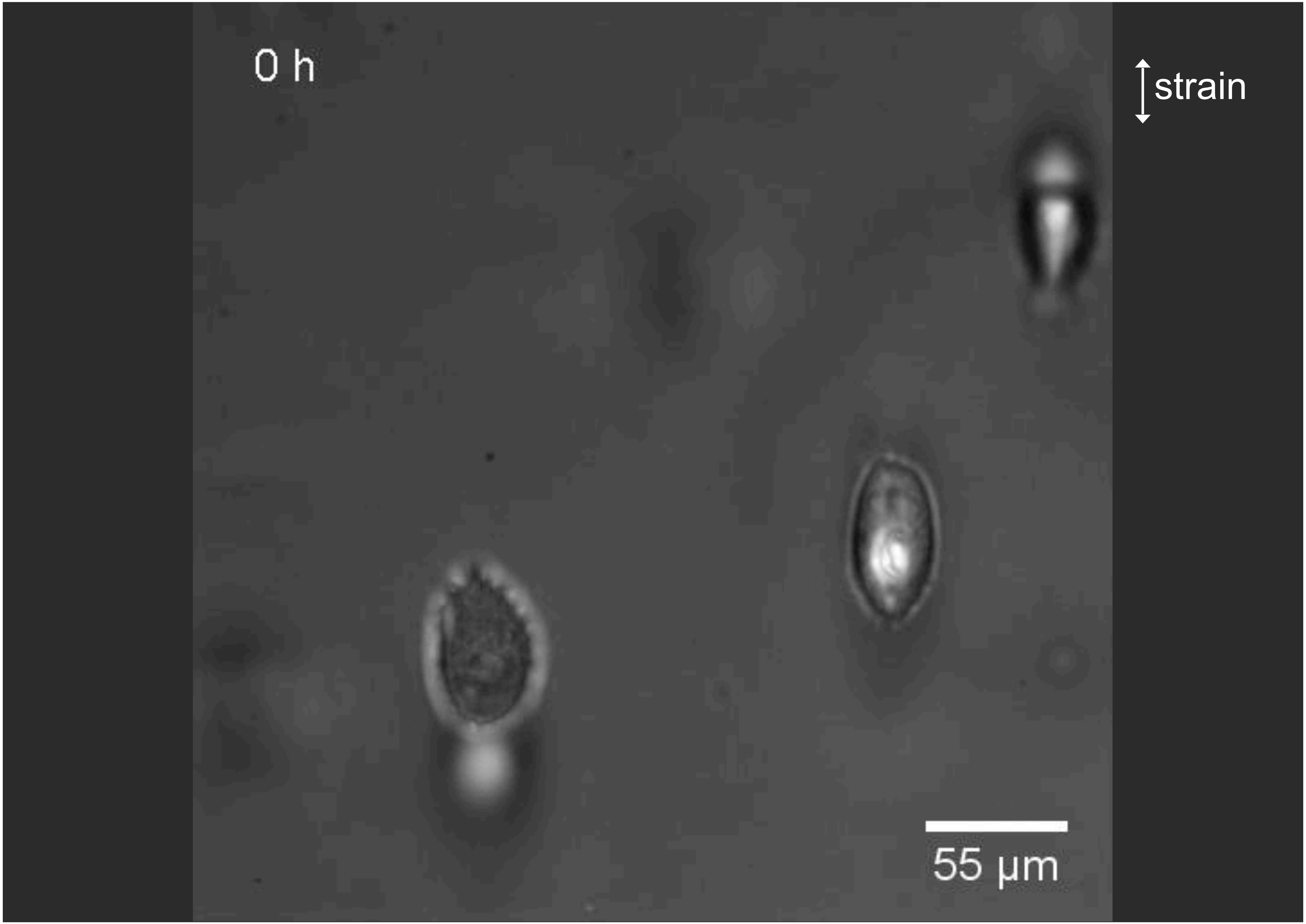
equal area & perimeter
different orientation

μ-pattern infer polarization

Guiding 3D cell migration in deformed synthetic hydrogel microstructures



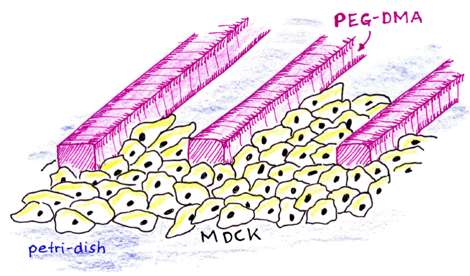
Dietrich, Miriam, Hugo Le Roy, David B Brückner, Hanna Engelke, Roman Zantl, Joachim O Rädler, and Chase P Broedersz. Soft Matter 19 (2018): 1592.


0 h
strain
55 µm

Conclusion

Collective Cell migration in microchannels described by flow and diffusion

Tina Marel, Felix Segerer, Matthias Zorn



Cell polarization produces spontaneous swirls (Cellular Potts Modell)

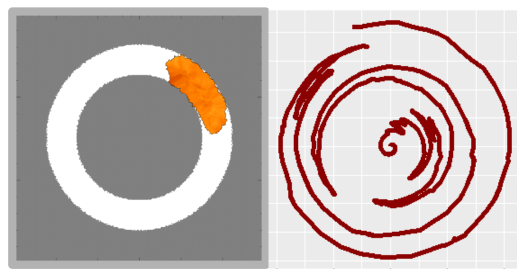
Felix Segerer

Cooperation: Florian Thürhoff, Andriy Goychuk, Erwin Frey

Single Cell migration on micro-lanes allows for migratory fingerprints

Christoph Schreiber

Cooperation: E. Wagner, A. Roidl



Cell migration on two-state micropattern described by inferred force and noise maps

Alexandra Fink, Christoph Schreiber

Sophia Schaffer, Fang Zhou

Cooperation: D. Brückner & C. Broedersz