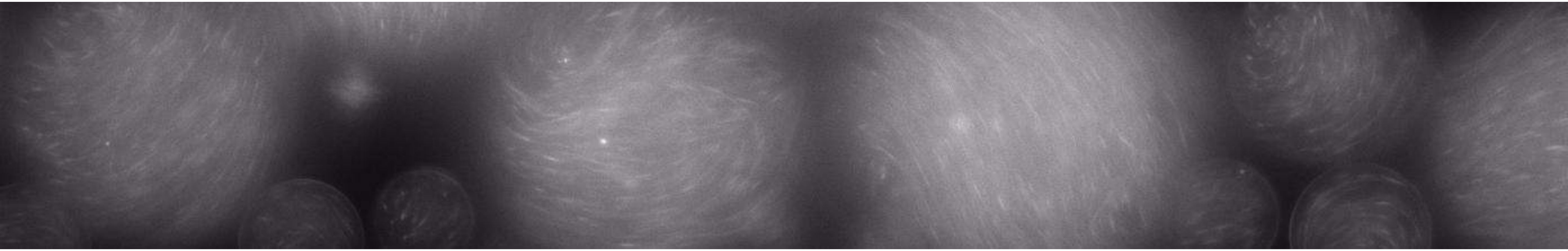
# Active nematic liquid crystals in biological materials: from multicellular tissues to active bio-polymers

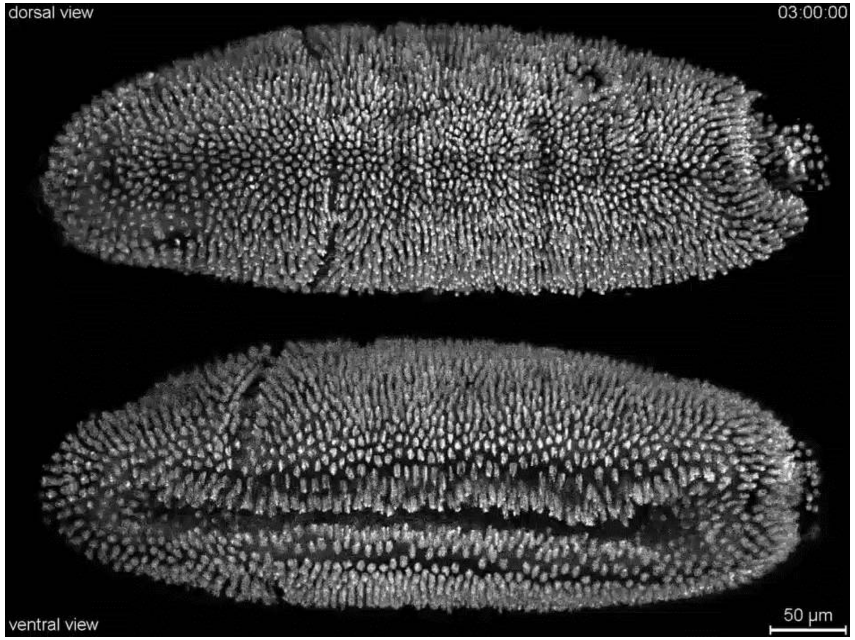
Guillaume Duclos, Brandeis University, Waltham MA

Rencontres Jeunes Physicien.ne.s, College de France, 23 Novembre 2018



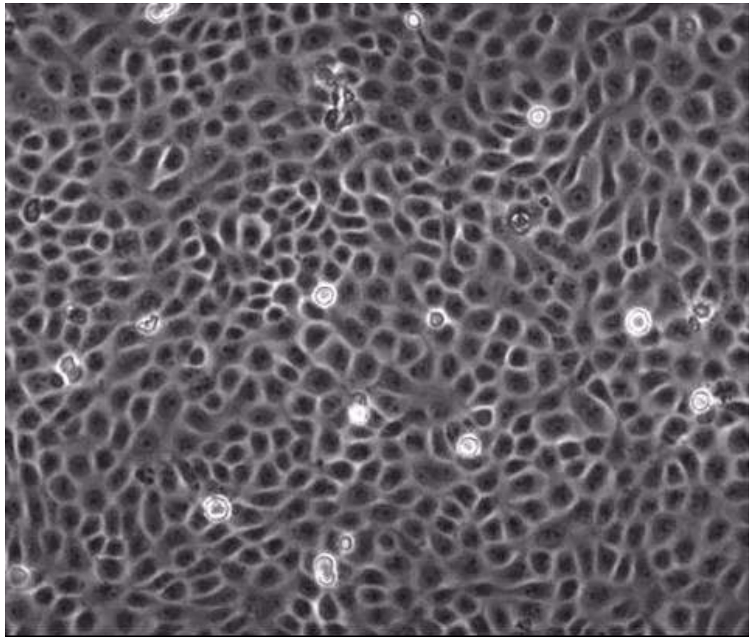
# Emergence of collective behaviors in biological systems

Organism



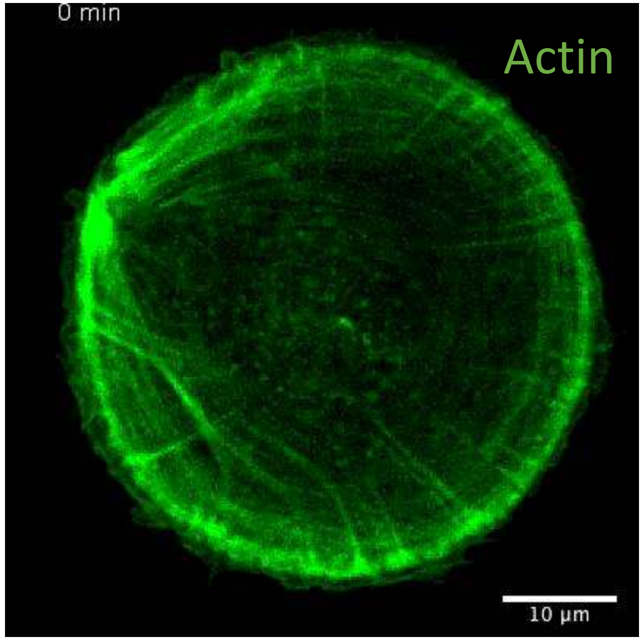

100 µm

Tissue



50 µm

Single cell



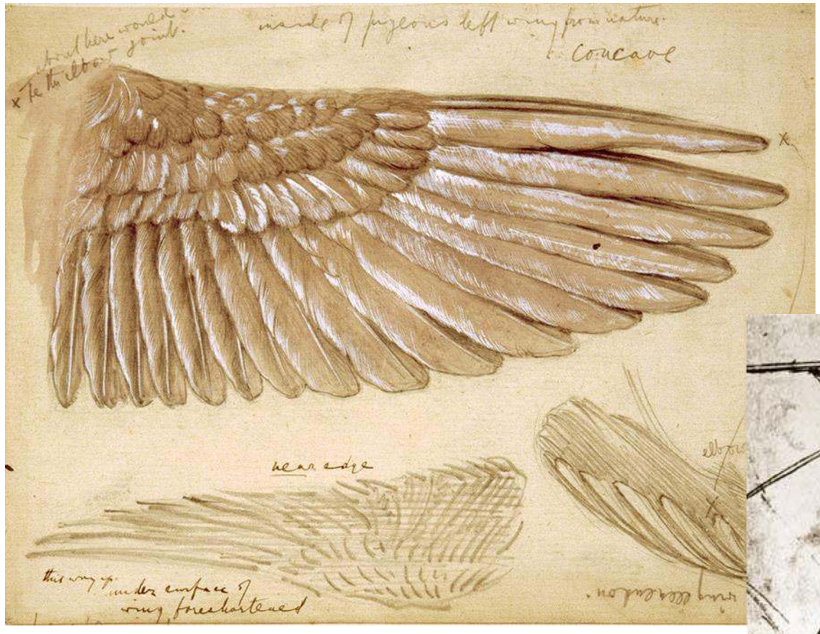

20 µm

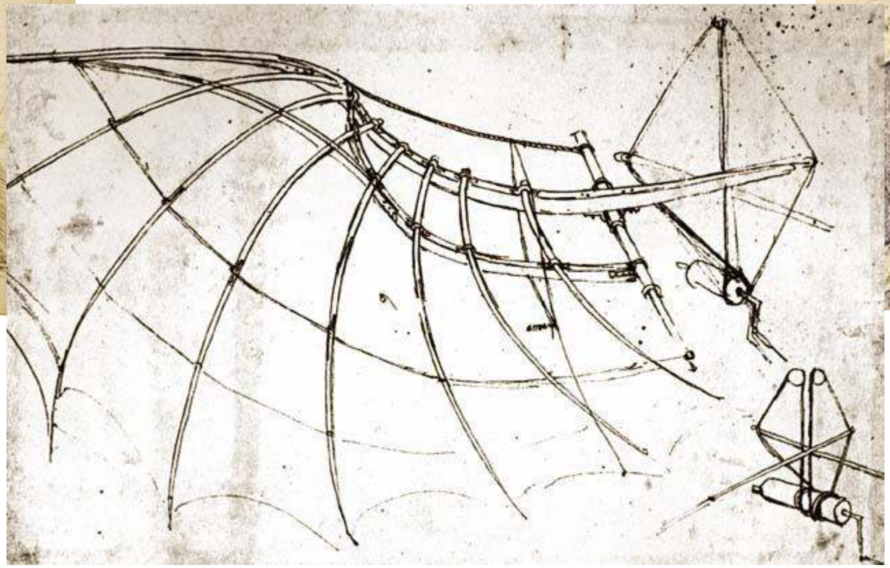
# Emergence of collective behaviors in biological systems

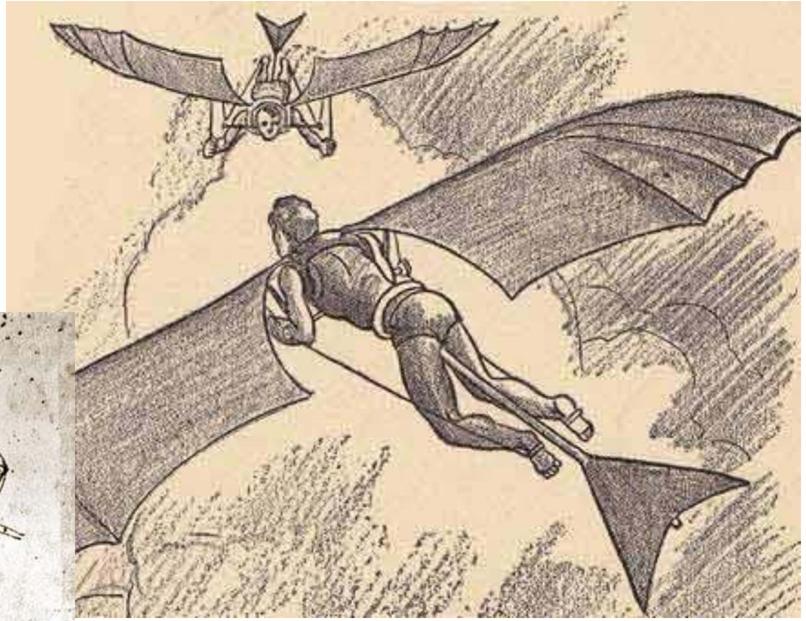
1. Study the fundamental design principles underlying biological functions.

2. Use this knowledge to create new materials that are endowed with properties found only in living organisms.

# Getting inspiration from living systems

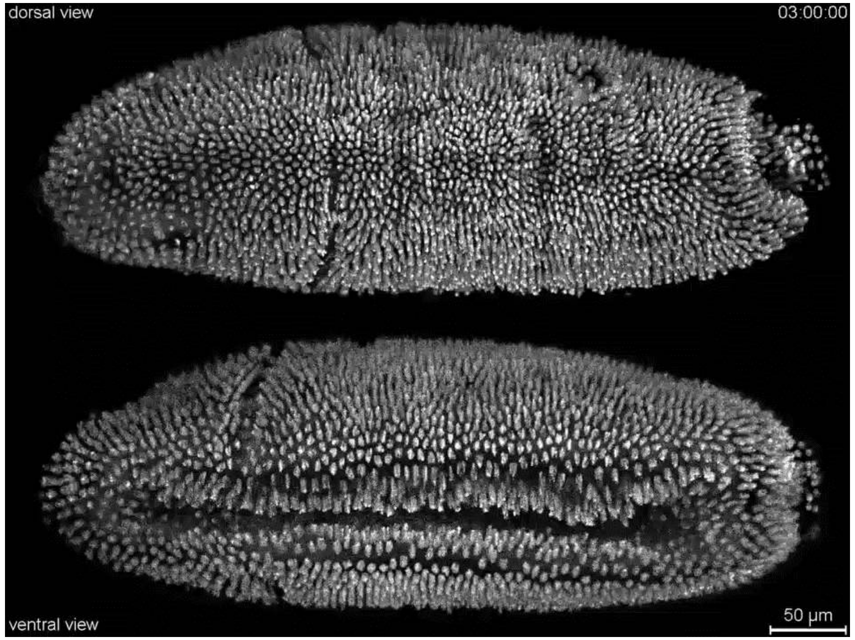






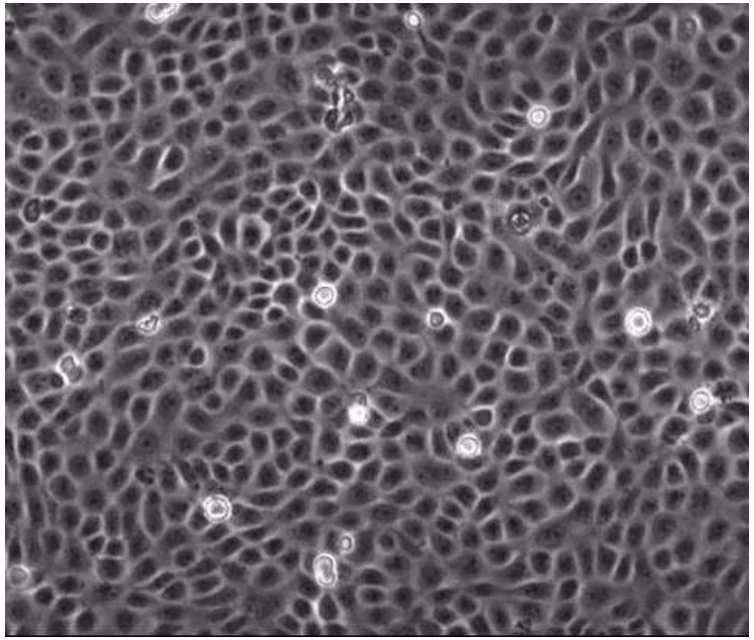
# Emergence of collective behaviors in biological systems

Organism



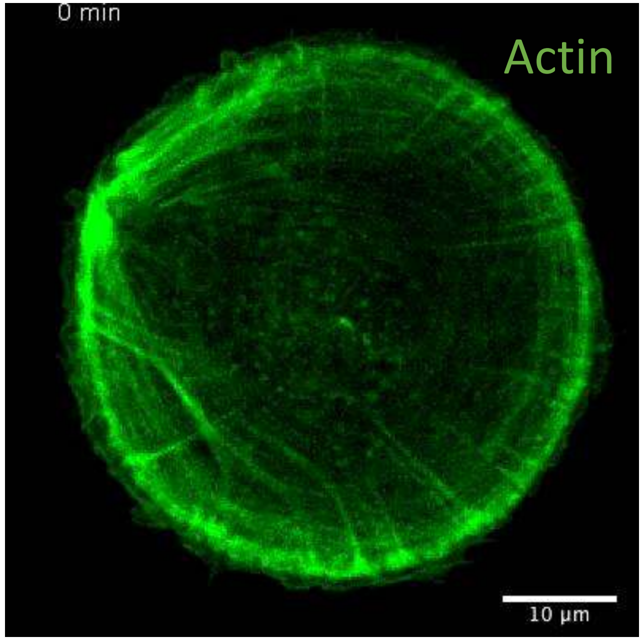

100 µm

Tissue



50 µm

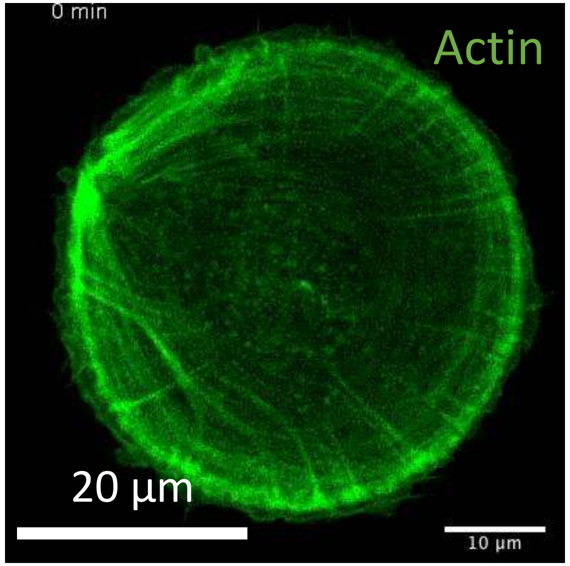
Single cell



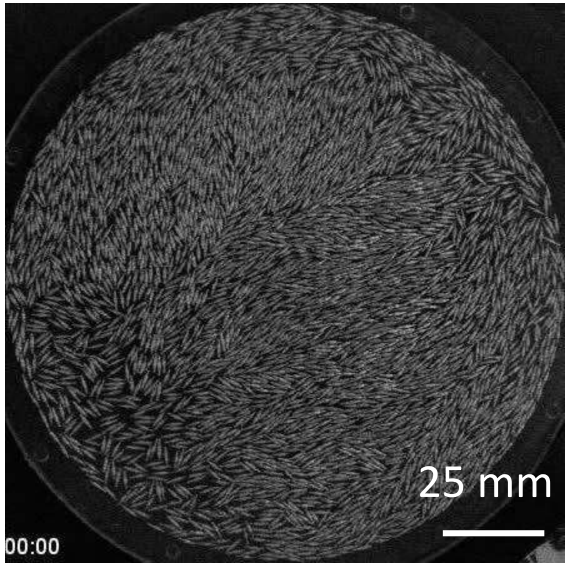

20 µm

# **Active matter:** Biological systems and non-living systems

**Definition :** Out of equilibrium systems composed of particles that convert free energy into mechanical work (self-propelled particles)




Confined **single-cell**
Tee et al, NCB, 2015

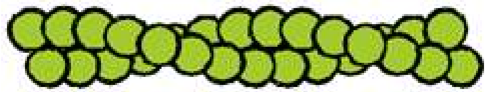



**Vibrated granular rods (rice)**
Narayan *et al*, Science 2006

Nematic order of apolar particles

Apolar active particle

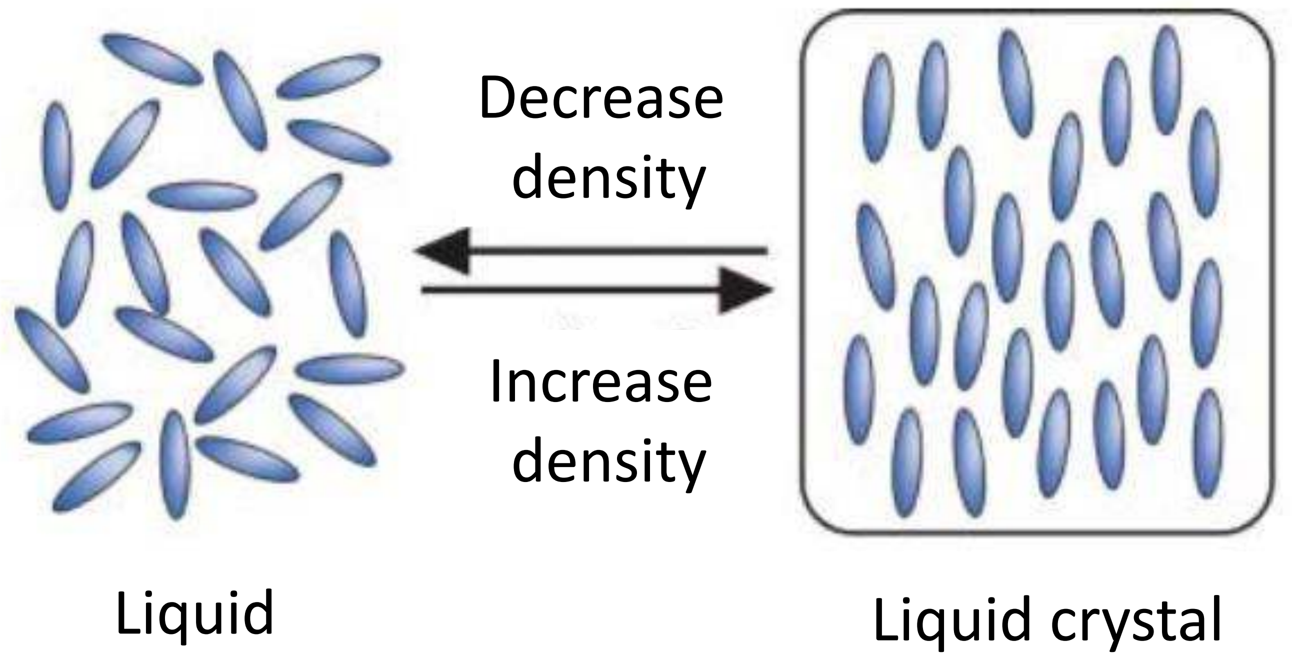
F actin



Grain of rice

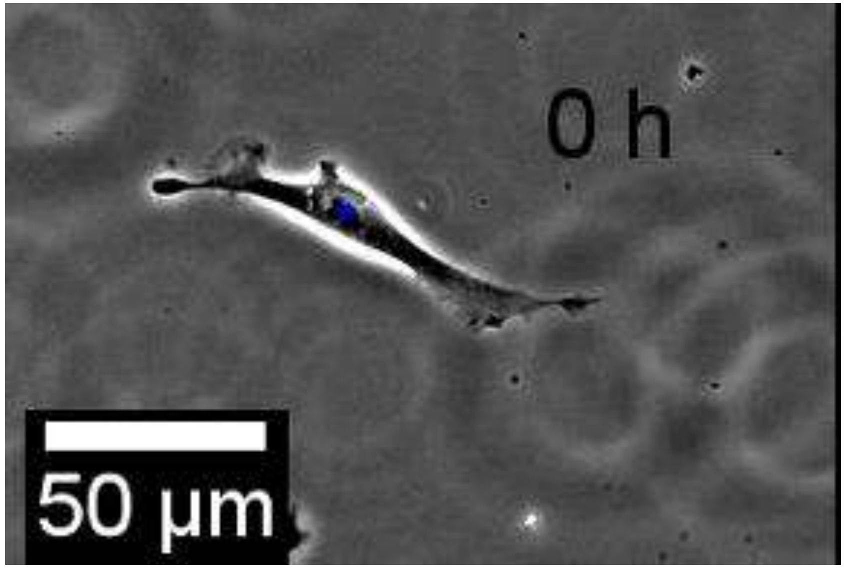
# Increase of density induces an Isotropic/Nematic transition in lyotropic liquid crystals

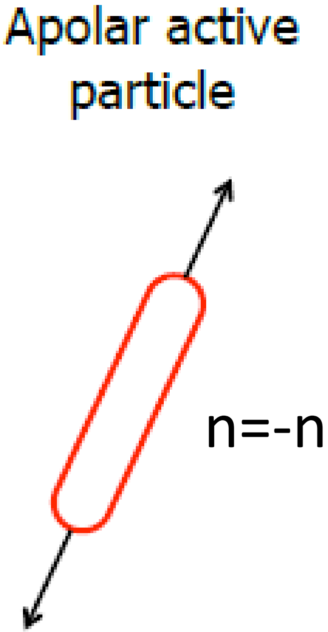
Nematic Liquid crystals have:
- High orientational order as in crystalline solids
- Low positional order as in liquids



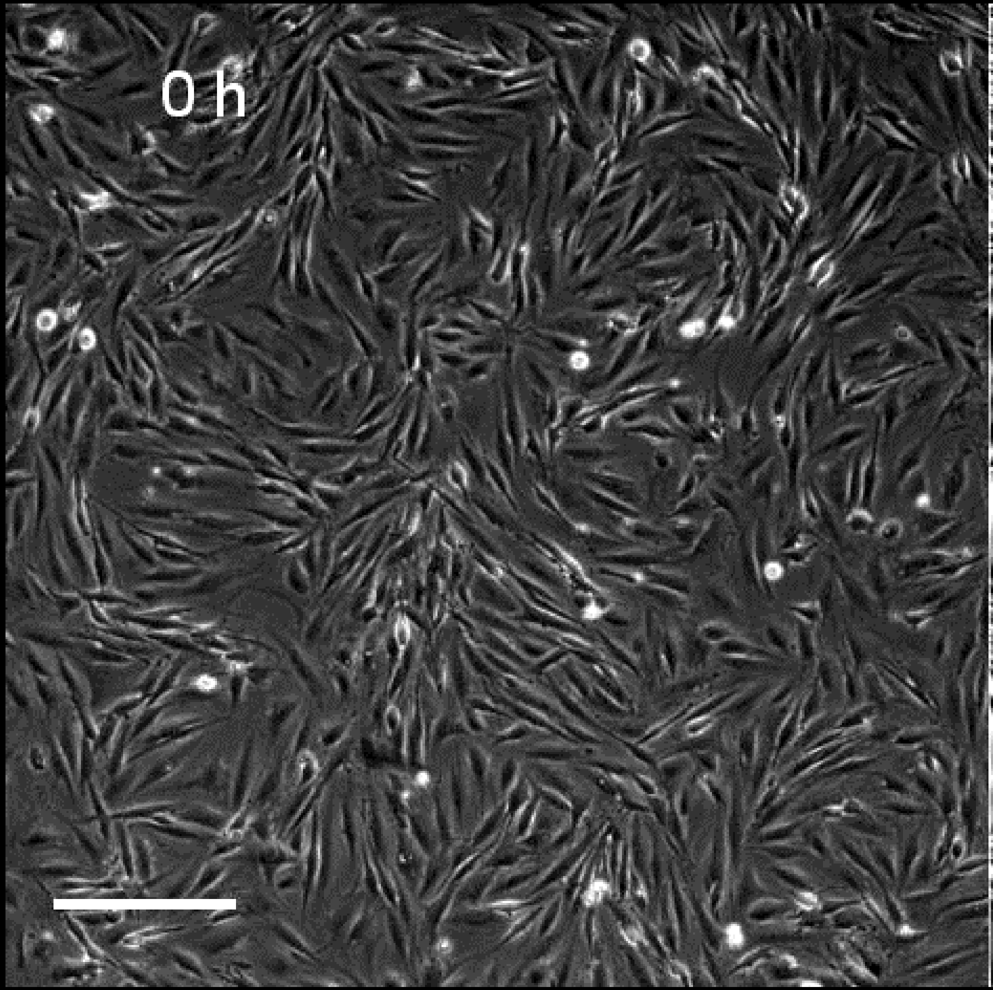
# Elongated cells migrate as an apolar active particle

Elongated apolar migrating cell

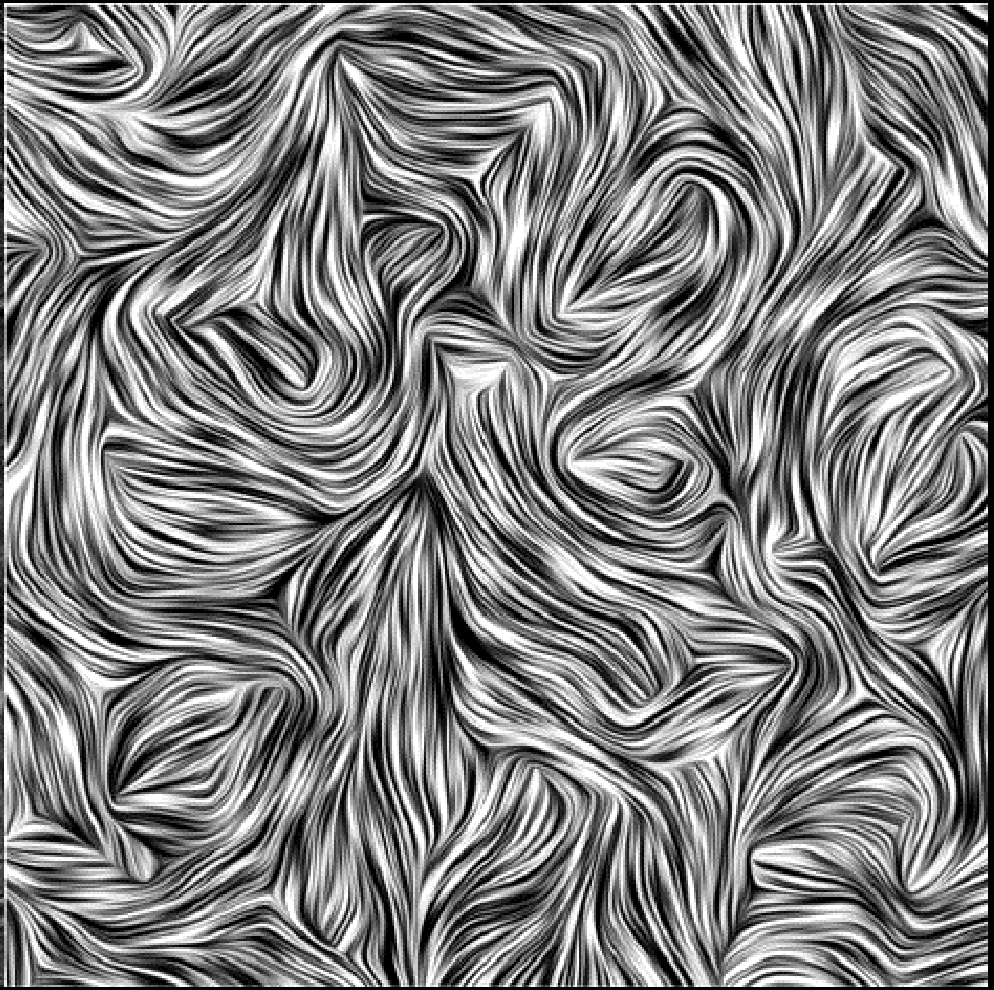


Elongated cells



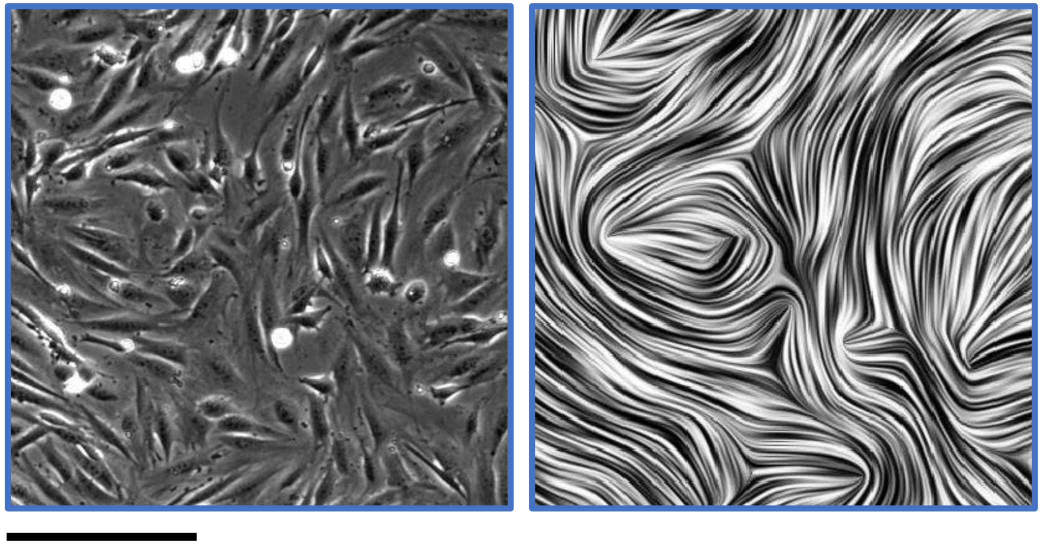

2D Orientation



250 µm

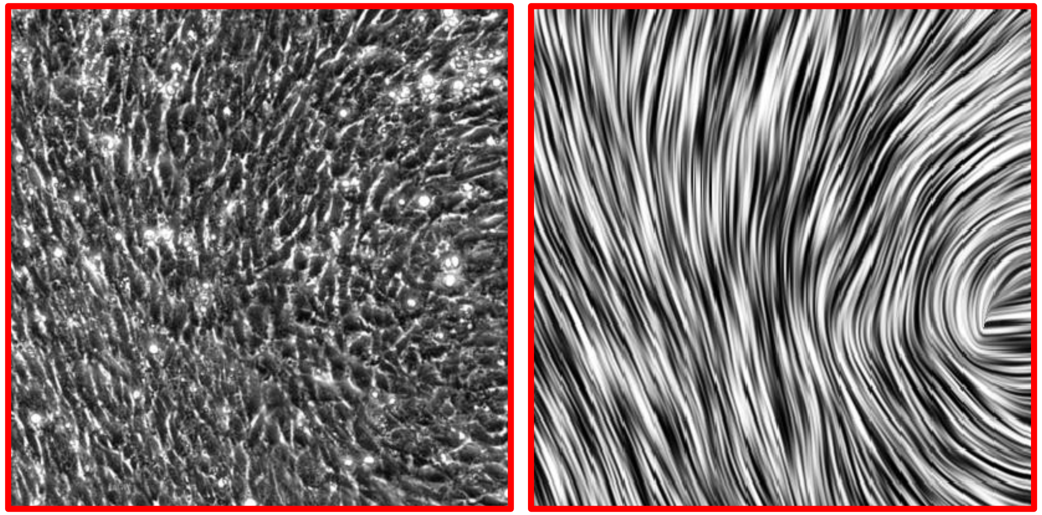
Duclos et al., Soft Matter 2014

# Disorder to order transition controlled by cell density

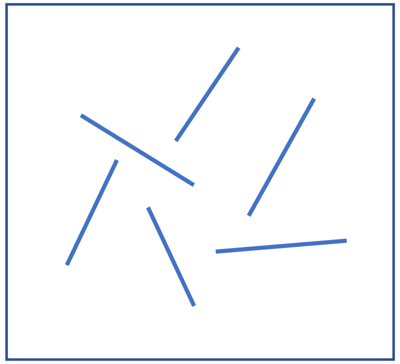


250 µm

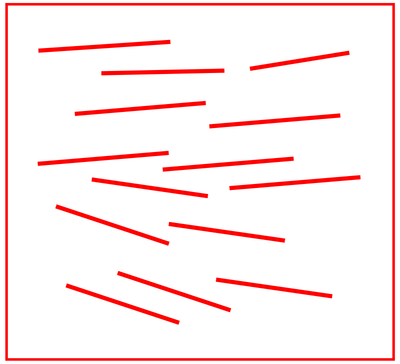
Increasing density



Low density
Low order

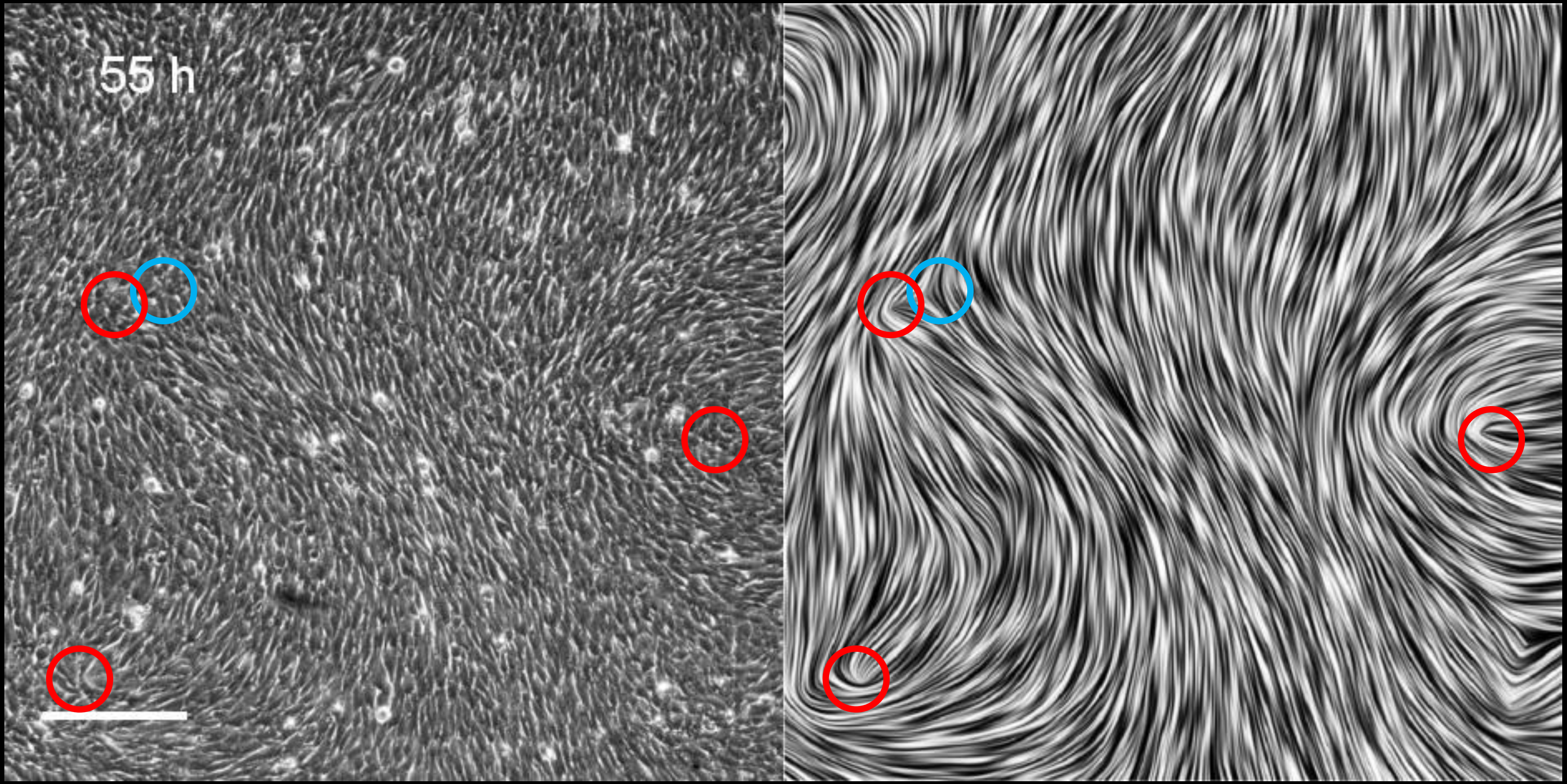


High density
High order



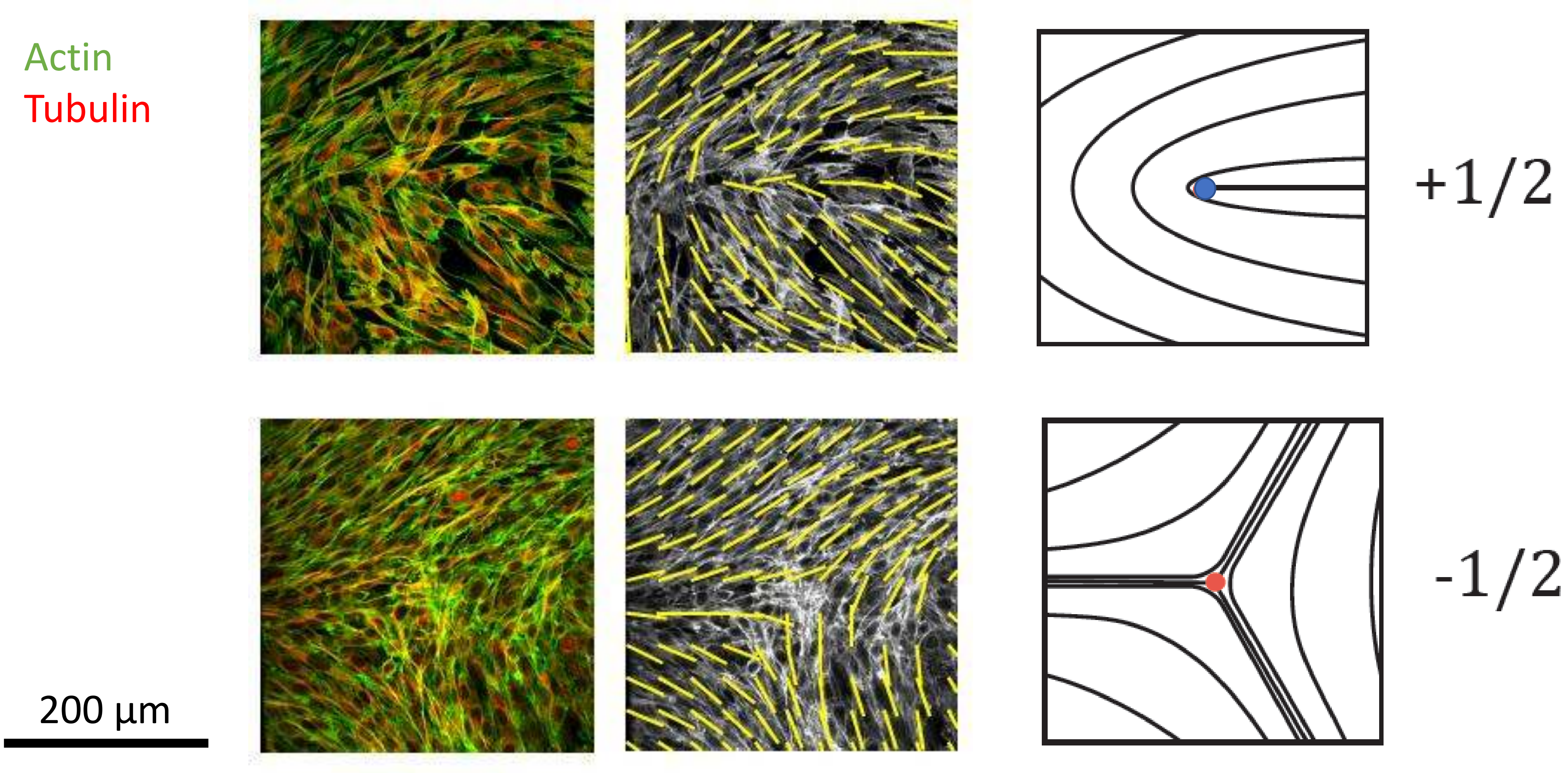
Elongated cells

2D Orientation



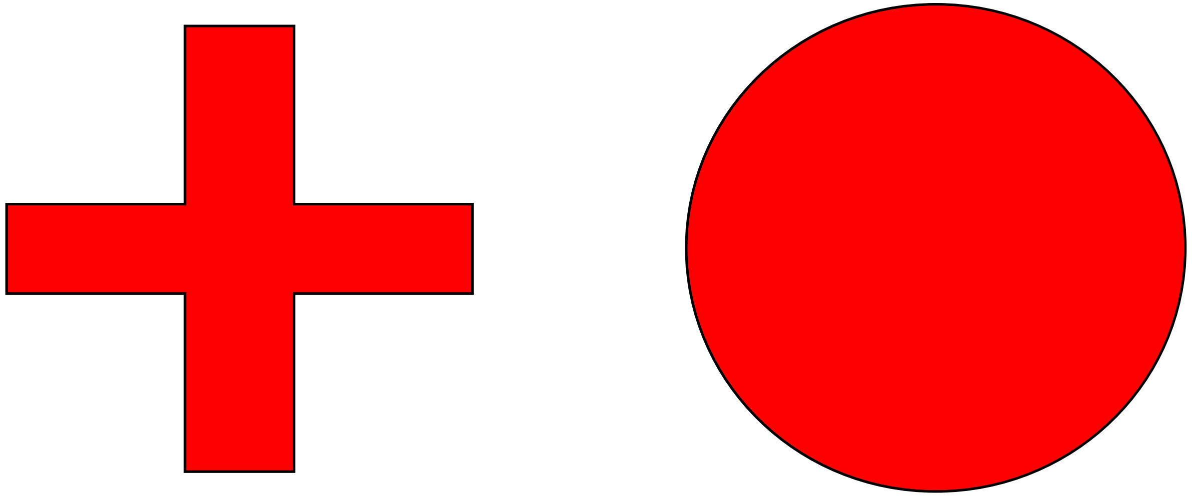

250 µm

# Two types of topological defects in the nematic cellular tissue




Duclos et al., Nat Phys 2017

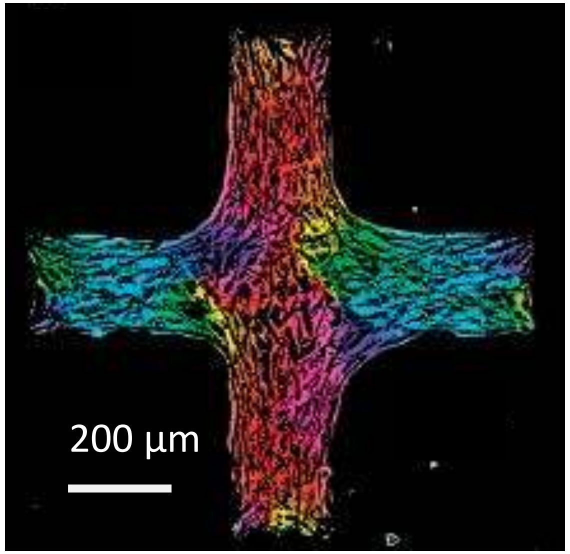
# Topological confinement of active cellular nematics



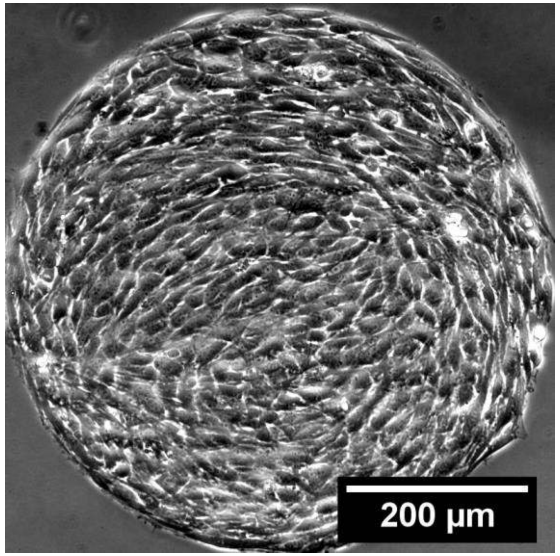
$S_{tot} = +1$

$S_{tot} = 0$

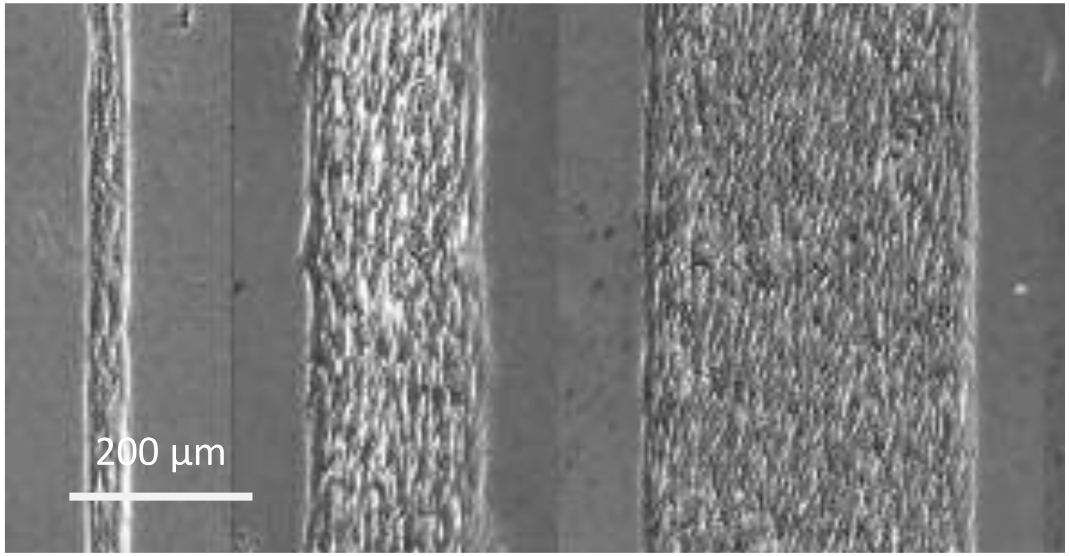
# Topological confinement of active cellular nematics




Duclos et al., Soft Matter 2014

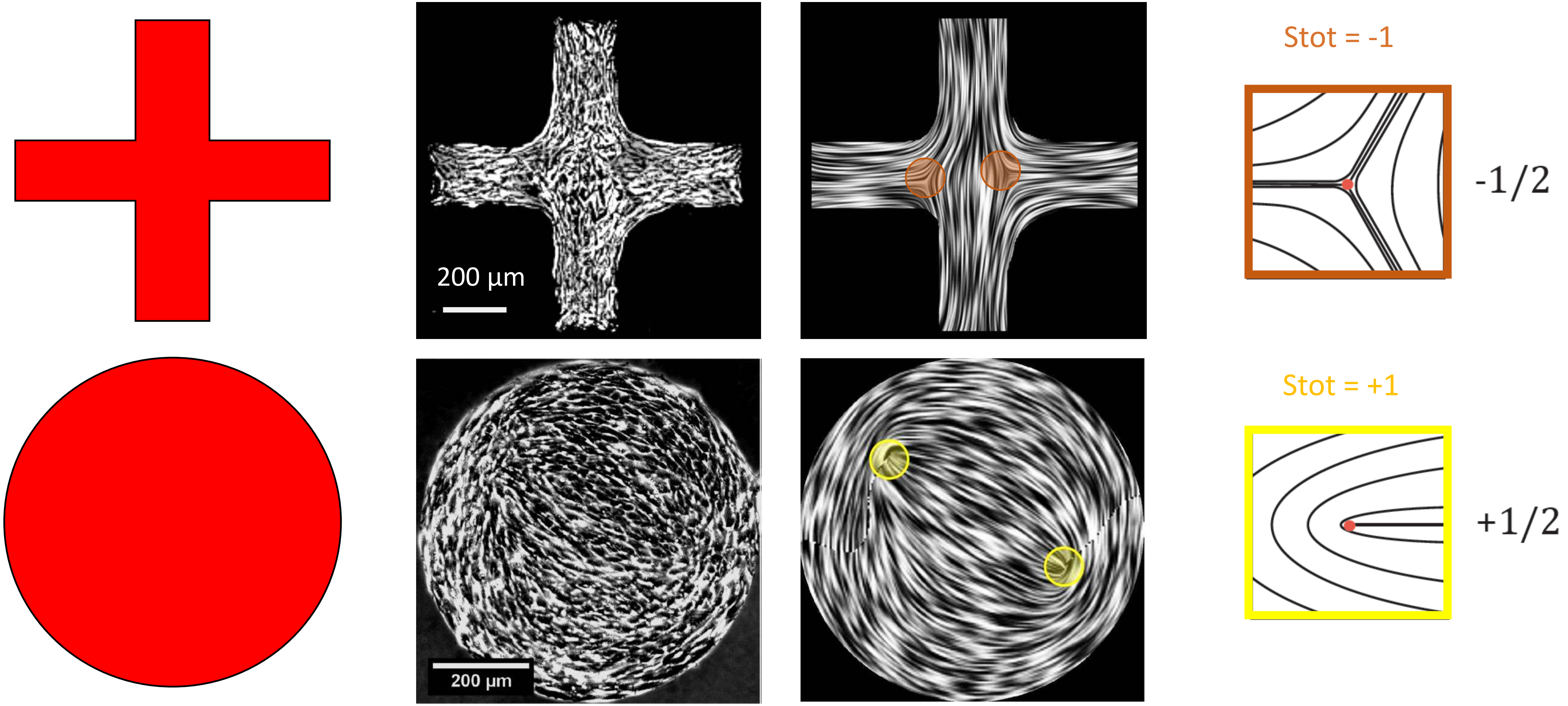



Duclos et al., Nat Phys 2017

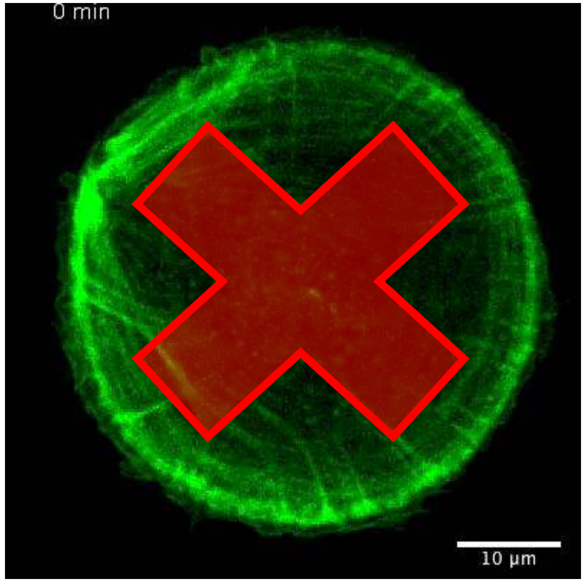



Duclos et al., Nat Phys 2018

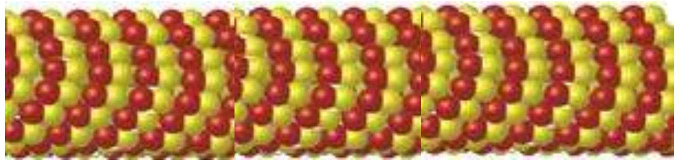
# Topological confinement of active cellular nematics



# Postdoc: Biomimetique active gel

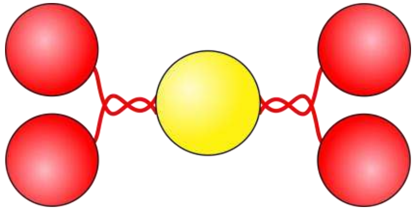


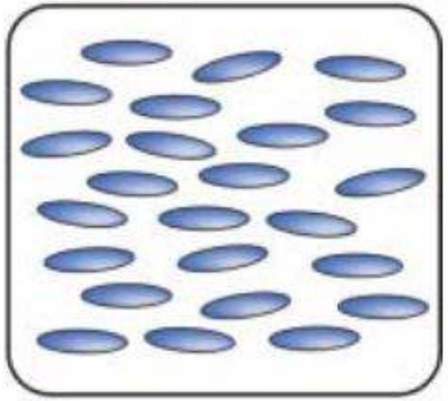

Microtubules



+

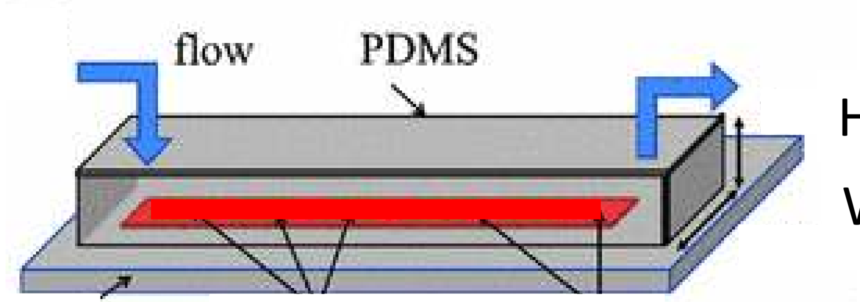
Molecular motors





Liquid crystal

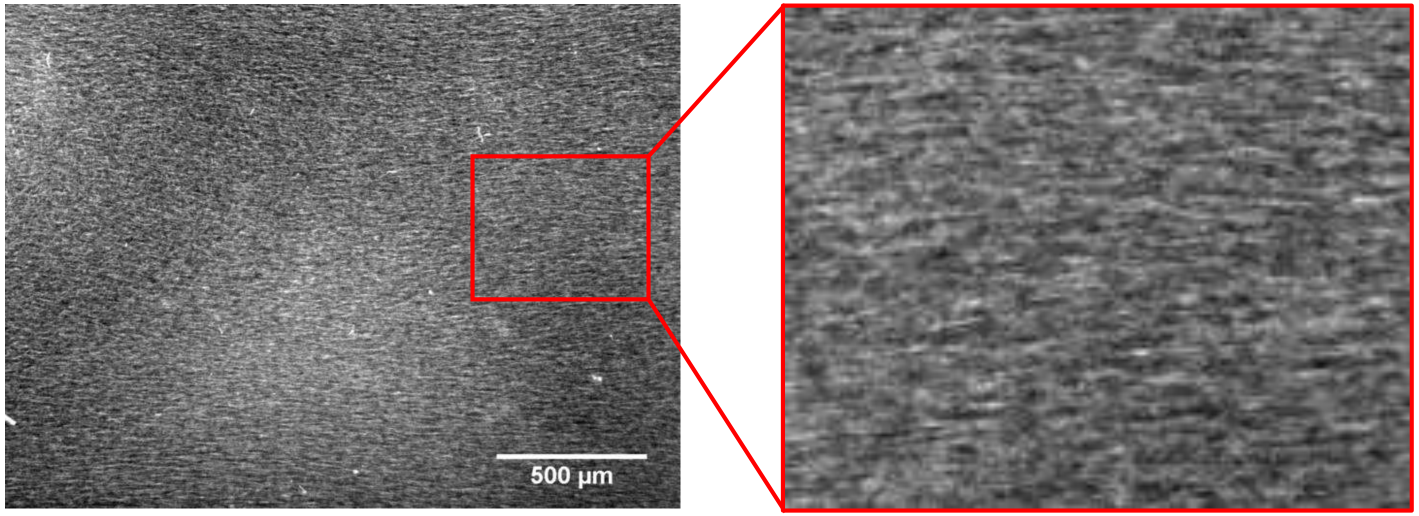
# Shear flows align the microtubules in a well defined initial state



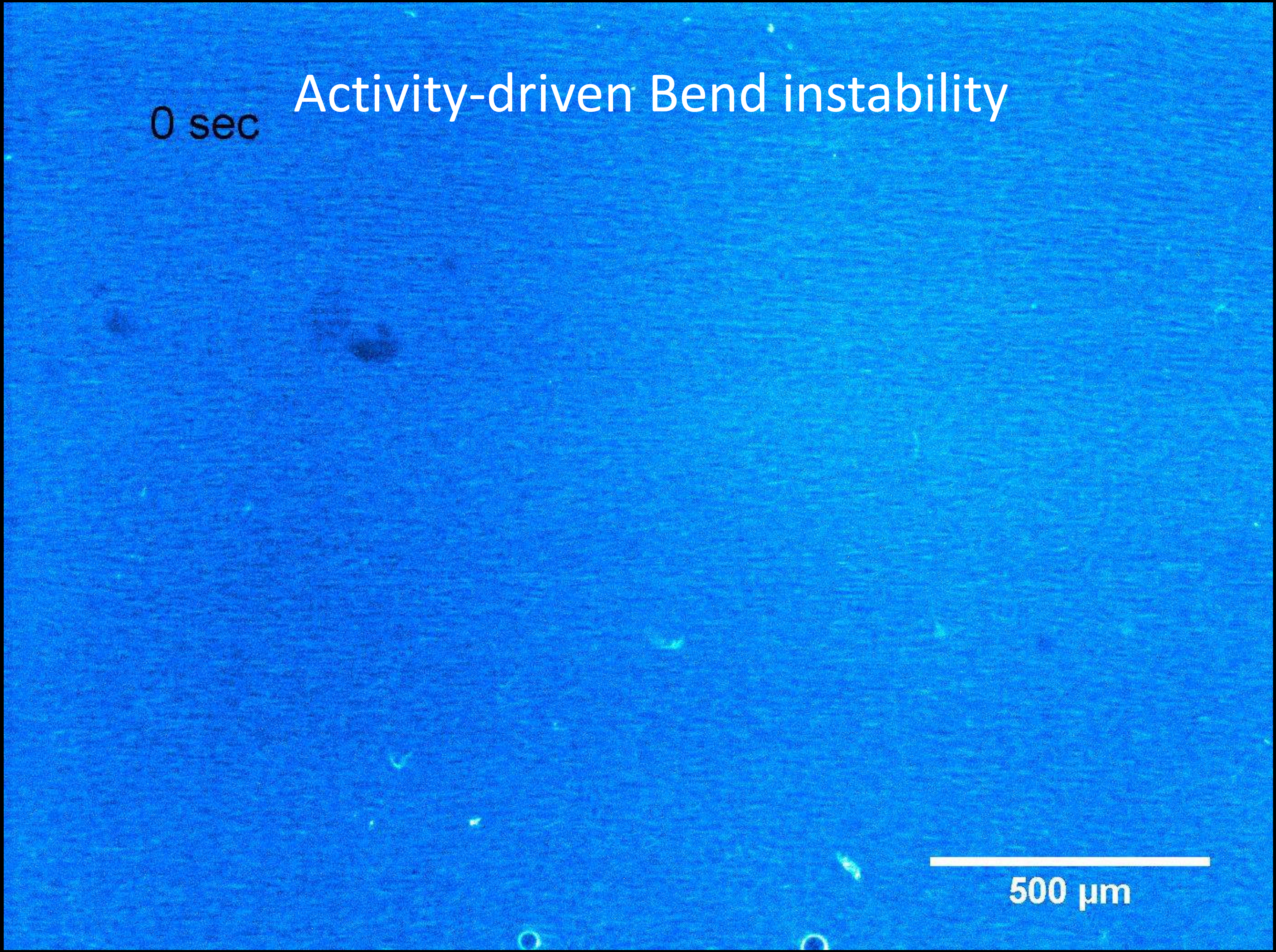

Height: 100 µm

Width: 3 mm

glass active material




Flow aligned microtubules


Activity-driven Bend instability
0 sec
500 µm

# Activity-driven bend instability

The wavelength of the instability $\lambda$ depends on:

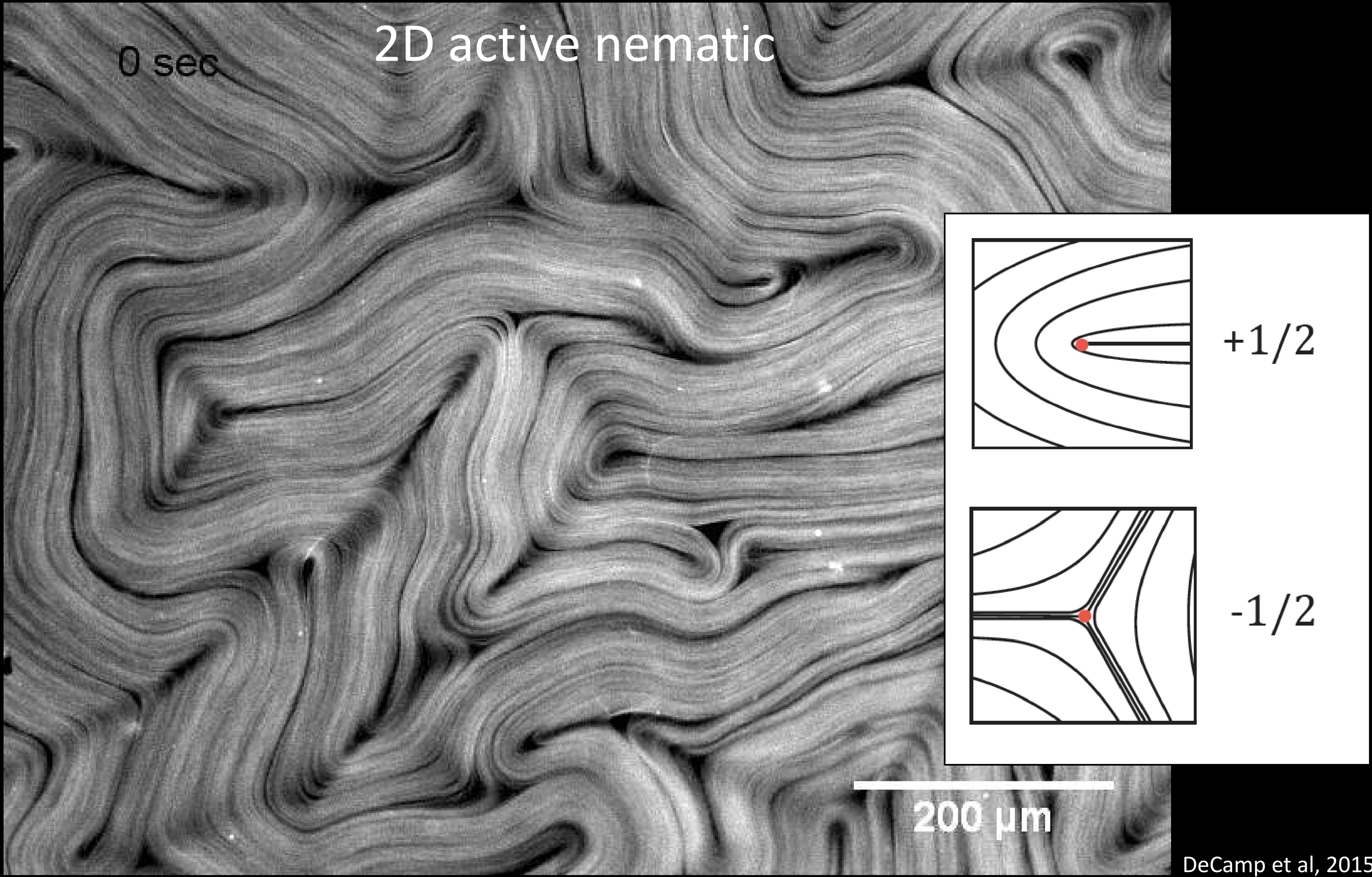
- Nematic elasticity **K**
- Activity **α**

$$\lambda \propto \sqrt{\frac{K}{\alpha}}$$

Nematic elasticity >> Activity

Activity >> Nematic elasticity

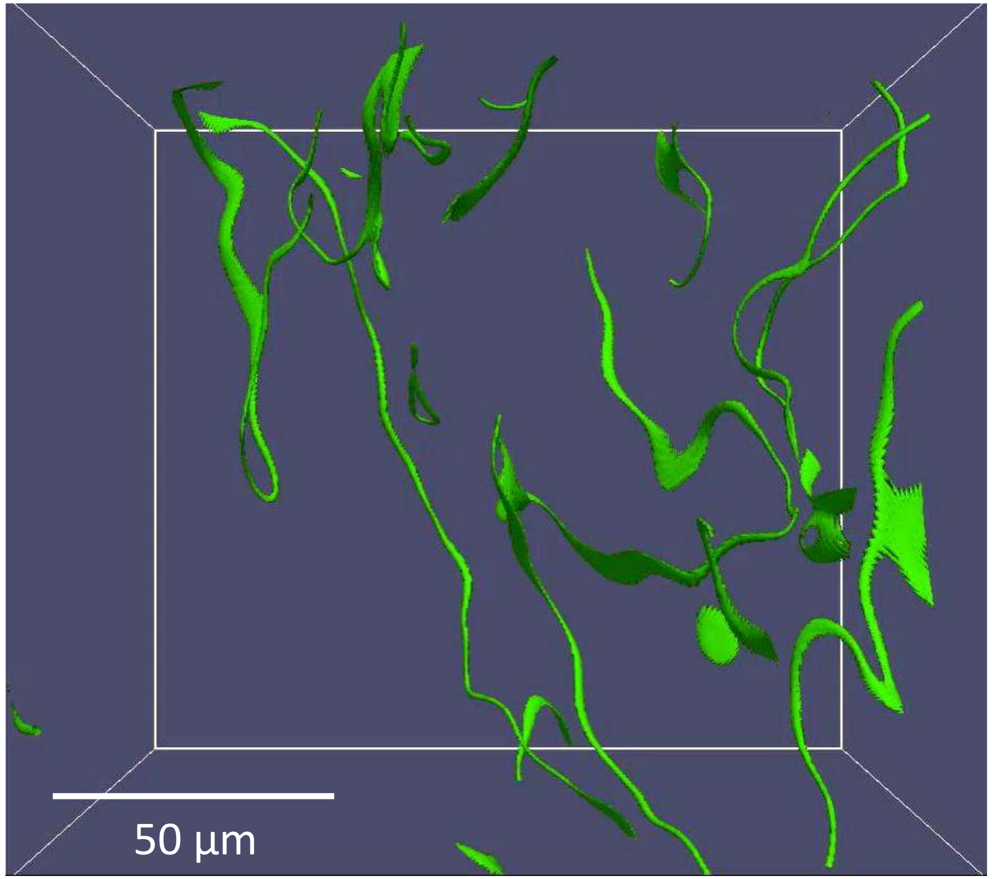
# 2D active nematic



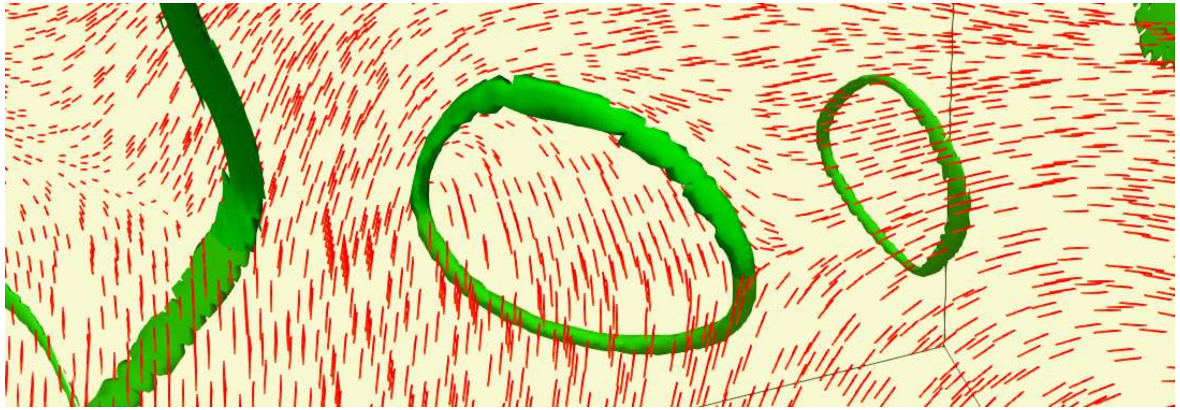

DeCamp et al, 2015

# Topological defects form loops in 3D

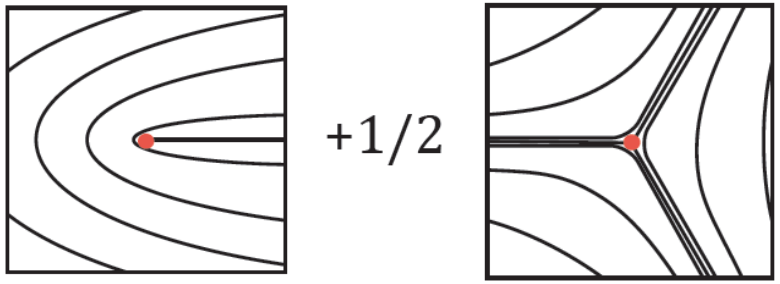
Defect lines




Defect line Orientation

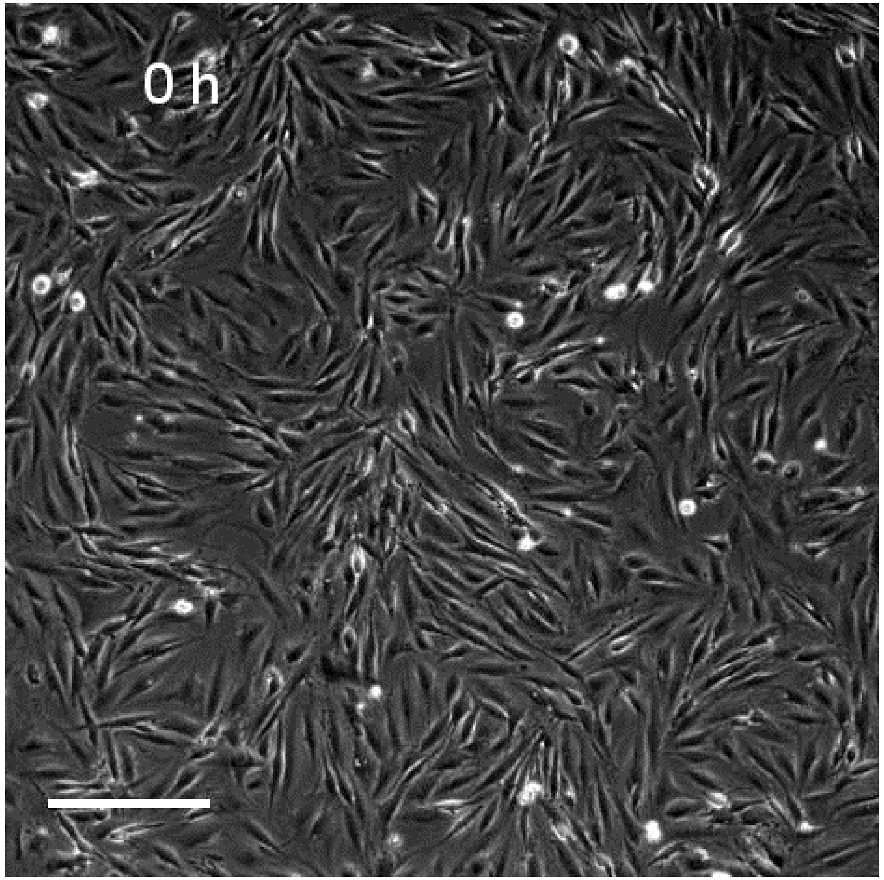


In 2D :

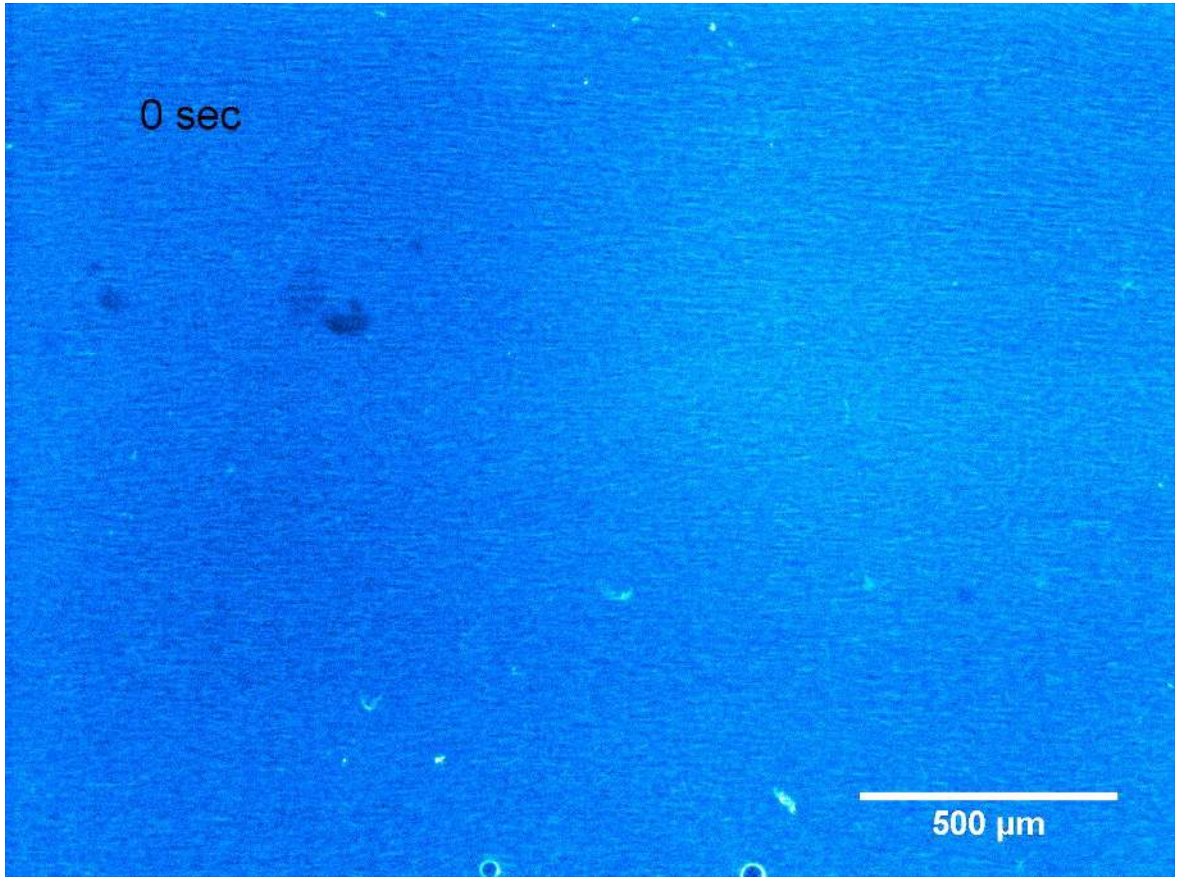


# **Conclusion**: Active nematics in biological materials

Living cells




Active polymers



# Thank you

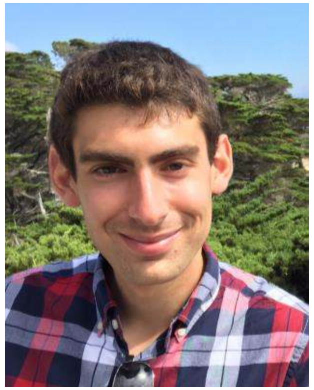

Active cellular nematic:
Pascal Silberzan @ *Curie Institute, CNRS UPMC* Paris
Jean-Francois Joanny, Jacques Prost
Hannah Yevick, Simon Garcia, Victor Yaschunsky, Carles Blanch-Mercader, Sarah Moitrier, Alex Bugion, Isabelle Bonnet

Dogic Lab :
Zvonimir Dogic, Pooja Chandrakar, John Berzeny, Linea Metcalf, Bez Laderman, Joia Miller, Joanna Robaszewski

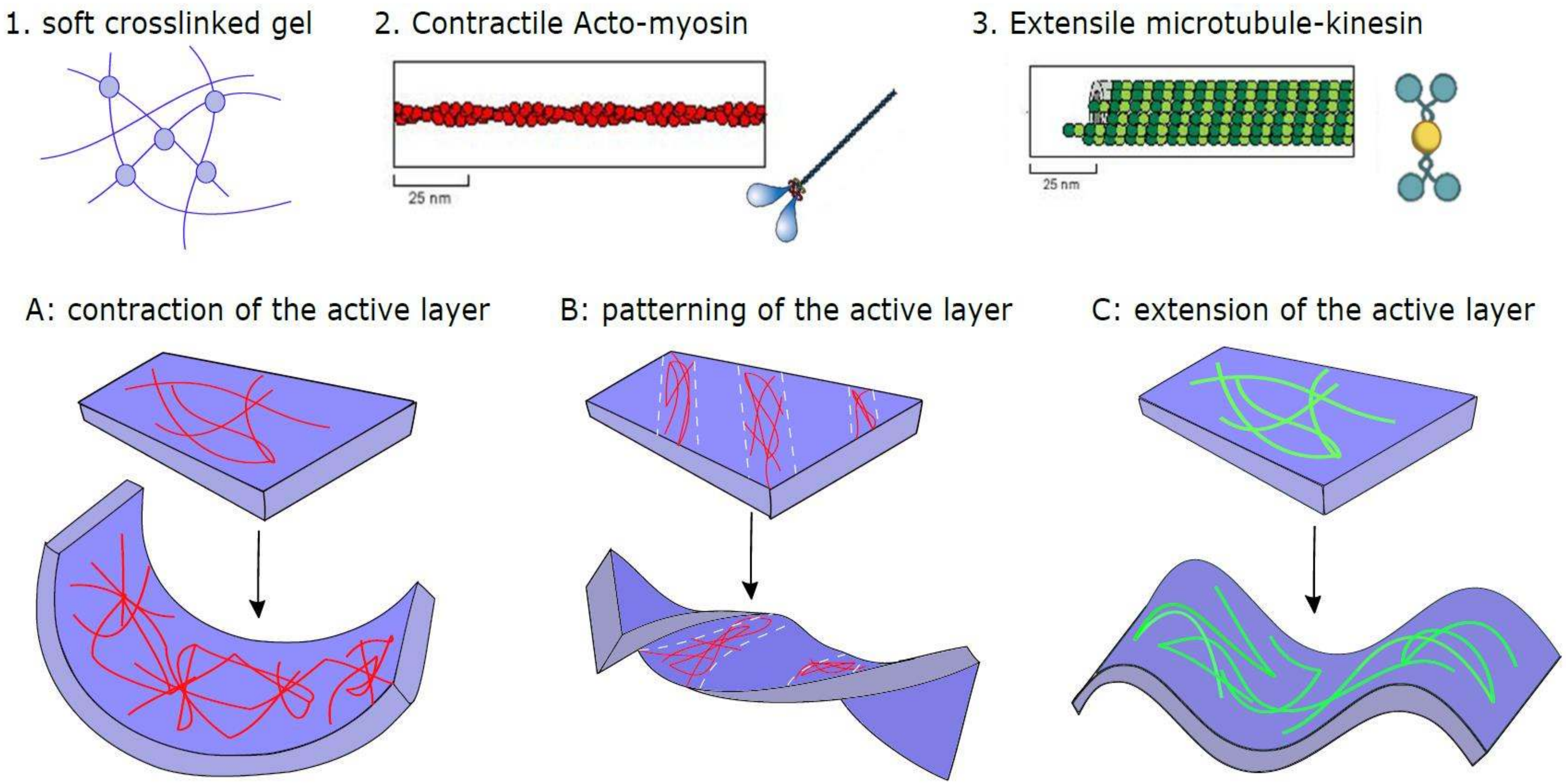
Theory: Arvind Baskaran, Zack Sustiel, Minu Varghese, Aparna Baskaran, Mike Hagan

Dan Beller, Bob Pelcovits, Thomas Power

Sebastian Streichan, UCSB

# **Perspective:** Use activity to control the morphogenesis of biomimetic elastomer



# Thank you

Dogic Lab :

Zvonimir Dogic
Pooja Chandrakar
John Berzeny
Linea Metcalf
Bez Laderman
Masha Siavashpouri
Joia Miller
Andrew Balchunas
Joanna Robaszewski

Marc Ridila (former)
Achini Orpathalage (former)
Mohamed Gharbi (former)
Kun-Ta Wu (former)
Steve DeCamp (former)
Feodor Hiliski (former)

Sebastian Streichan, UCSB

Theory: Arvind Baskaran, Zack Sustiel, Minu Varghese, Aparna Baskaran, Mike Hagan
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*Brown University, RI*

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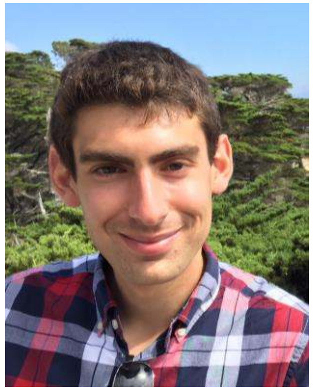
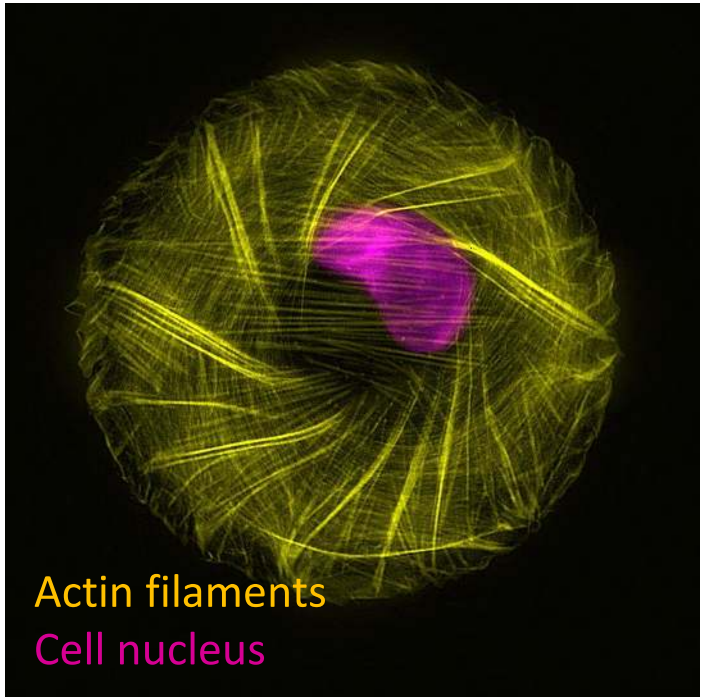


# Cytoskeleton filaments: bio-polymers driven out of equilibrium by molecular motors

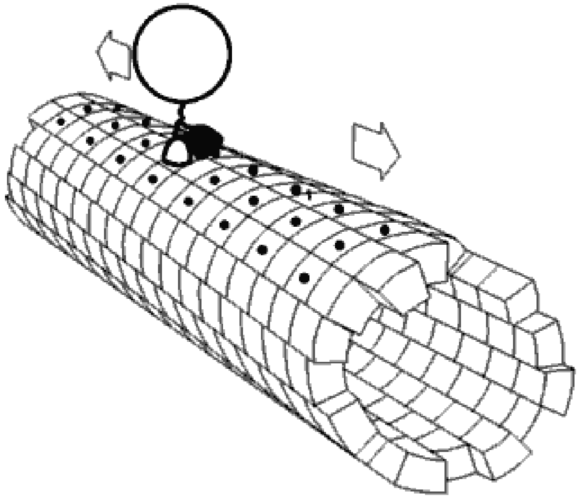
## Polymer network



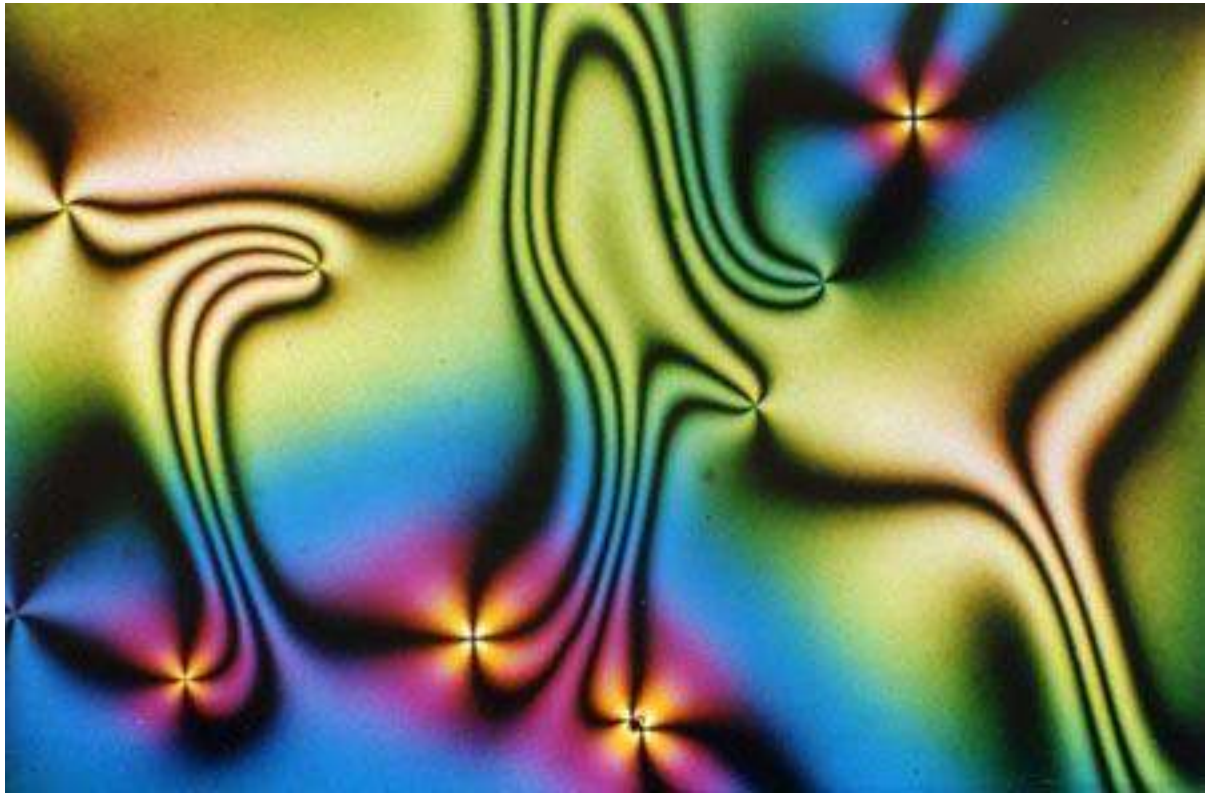

Bershadsky lab, National University of Singapore

## Molecular motor

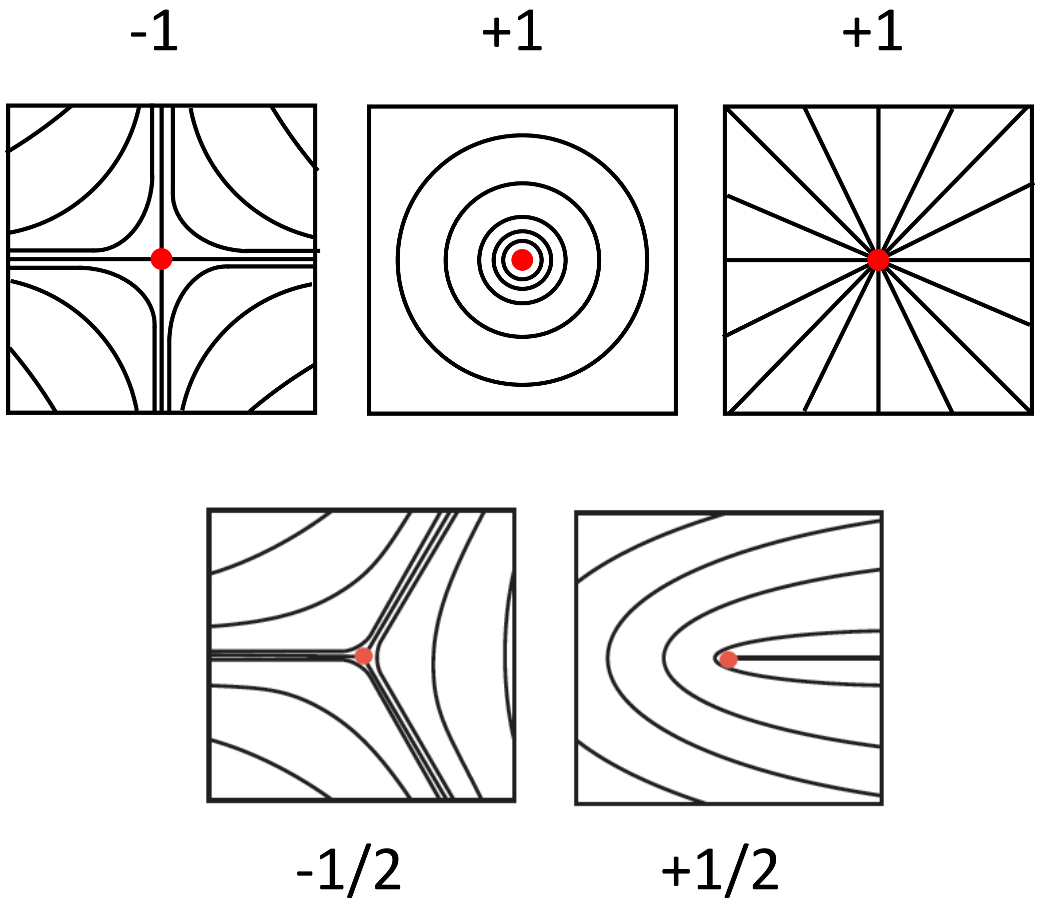
Kinesin-1 motors



# Topological defects in nematic Liquid crystals

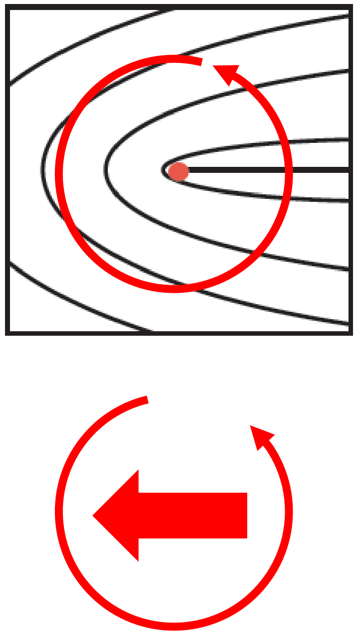


Oleg D. Lavrentovich, Liquid Crystal Institute, Kent State University

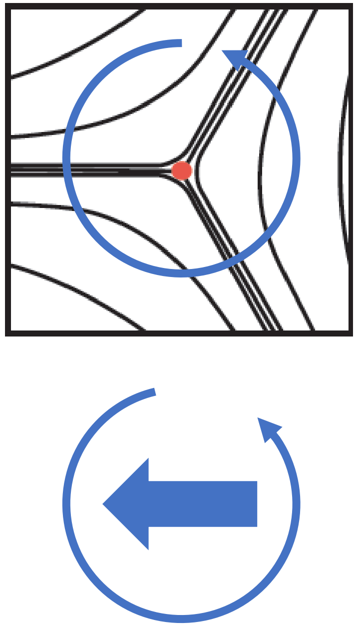


# Topological defects in nematic Liquid crystals

Topological charge $Q = \frac{1}{2\pi} \oint \frac{d\theta}{ds} ds$



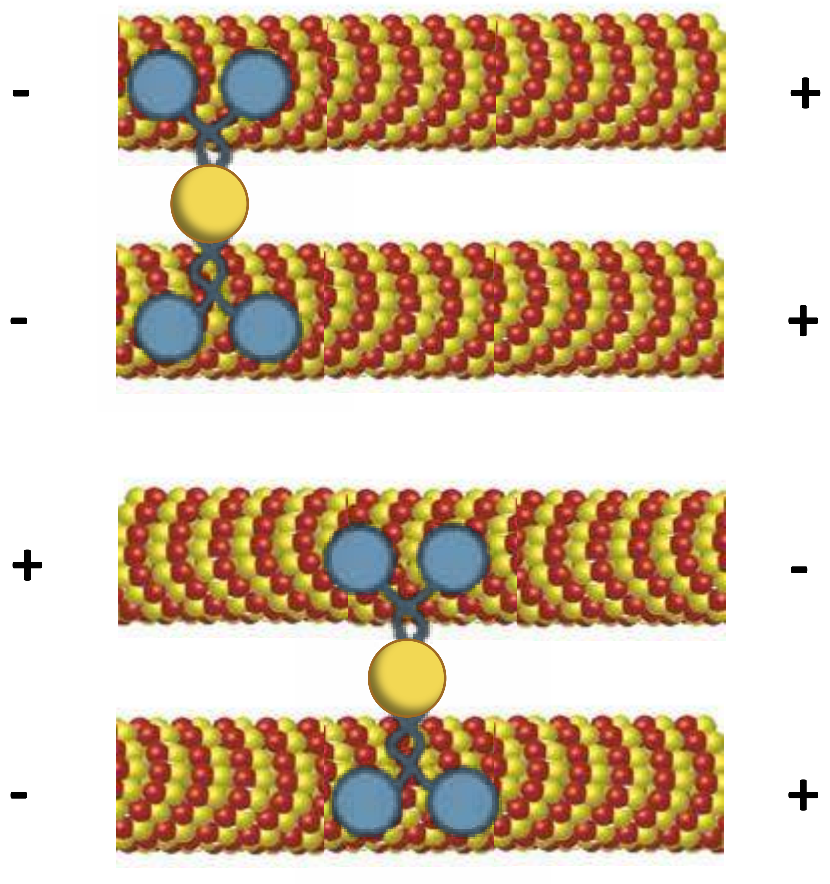
+1/2



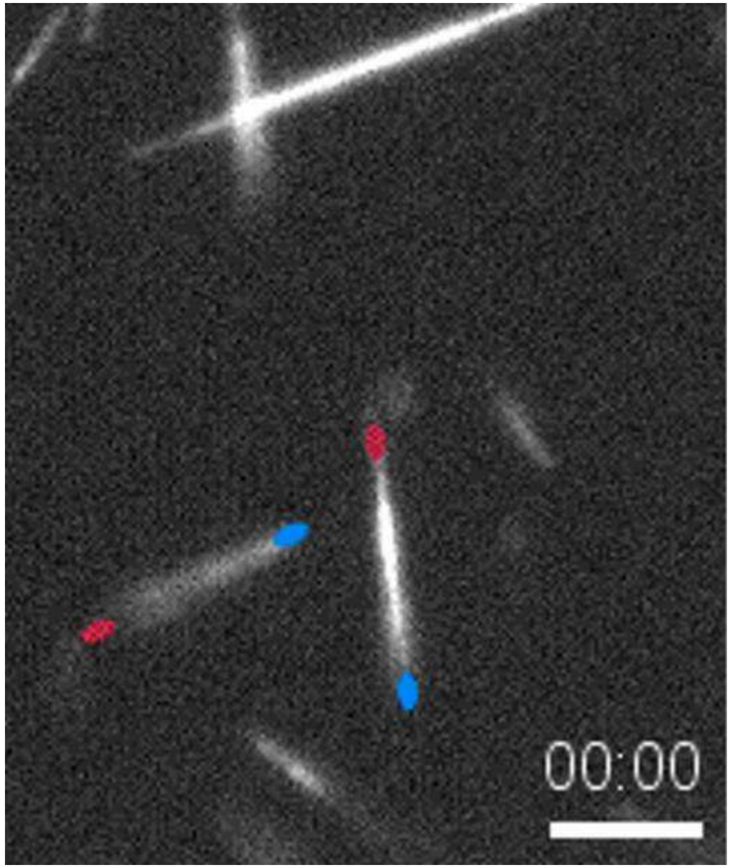
-1/2

# Bend instability suplement

# Kinesin clusters induce the sliding of anti-parallel microtubules

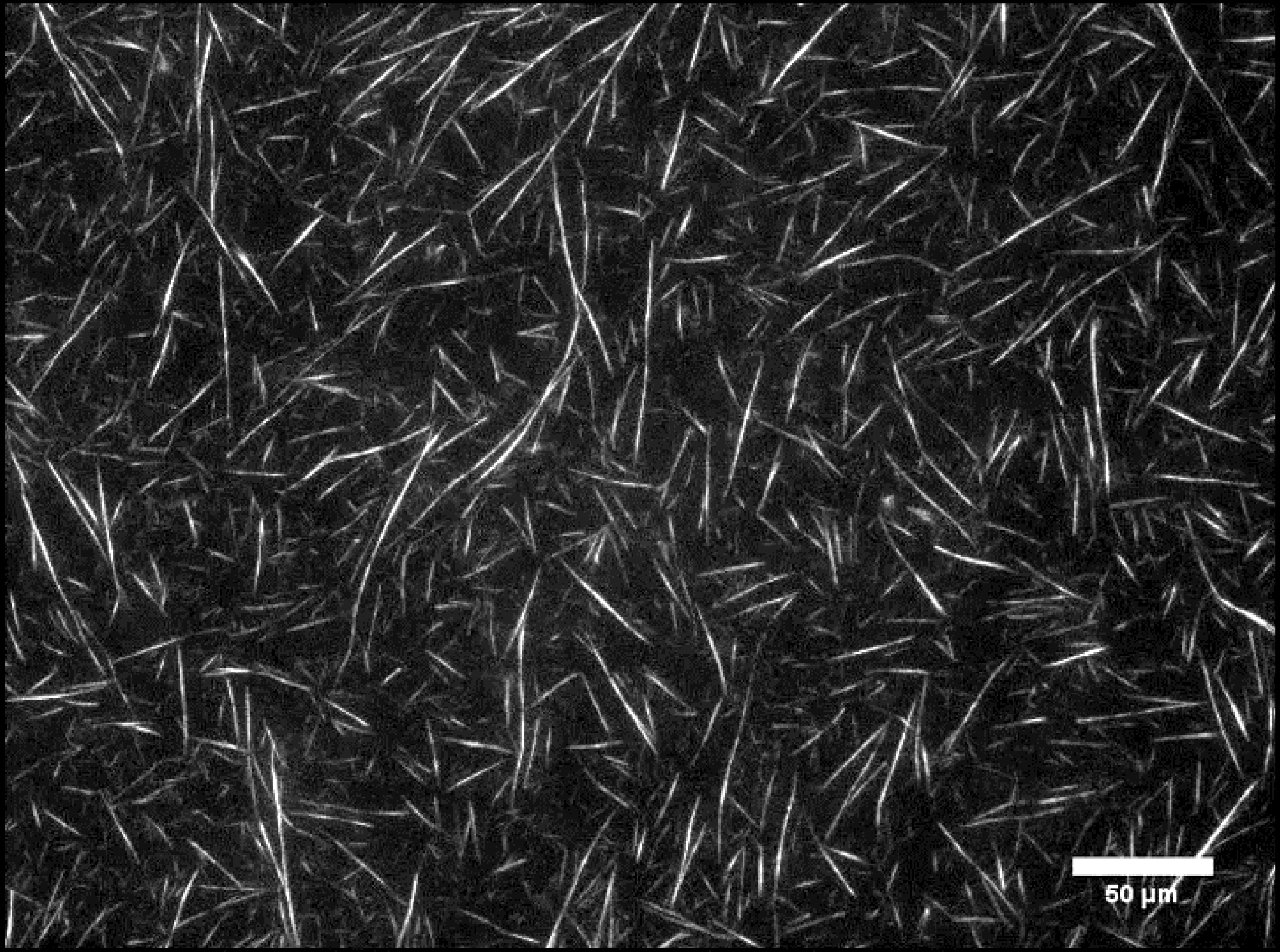



Fluorescent MT, polar ends labeled in blue and red



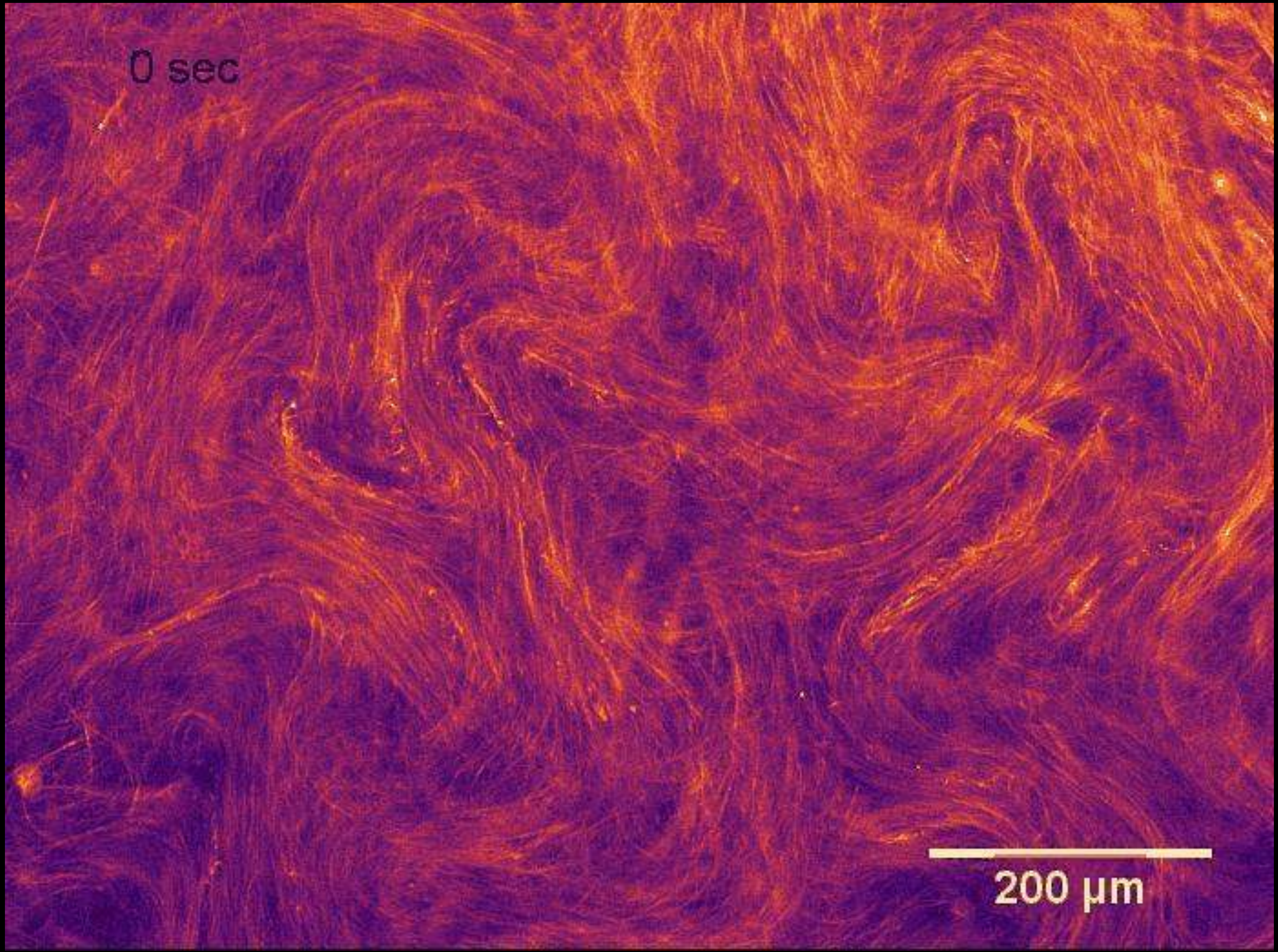

Sanchez et al, 2012

# Low MT concentration on a 2D oil-water interface

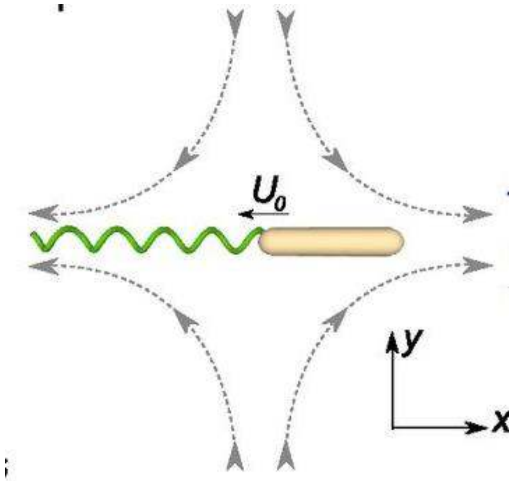


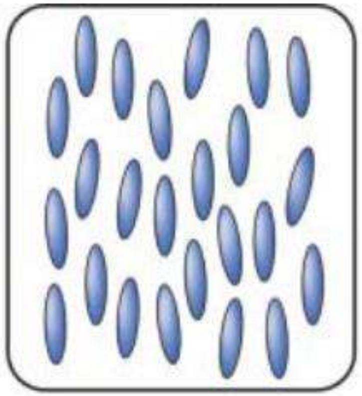

DeCamp et al, 2015

Fluorescently labelled Microtubules in a 3D flow channel



# Instability in “Living Liquid Crystals”

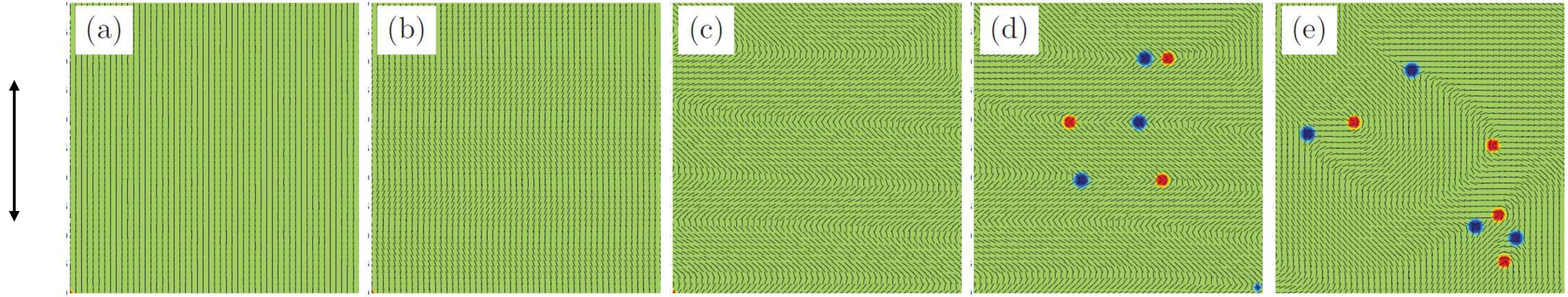



Zhou et al., PNAS 2013

# Theoretical approach: Bend instability is a 2D active extensile nematic

Continuum model of an extensile active nematic



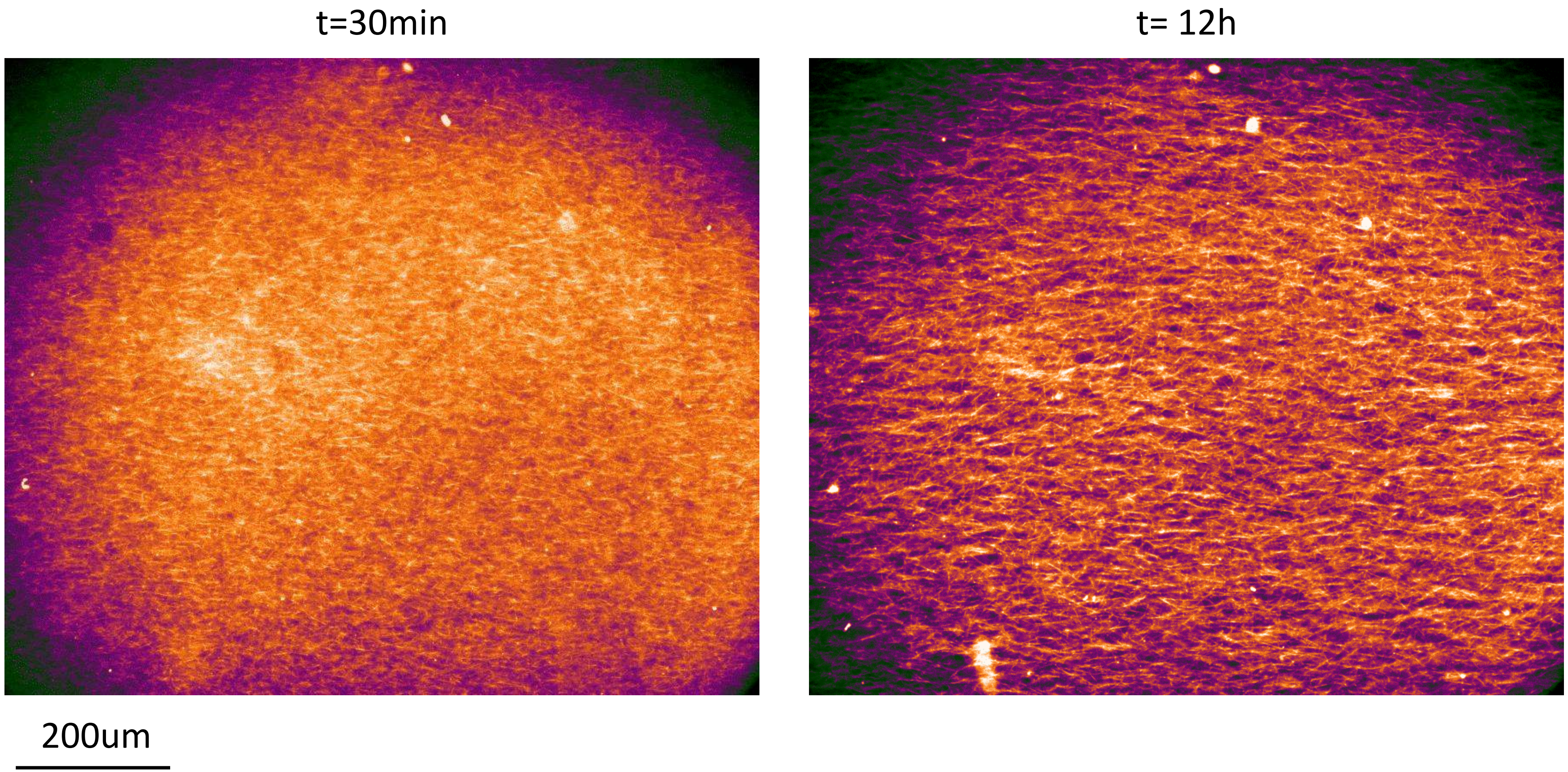

Thampi et al., Instability and topological defects in active nematics, Europhysics Letter 2013

$$\lambda \propto \sqrt{\frac{K}{\alpha}}$$

**K** nematic elasticity (Frank constant)
**α** activity

# The instability is an active process

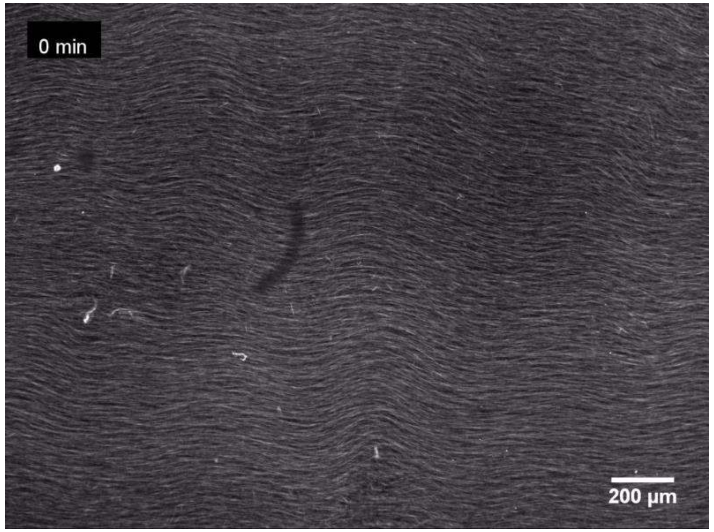
No ATP and no Motor complexes



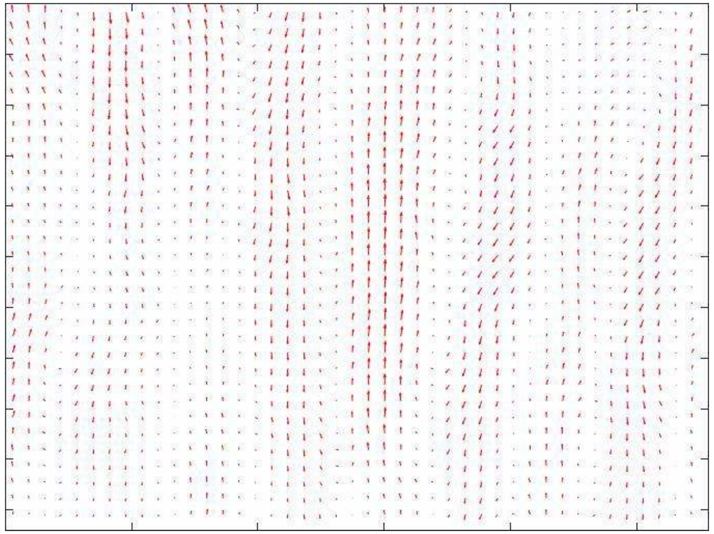
# Dynamics of the instability

Mapping of the displacement field using Particle Image Velocimetry (PIV)

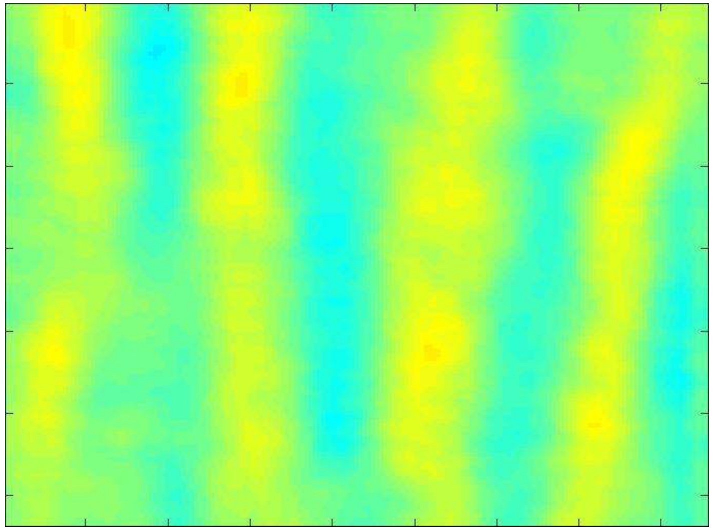
Microtubules



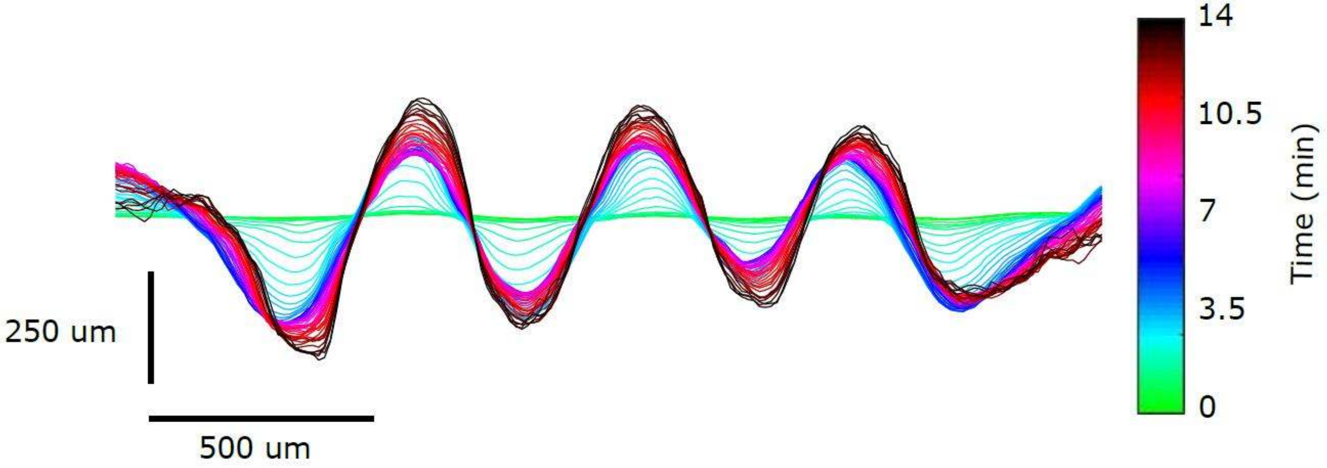

Velocity field

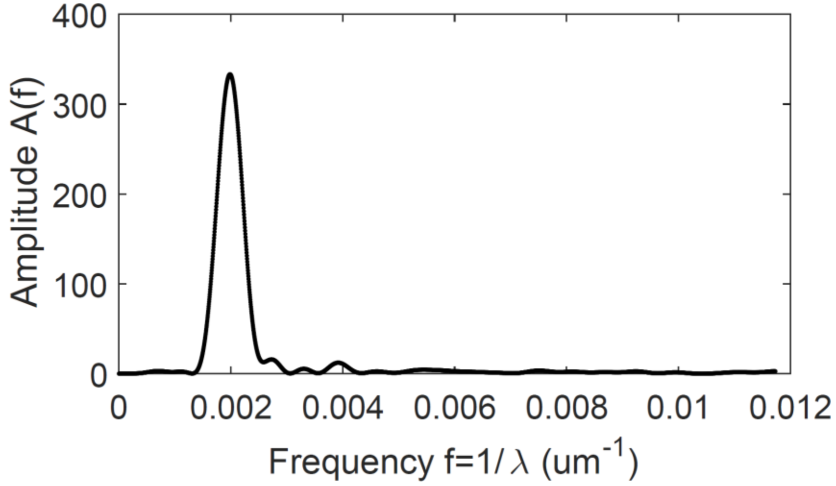


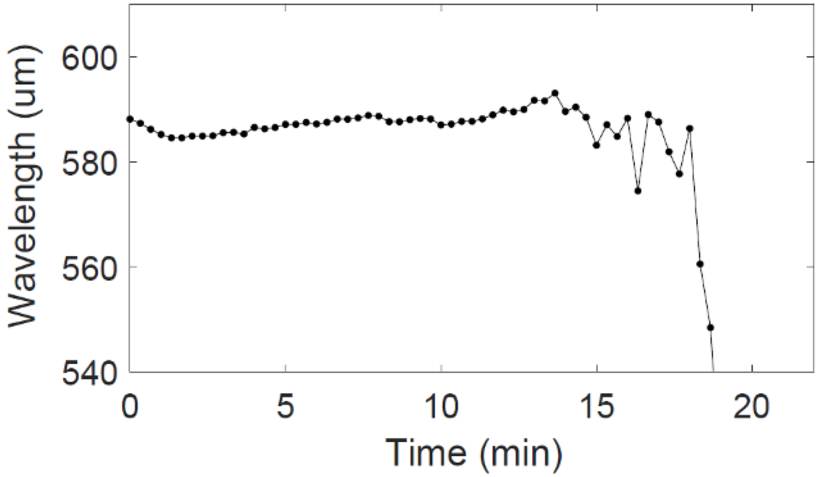
Vorticity

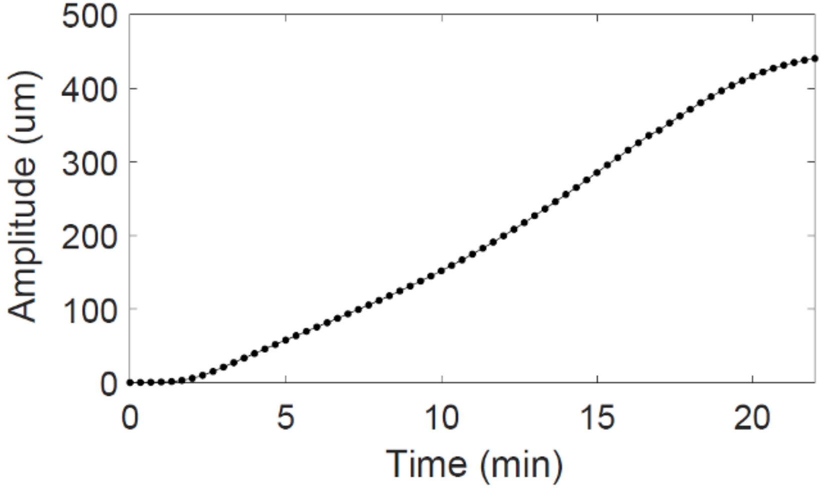


# Dynamics of the instability

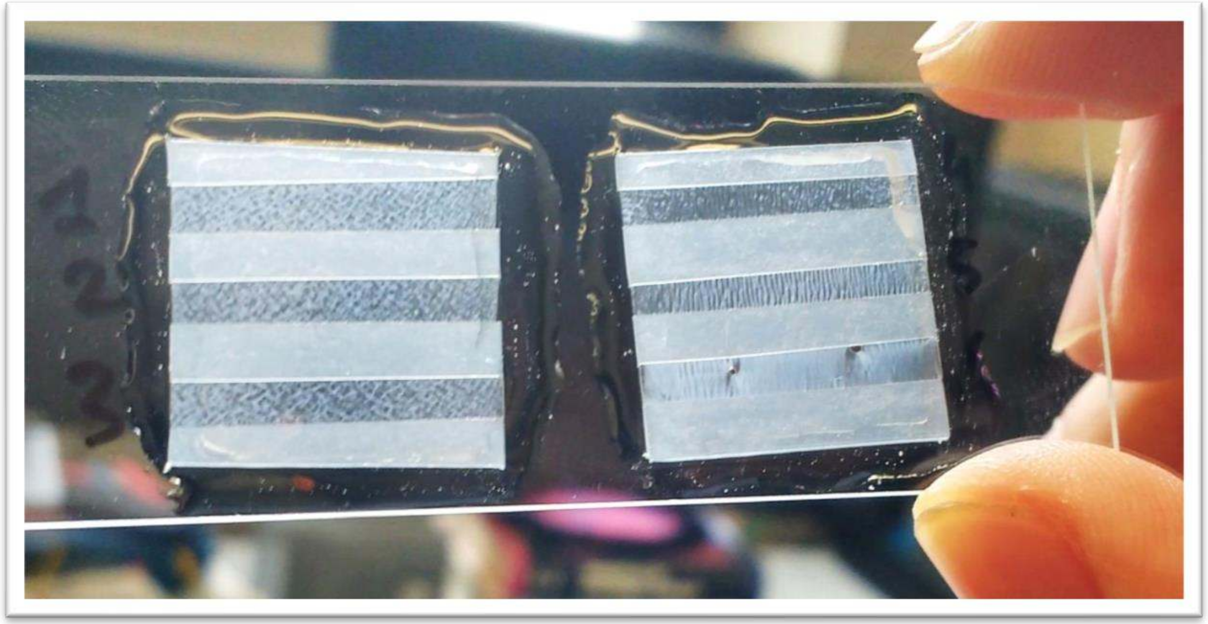


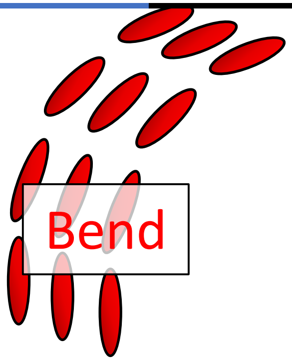



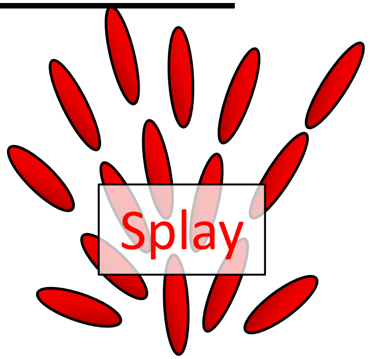
# Macroscopic instability



5 mm

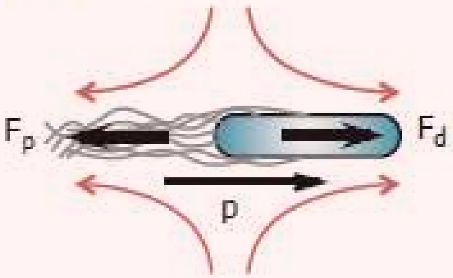
# Instability in extensile vs. contractile active nematics

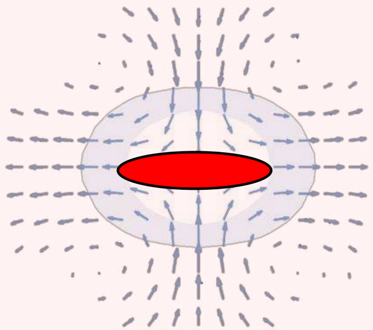



Pusher

a) Extensile



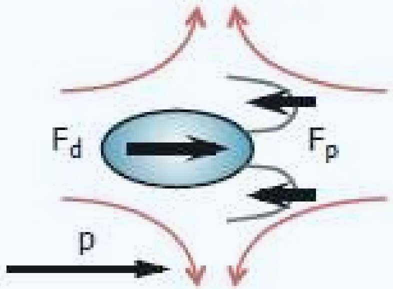



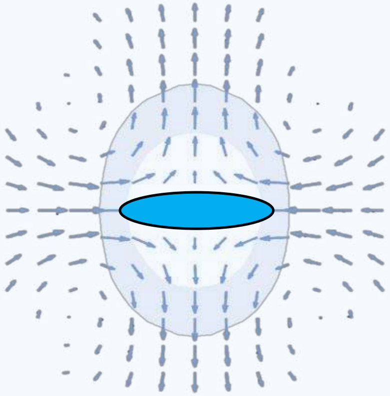
Unstable

Stable

Puller

b) Contractile

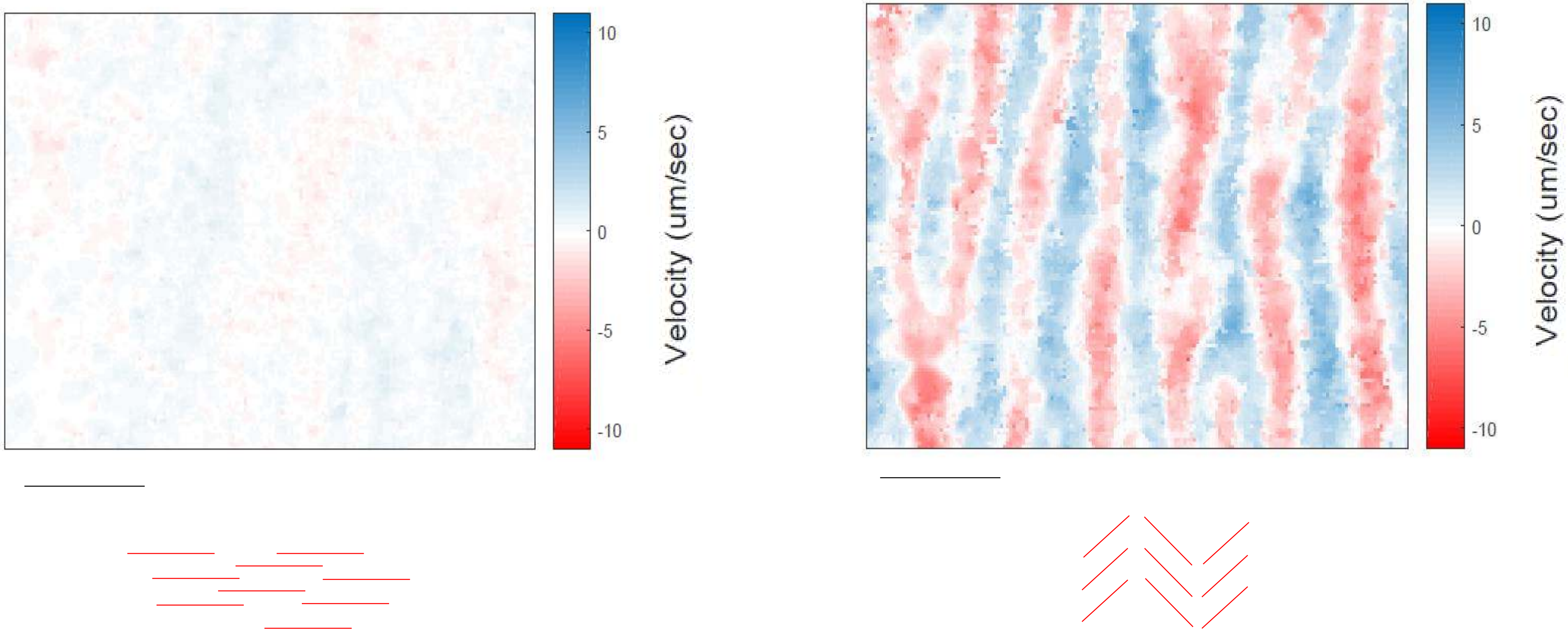


Stable

Unstable

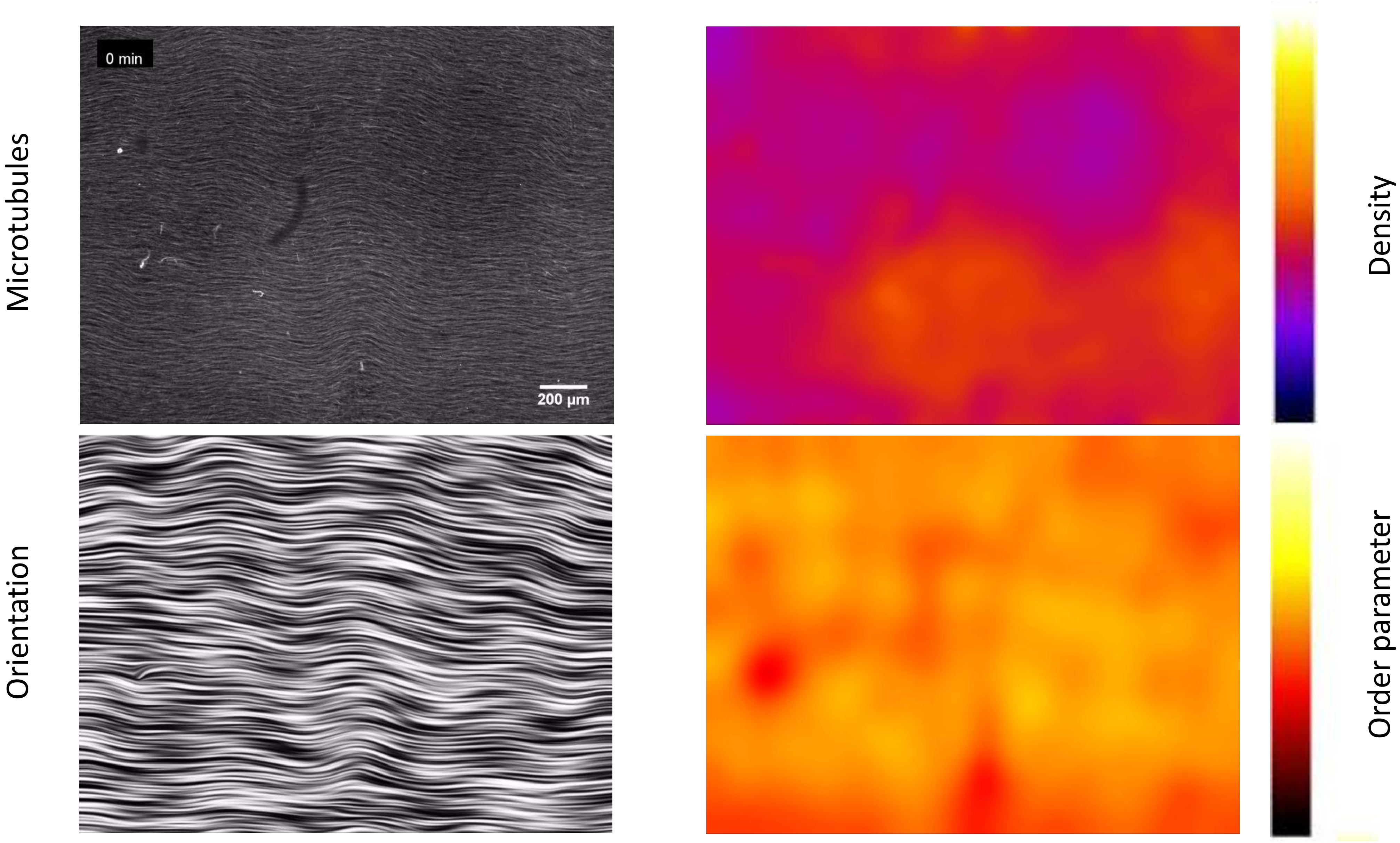
# Velocity along the Y axis



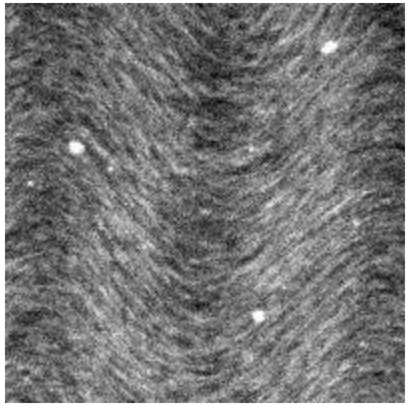

Y axis

X axis = channel axis

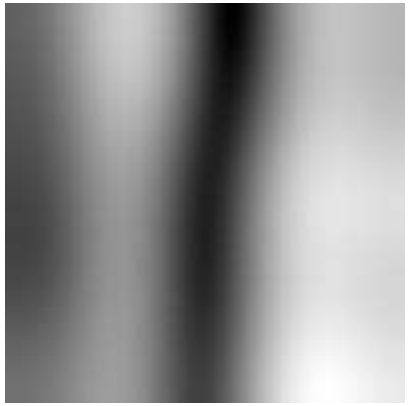
# Density – Orientation – Order parameter



Fluorescent MT

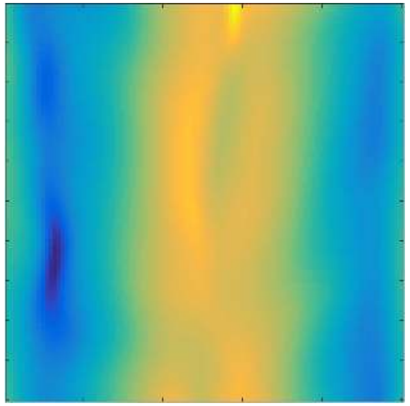


S - Order Param

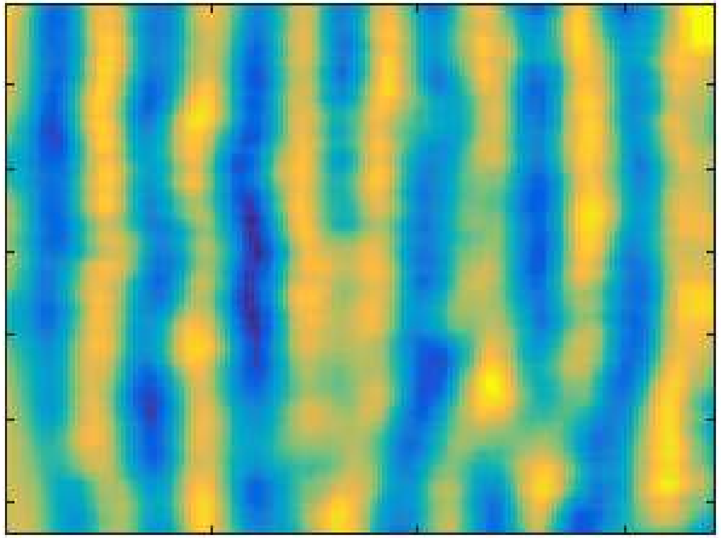


Orientation $\vec{n}$

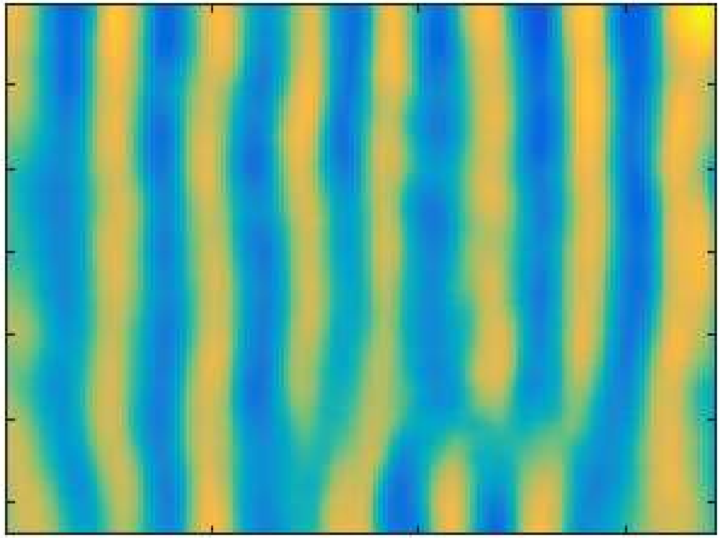
Curl ( $S.\vec{n}$ )



Velocity along Y axis



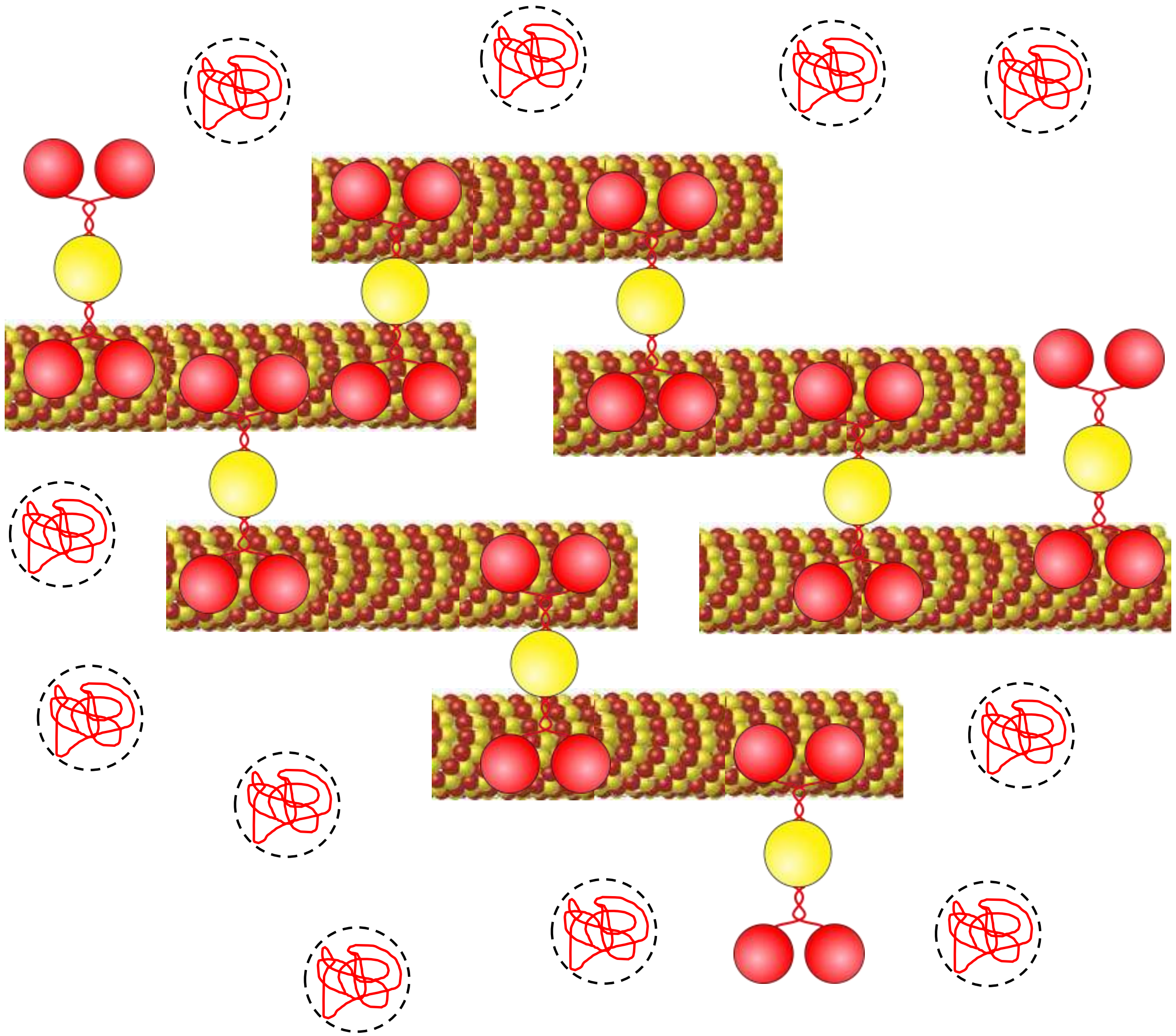
Curl ( Q )



500 um

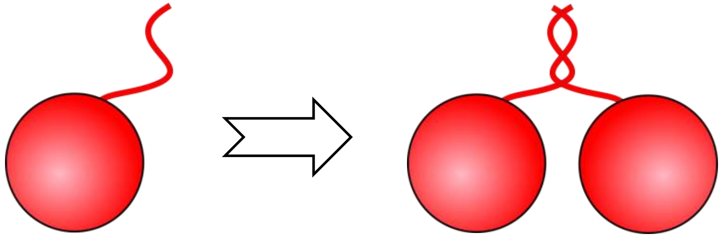
$$v \propto \nabla \times Q$$

# Wavelength vs. Kinesin-Streptavidin concentration

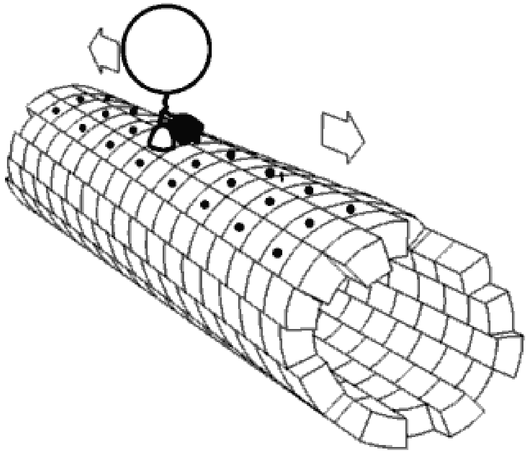


## Active effect or viscoelastic effect ?

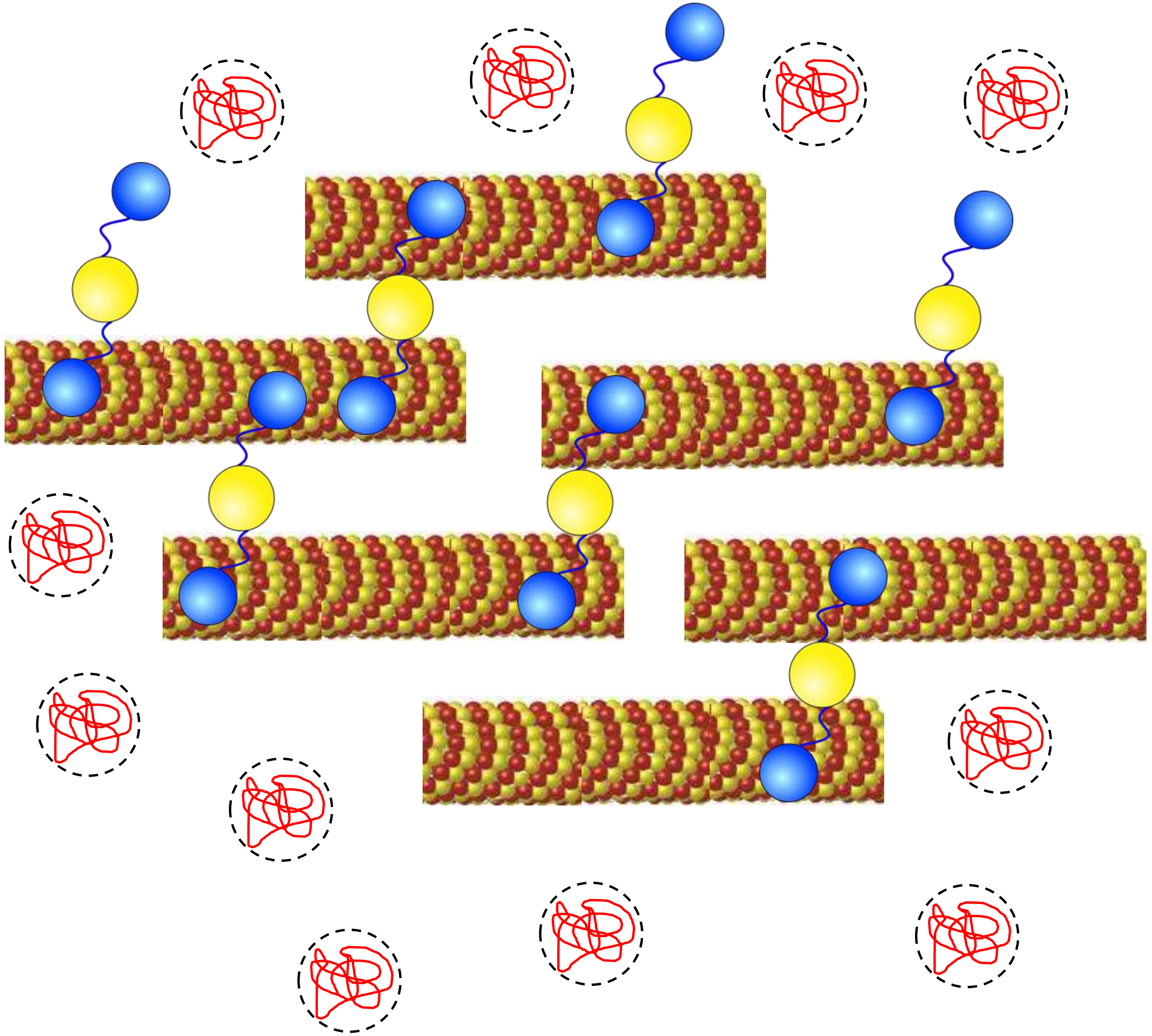
K401, is a double-headed processive motor



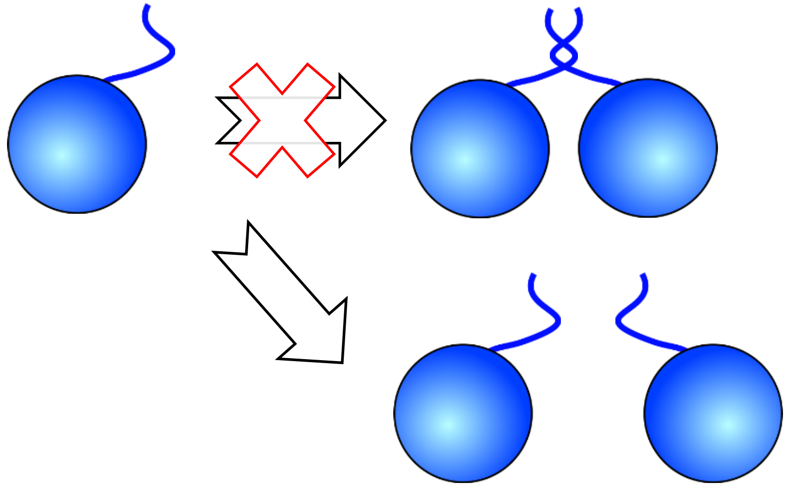
Processive: go through repeated complete enzymatic cycles while remaining bound to the microtubule (~100 cycles)



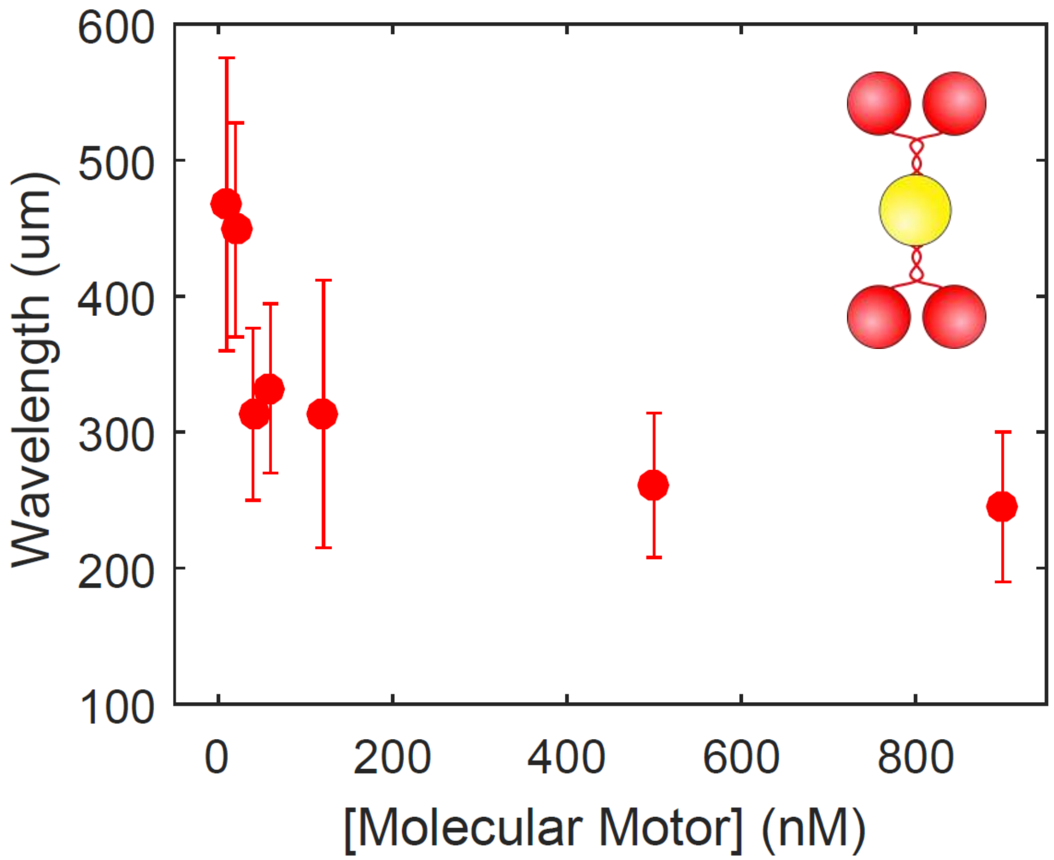
# Wavelength vs. Kinesin-Streptavidin concentration

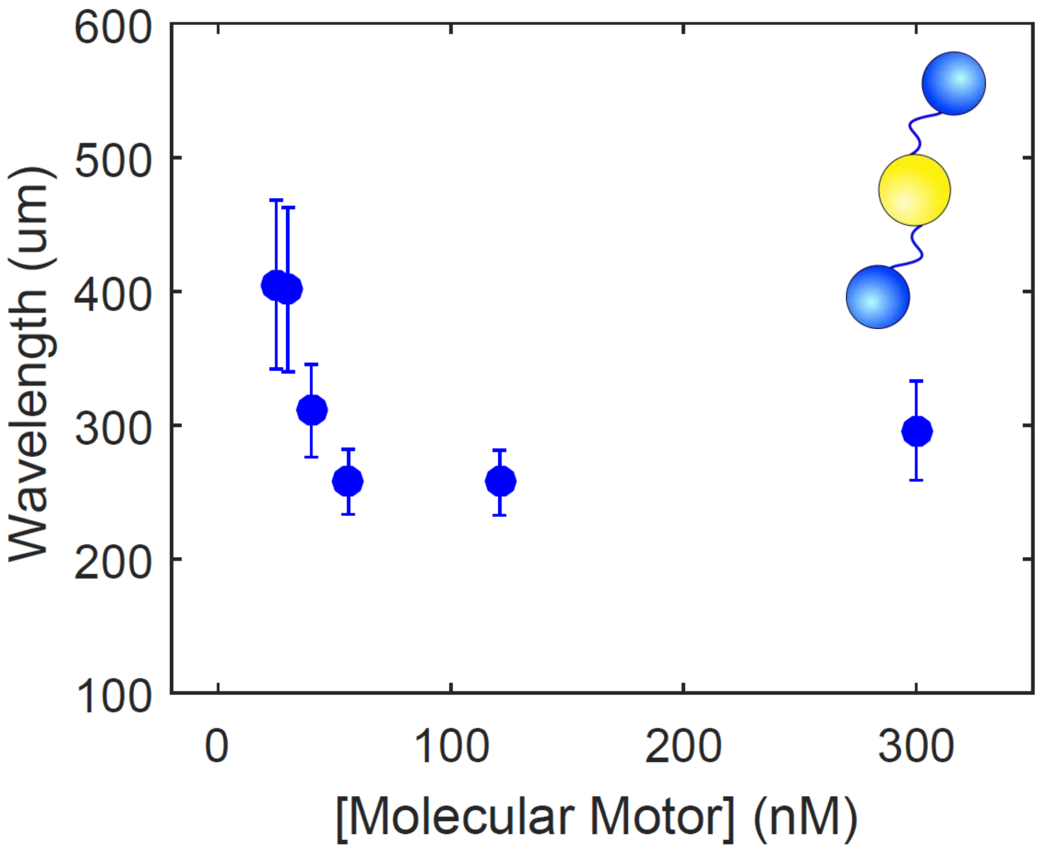


K365 is a single-headed non processive motor



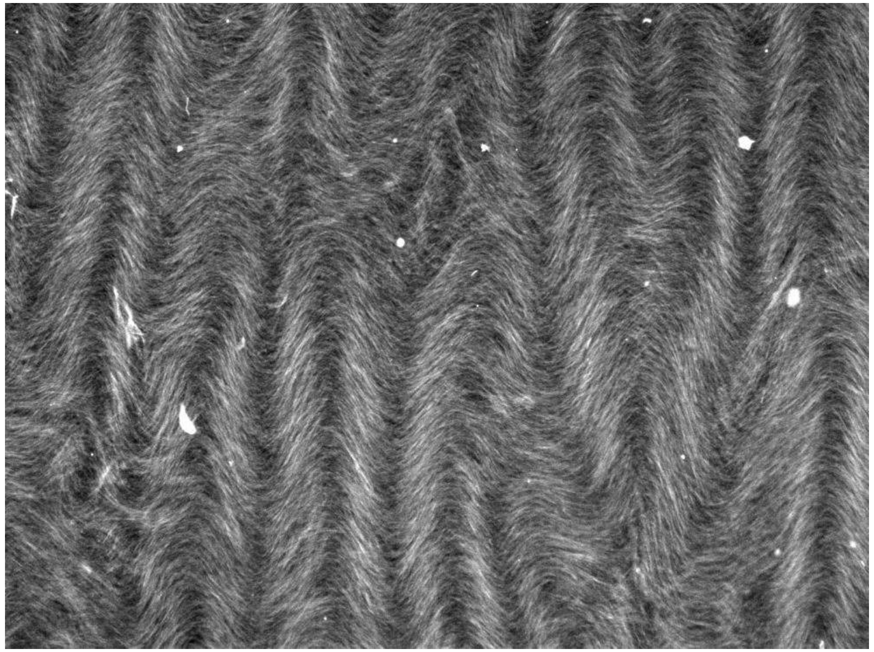
# Wavelength vs. Kinesin-Streptavidin concentration (single-headed K365)



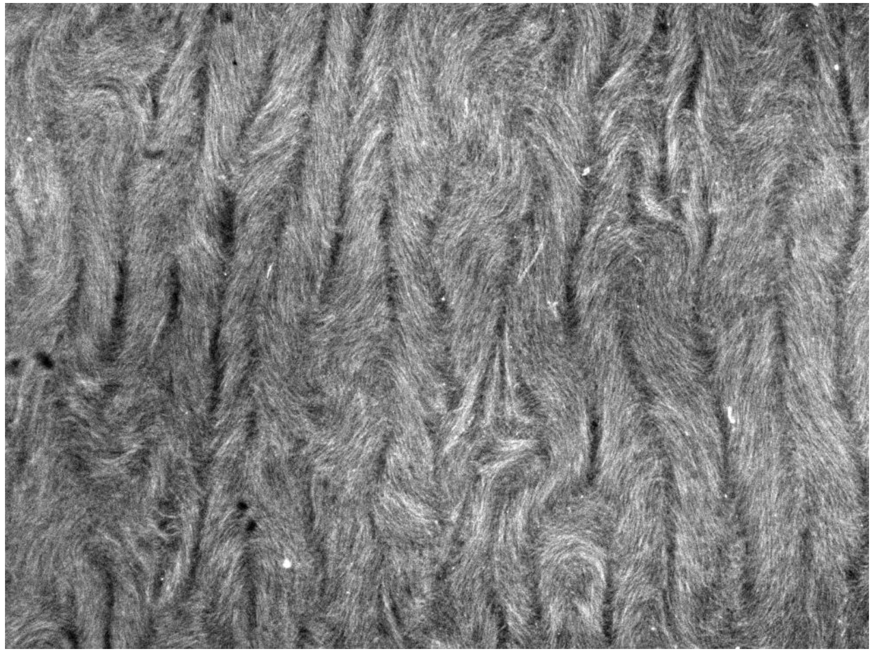
# Wavelength vs. ATP concentration

[ATP] = 100uM



500um

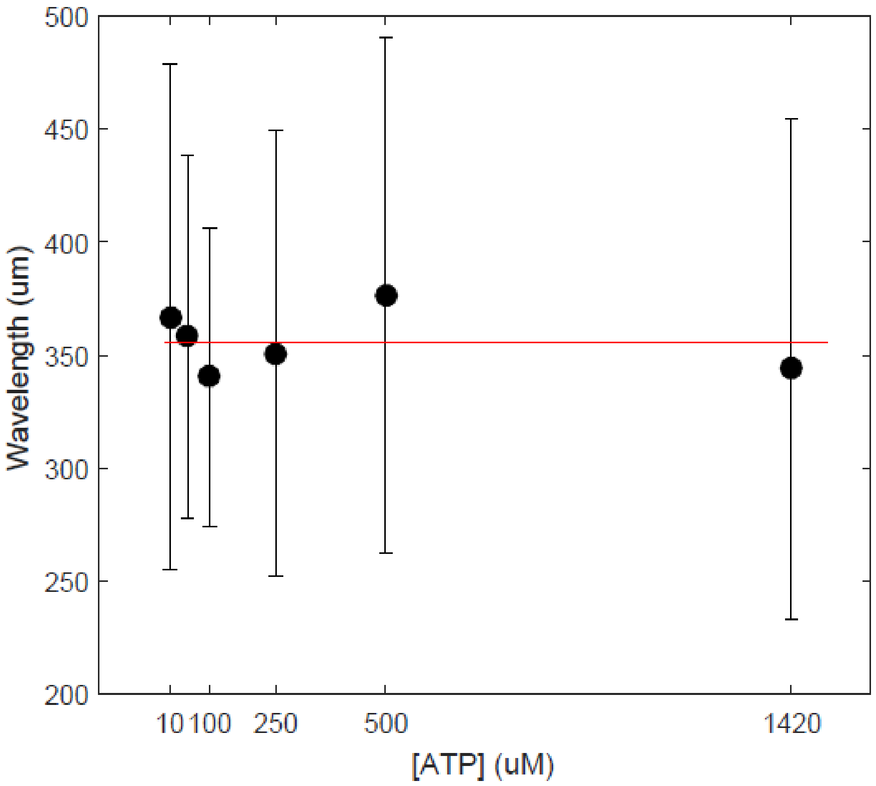
[ATP] = 1420uM

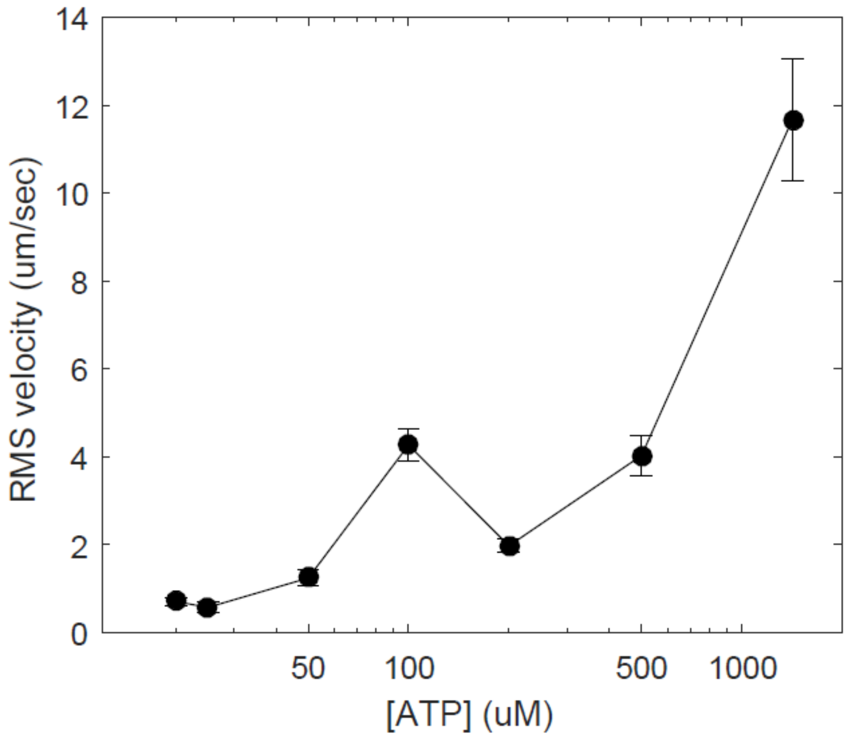


500um

[Tubulin]=1.3mg/mL, [KSA]=121nM, [Pluronic]=2%

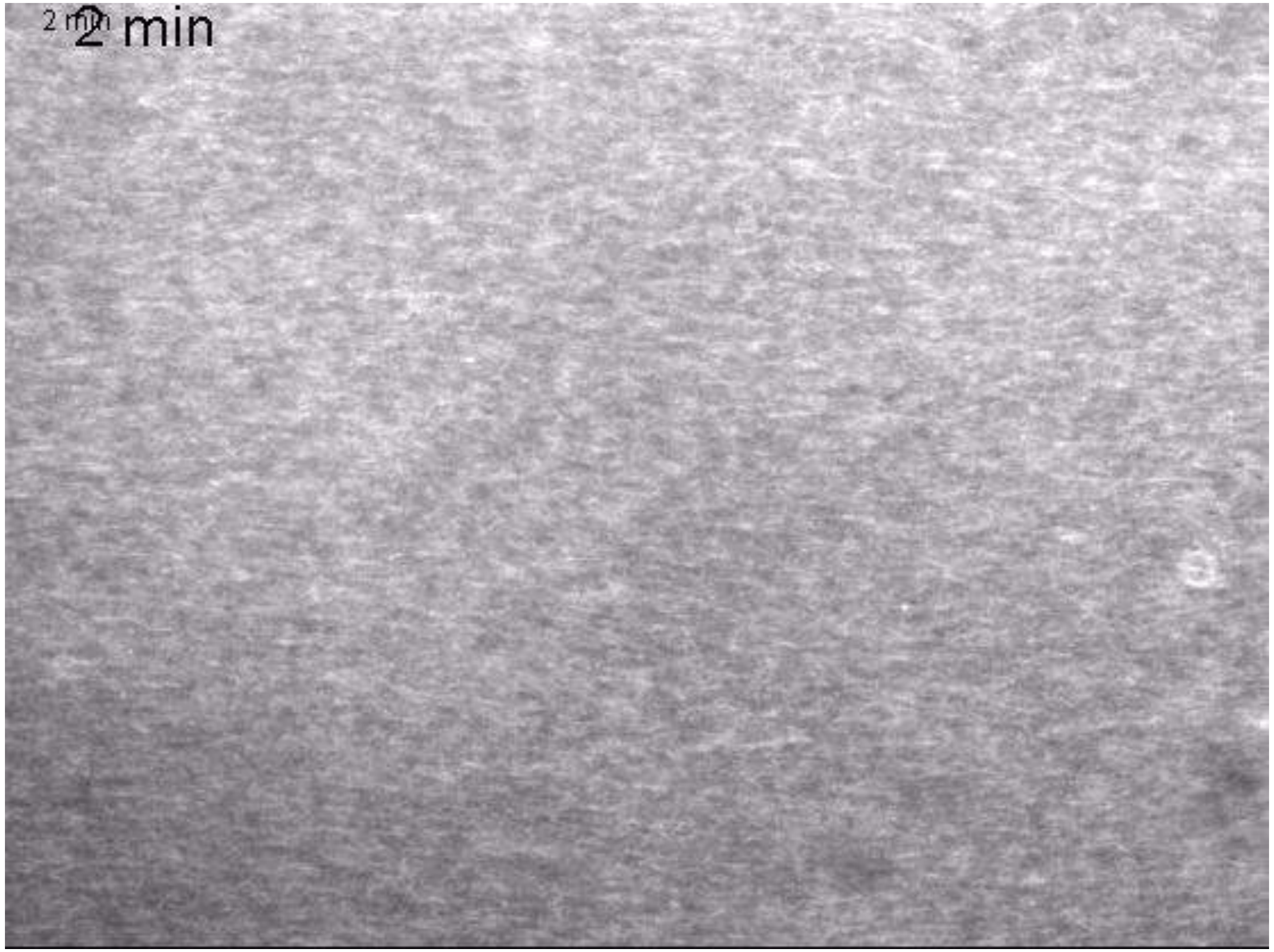
# Wavelength vs. ATP concentration




[Tubulin]=1.3mg/mL, [KSA]=121nM, [Pluronic]=2%

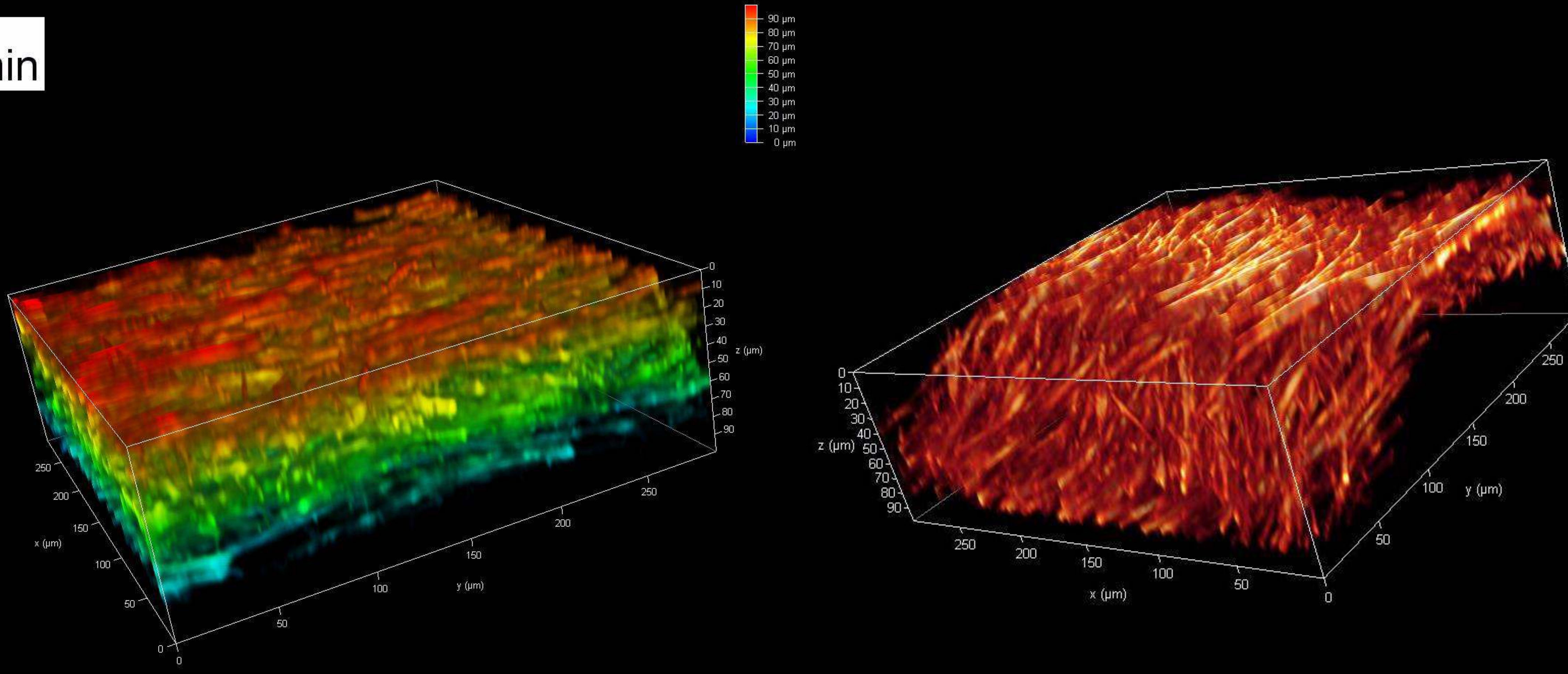
# Low ATP concentration (10uM)




200um

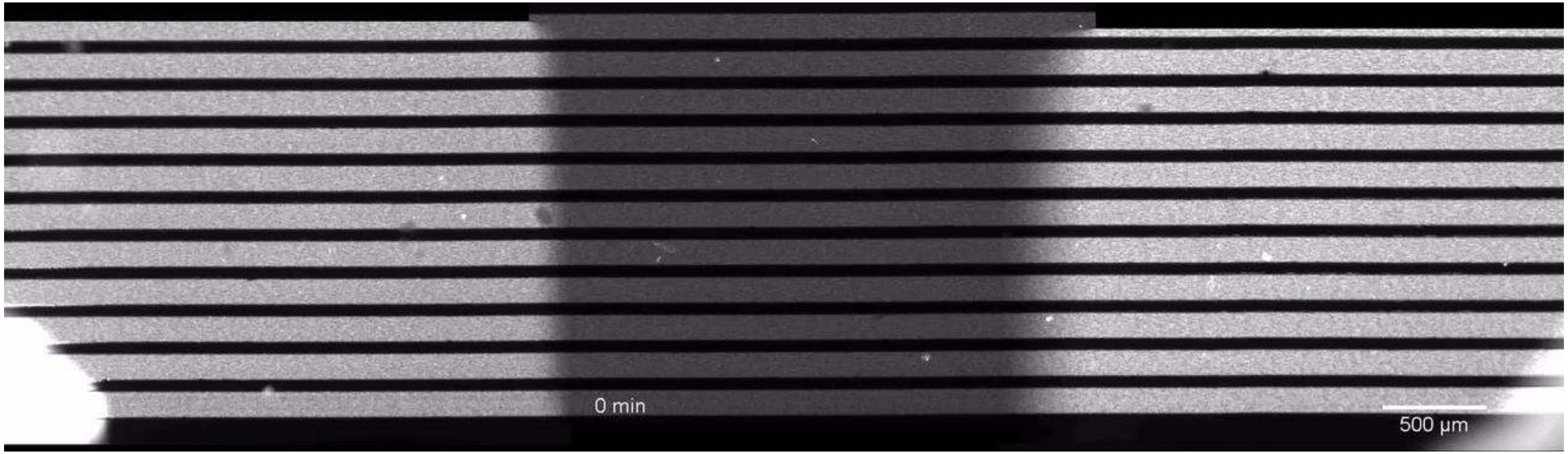
# Low ATP concentration (10uM)

0 min




100um

100um

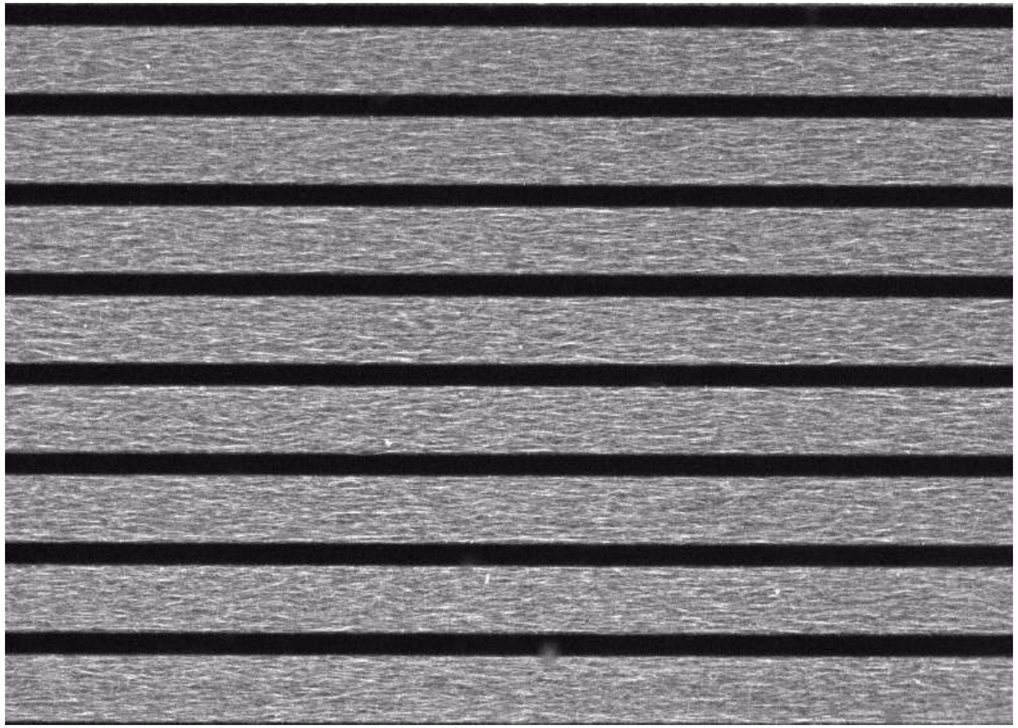



W=100um
H=50um

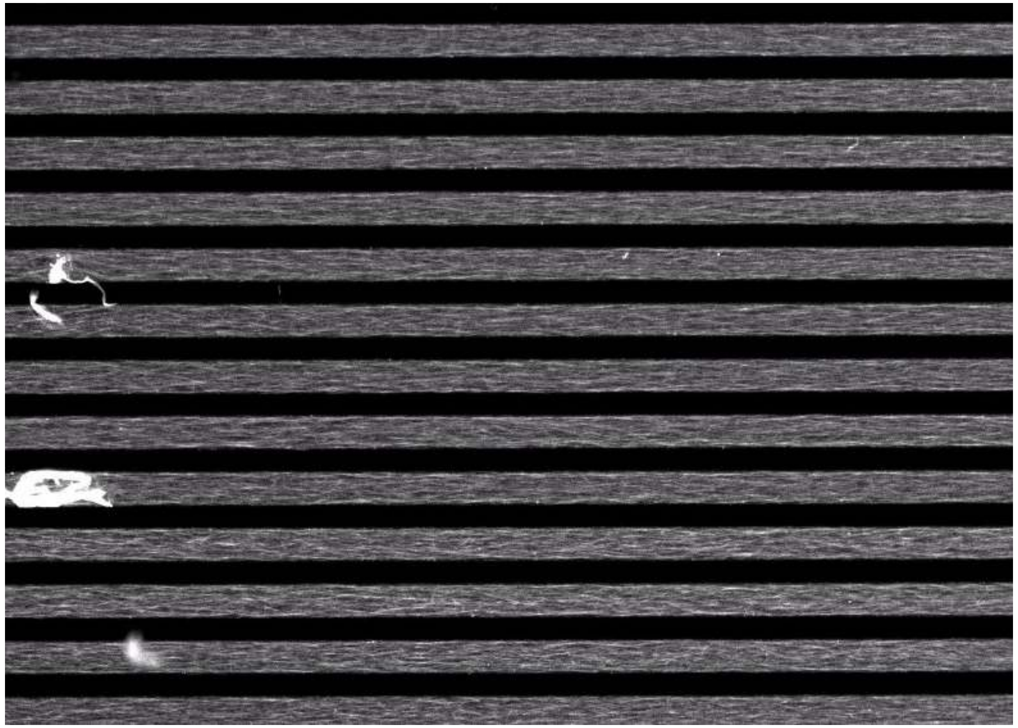
[Tubulin]=1.3mg/mL,
[KSA]<20nM,
[ATP]=1420uM,
[Pluronic]=2%

# Effect of confinement on the instability

W=150um
H=50um

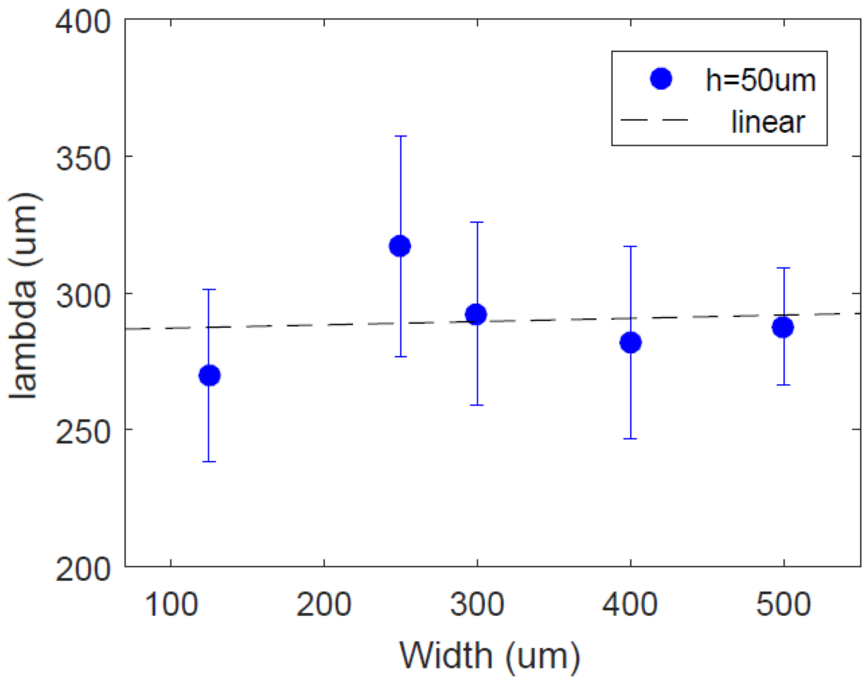


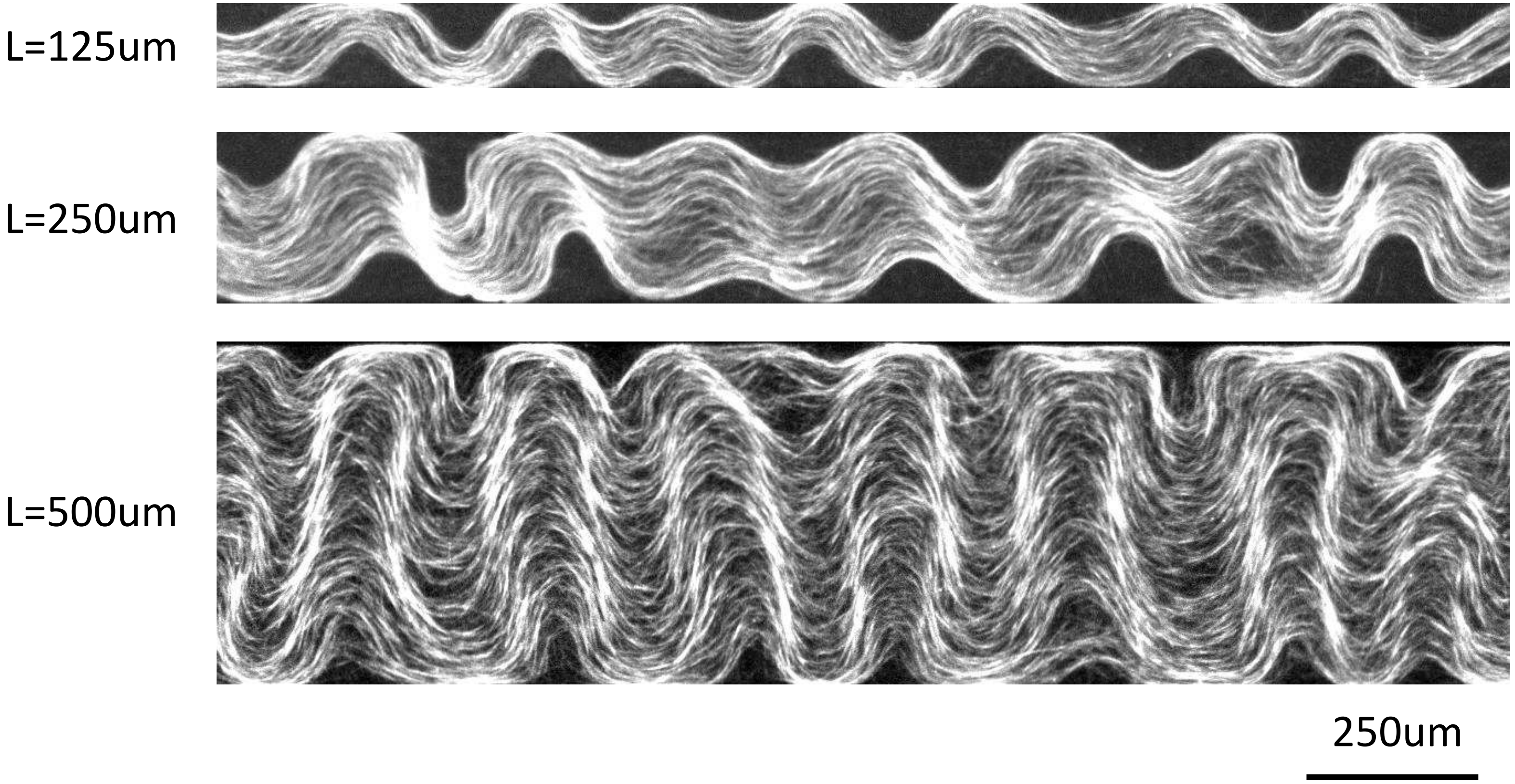
W=75um
H=50um



[Tubulin]=1.3mg/mL, [KSA]=20nM,
[ATP]=1420uM, [Pluronic]=2%

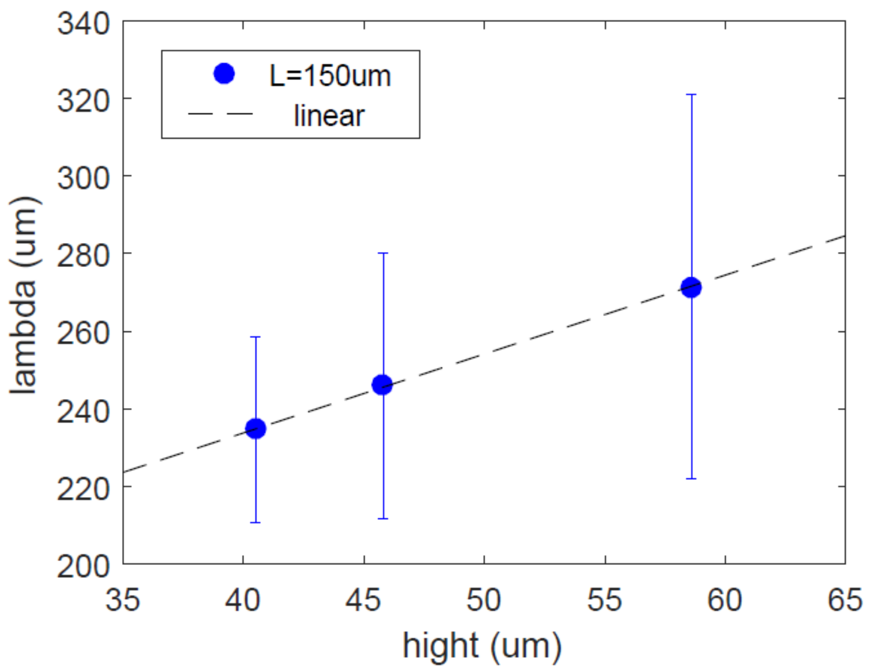
# **Effect of confinement:** Wavelength vs. channel width

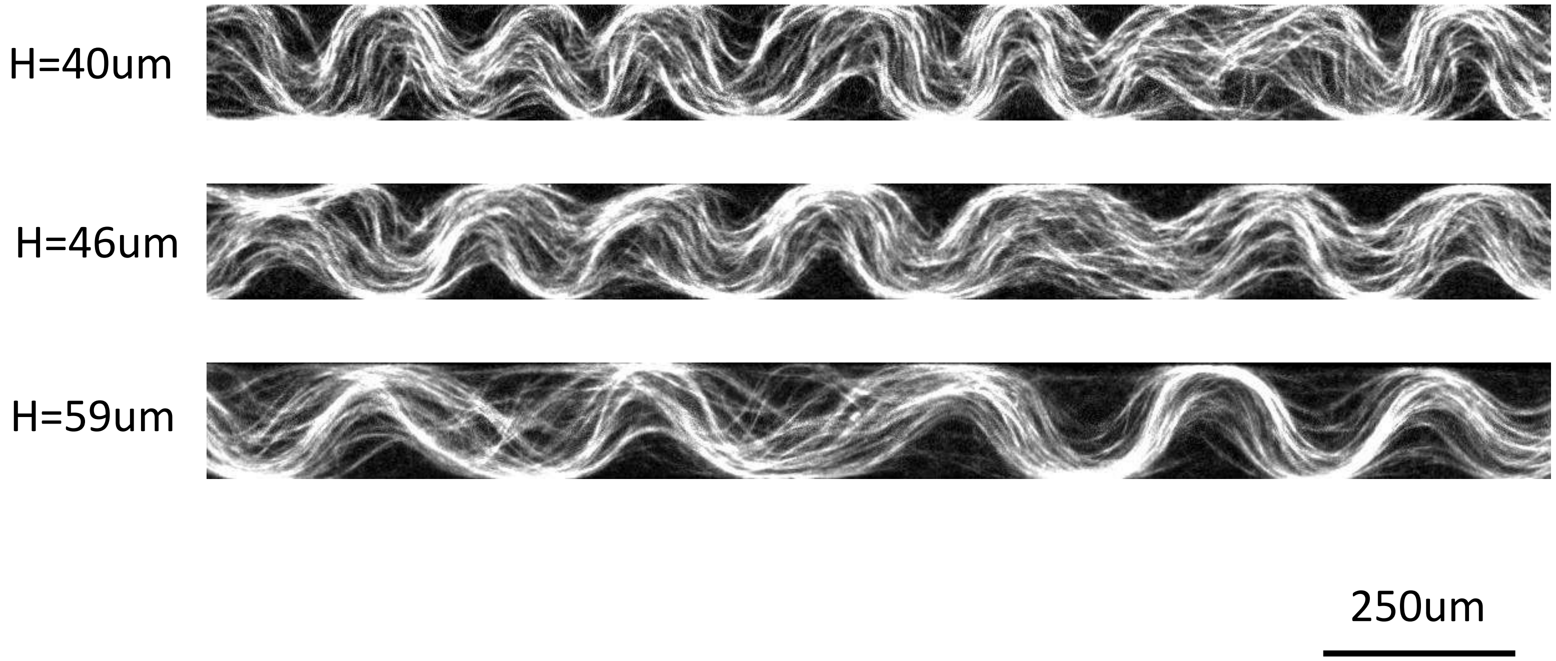



[Tubulin]=1.3mg/mL, [KSA]=20nM, [ATP]=1420uM, [Pluronic]=2%, height=50um

# **Effect of confinement:** Wavelength vs. channel height



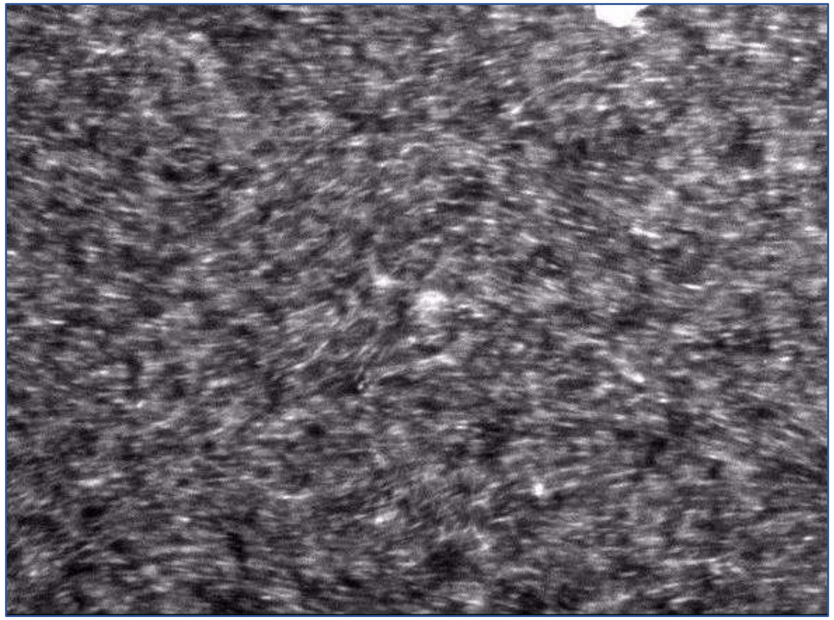




[Tubulin]=1.3mg/mL, [KSA]=20nM, [ATP]=1420uM, [Pluronic]=2%, height=50um

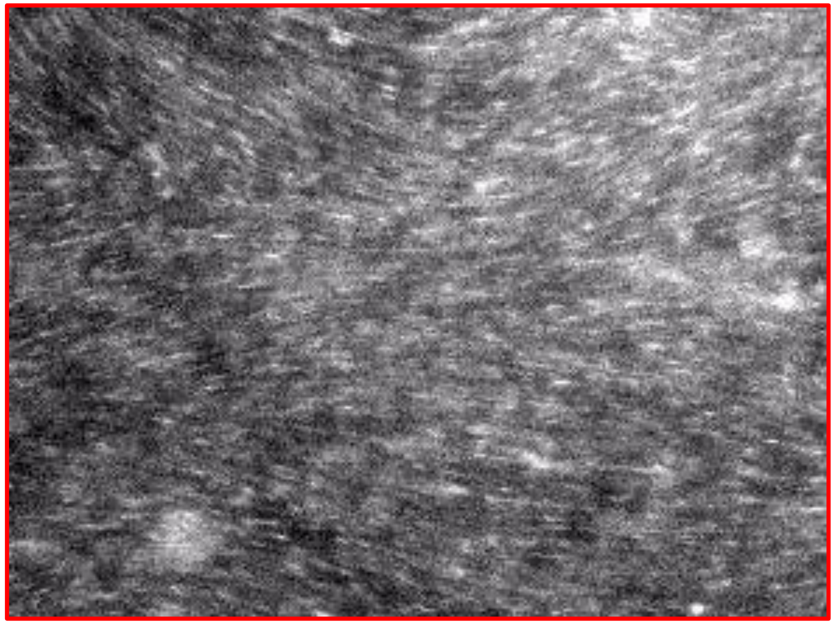
# Active 3D active LC suplement

# Are the MT still actively sliding in the stable phase ?

[ - ] ATP

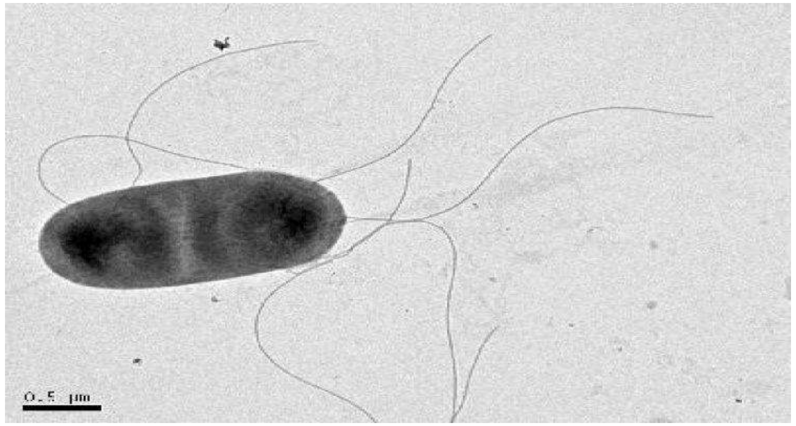


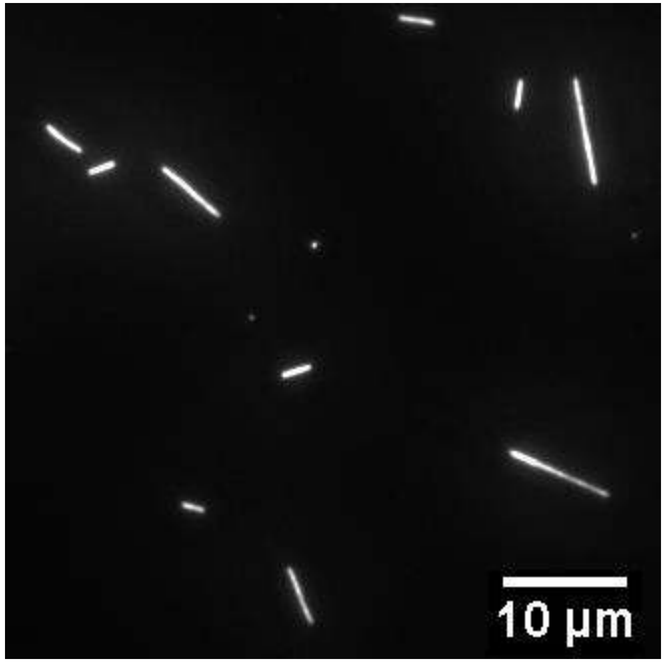
[+] ATP

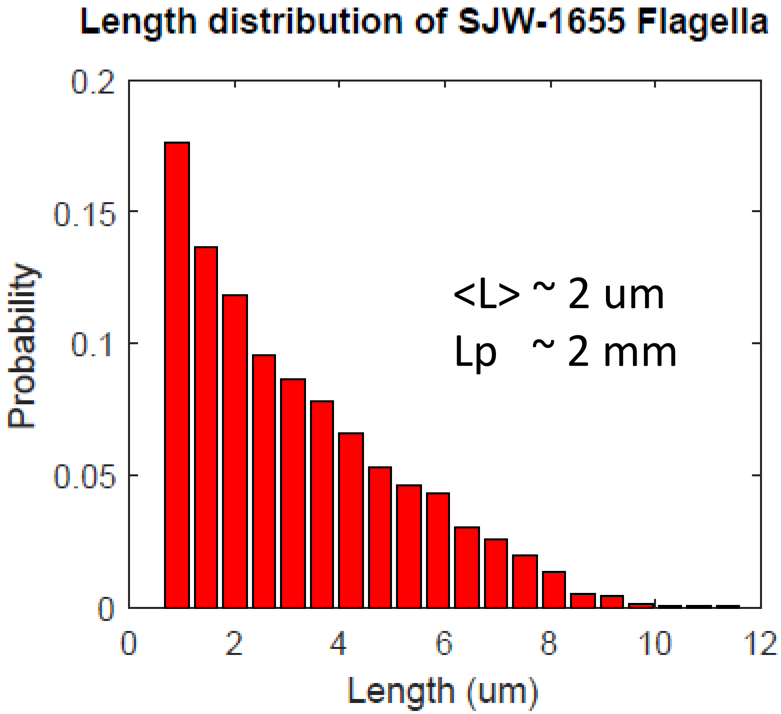


100um

# Salmonella Bacteria Flagella



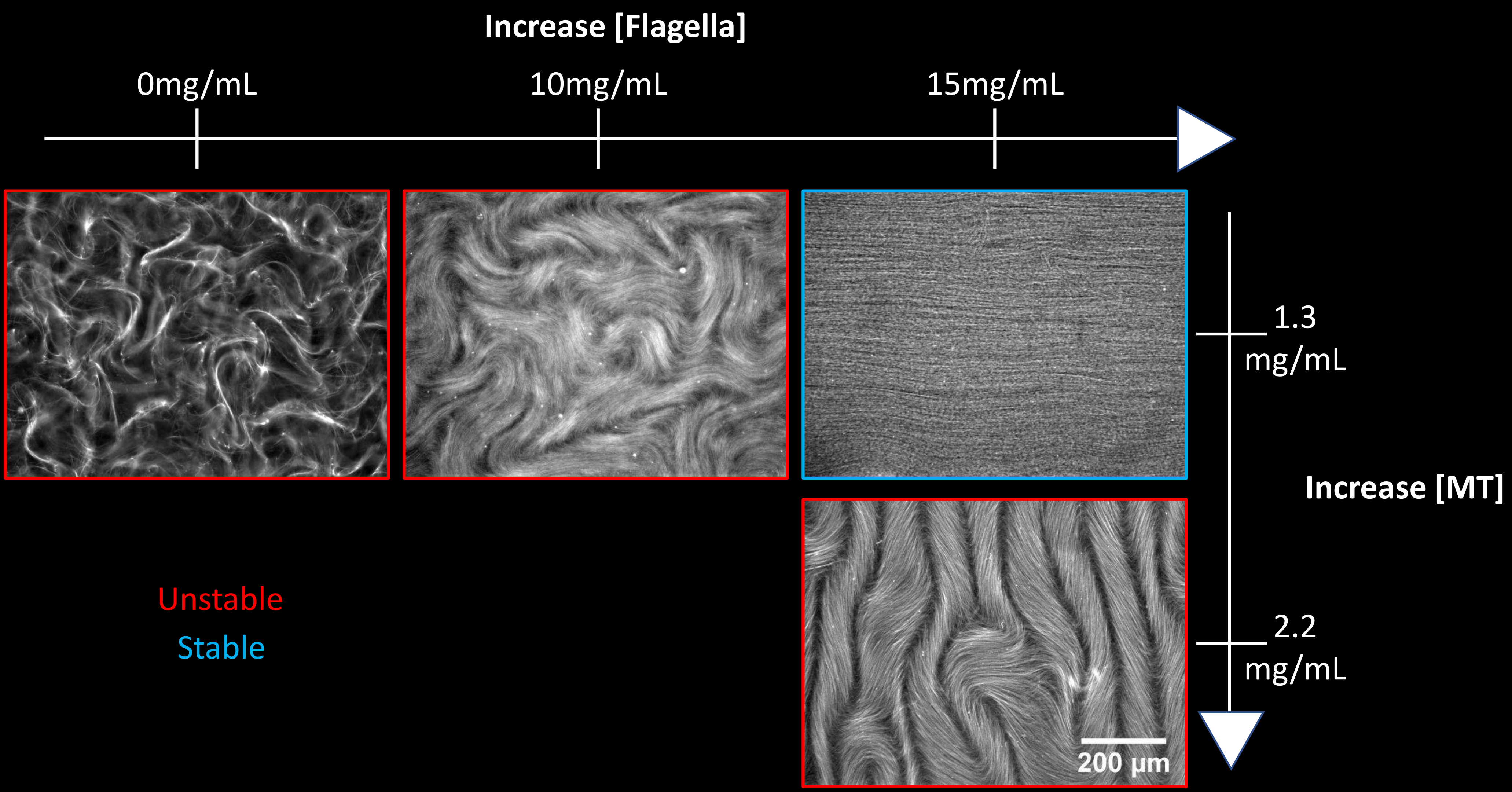




EM

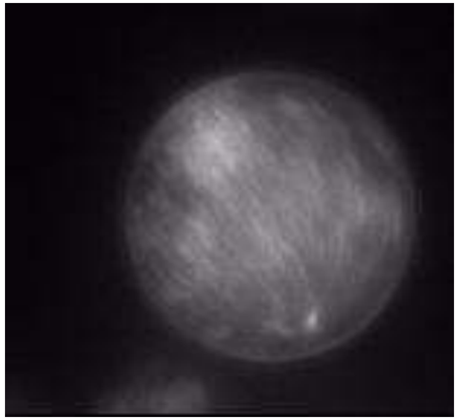
Fluorescent

Dark-field

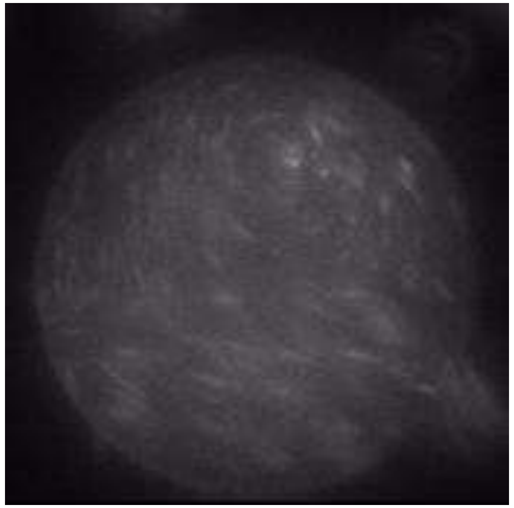
# Stability depends on the ratio of MT to flagella



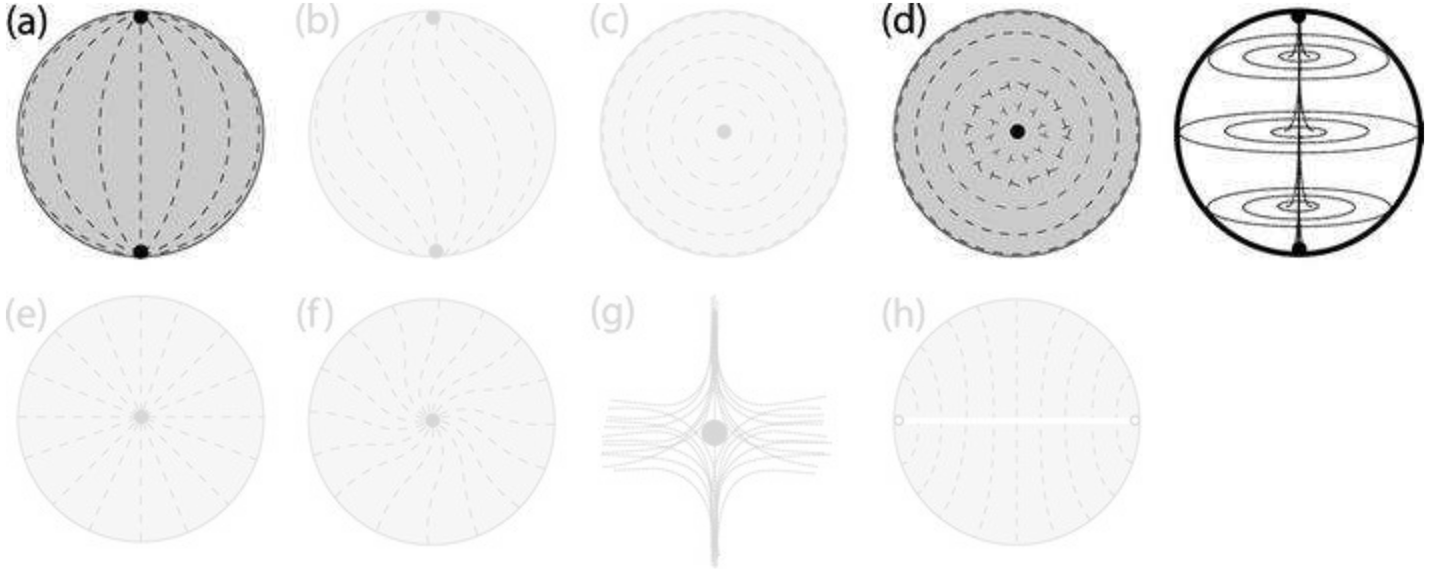
# Confinement below the critical radius



**R=10um**

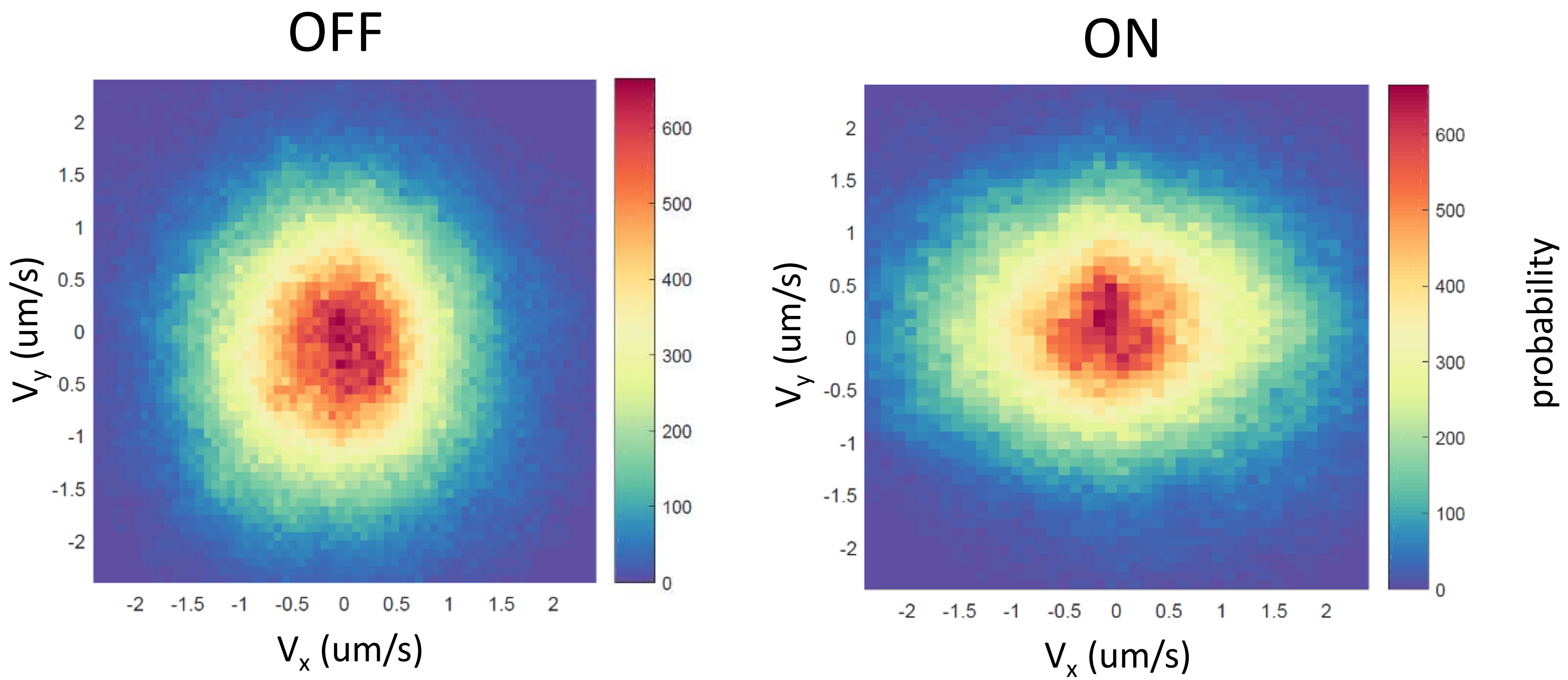


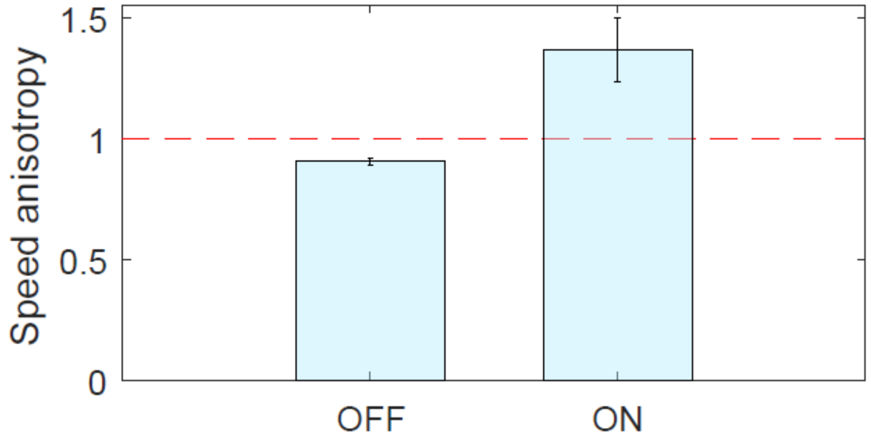
**R=25um**




Lopez-Leon and  Fernandez-Nieves (2011)

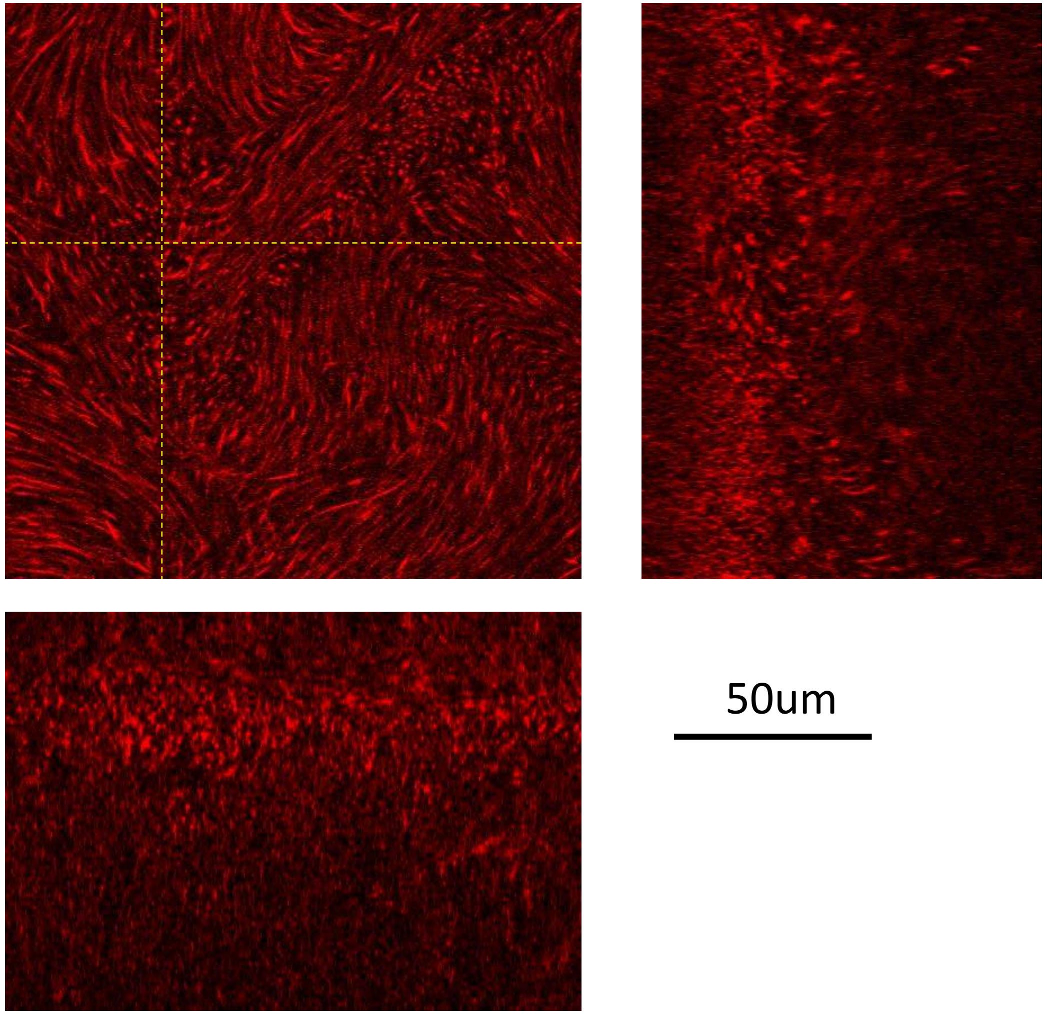
# Effect of an external magnetic field

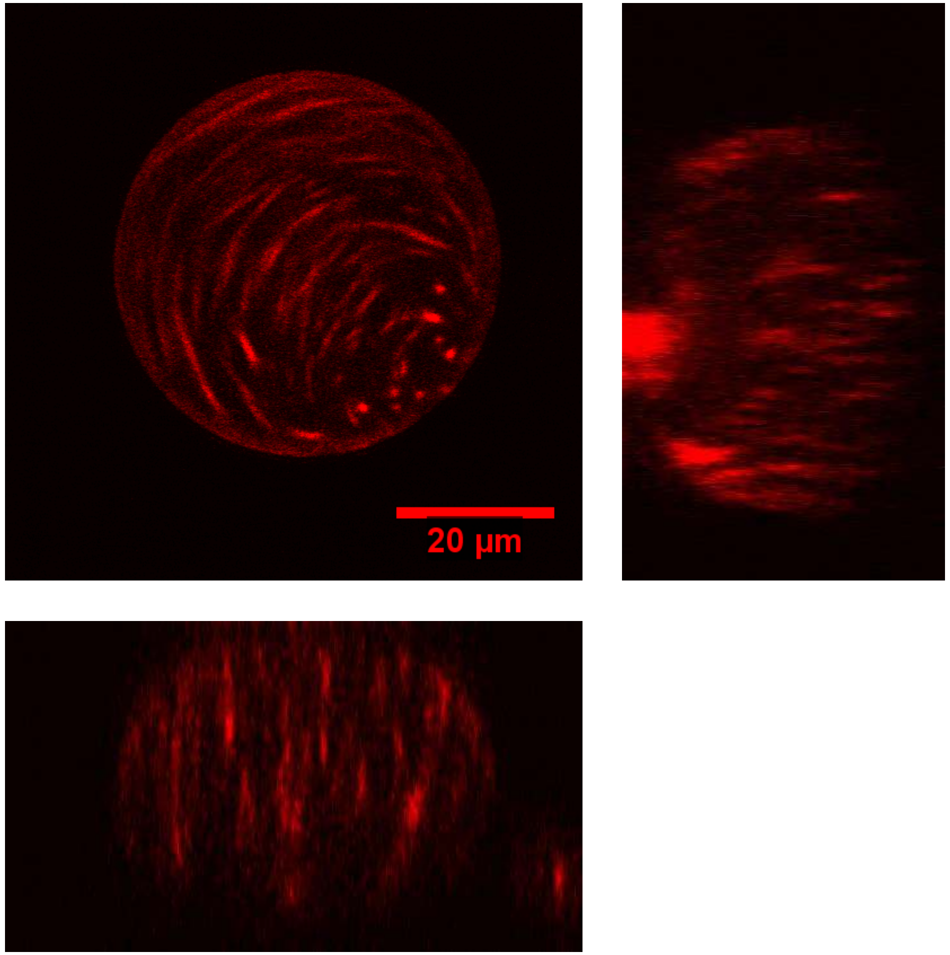


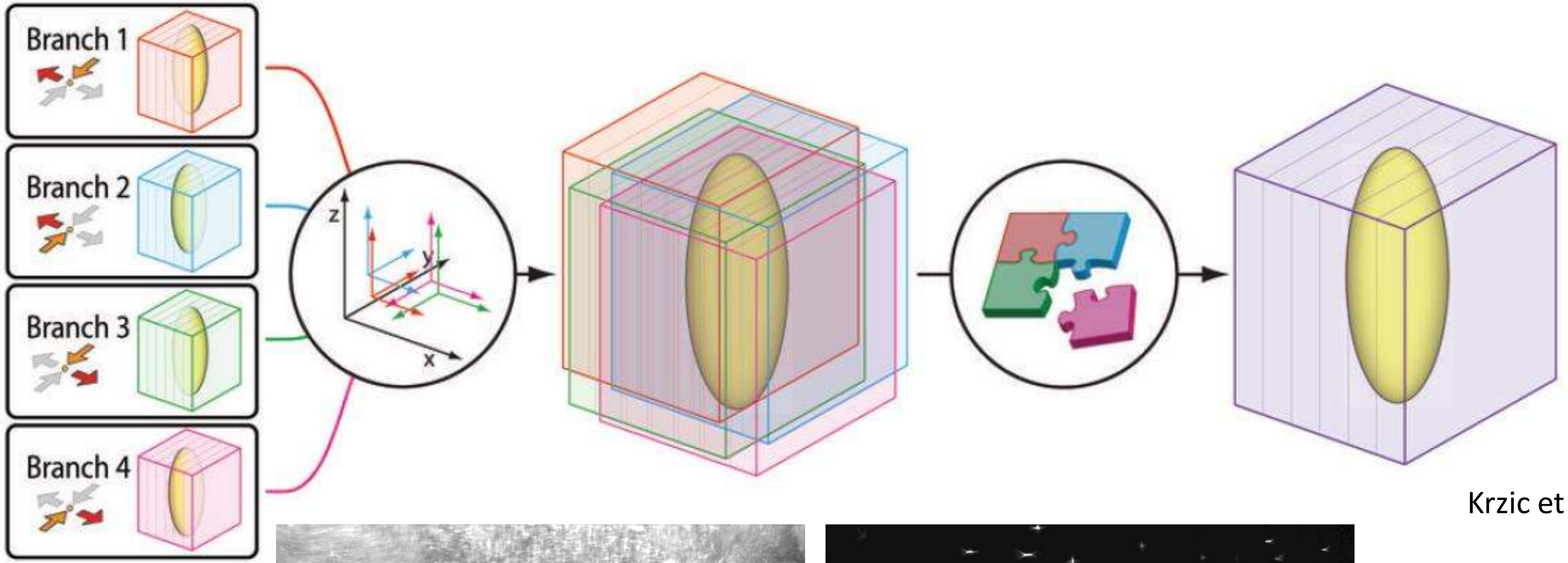
# 3D Samples: 3D confocal microscopy

FOV (X,Y,Z): 150*150*100um

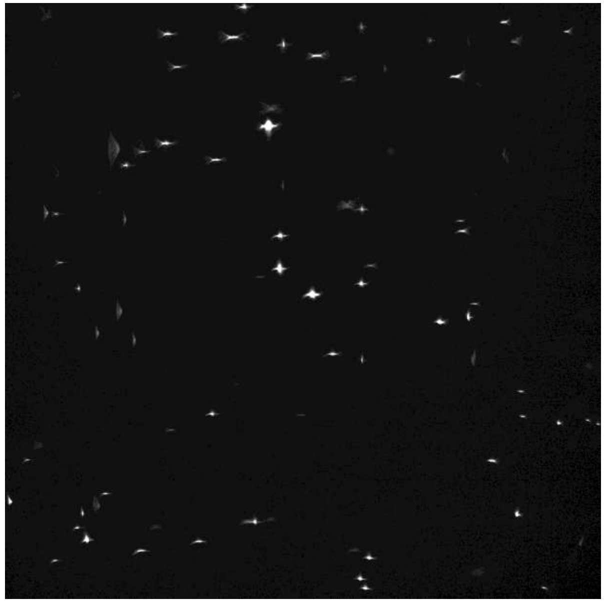


# Multi-view light-sheet microscopy (S. Streichan, UCSB)

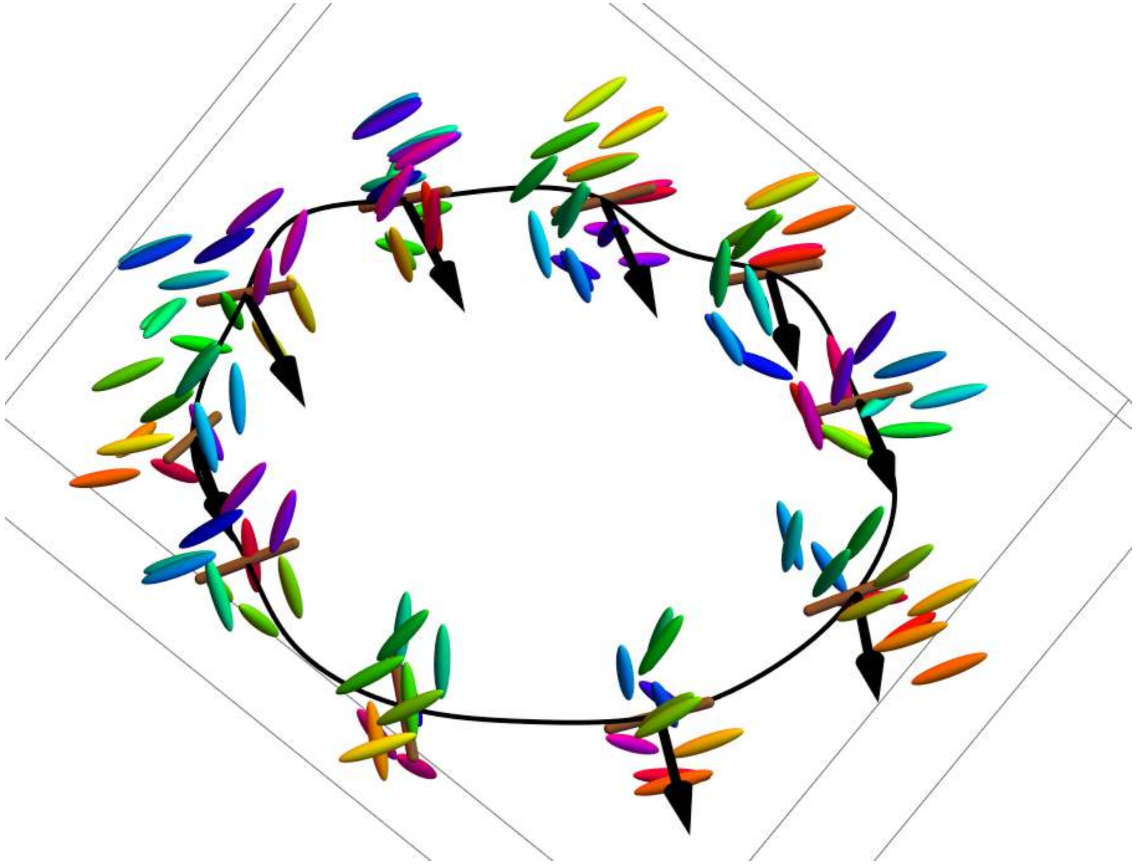


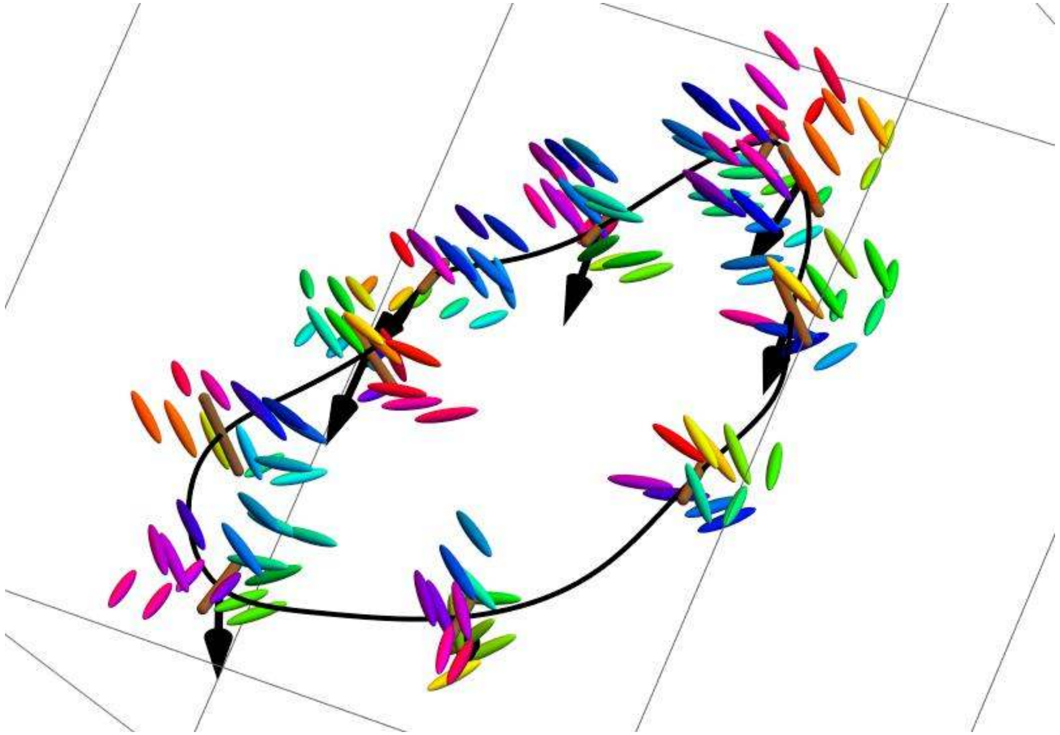

Krzic et al., Nat. Methods (2012)



200um

# Topological defects form loops in 3D

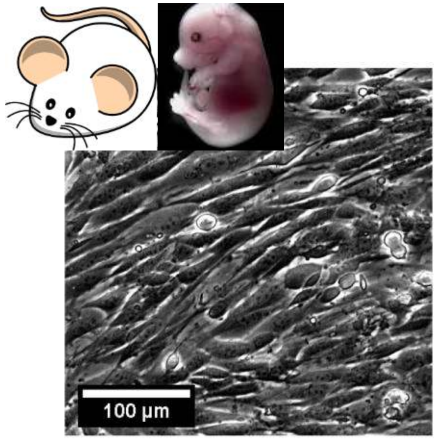




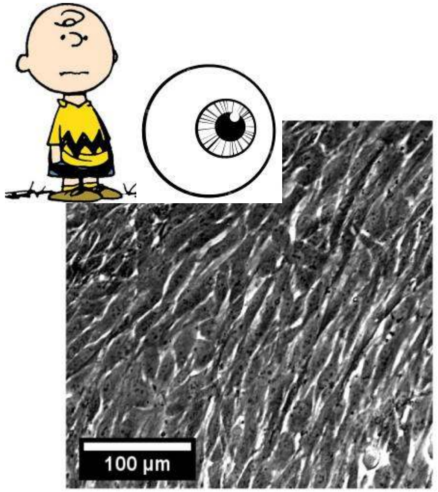
# Active cellular nematic suplement

# Active nematic Liquid crystals in biological materials

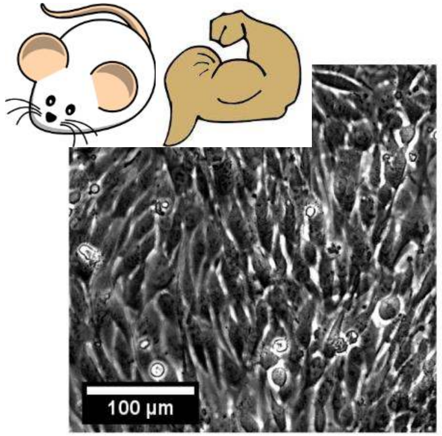





NIH-3T3

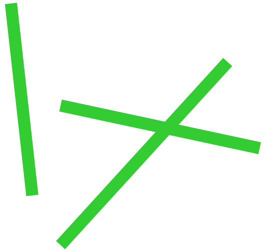



RPE1

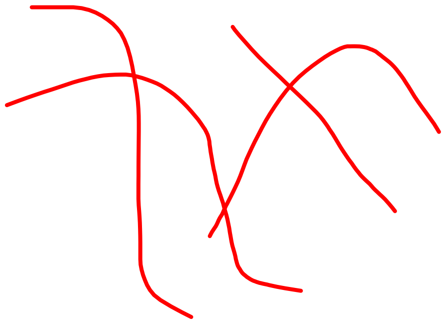



C2C12

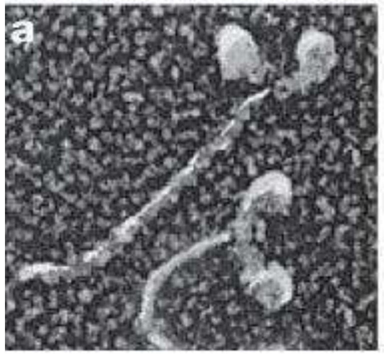
MT



Actin filaments



Molecular motors

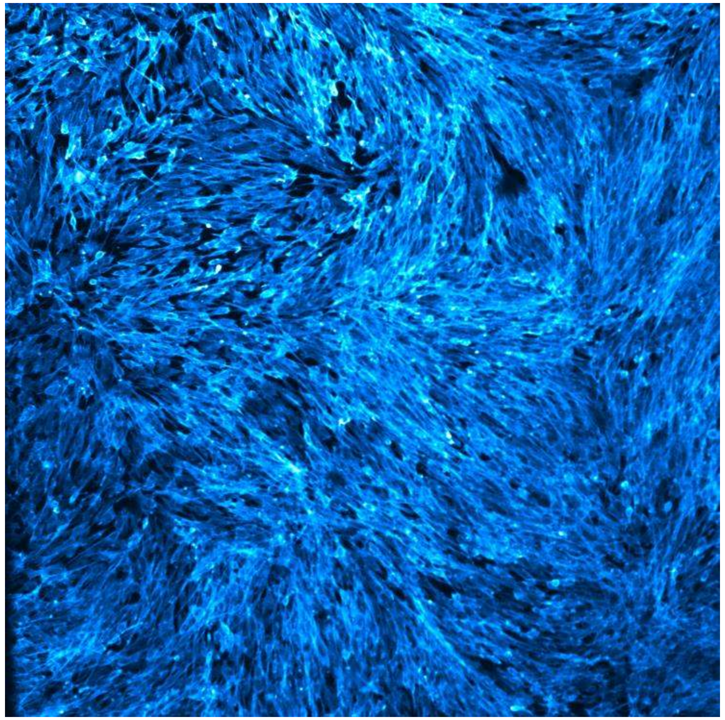



Schliwa and Woehlke, Nature 2003

DNA, membranes…

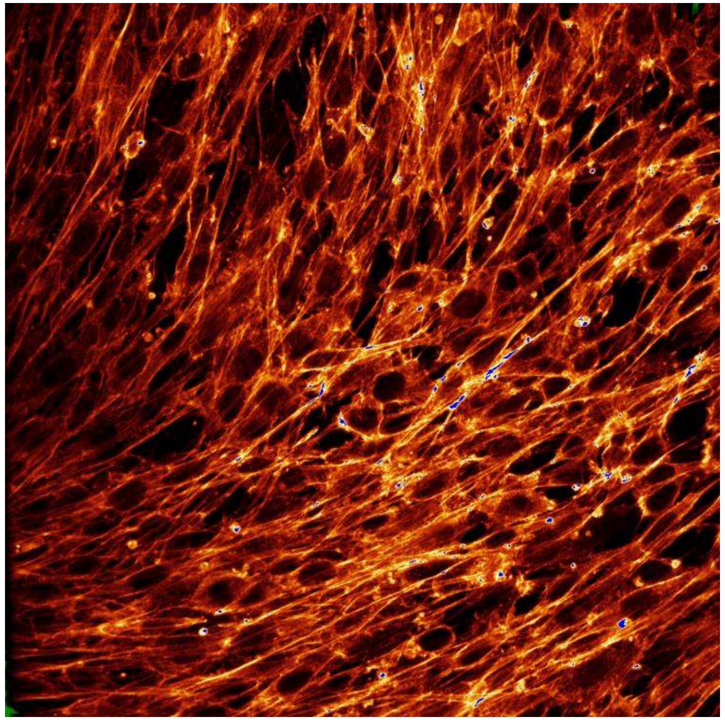
# Actin cytoskeleton at different magnification

10X



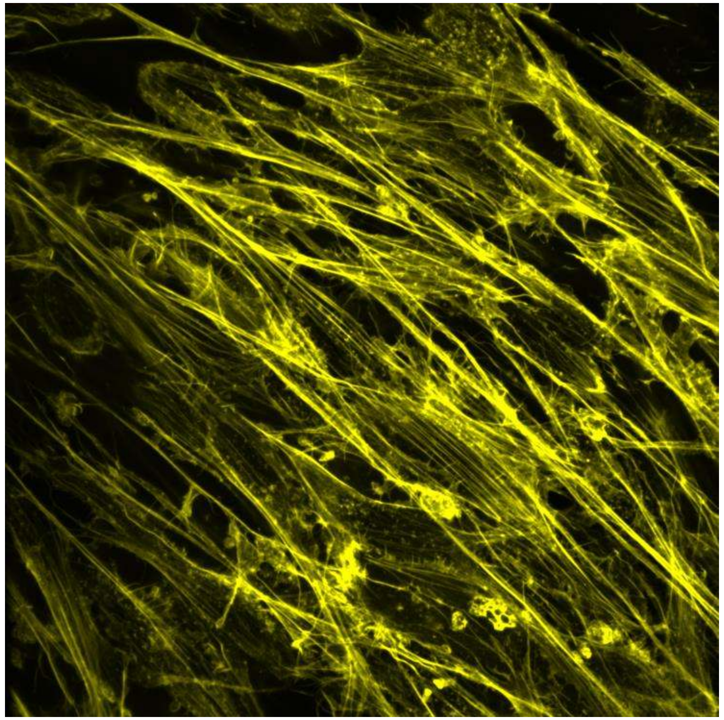
500 um

40X



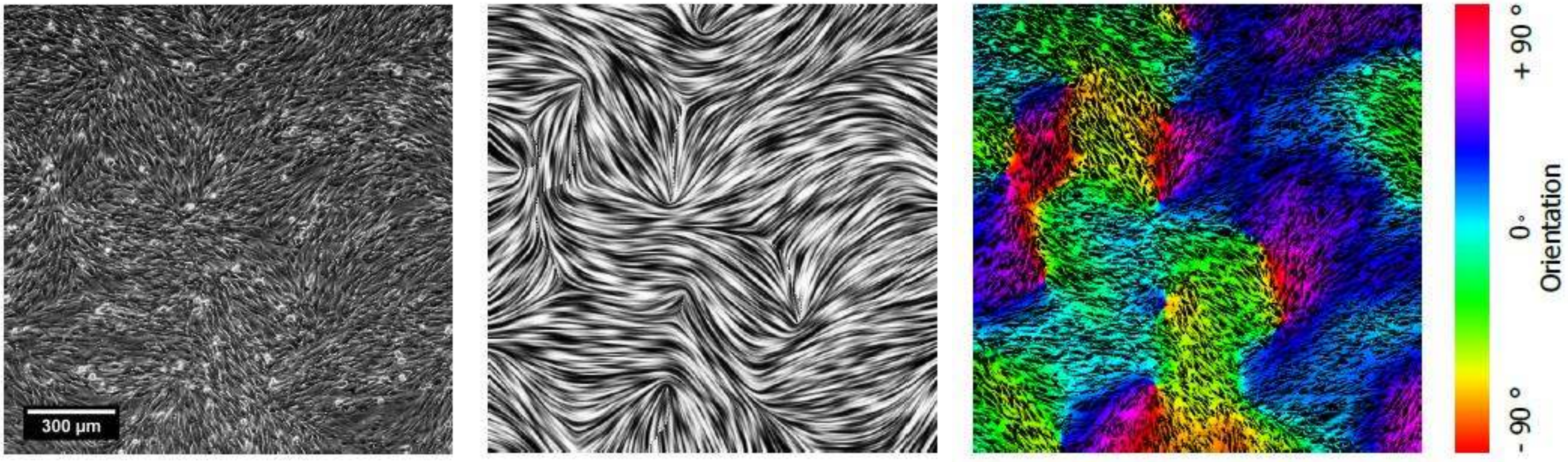
125 um

100X



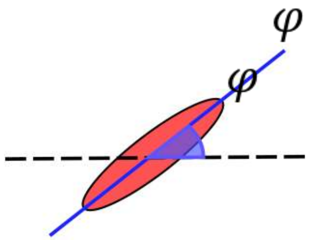
50 um

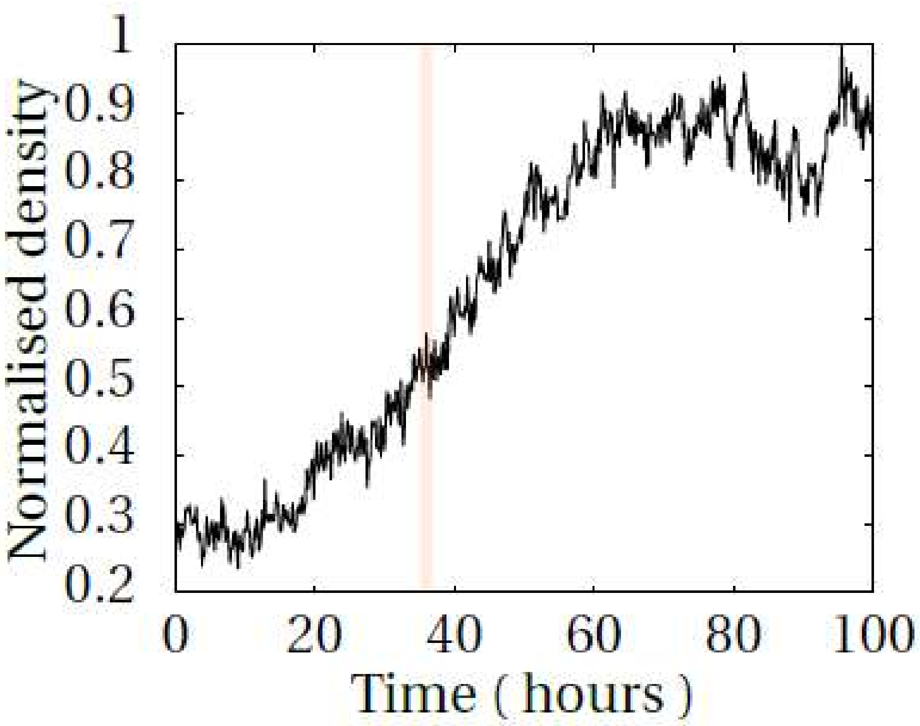
# Coarse-grained orientation field on a fibroblast monolayer

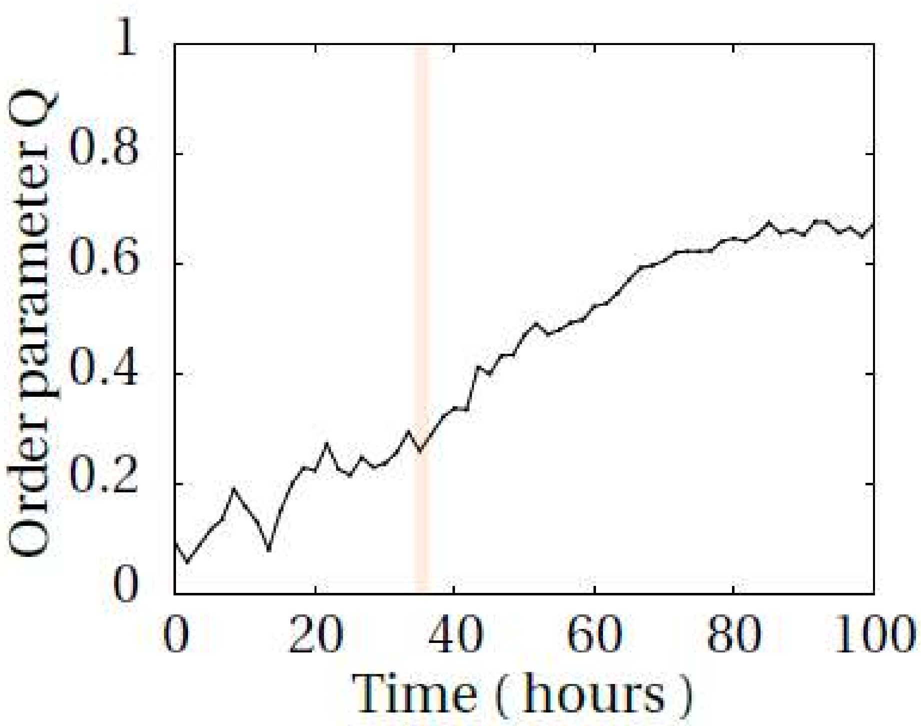


# Nematic order increases over time

$$Q = \sqrt{< \cos 2\varphi >^2 + < \sin 2\varphi >^2}$$



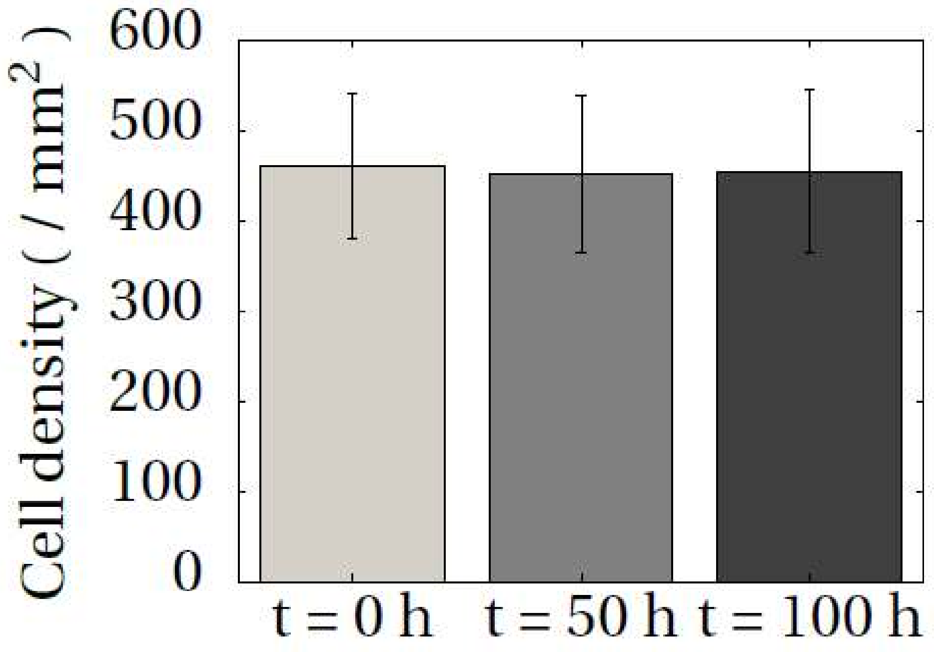



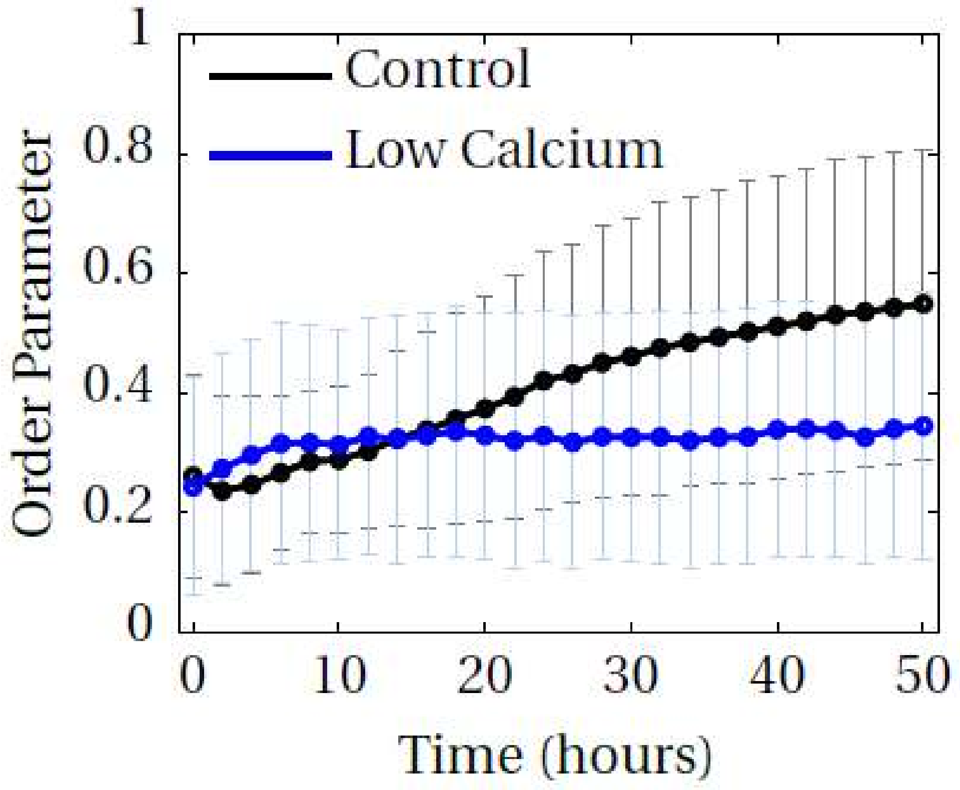




Duclos et al., Soft Matter 2014

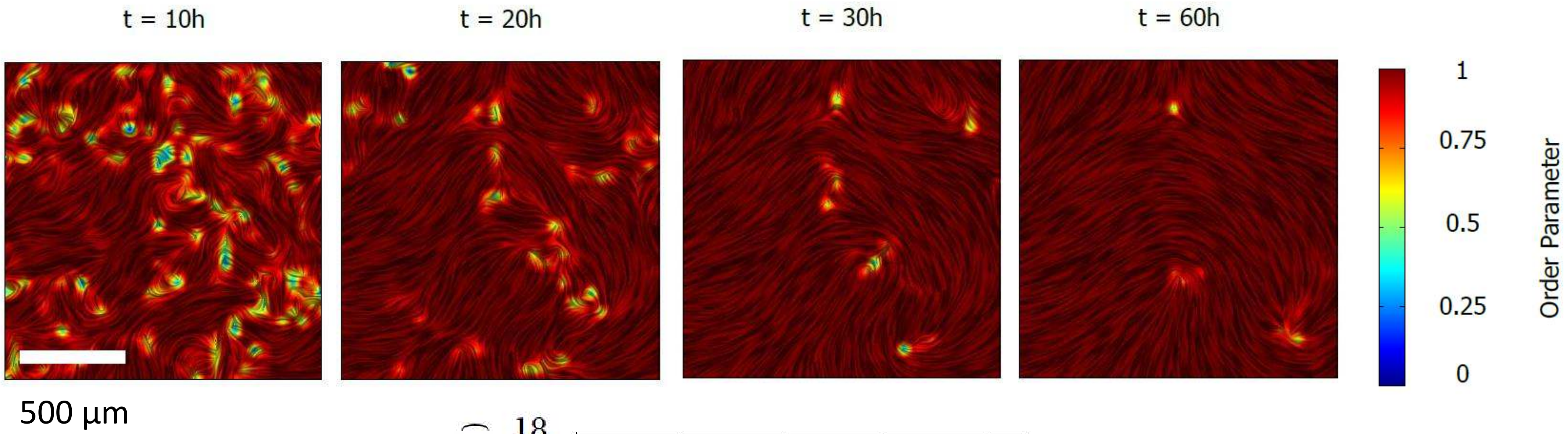
# Cell density increase drives an increase in nematic order

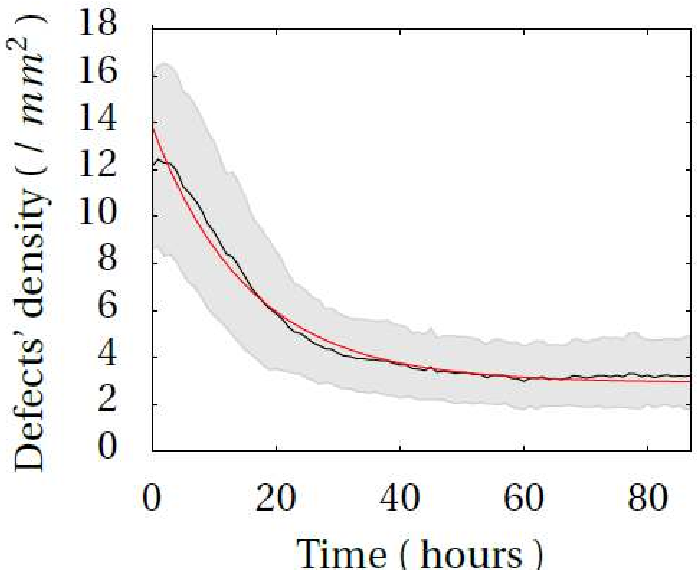
Inhibition of cell proliferation



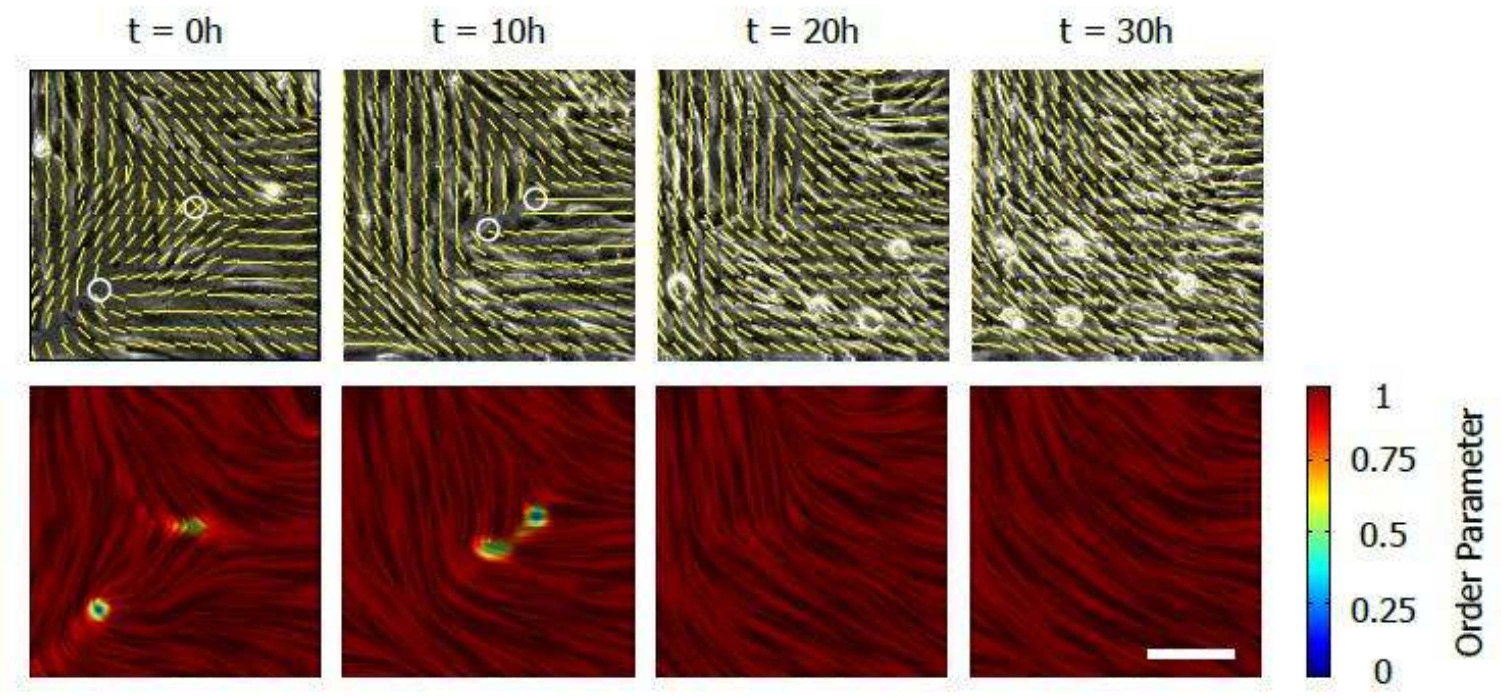
# Defect density decreases with time



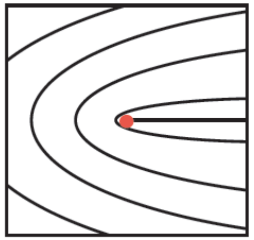



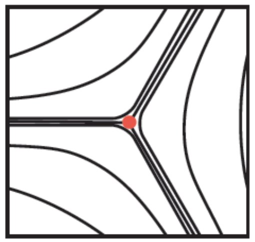

No defect creation !

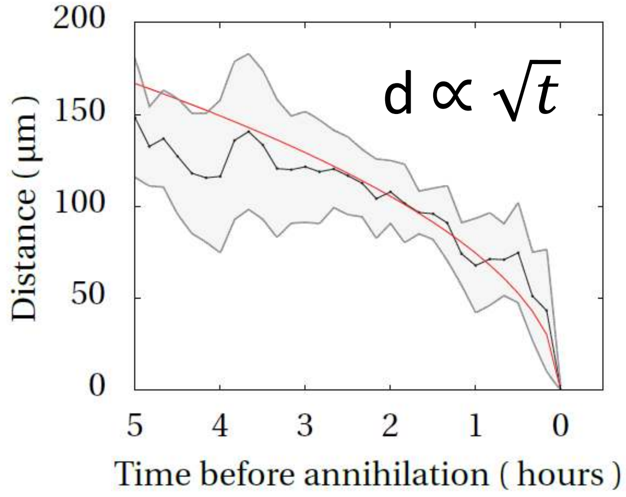
# Pairwise defects annihilation: topological attraction

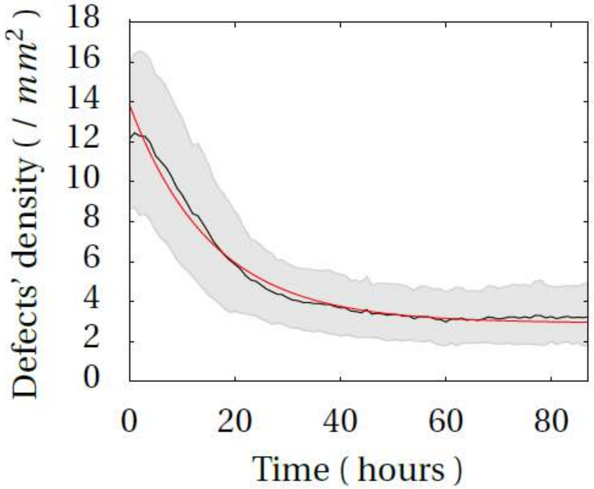



100 µm

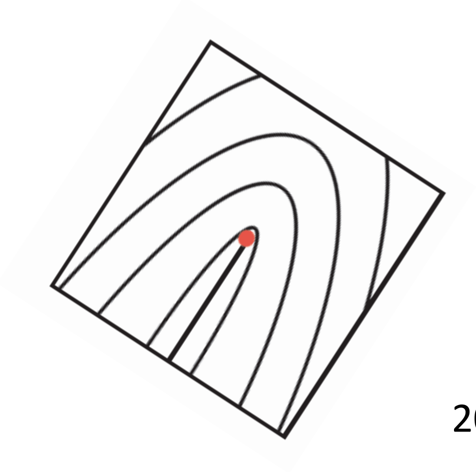


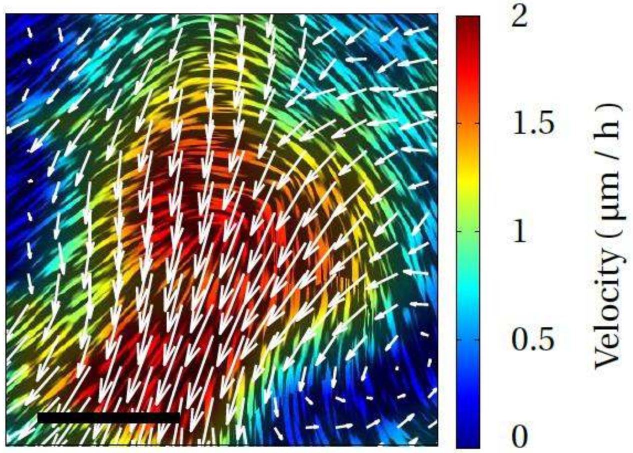



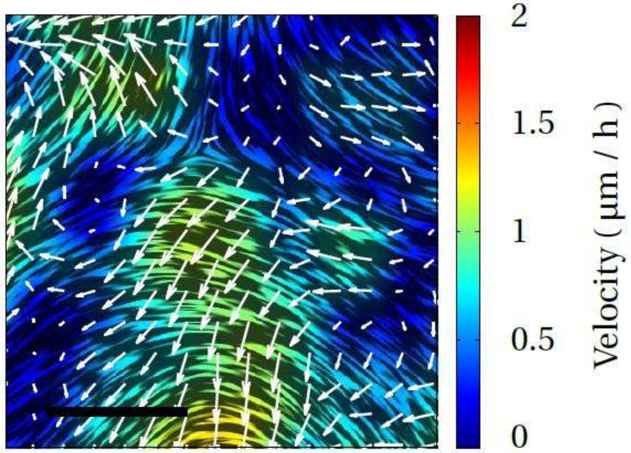
# Self-propulsion of +1/2 topological defects



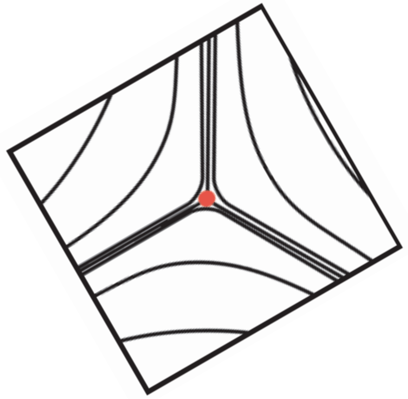
200 µm

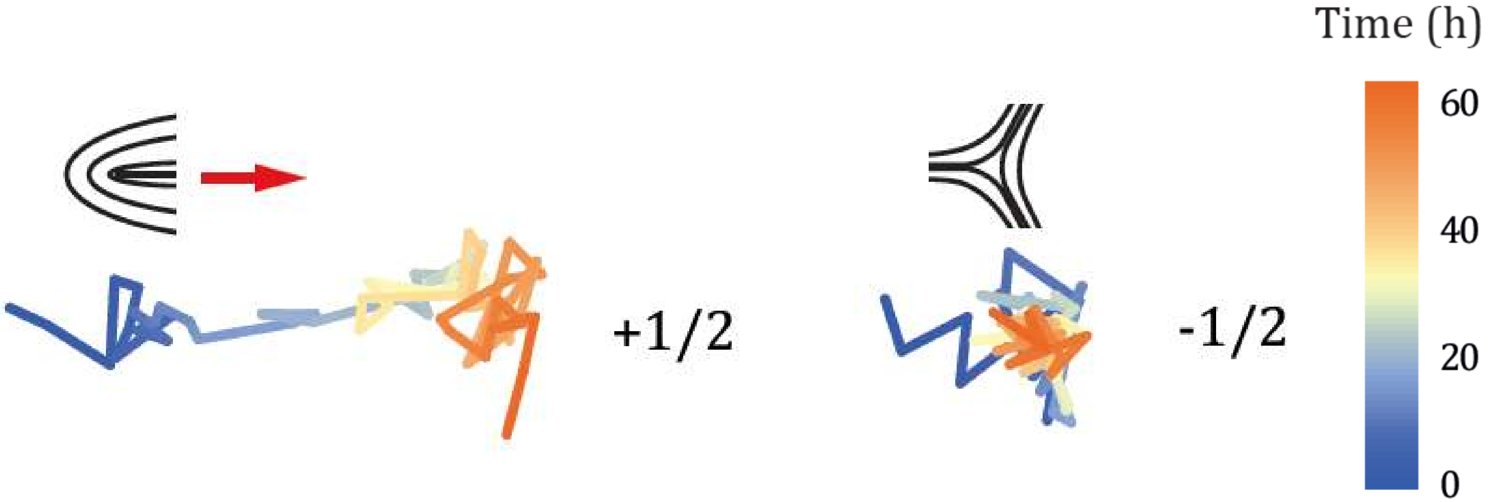



(a) s = +1/2 defects



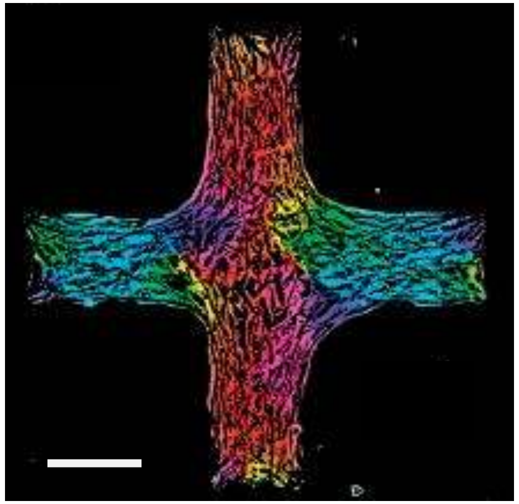

(b) s = -1/2 defects



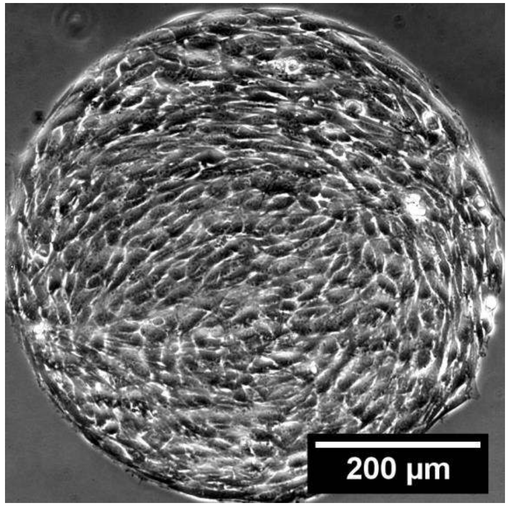


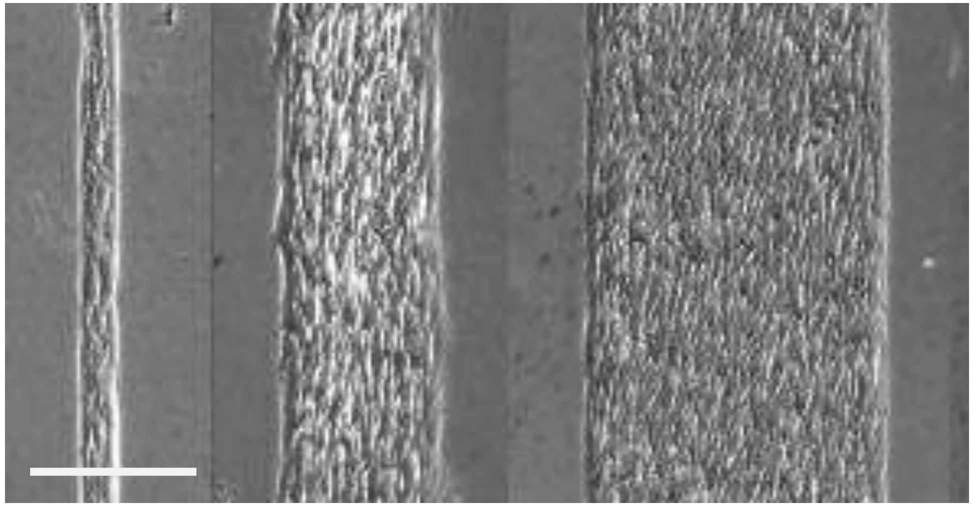

Contractile active nematics

# Topological confinement of active cellular nematics



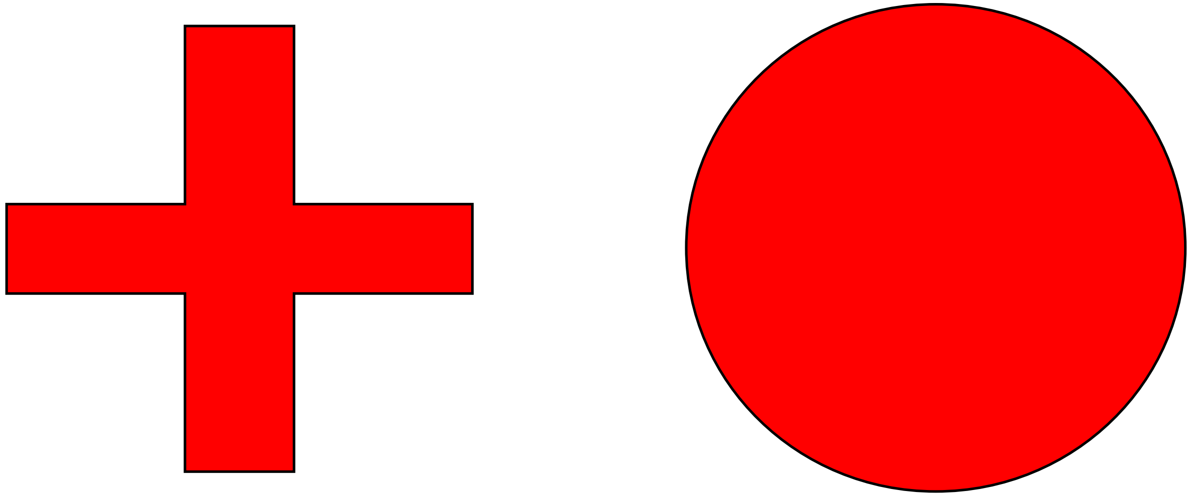
200 µm



200 µm

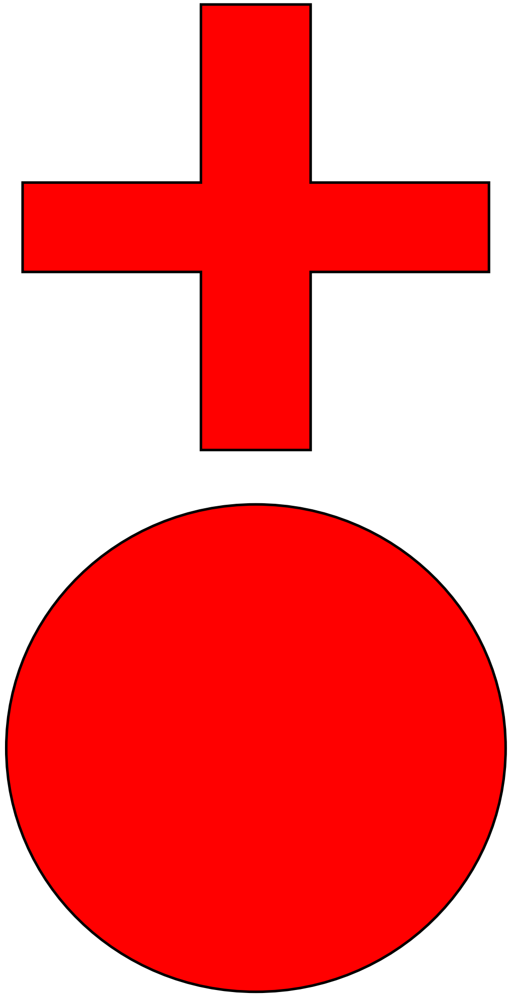
# Topological confinement of active cellular nematics

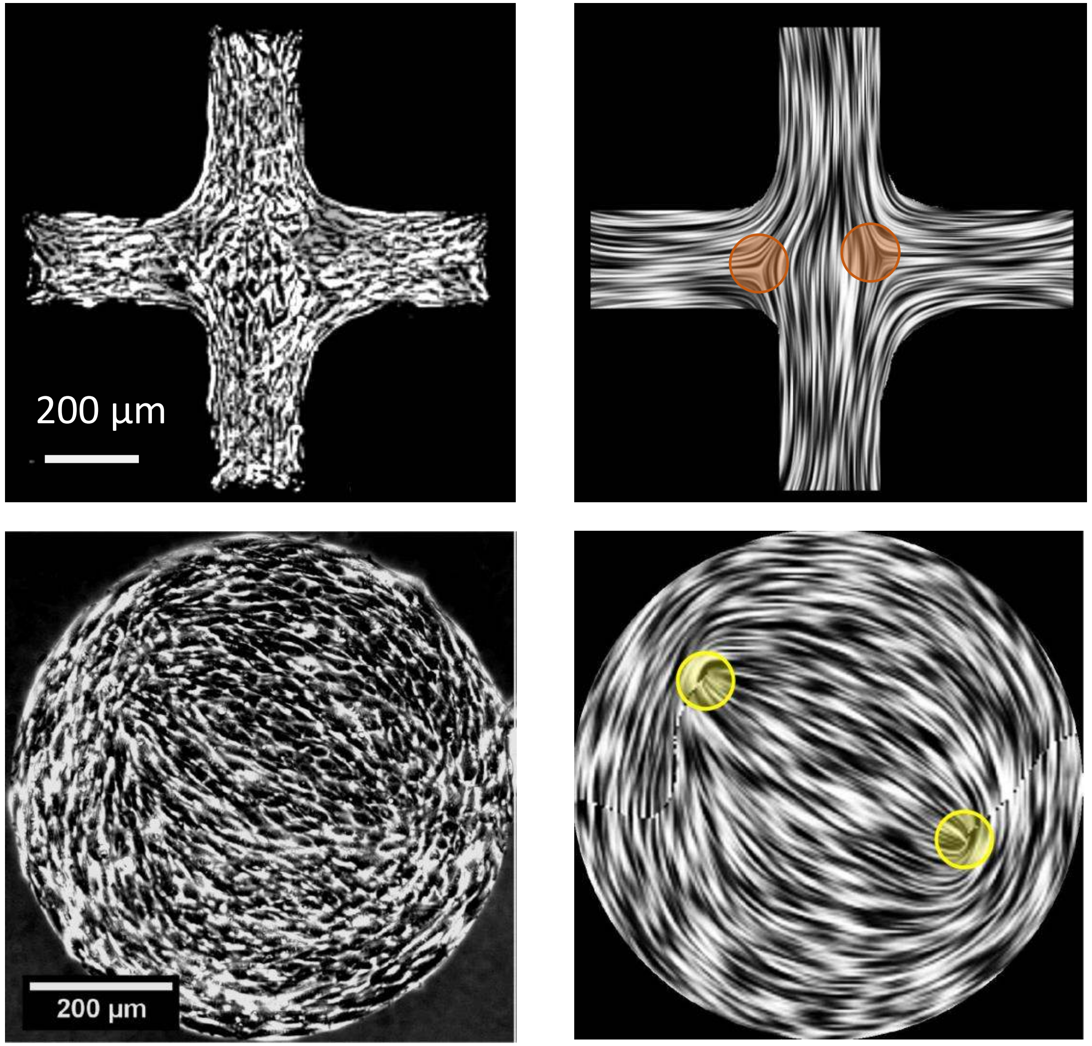


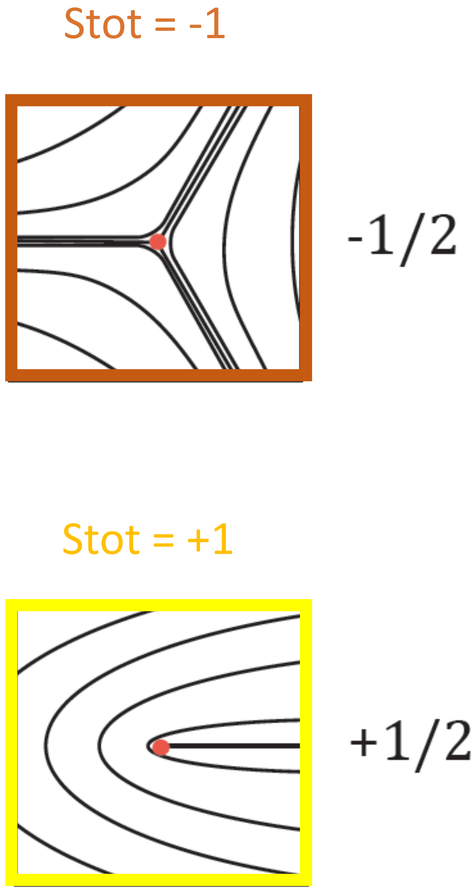
$S_{tot} = +1$

$S_{tot} = 0$

# Topological confinement of active cellular nematics

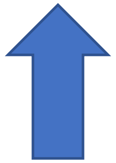




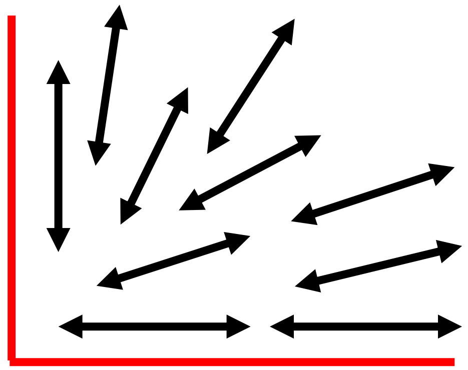




Duclos et al., Nat Phys 2017

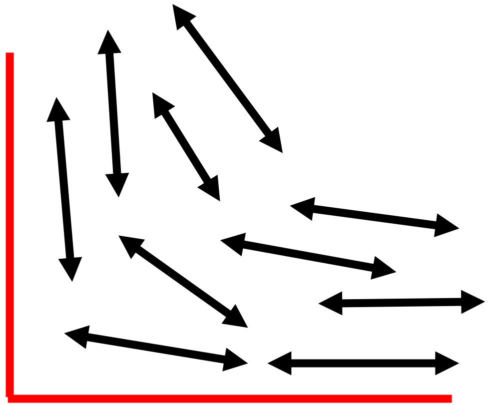
# Confinement in squares



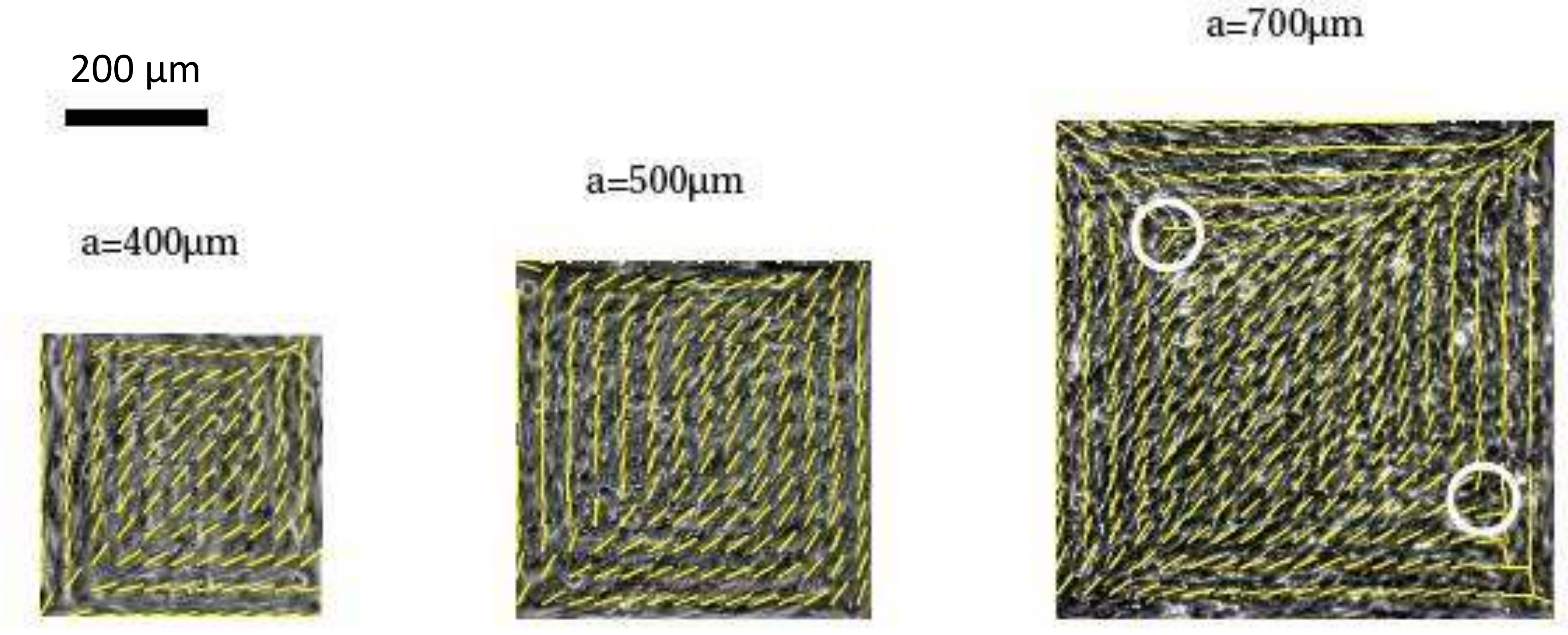
Splay corner

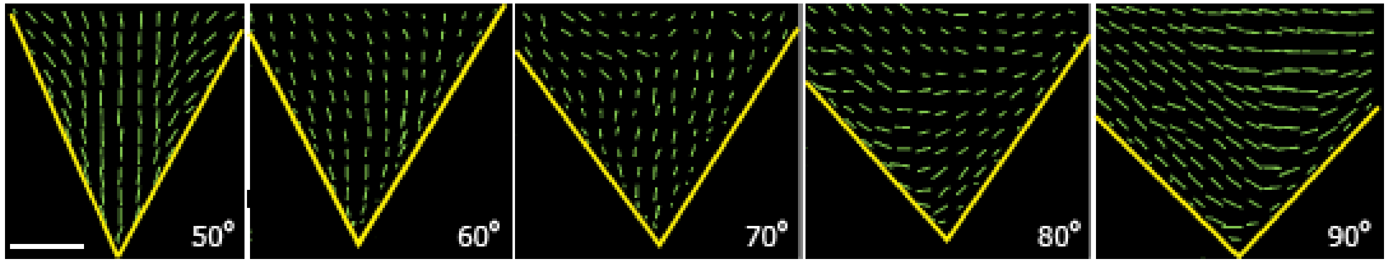


Bend corner



# Active nematic Liquid crystals in biological materials

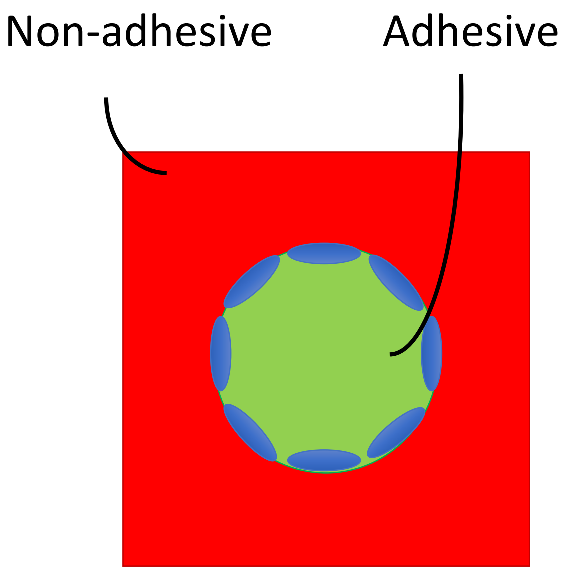


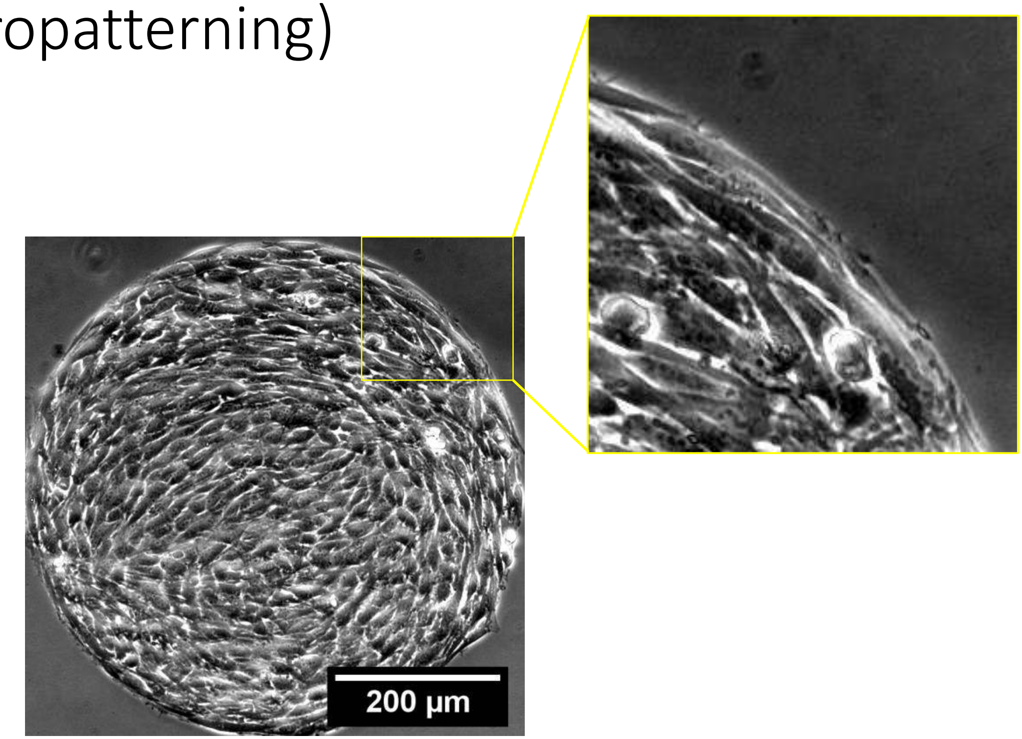

Dammone et al, PRL, 2012

# Confinement in disks (micropatterning)

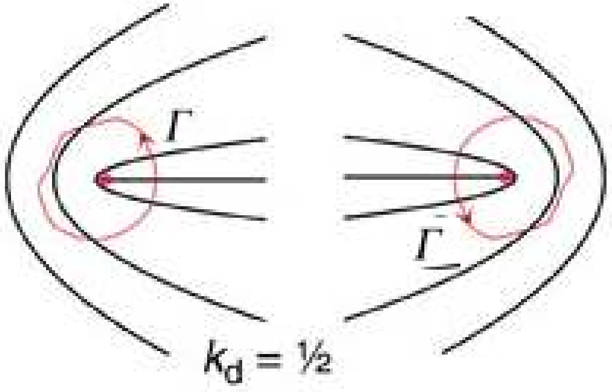
R = 250 µm – 400 µm



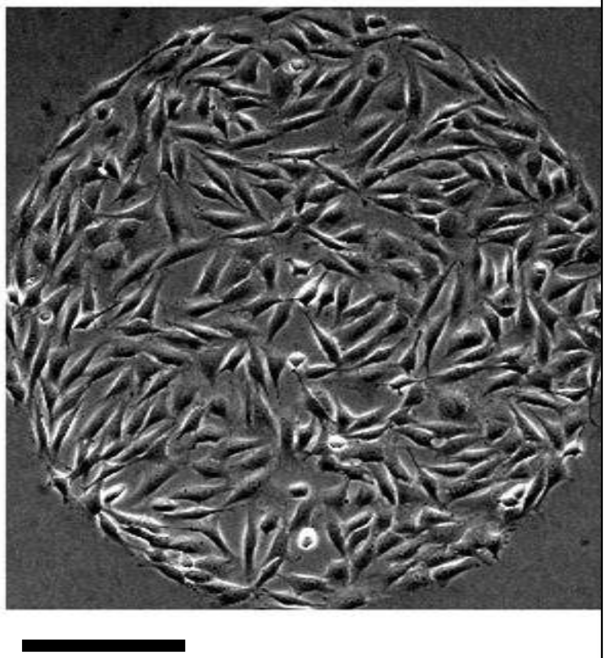

Total charge = +1



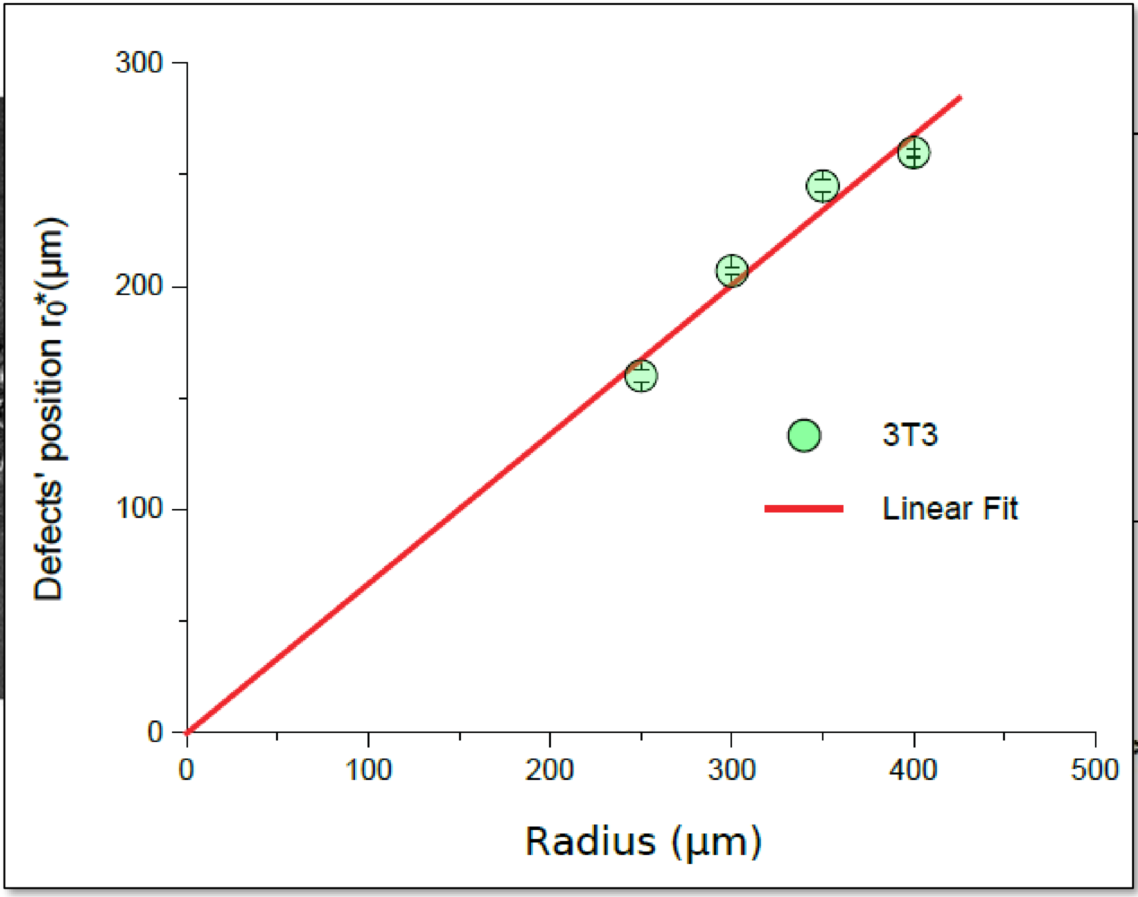

+1 defect instable
Two +1/2 defects

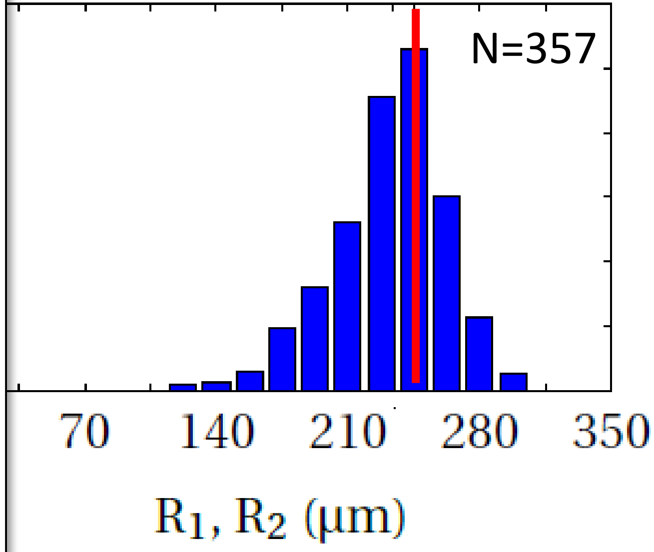


# Topological confinement of active cellular nematics



200 µm



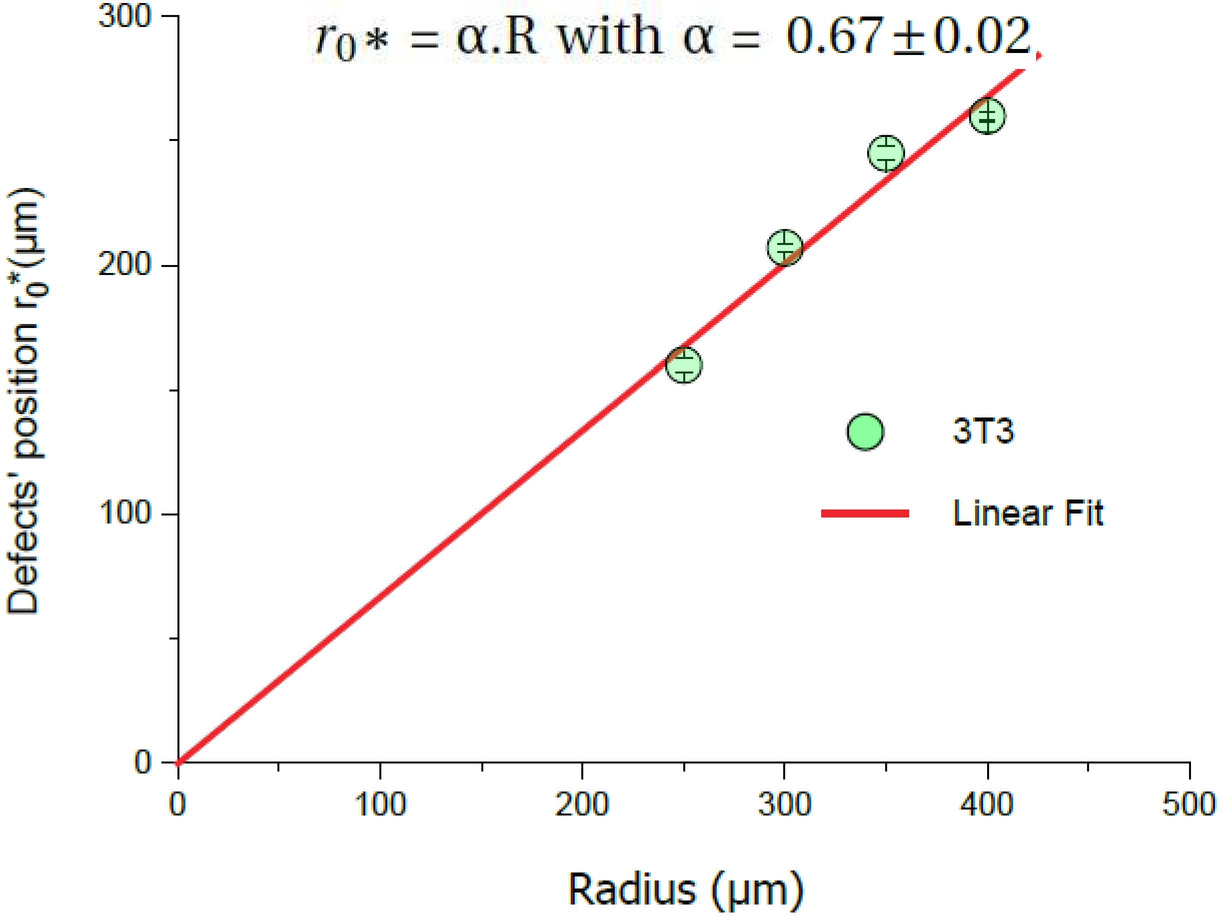




$* = \alpha.R$ with $\alpha = 0.67 \pm 0.02$

Duclos et al., Nat Phys 2017

# Topological confinement of active cellular nematics

**$r_0$***, the defects' radial position scales with **R**, the disk radius




Independant of:

- Cell contractility
- Cell type

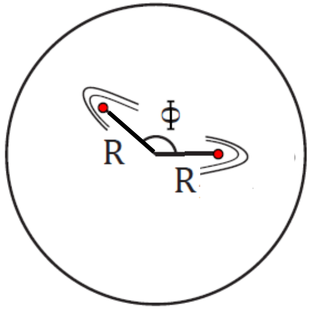
# Theoretical model (Christoph Erlenkaemper, Jean-François Joanny)

**Hypothesis:**

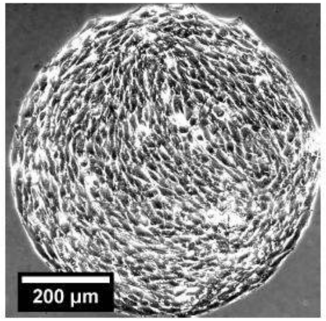
Parallel alignment at the edges
$K_1 = K_3 = K$
No active stress

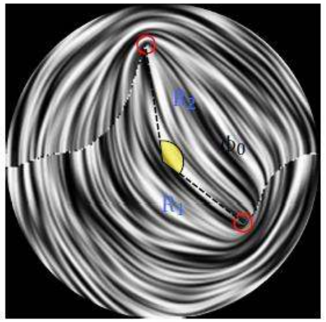
**2 degrees of freedom**

R and Φ
(Defect position uncorrelated)

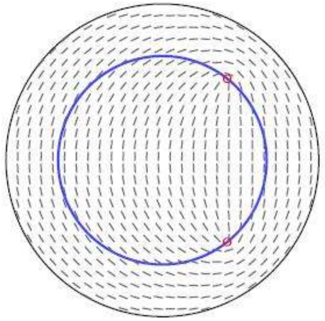


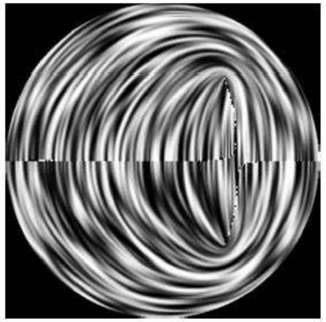

Experimental data



Model



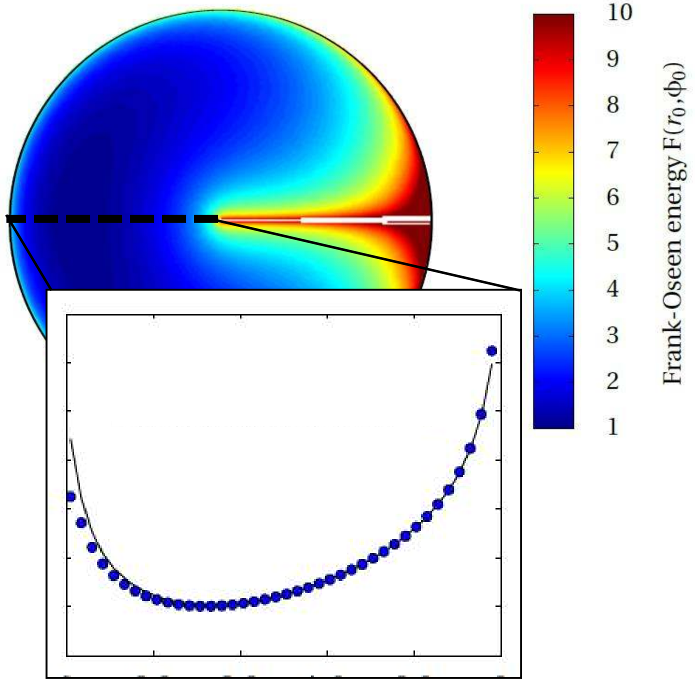


# Nematic drop model

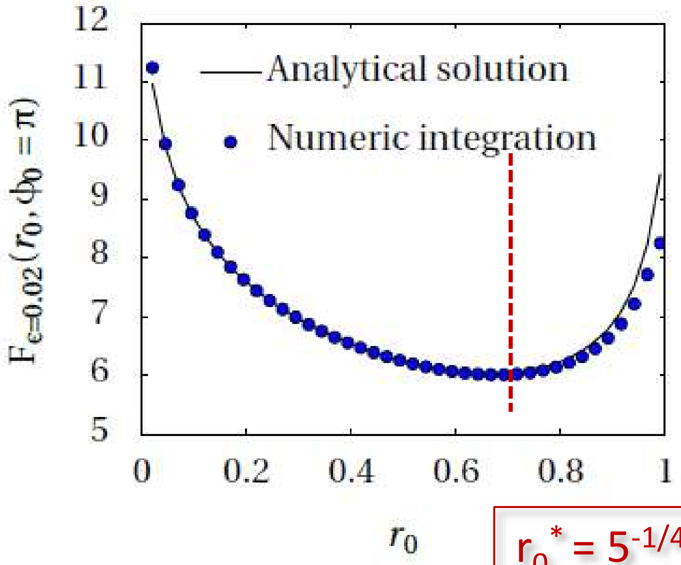
## Frank-Oseen free energy

$$F(r_0, \phi_0) = \frac{K}{2} \int_{\Omega} (\nabla \vec{n})^2 dS$$

2D Energy map (polar)

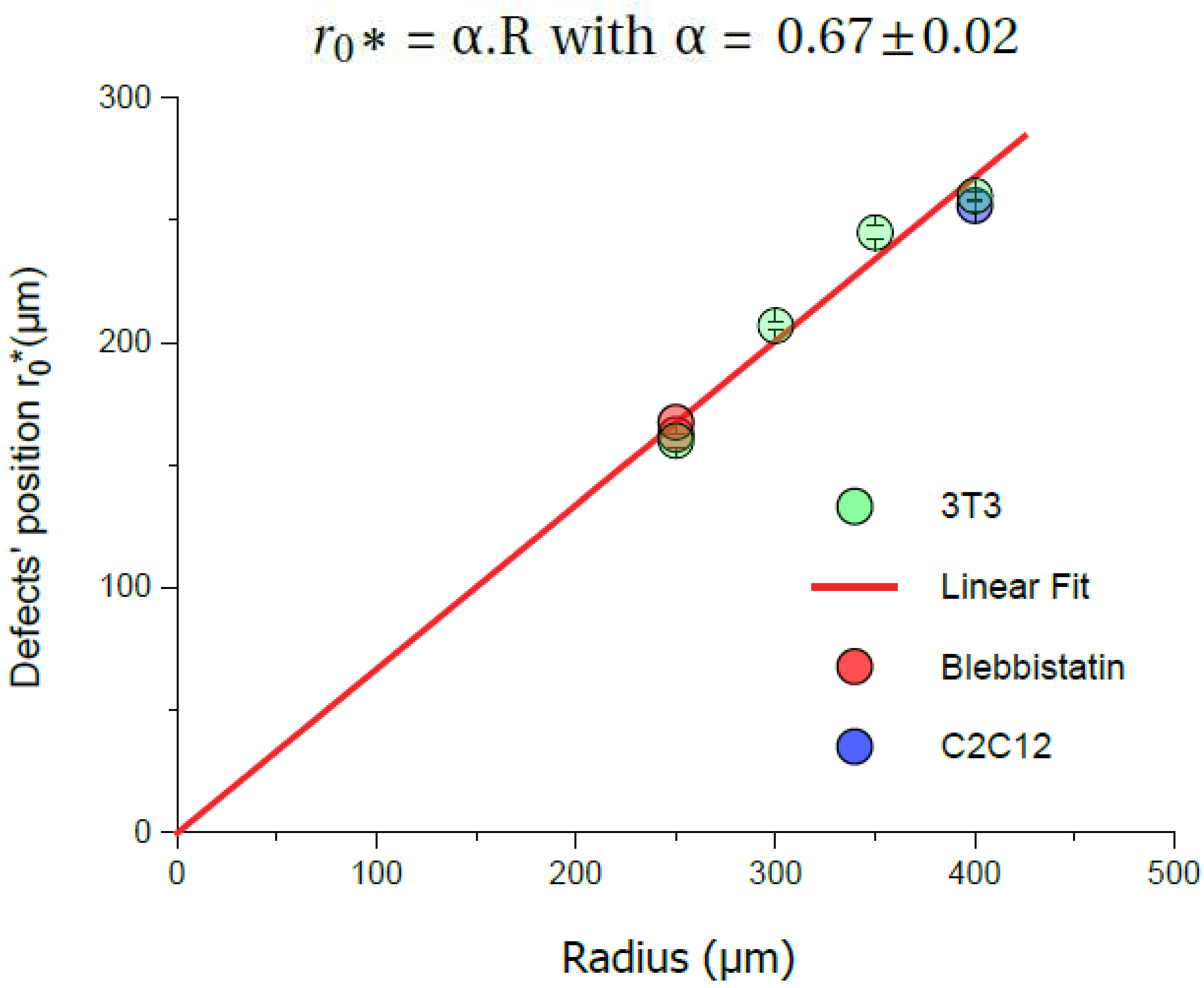



1D Energy map (Φ=π)




$r_0^* = 5^{-1/4} \approx 0{,}67 * R$

# $r_0$*, the defects' radial position scales with **R**, the disk radius



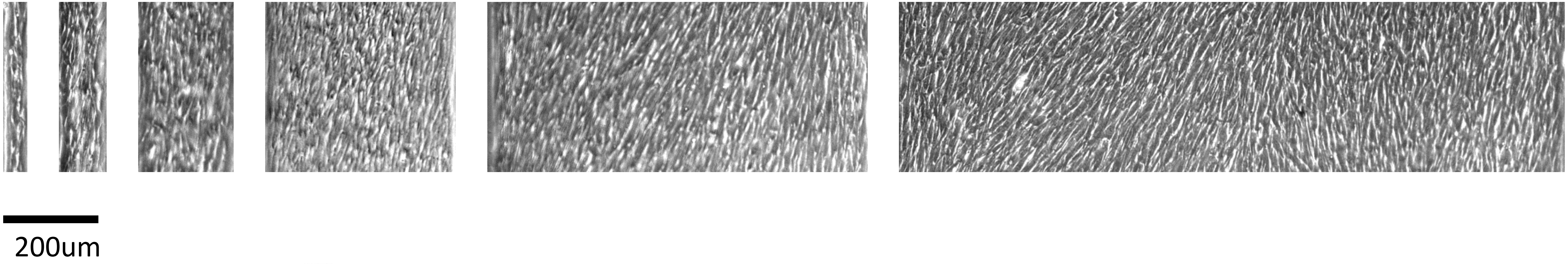

$\alpha_{theory} = 5^{-1/4} \approx 0.67$

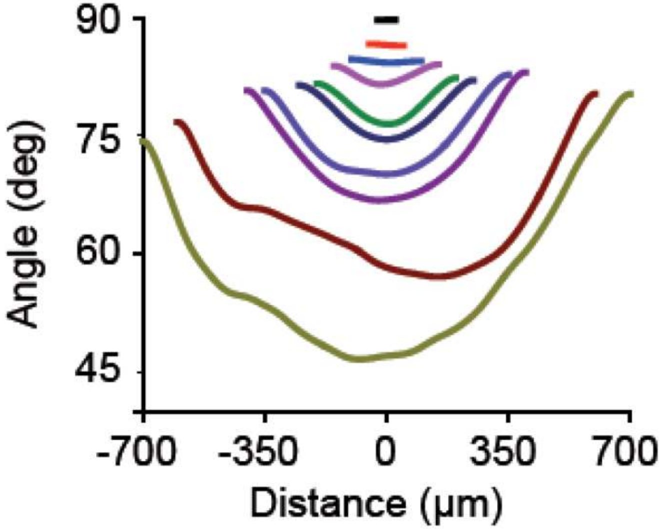
$\alpha_{exp} = 0.67 \pm 0.02$

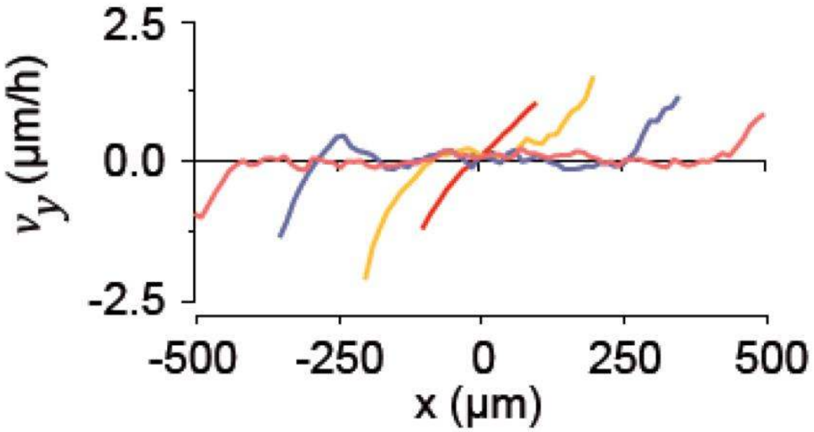
Independant of:

- Activity
- Nematic elasticity K

# Topological confinement of active cellular nematics ( L > 50 um )

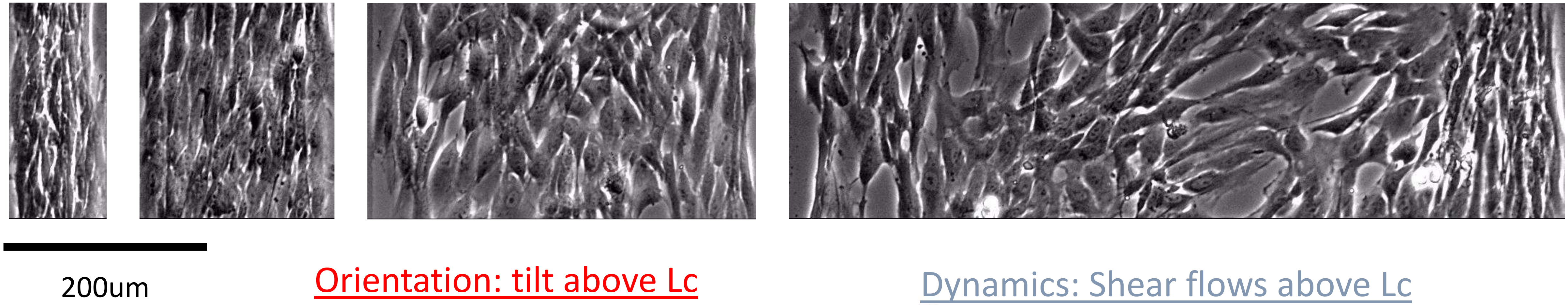


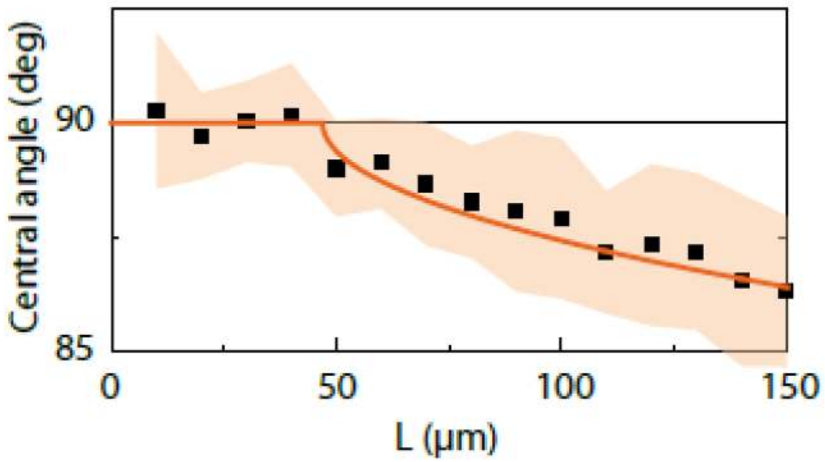




Duclos et al., in review

# Topological confinement of active cellular nematics ( L > 50 um )




## Orientation: tilt above Lc




## Dynamics: Shear flows above Lc