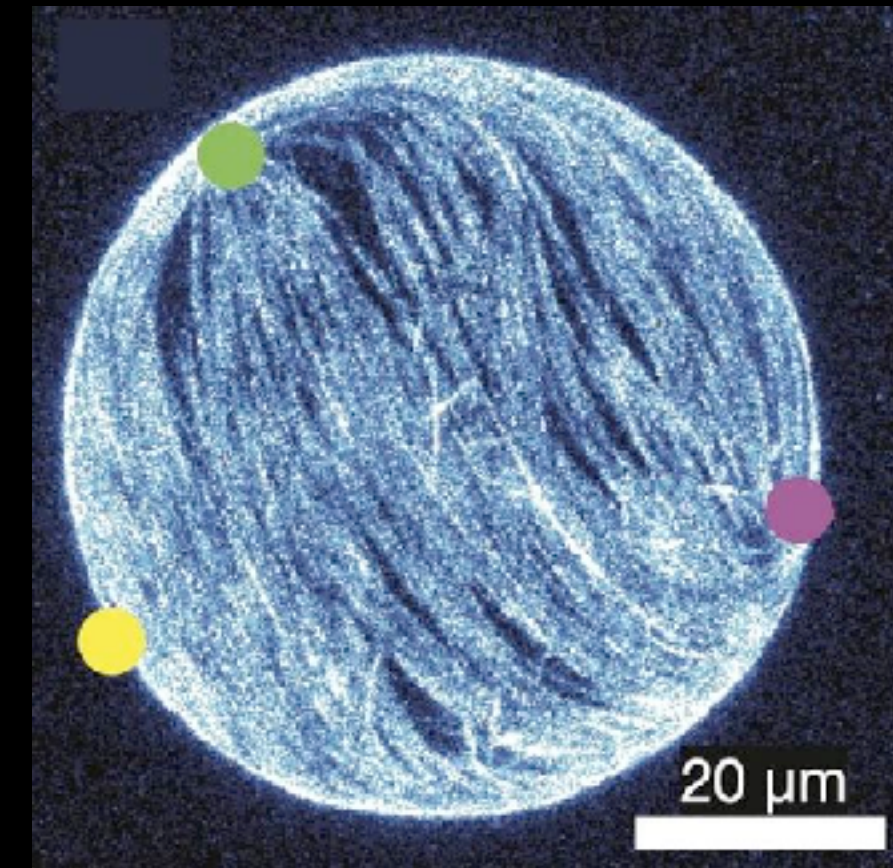
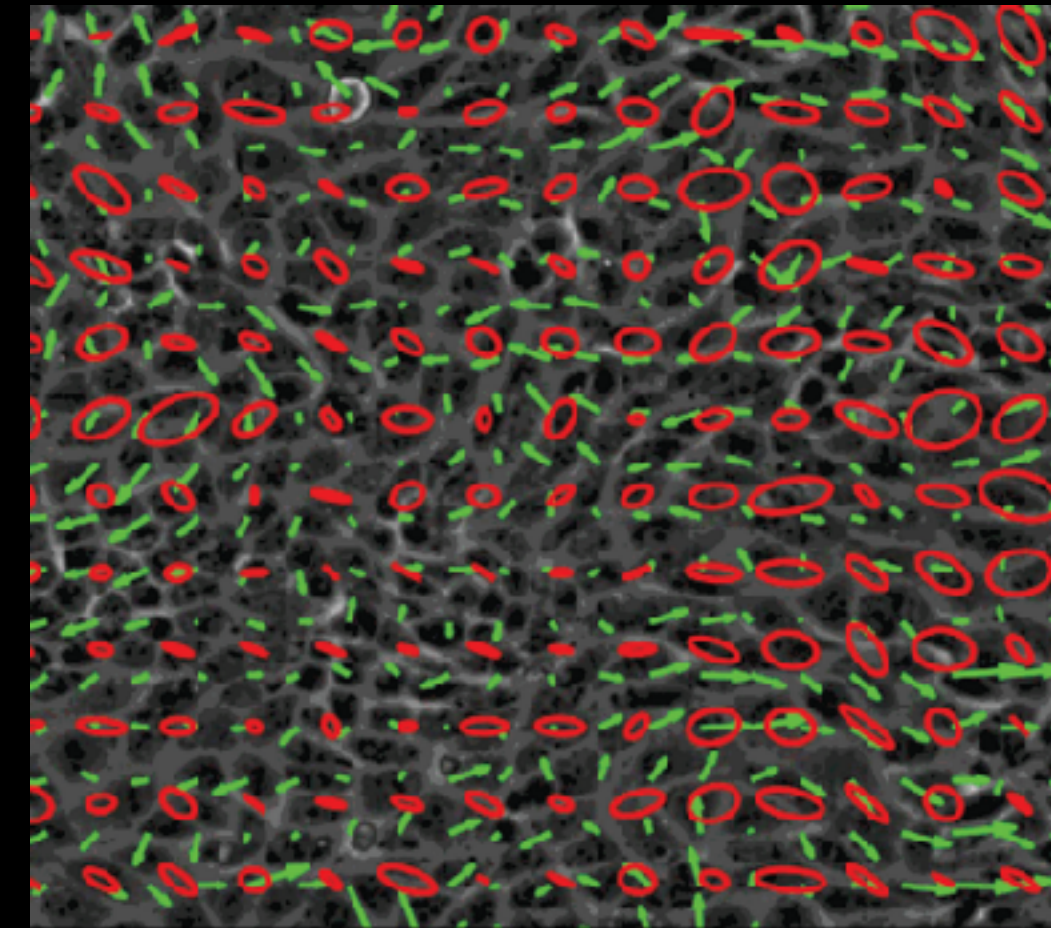
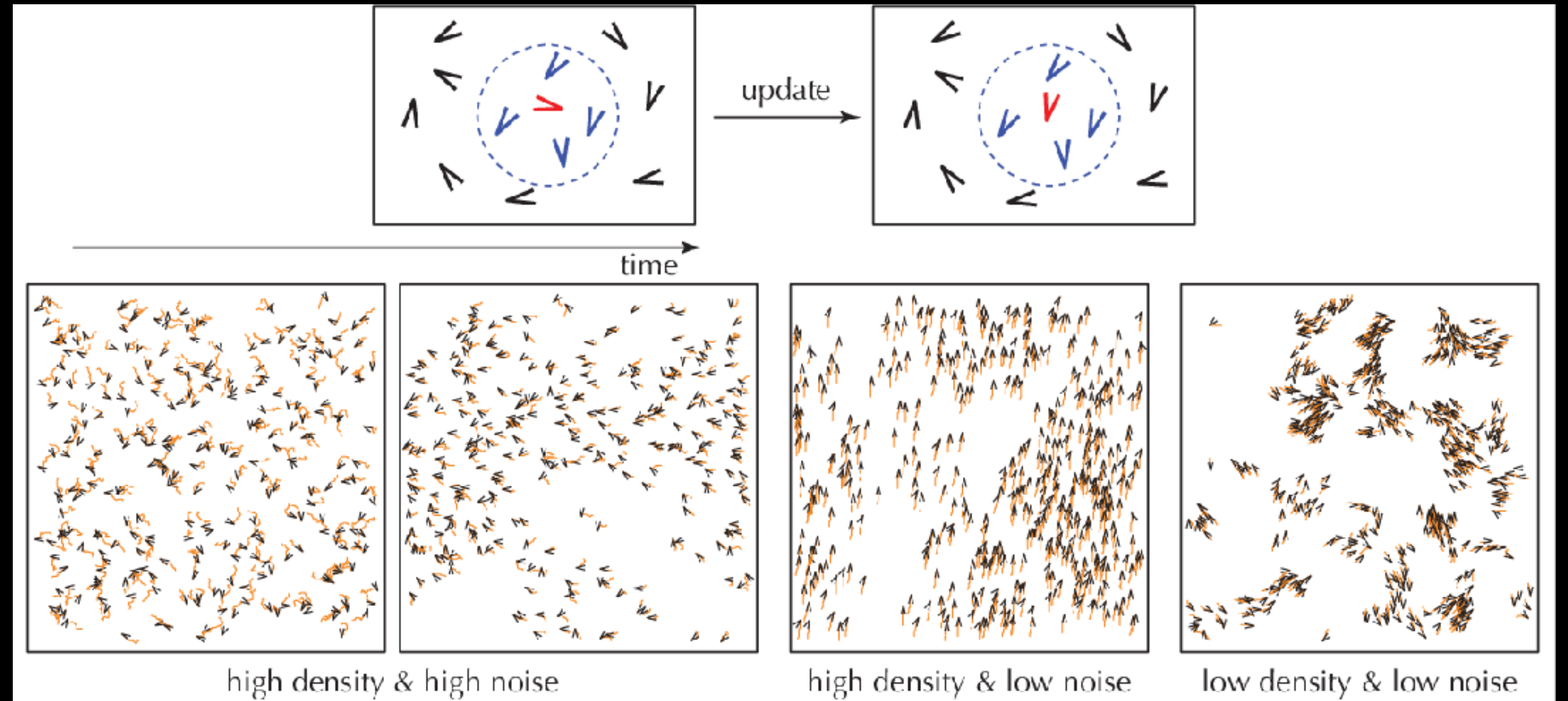


# Biological active matter



# Flocking

## Vicsek model



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

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

$$v_a = \frac{1}{Nv} \left| \sum_{i=1}^N \mathbf{v}_i \right|$$

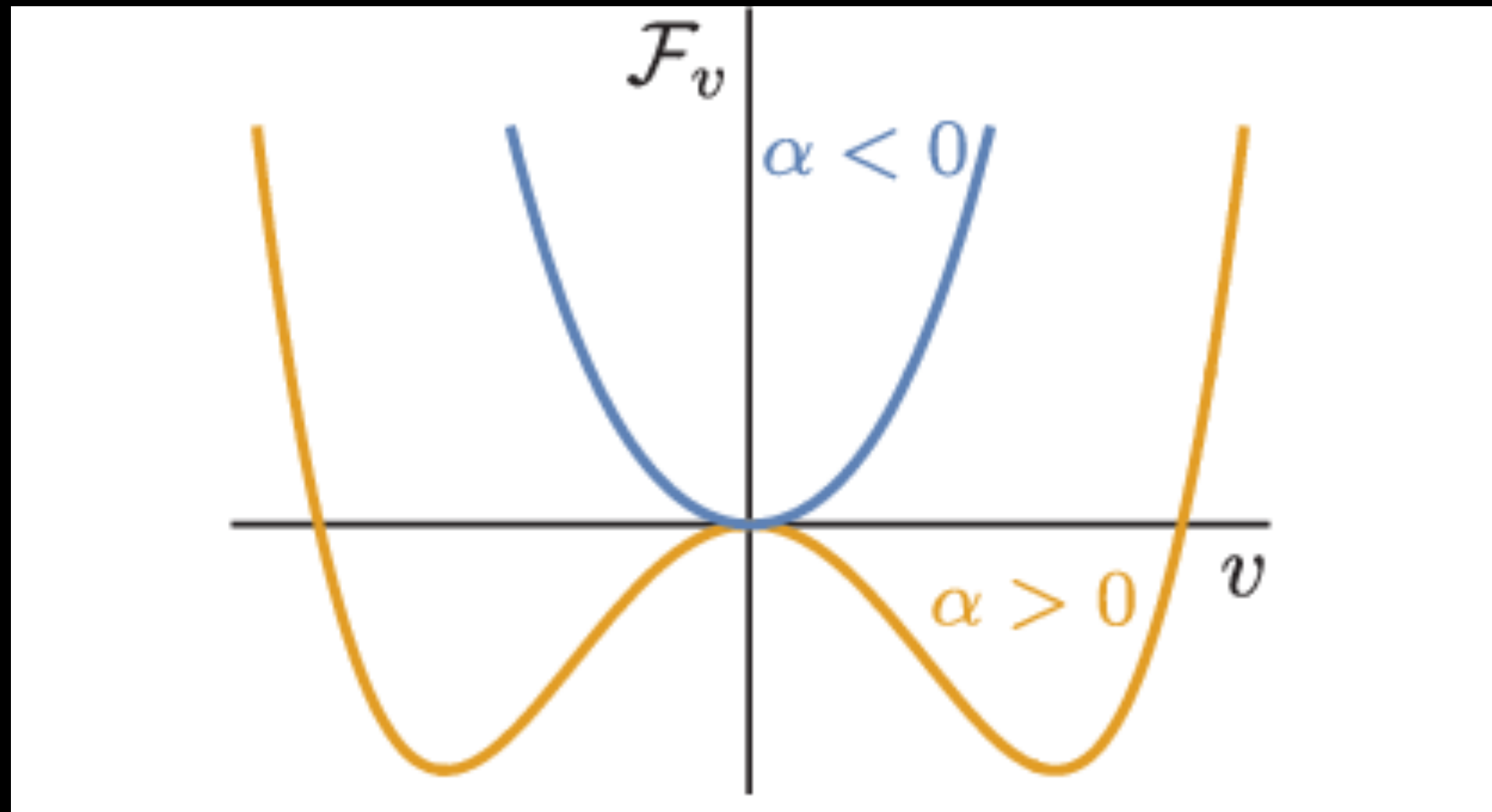
Velocity is the  
Order parameter

Vicsek et al *Phys. Rev. Lett* 1995

Simulation: [https://youtu.be/L0\\_sRESiPjY](https://youtu.be/L0_sRESiPjY)

# Toner-Tu theory

## Hydrodynamic/continuum theory



$$\mathcal{F}_v = -\frac{1}{2}\alpha|\vec{v}|^2 + \frac{1}{4}\beta|\vec{v}|^4$$

$$\partial_t \rho + \vec{\nabla} \cdot (\rho \vec{v}) = 0 \quad \text{Continuity equation for density of particles}$$

$$\partial_t \vec{v} + \lambda_1 (\vec{v} \cdot \vec{\nabla}) \vec{v} = -\vec{\nabla} P + \eta \nabla^2 \vec{v} + \alpha \vec{v} - \beta |\vec{v}|^2 \vec{v}$$

N-S terms with  $\lambda$  a phenomenological parameter  
P the pressure  
 $\eta$  the viscosity originating from noise term in Viscek

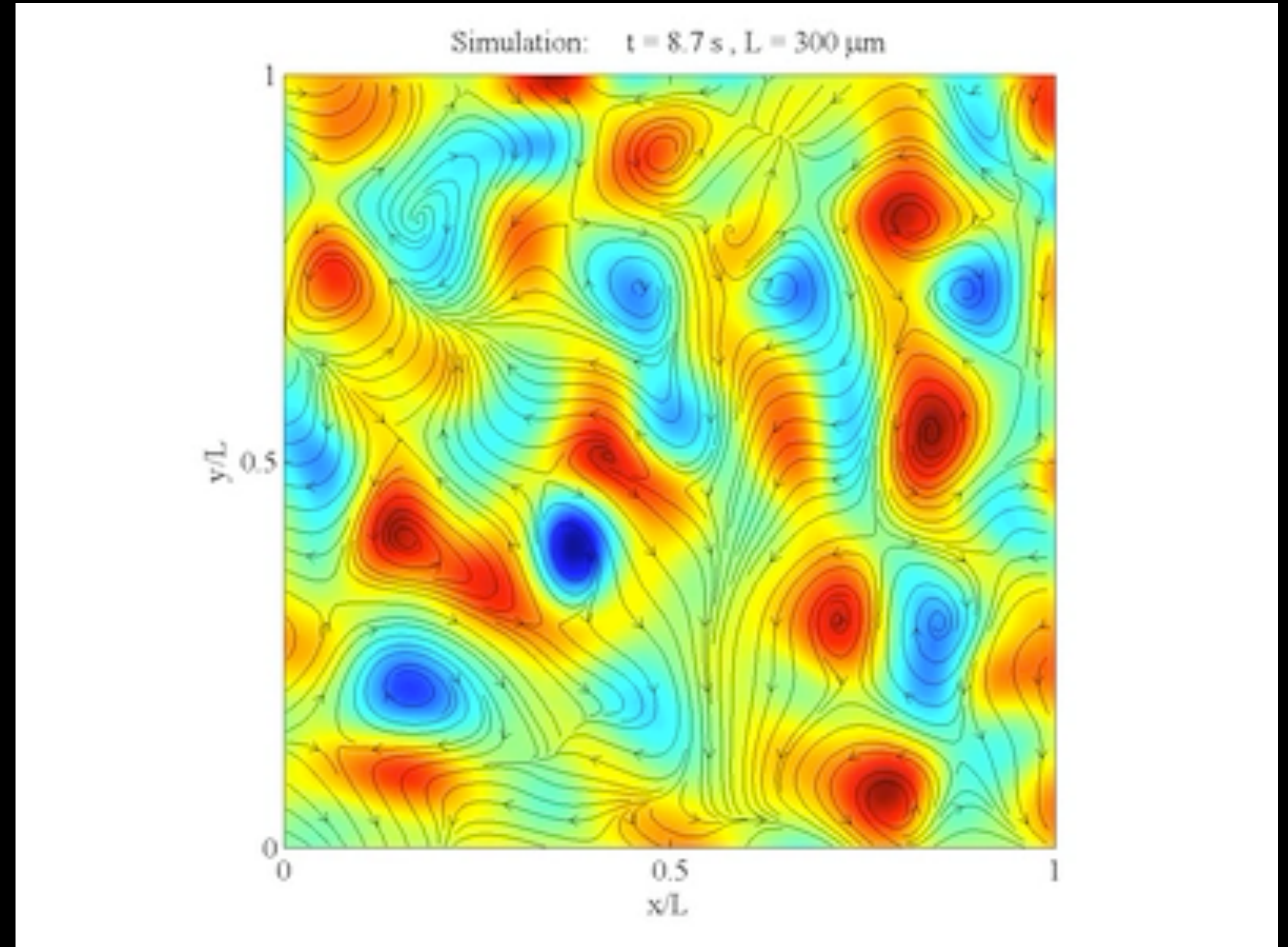
Propensity of system to acquire a common velocity

Stationary states correspond to the minimum of this effective potential density

# Bacteria turbulence



Dunkel Phys. Rev. Lett. , 2013



$$(\partial_t + \lambda_0 \mathbf{v} \cdot \nabla) \mathbf{v} = -\nabla p + \lambda_1 \nabla v^2 - \beta (v^2 - v_0^2) \mathbf{v} + \Gamma_0 \nabla^2 \mathbf{v} - \Gamma_2 (\nabla^2)^2 \mathbf{v}$$

Advection and nematic Interactions  $\uparrow$   $\lambda_0$   
 Active pressure  $\uparrow$   $\lambda_1$   
 $\beta \neq 0$   $\uparrow$   $\beta (v^2 - v_0^2) \mathbf{v}$  model doesn't conserve momentum  
 Passive and active stresses (due to hydrodynamic and steric interactions)  $\uparrow$   $\Gamma_0 \nabla^2 \mathbf{v} - \Gamma_2 (\nabla^2)^2 \mathbf{v}$

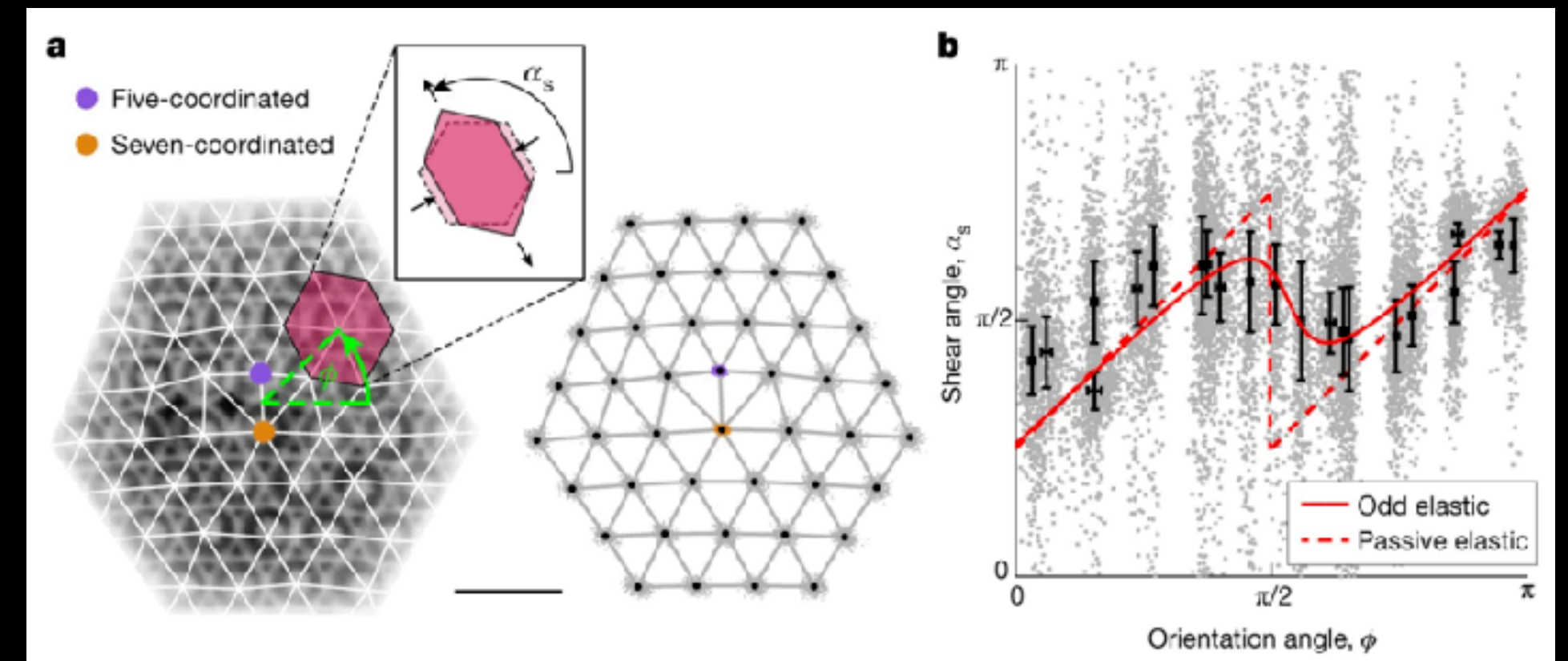
$\lambda_0 = 1, \lambda_1 = \beta = \Gamma_2 = 0$  and  $\Gamma_0 > 0$ , the model reduces to the incompressible Navier-Stokes equation

# Living crystals

## Odd Dynamics of Living Chiral Crystal

### Supplementary Video 1: Living chiral crystal (Fig. 1a).

Starfish embryos spontaneously self-assemble into a 2D chiral crystal below the air-water interface. This living chiral crystal persists for at least 30 hours before undergoing dissolution, a process driven by changes in the embryo's morphological and hydrodynamic properties as they continuously develop.



# Active nematics

Active 2D nematic  
Low curvature interface  
60X mag  
15 $\mu$ m bar

$$\nabla \cdot \mathbf{u} = 0,$$

$$\rho(\partial_t \mathbf{u} + \mathbf{u} \cdot \nabla \mathbf{u}) = \nabla \cdot \mathbf{\Pi},$$

where  $\mathbf{\Pi}$  is a general stress tensor, which includes the pressure,  $P$ , and the viscous, elastic, and active stresses:

$$\mathbf{\Pi}^{\text{viscous}} = 2\eta\mathbf{E},$$

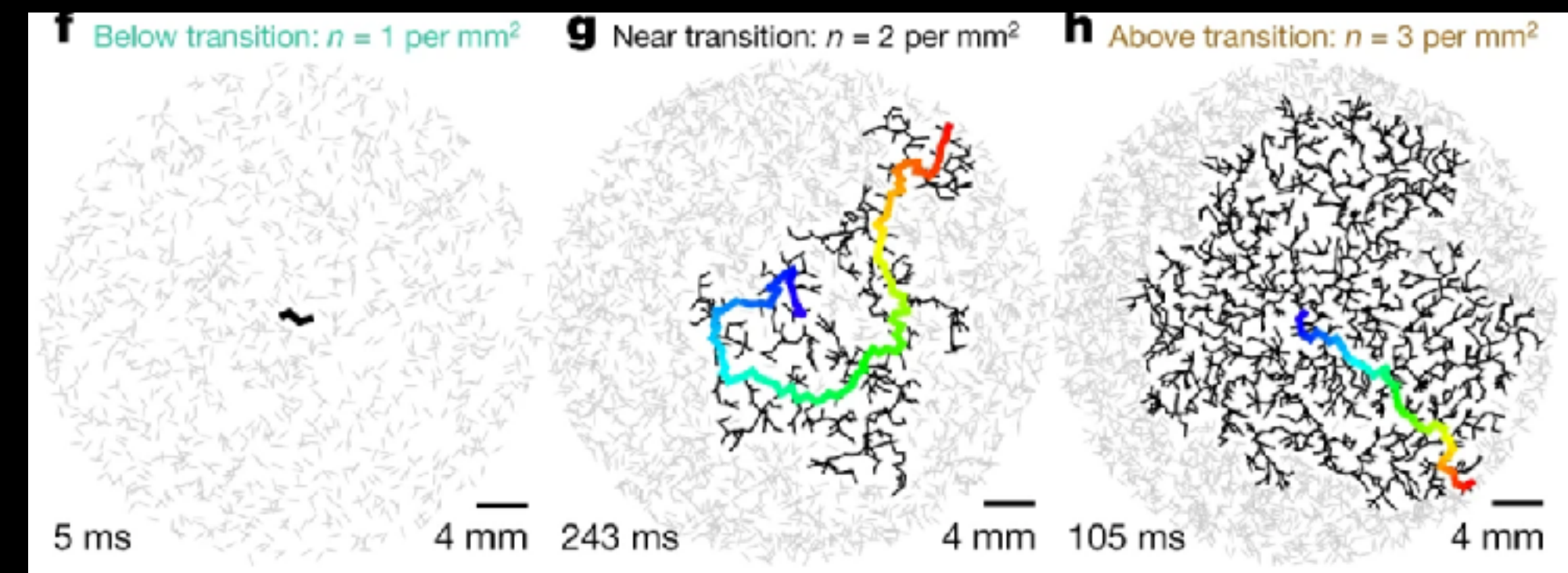
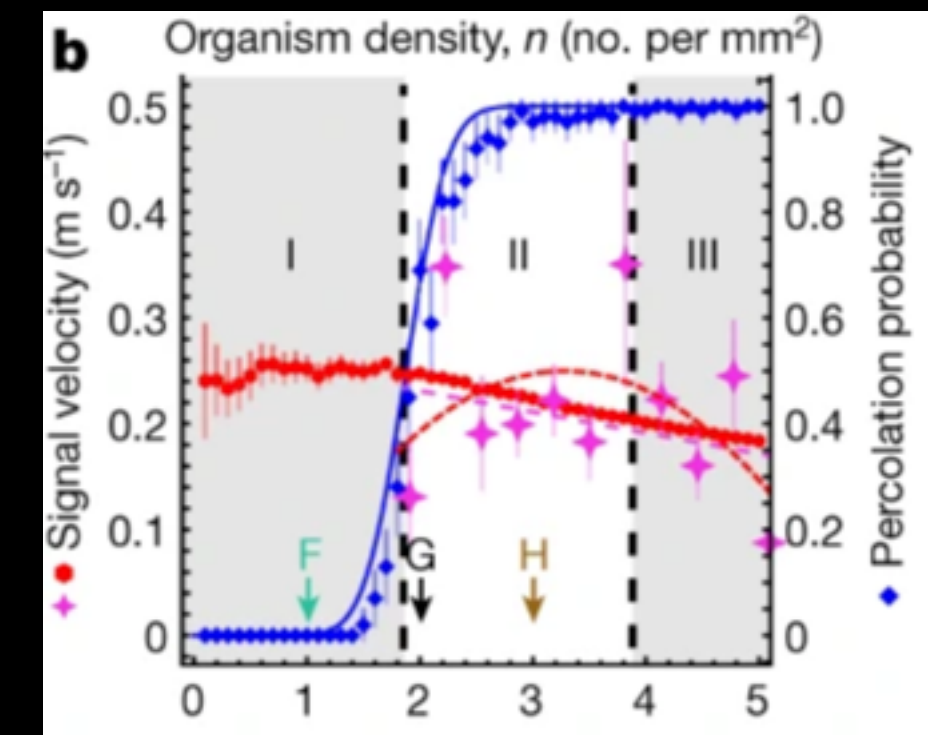
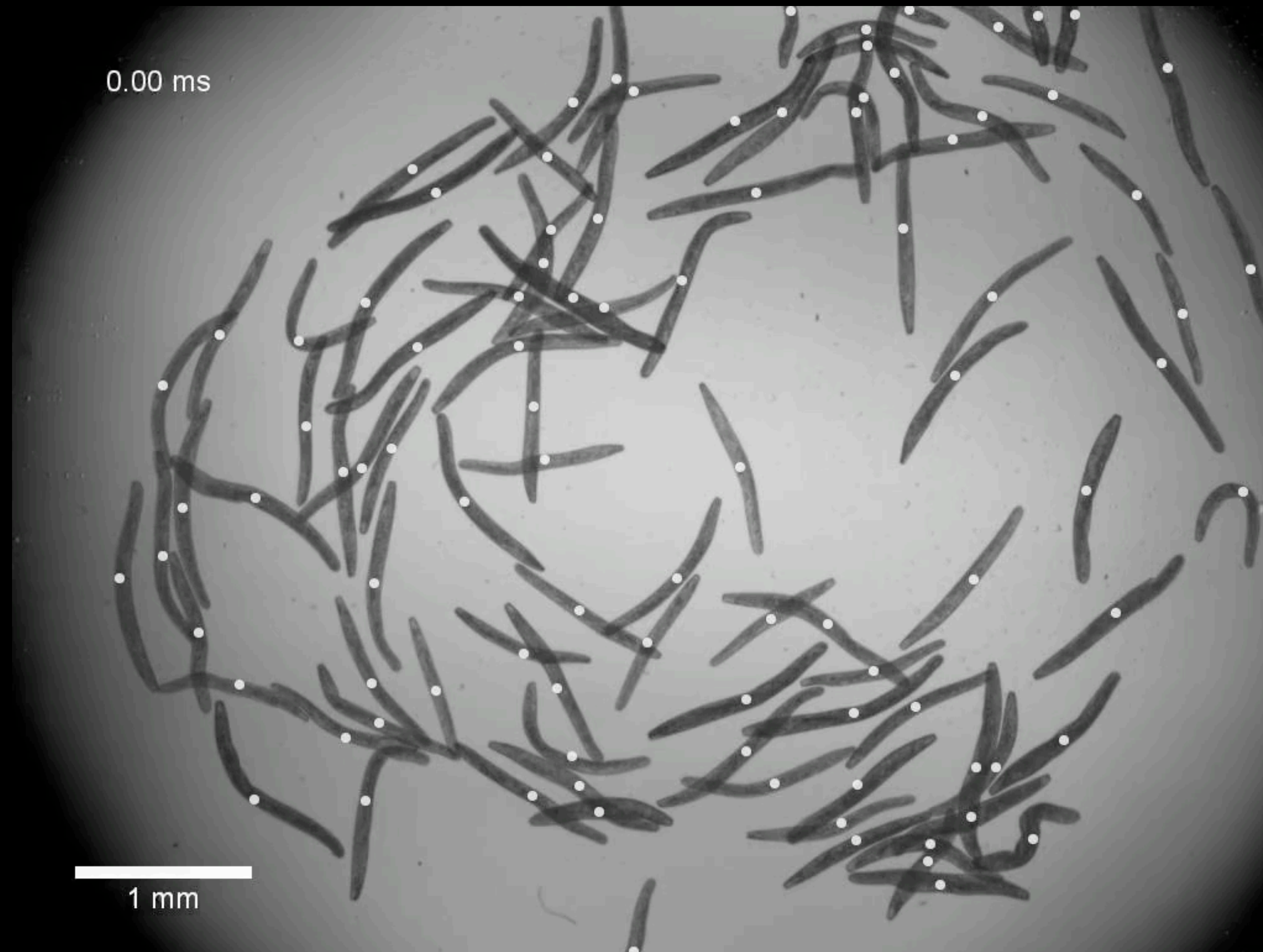
$$\mathbf{\Pi}^{\text{elastic}} = -P\mathbf{I} + 2\lambda(\mathbf{Q} + \mathbf{I}/3)(\mathbf{Q}:\mathbf{H})$$

$$-\lambda\mathbf{H} \cdot \left(\mathbf{Q} + \frac{\mathbf{I}}{3}\right) - \lambda\left(\mathbf{Q} + \frac{\mathbf{I}}{3}\right) \cdot \mathbf{H}$$

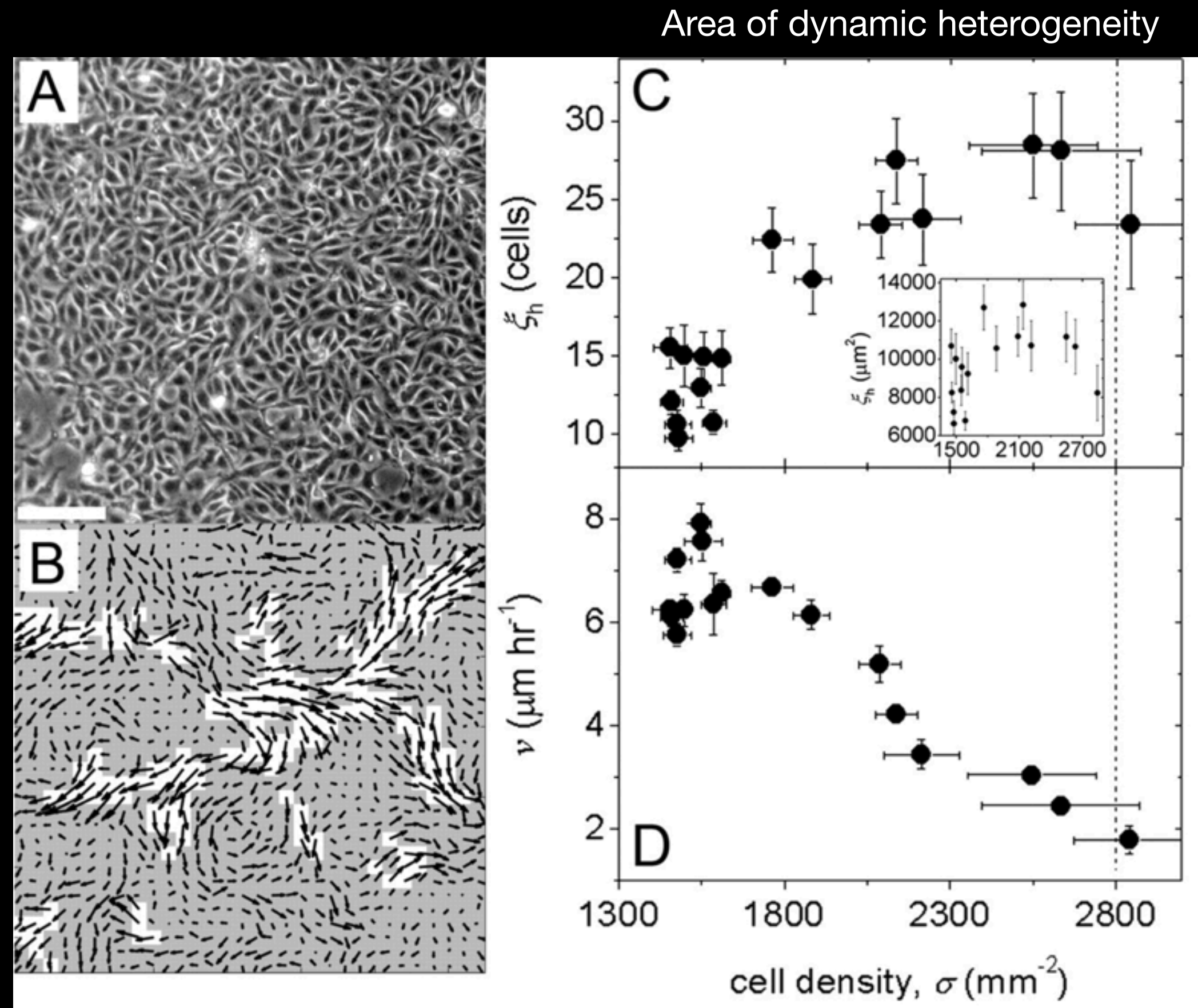
$$-\nabla\mathbf{Q} \frac{\delta\mathcal{F}}{\delta\nabla\mathbf{Q}} + \mathbf{Q} \cdot \mathbf{H} - \mathbf{H} \cdot \mathbf{Q},$$

$$\mathbf{\Pi}^{\text{active}} = -\zeta\mathbf{Q}.$$

# Hydrodynamic trigger waves



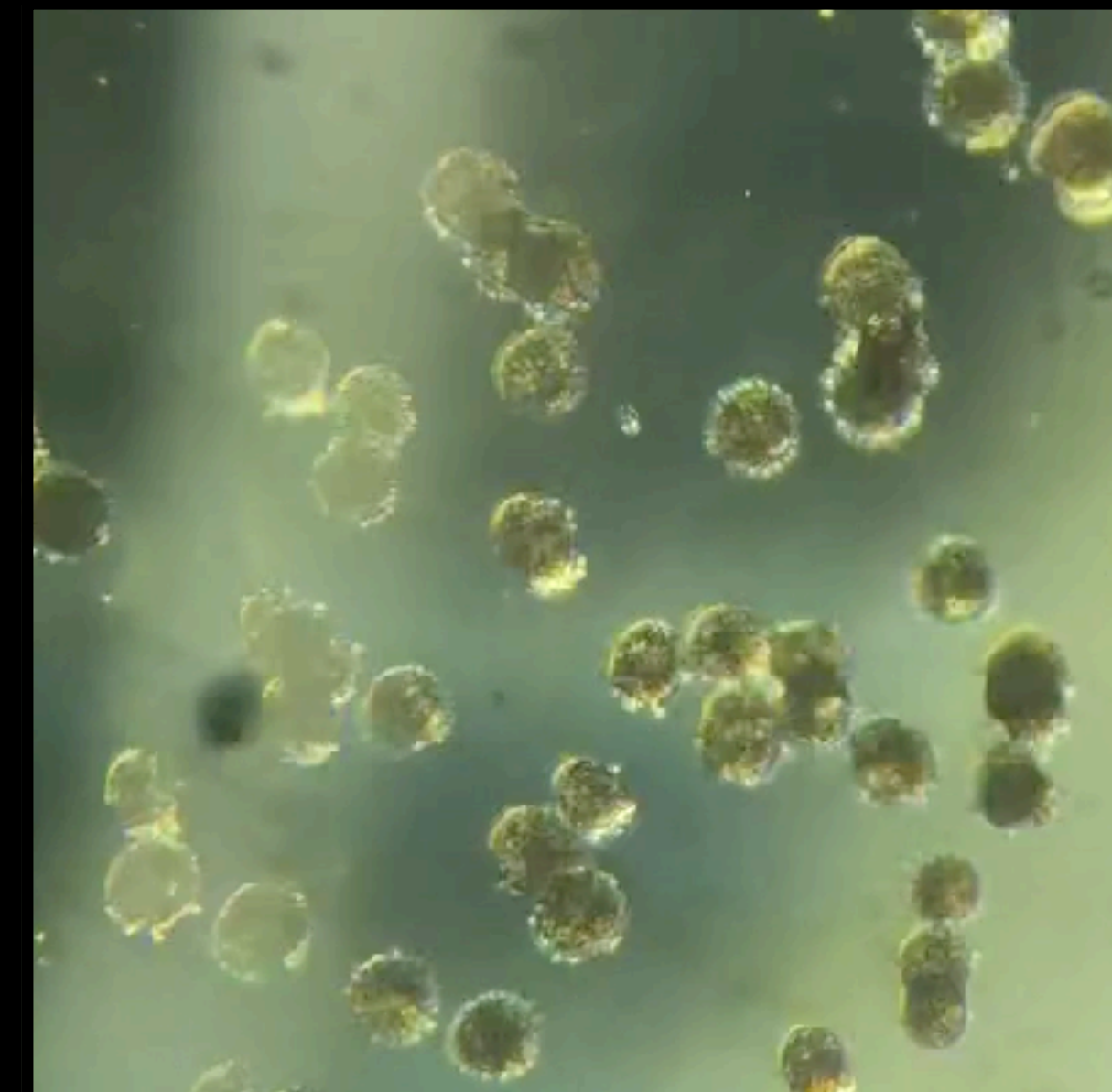
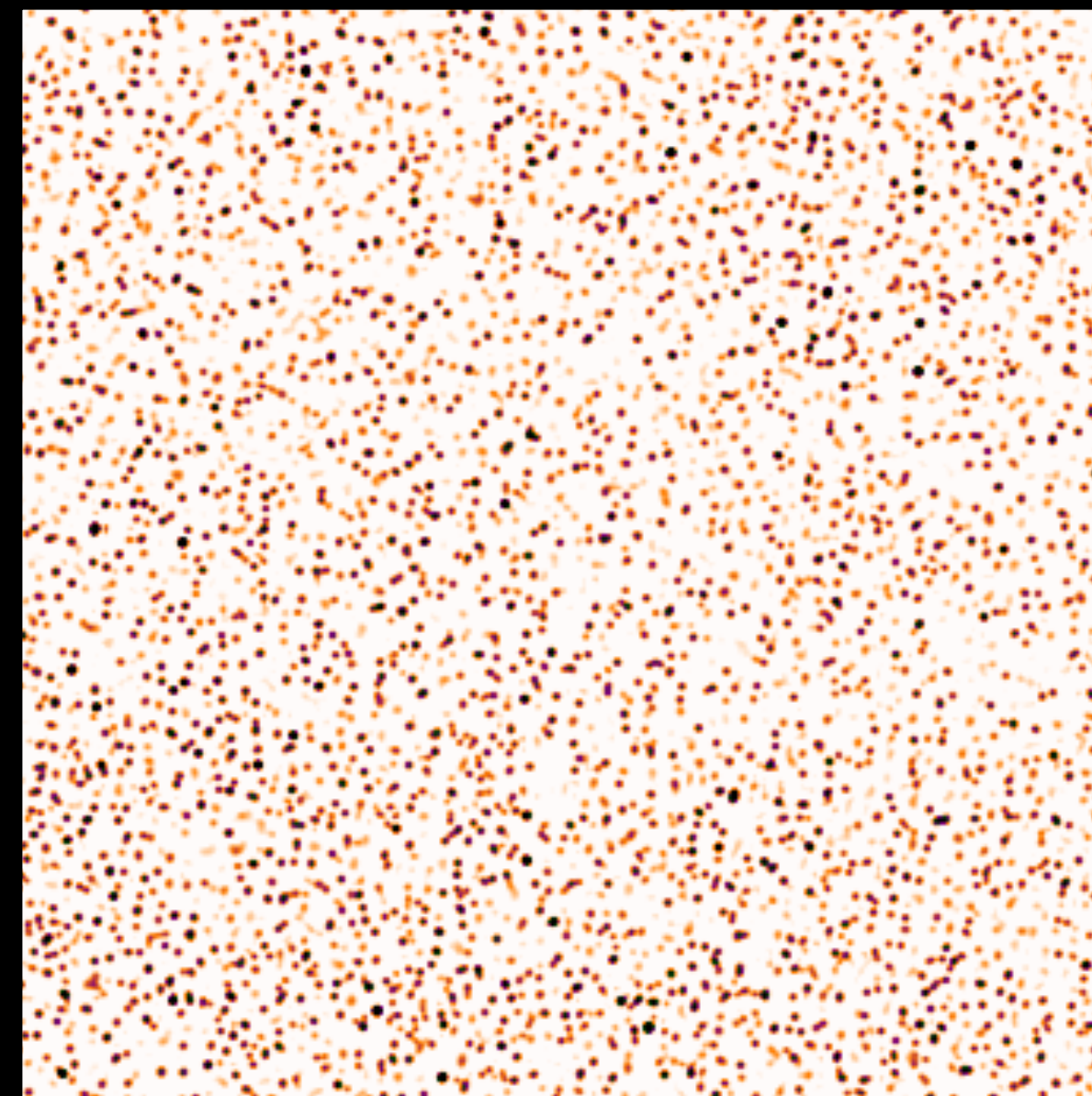
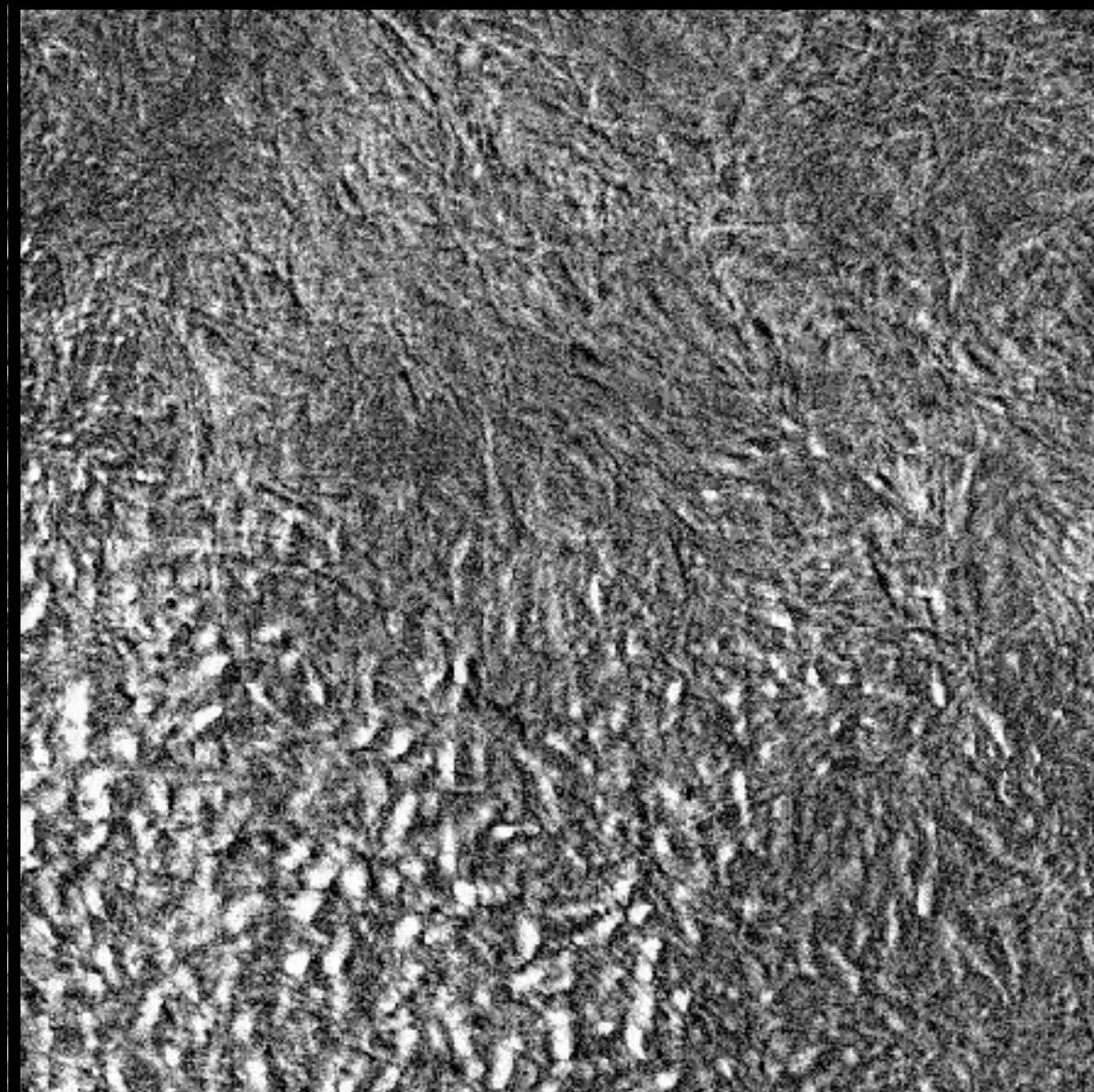
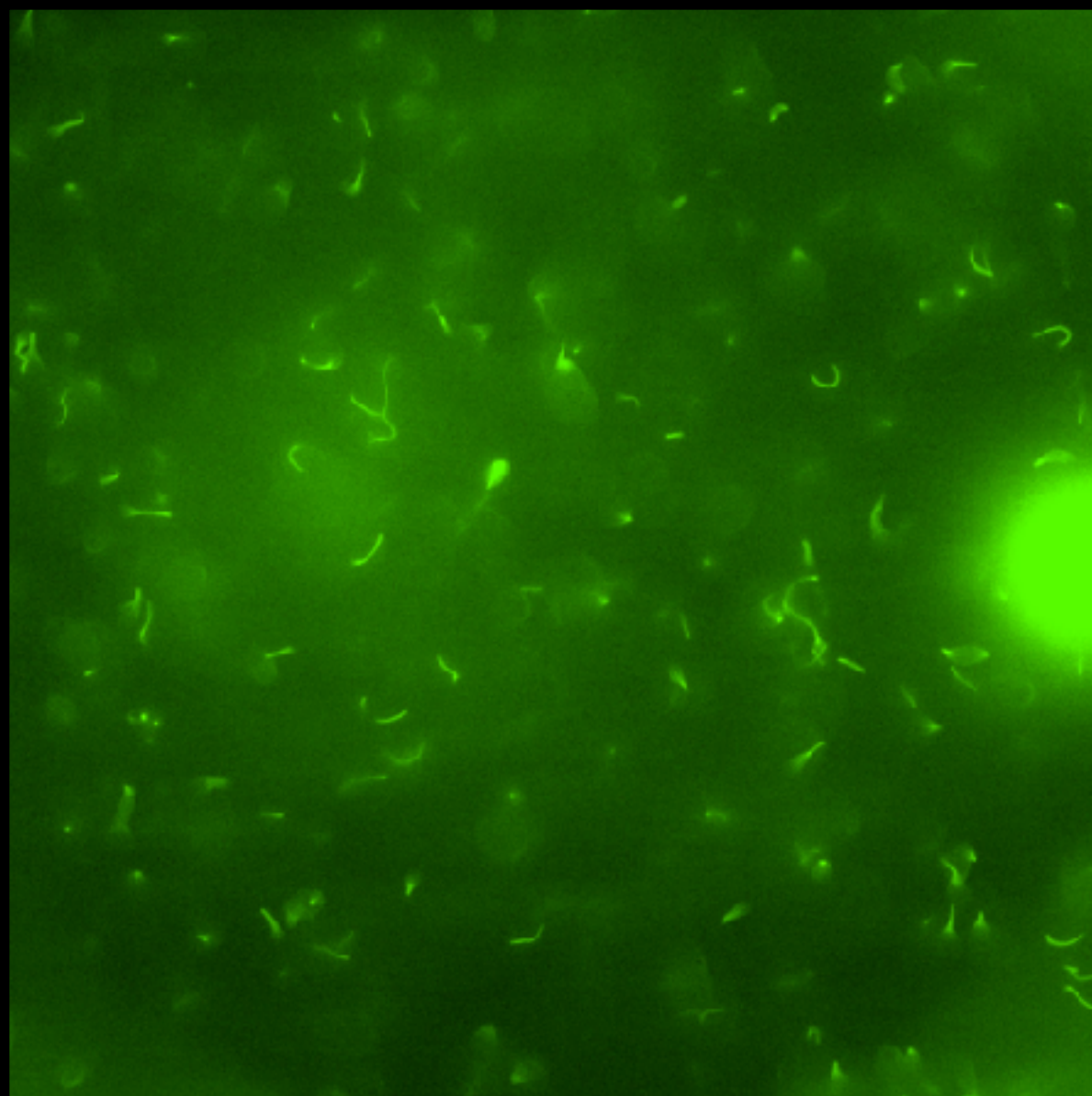
# Glass-like dynamics of collective cell migration



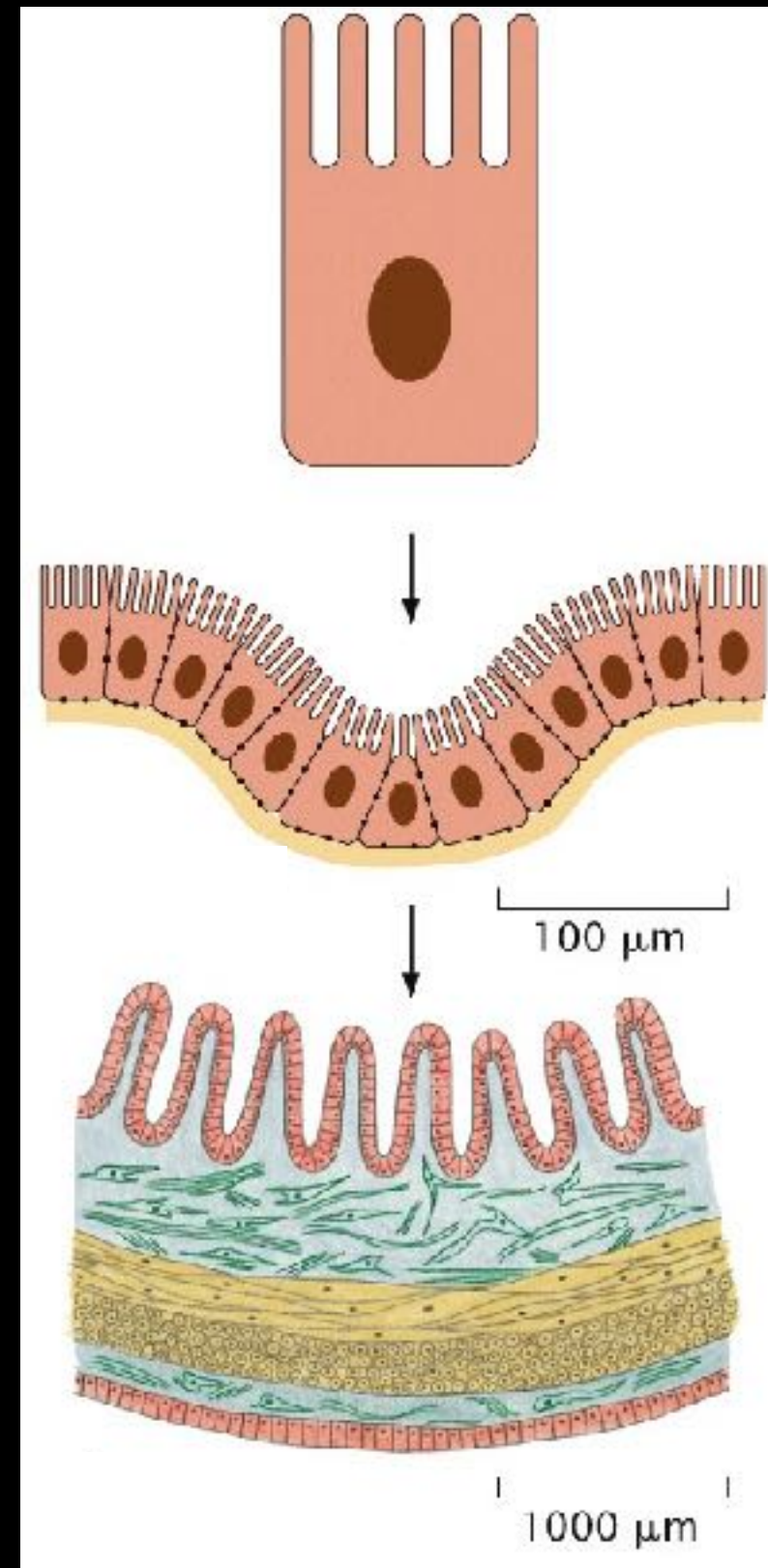
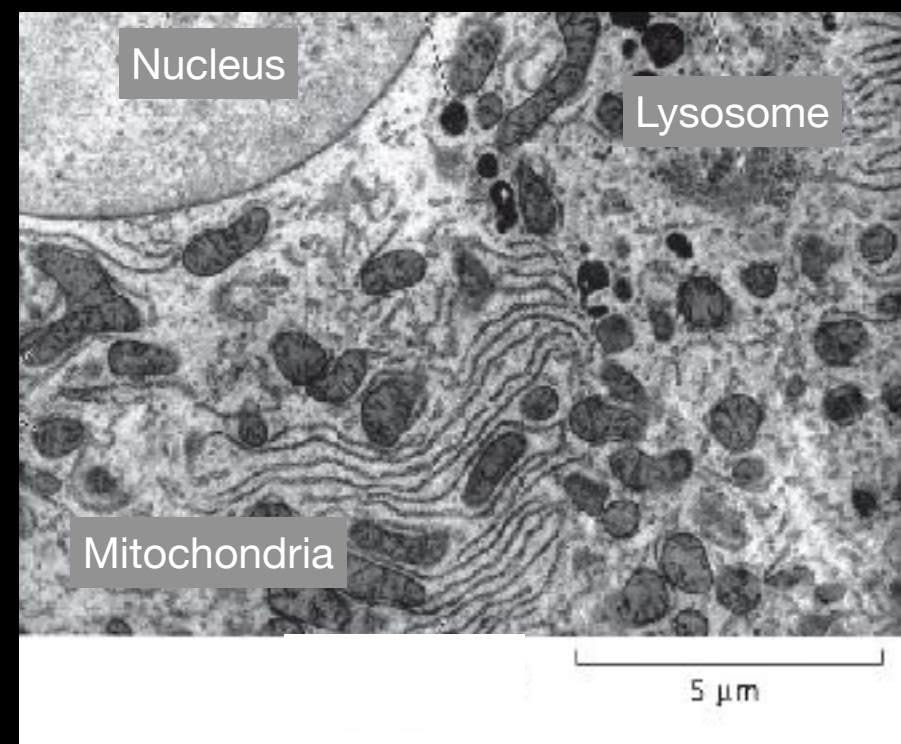
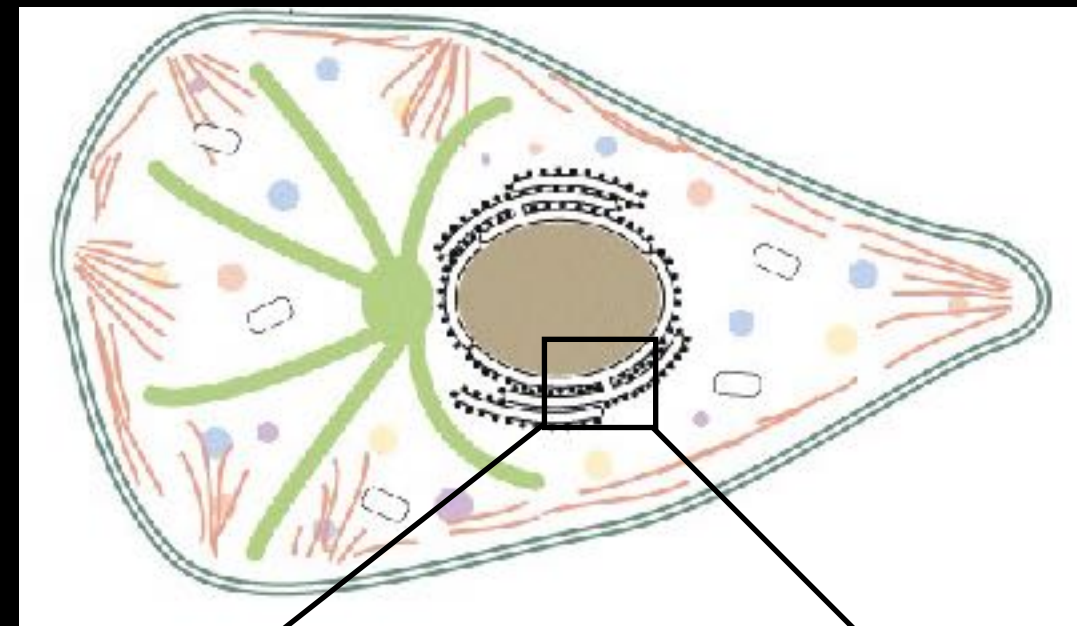
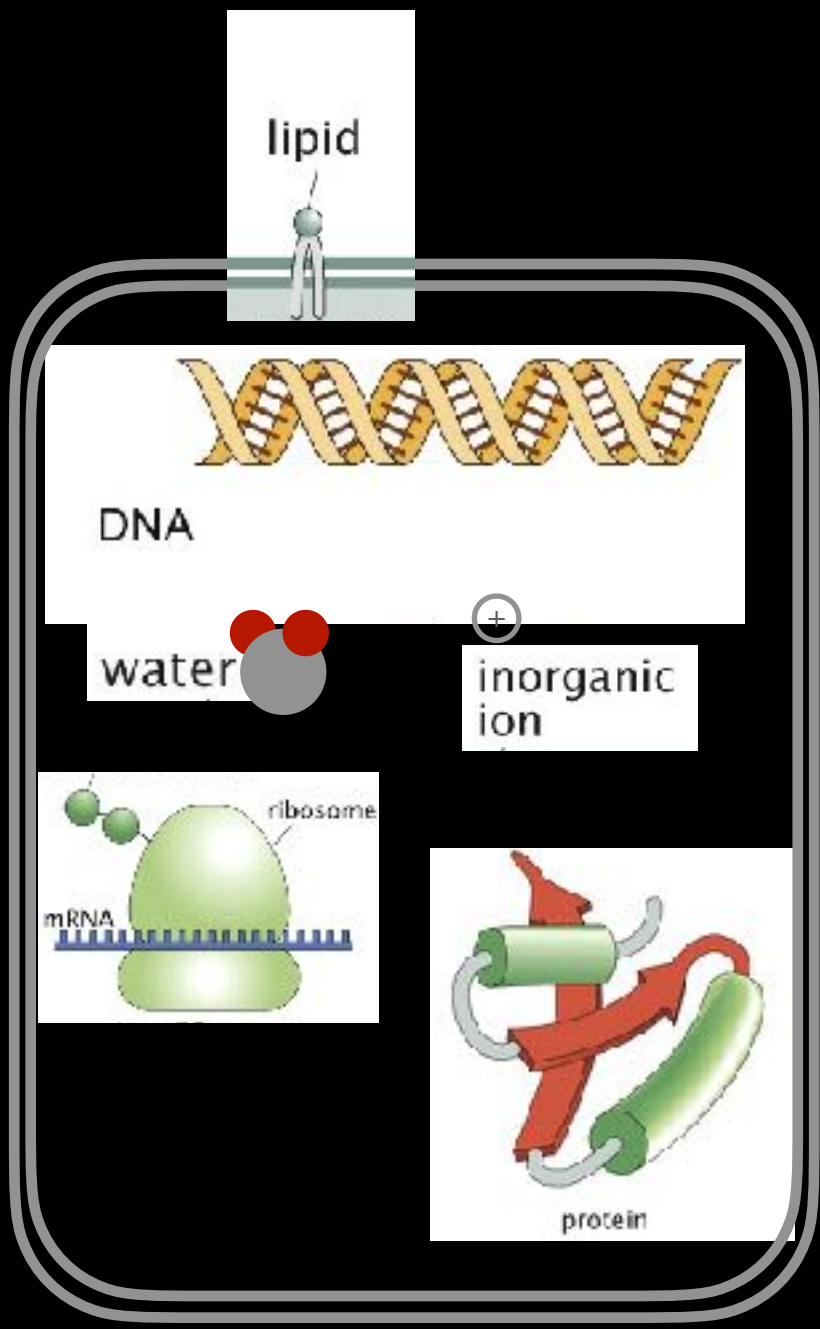
[https://www.youtube.com/watch?v=T2MWEc\\_rrIA](https://www.youtube.com/watch?v=T2MWEc_rrIA)

# Living patterns:

Linking microscopic properties with emergent macroscopic dynamics



# Living matter: The “stuff of life”



Molecules

Cell

Tissue

Organism

Environment

10<sup>-9</sup> m

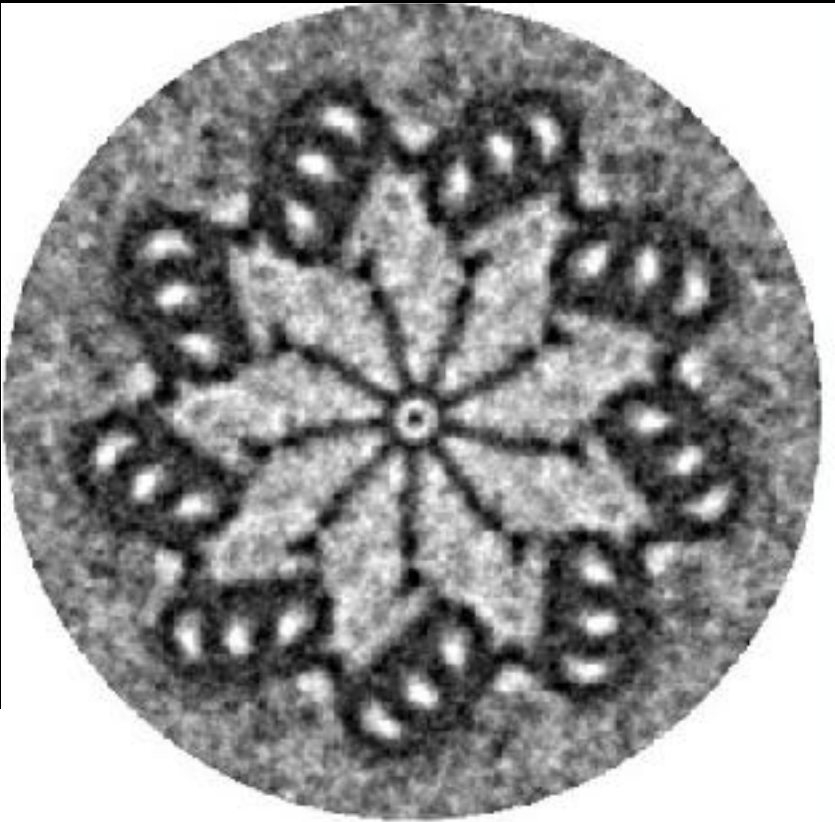
10<sup>-6</sup> m

10<sup>-3</sup> m

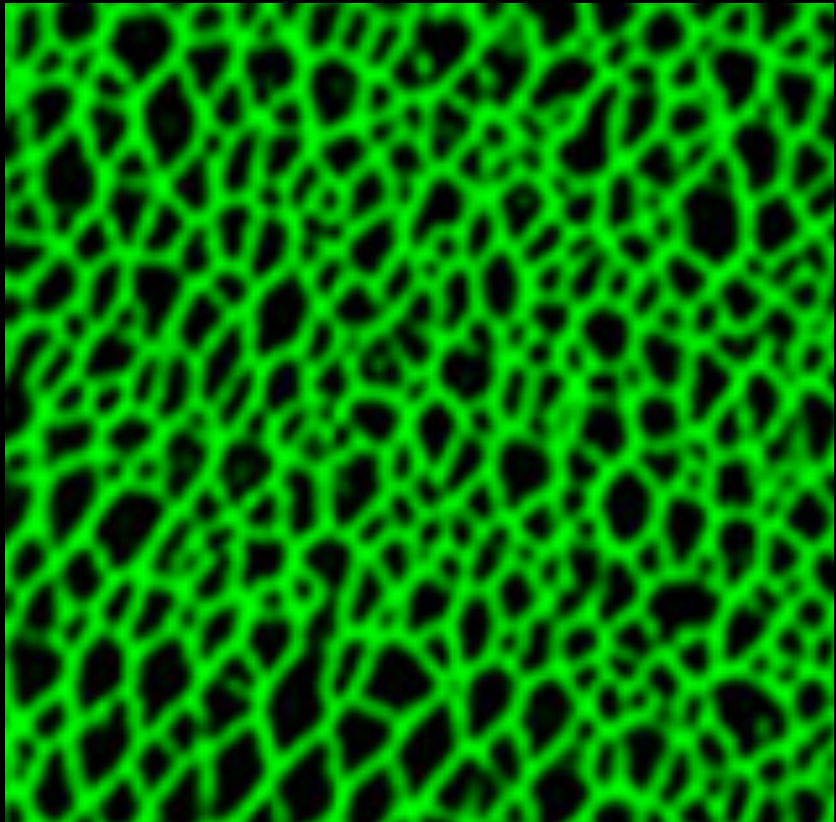
10<sup>0</sup> m

# Living matter is patterned across length scales

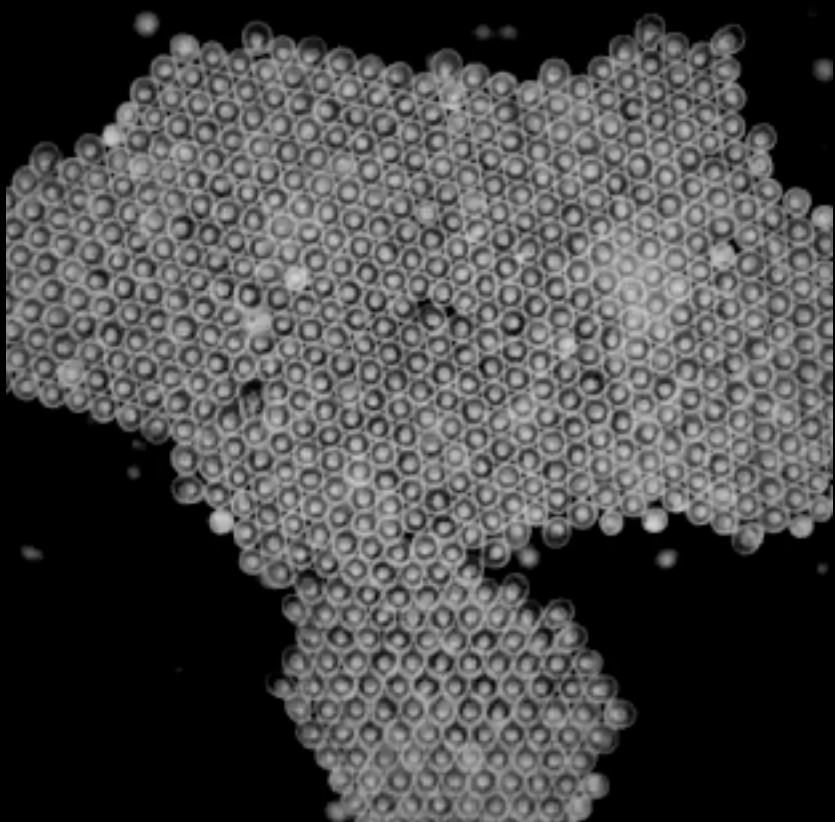
“Endless forms most beautiful”



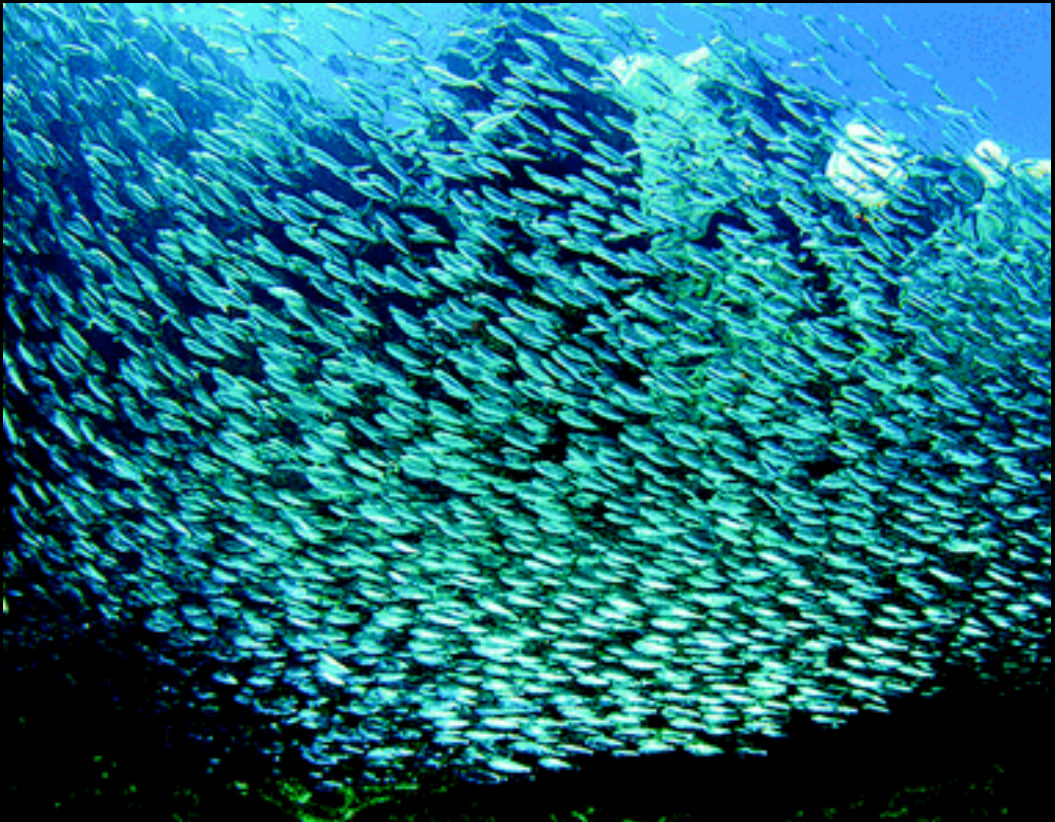
Nazarov S., *et al.* EMBO J.39:e106249 (2020)



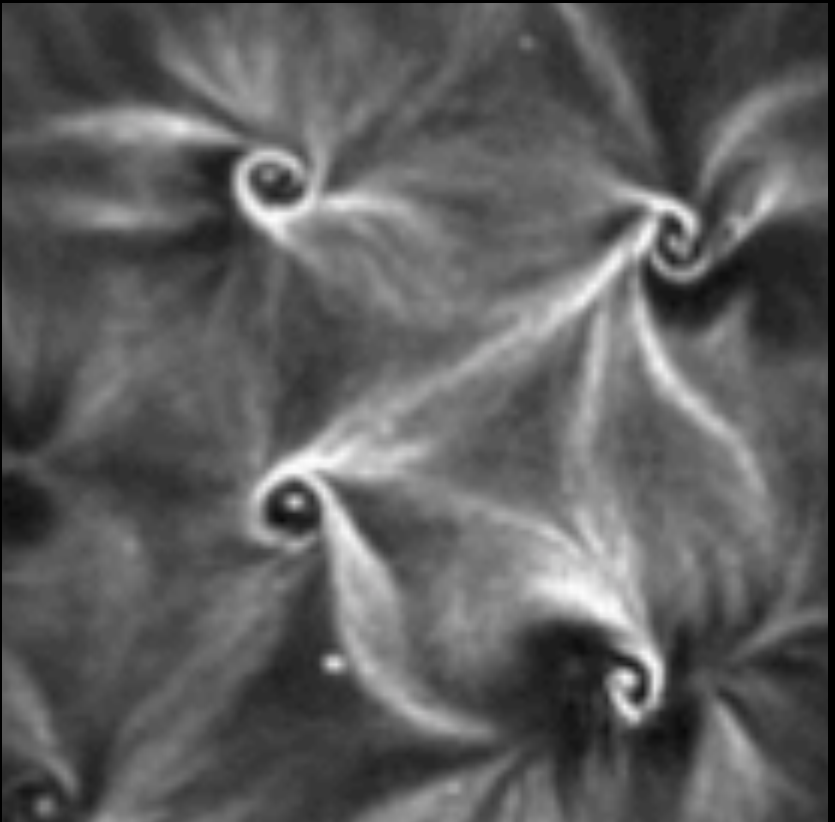
Aubusson-Fleury *et al.* Biology Open. 2017



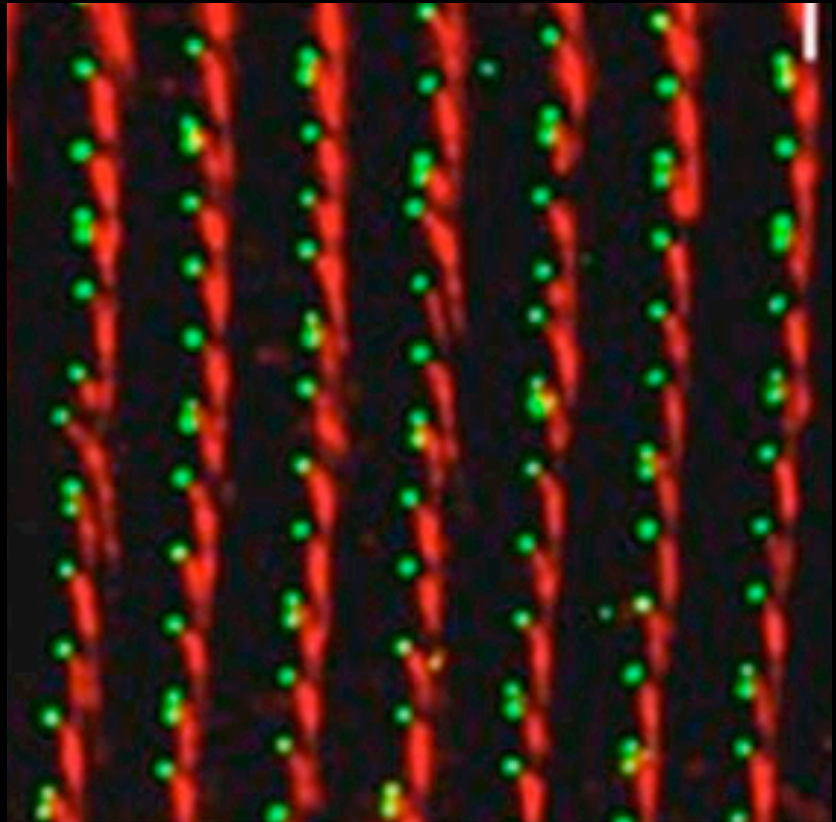
Tan, T.H., *et al.* Nature 607, 287–293 (2022)



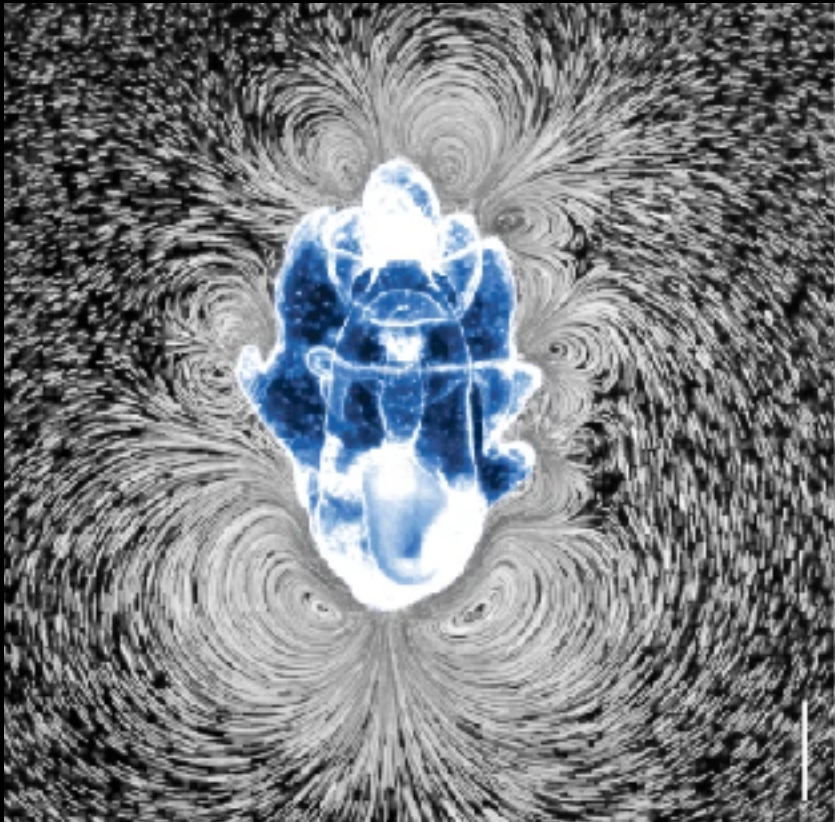
Marchetti M. C., *et al.* Rev.Mod.Phys. 85, 1143 (2013)



Surrey, T., F. *et al.*, Science 292, 1167 (2001)



Bengueddach, H. *et al.* Cilia 6, 6 (2017)



Gilpin W. *Et al* Nat Phys. 13, 380–386 (2017)



Hemelrijk C.K., J. Phys.: Condens. Matter 32 (2020)

Molecules

Cell

Tissue

Organism

Environment

$10^{-9}$  m

$10^{-6}$  m

$10^{-3}$  m

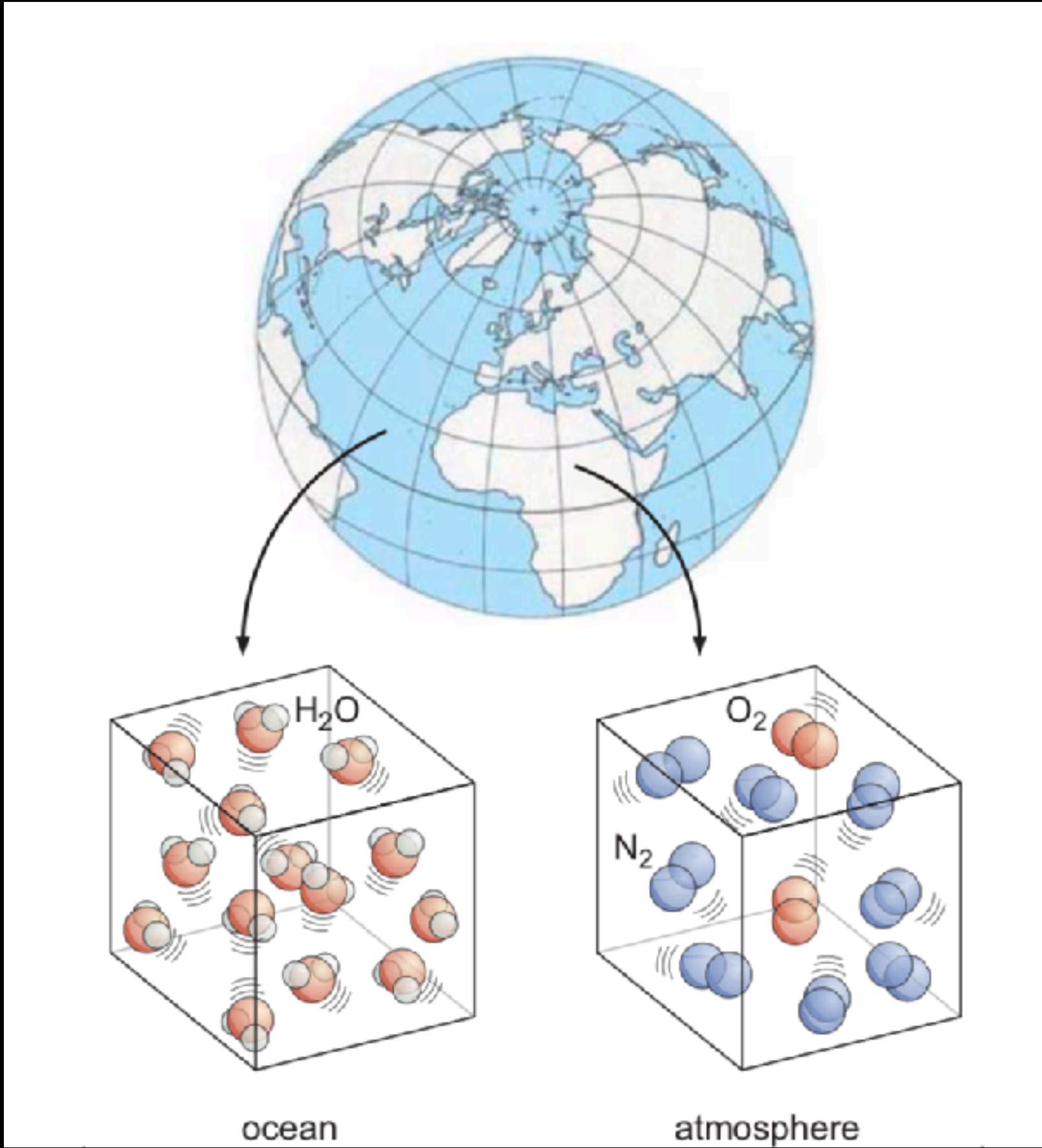
$10^0$  m

# How do we patterns emerge at different length scales?

- \* How are patterns formed in living systems? Statistical Mechanics
- \* How are they maintained/evolve? Dynamical systems
- \* What is the biological function of these patterns? Physiology/Development
- \* What are the properties of living/active matter? Material Science/Engineering

How do we integrate knowledge across levels of organization/length scales?

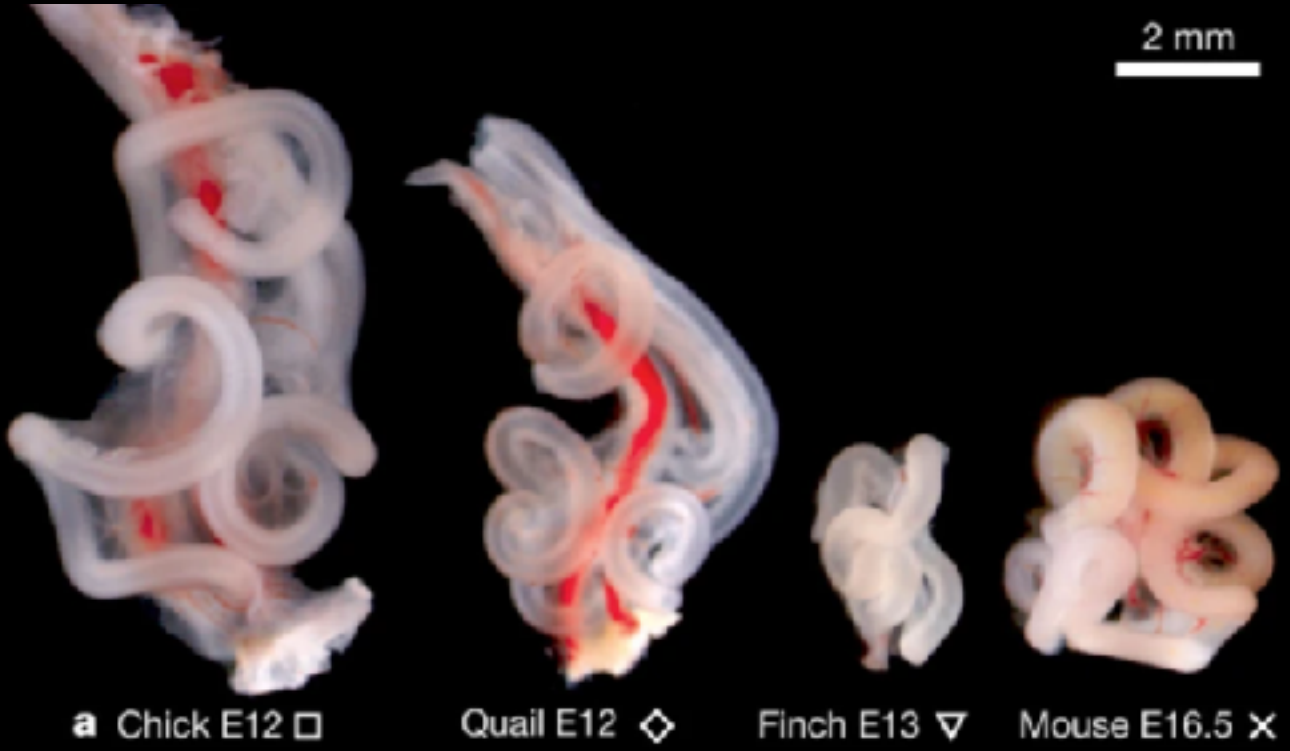
# Understanding mesoscale behavior is key to connect the micro- and macro-scales



Atmospheric wakes

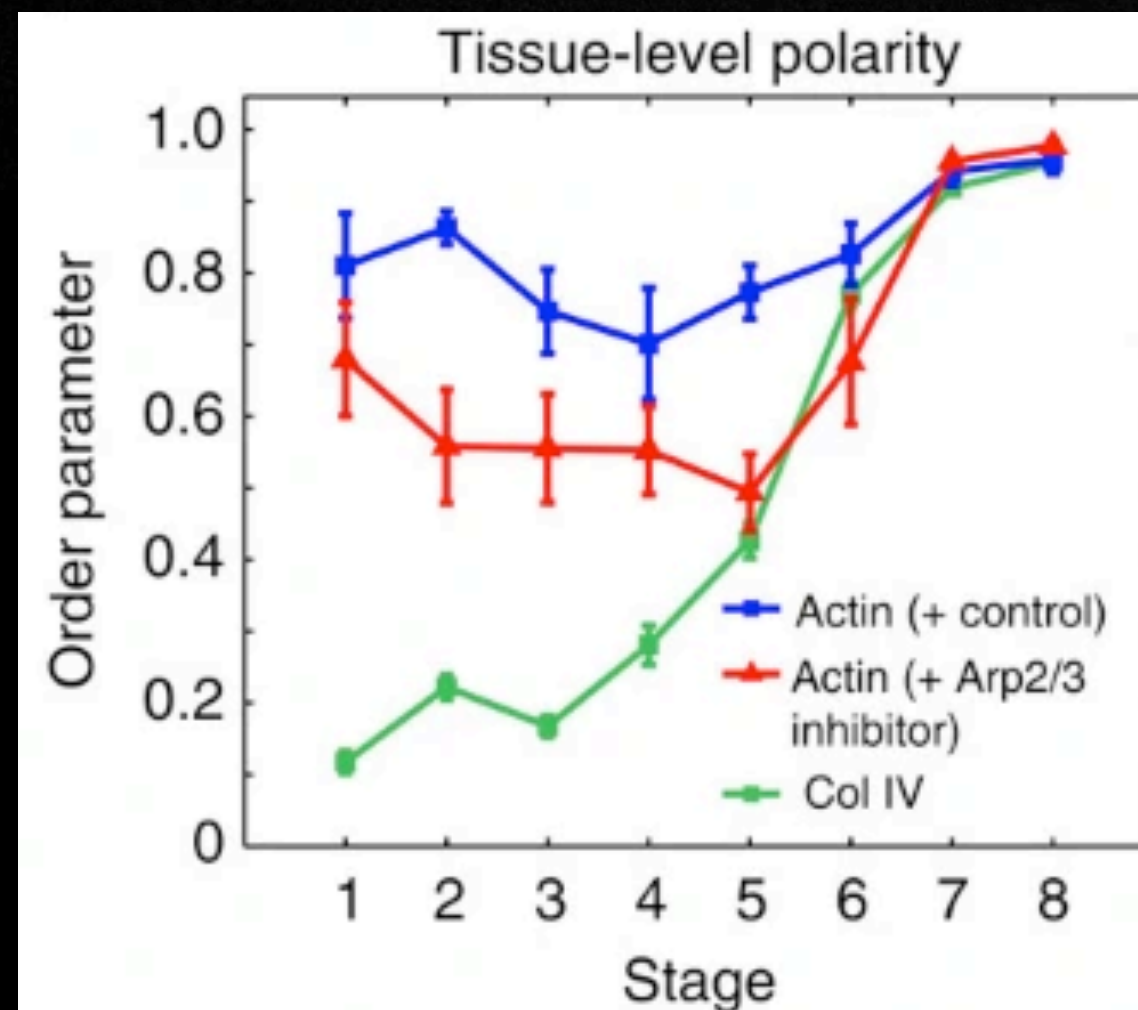
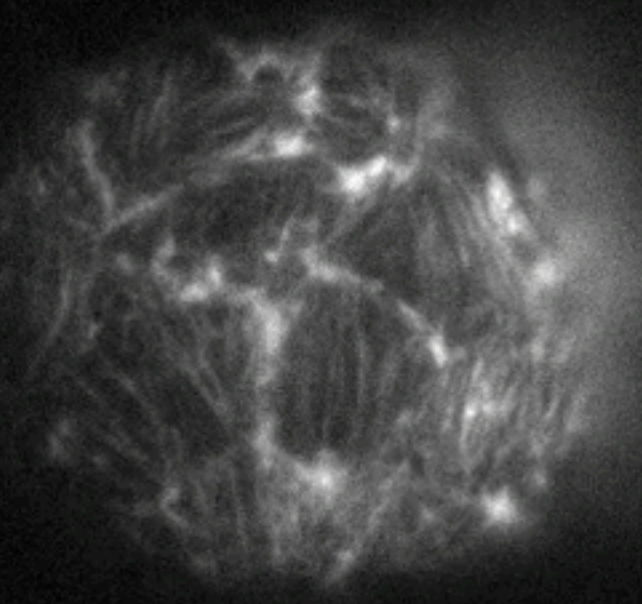


Looping of the gut



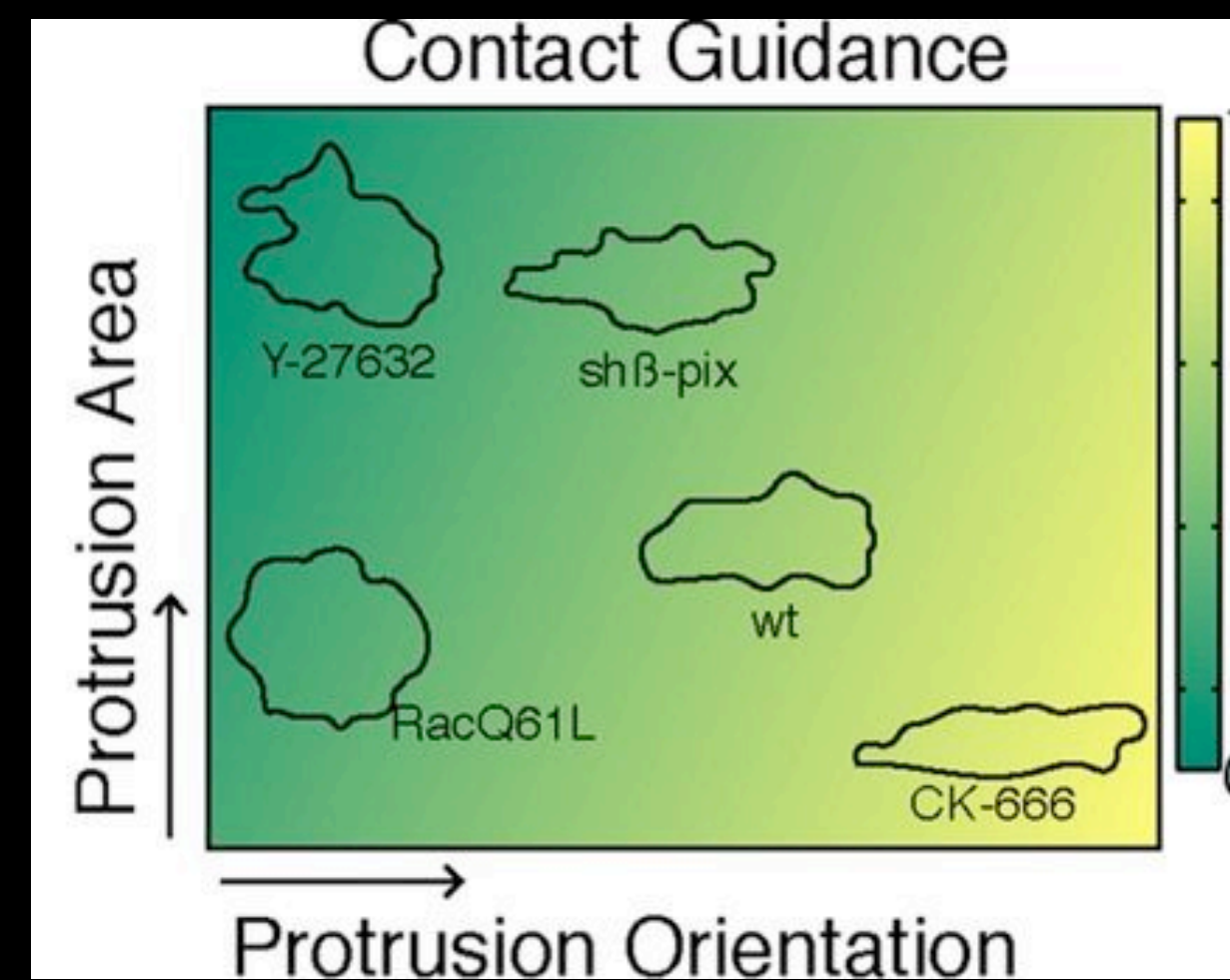
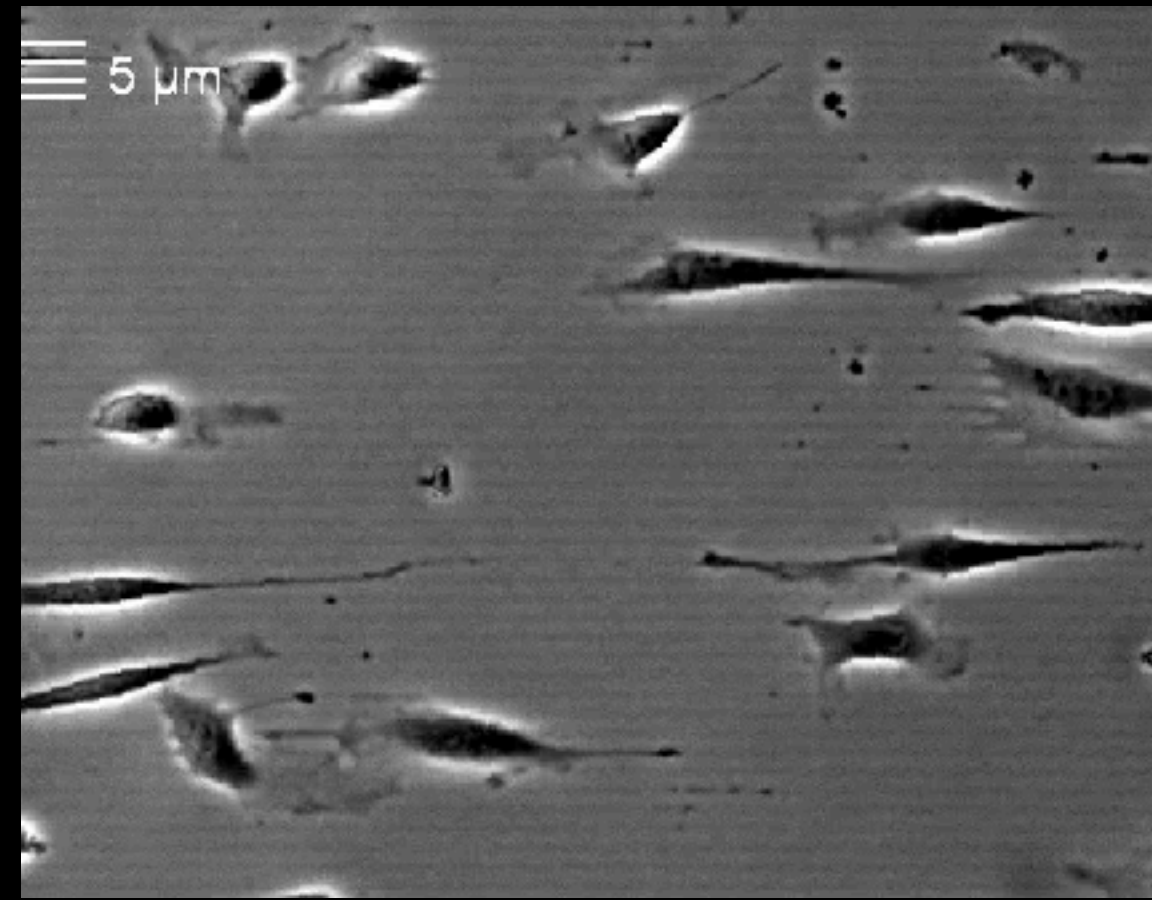
# Identifying mesoscale parameters is key to predict macroscopic behavior

Tissue shape changes



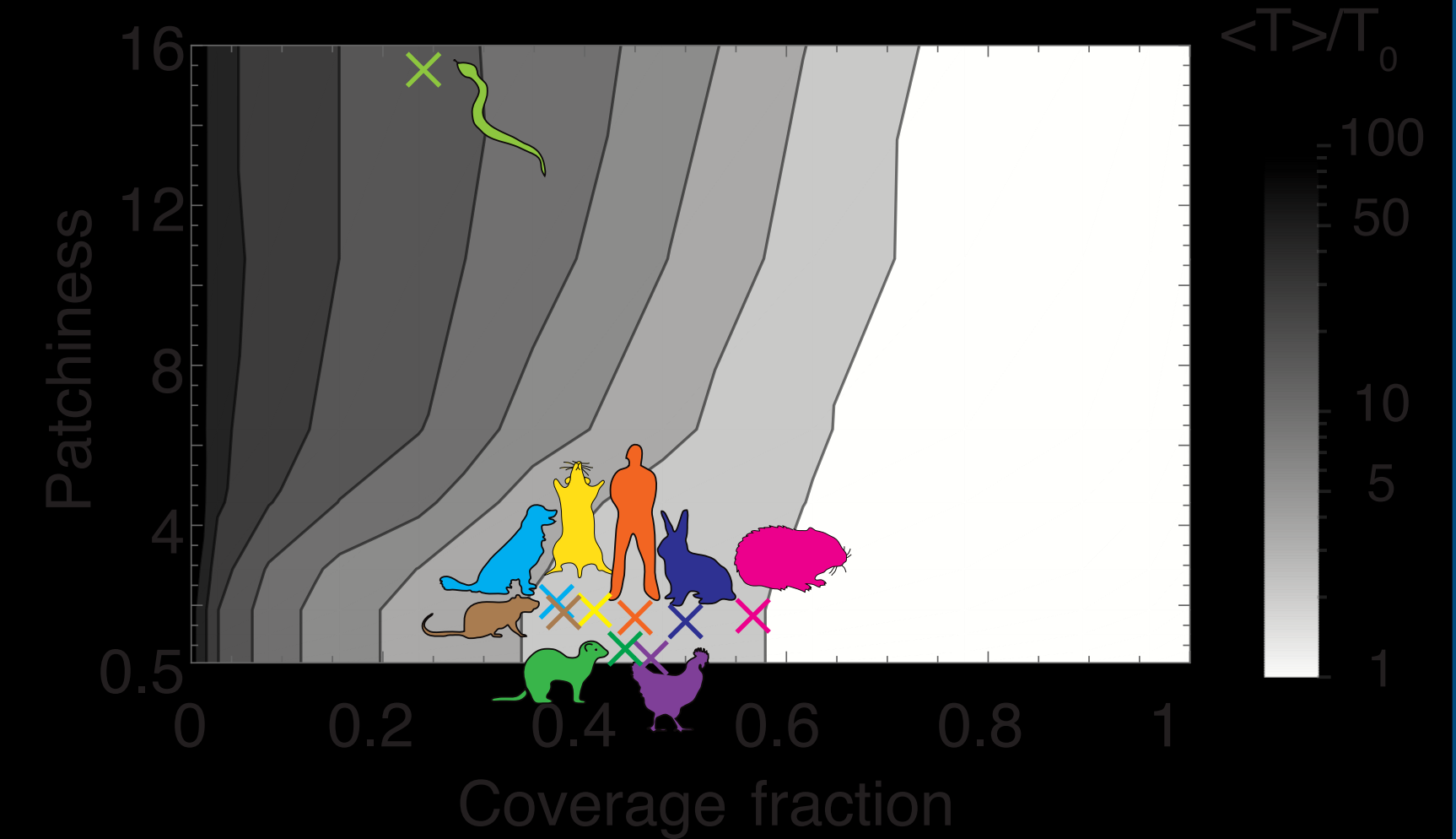
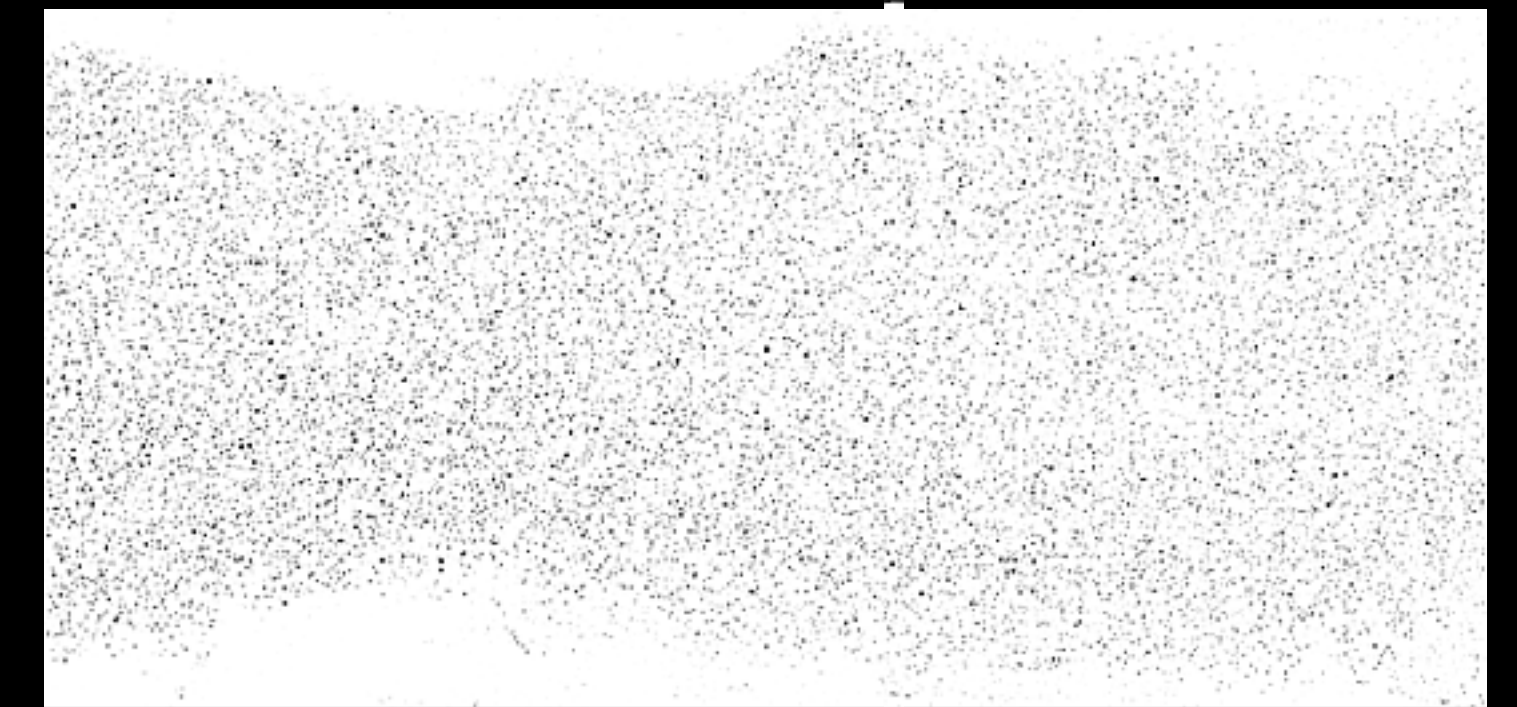
Ramirez-San Juan G.R. *et al. Nat. Comms.* 2014

Directed cell motility



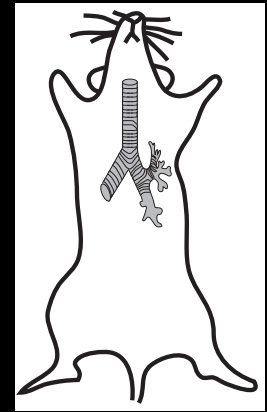
Ramirez-San Juan G.R. *et al. Mboc.* 2017

Flow generation

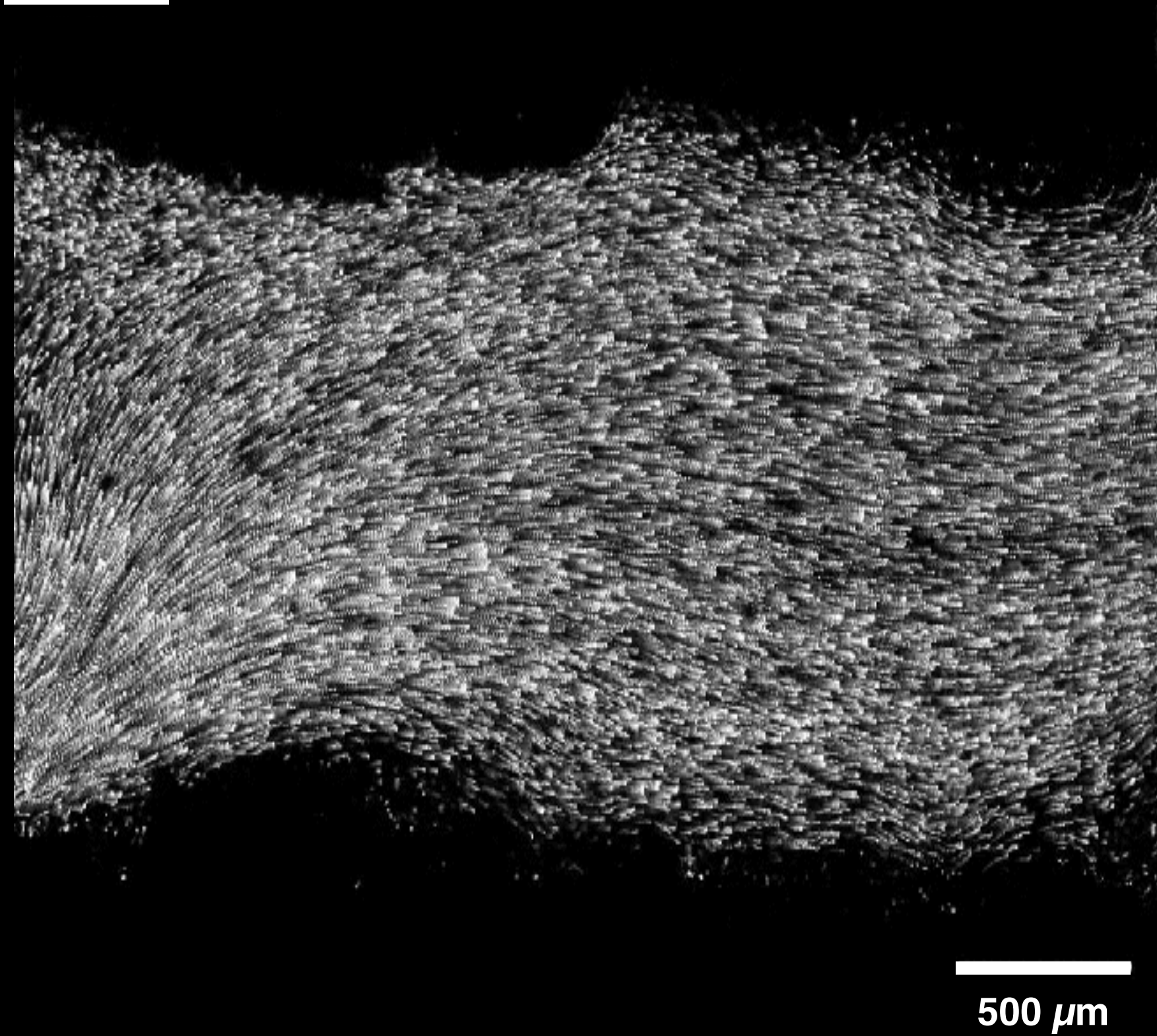


Ramirez-San Juan G.R. *et al. Nat. Phys.* 2020

# Integrated cilia activity generates flows tailored for specific biological functions



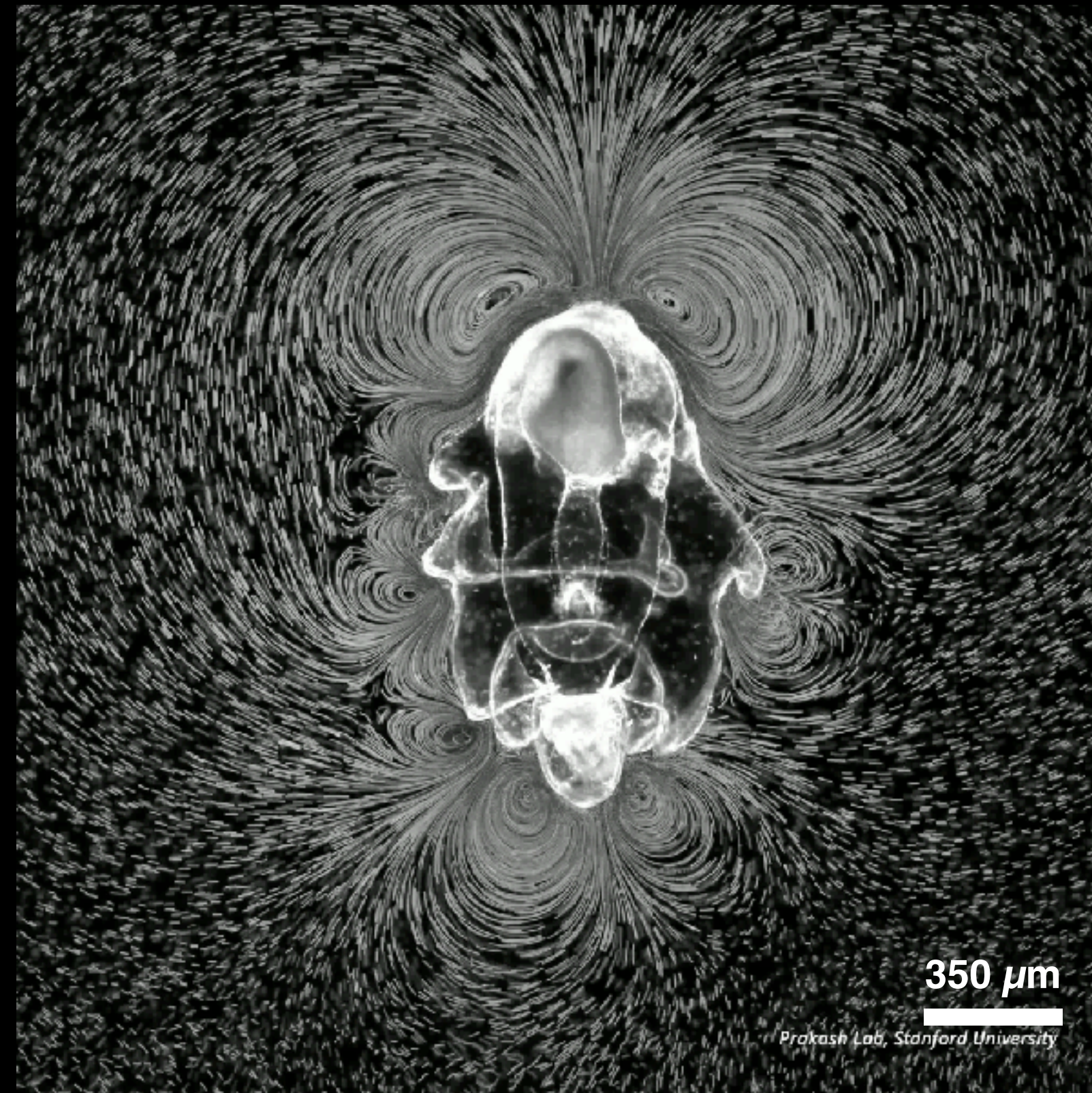
Mammalian airway



Ramirez-San-Juan et al. *Nat. Phys.* 2020.



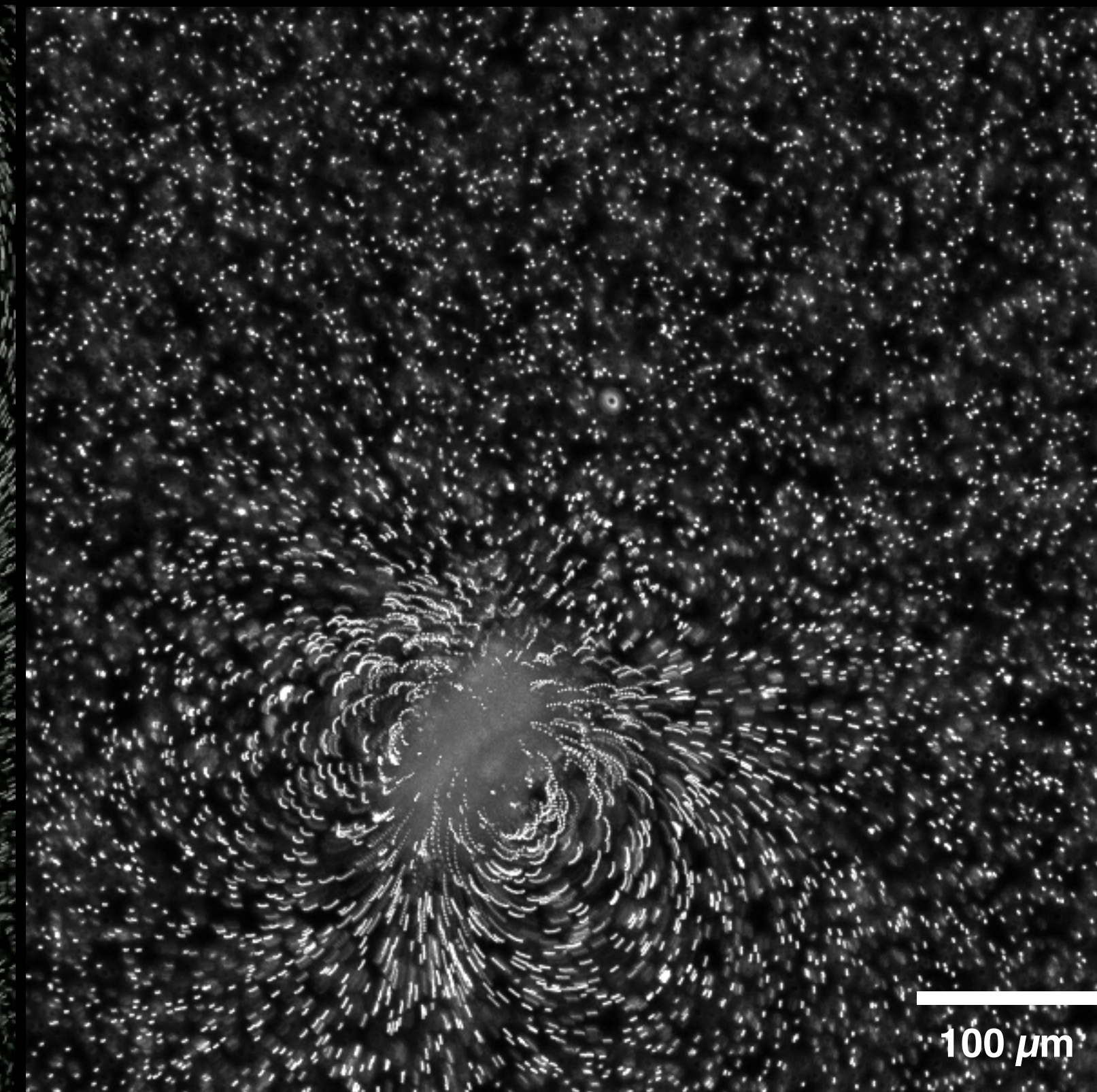
Marine larvae



Gilpin W et al. *Nat. Phys.* 2017.

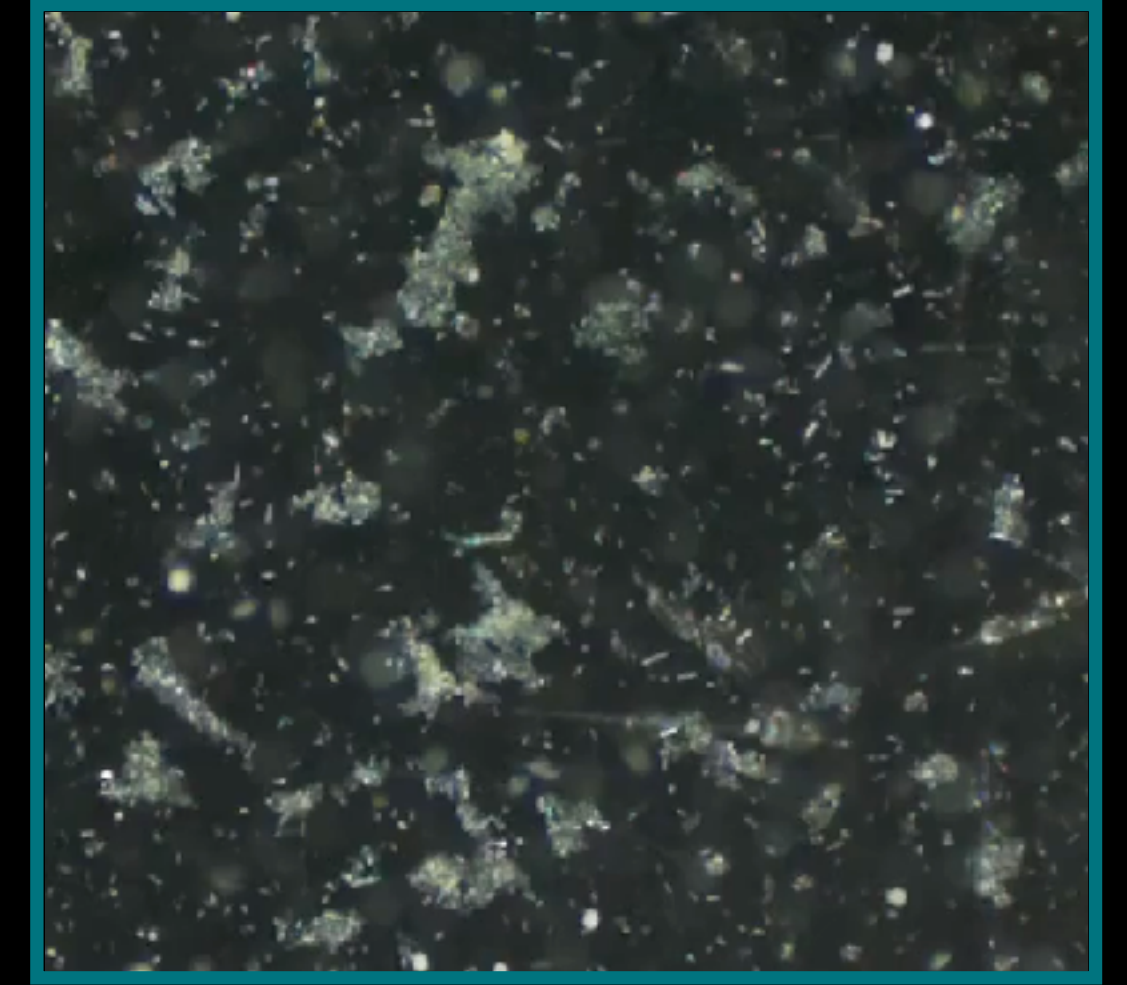
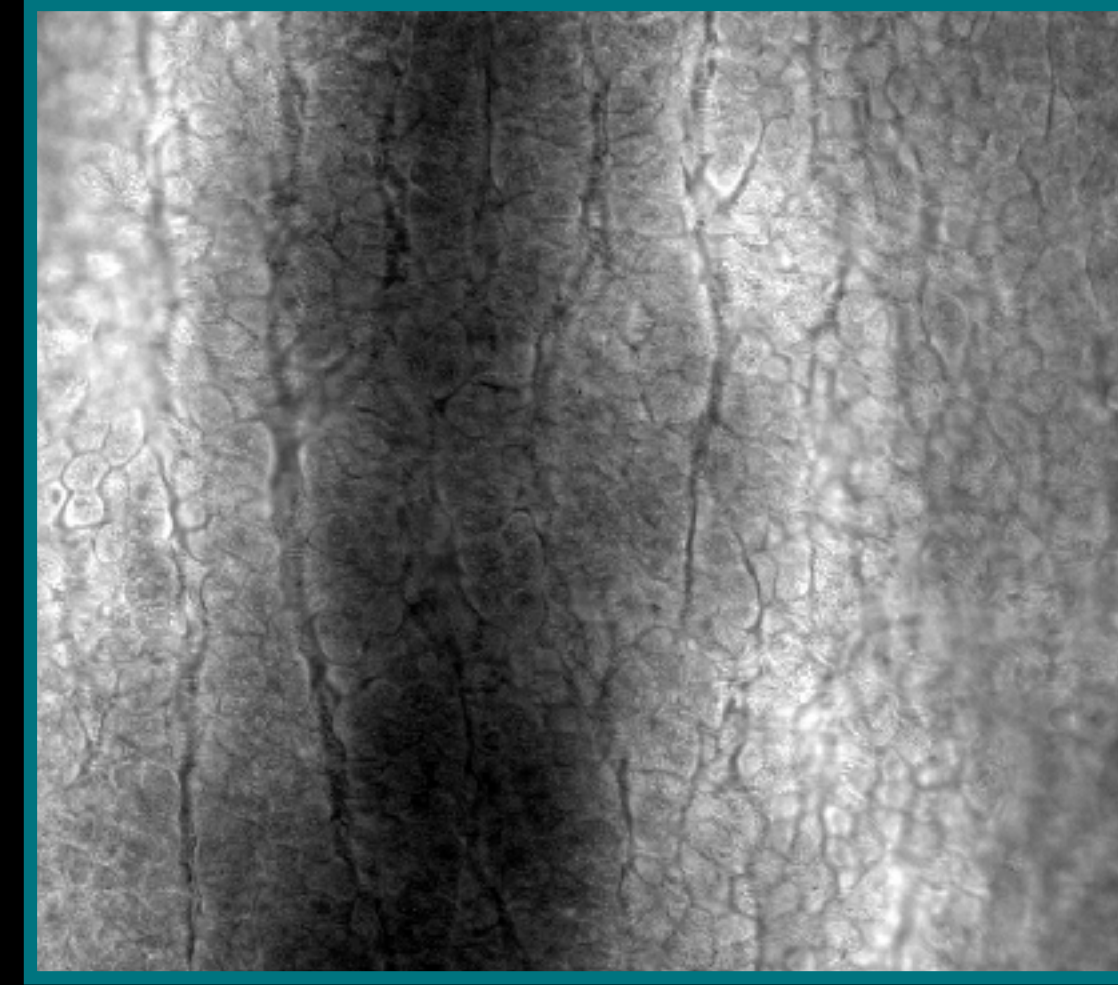
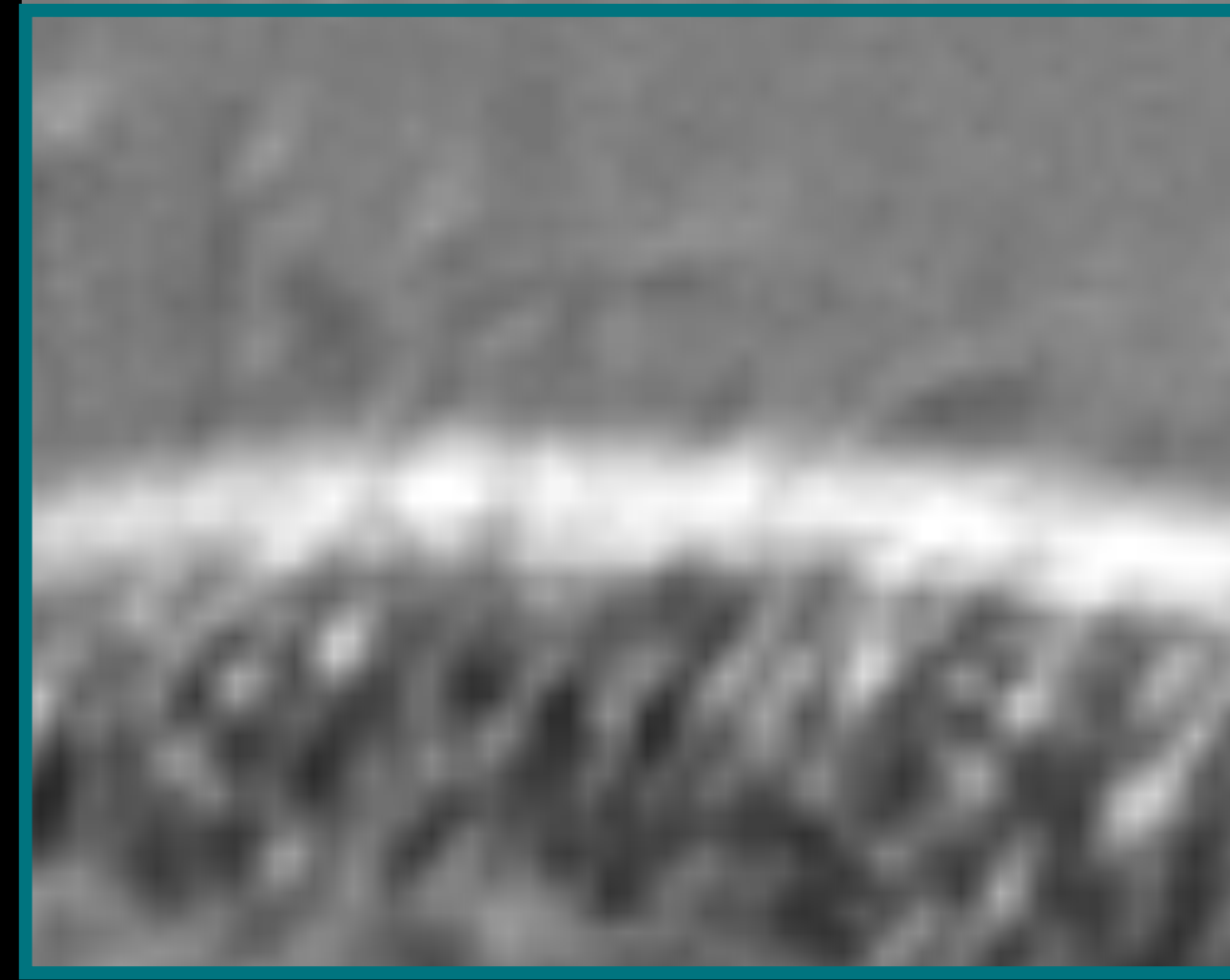


Unicellular protists

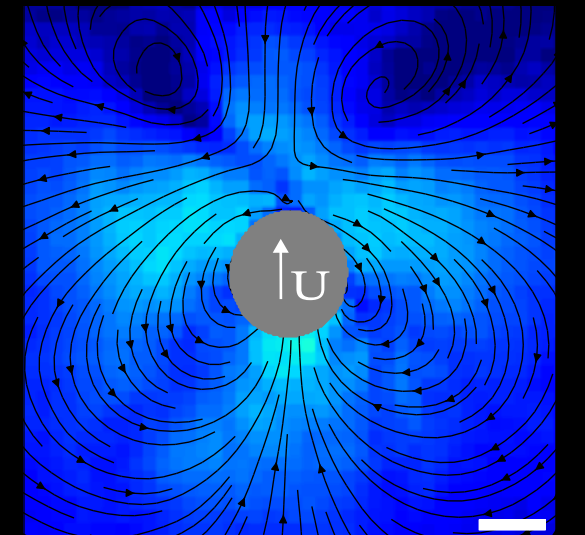
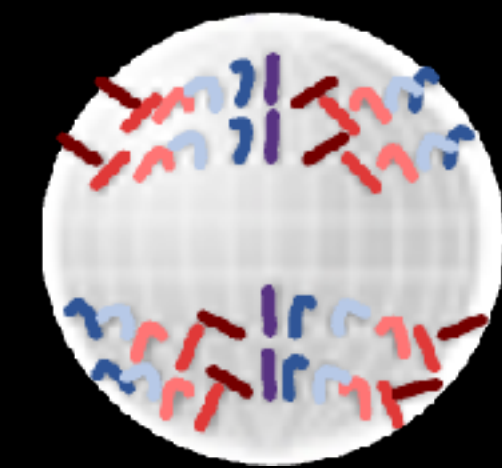
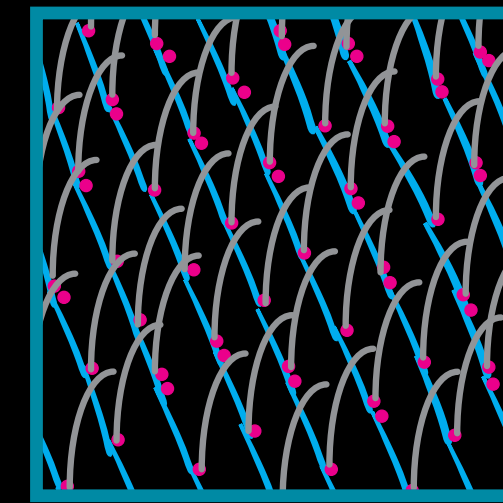
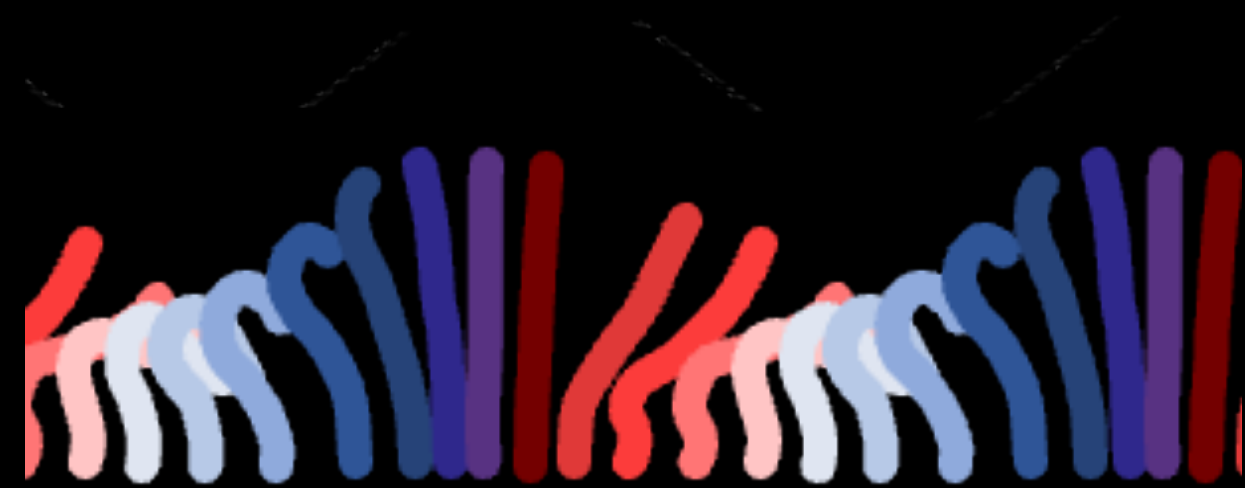
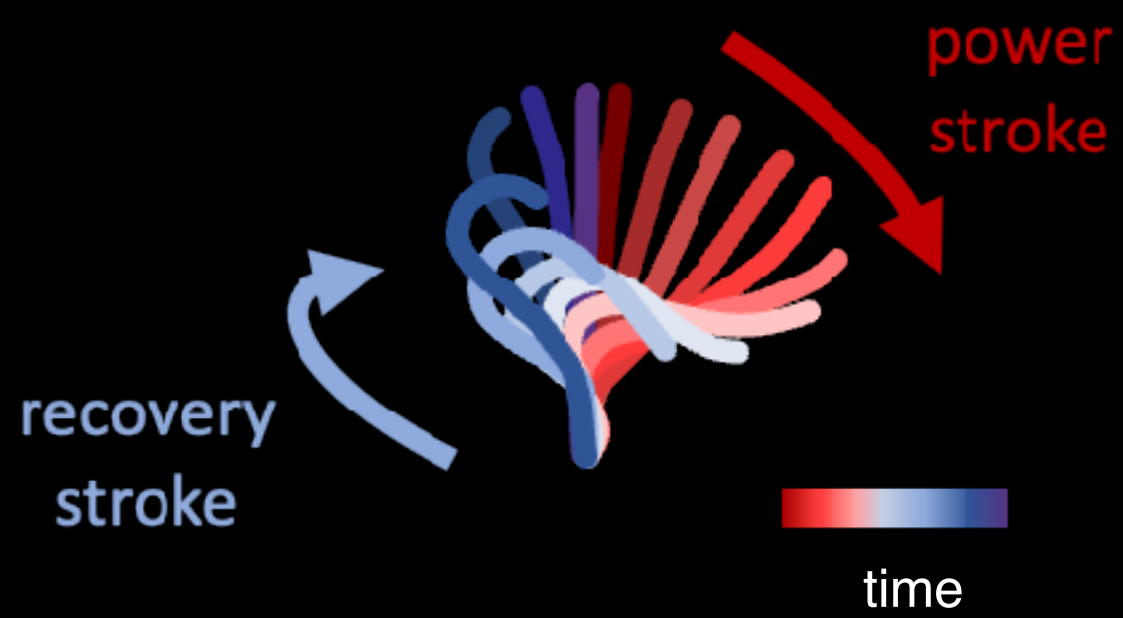


100 μm

# Function emerges from the spatio-temporal coordination of cilia across length scales



Brumley D et al. *eLife*. 2014.



Cilia beat

Metachronal coordination

Spatial patterning

Cellular gaits

Flow

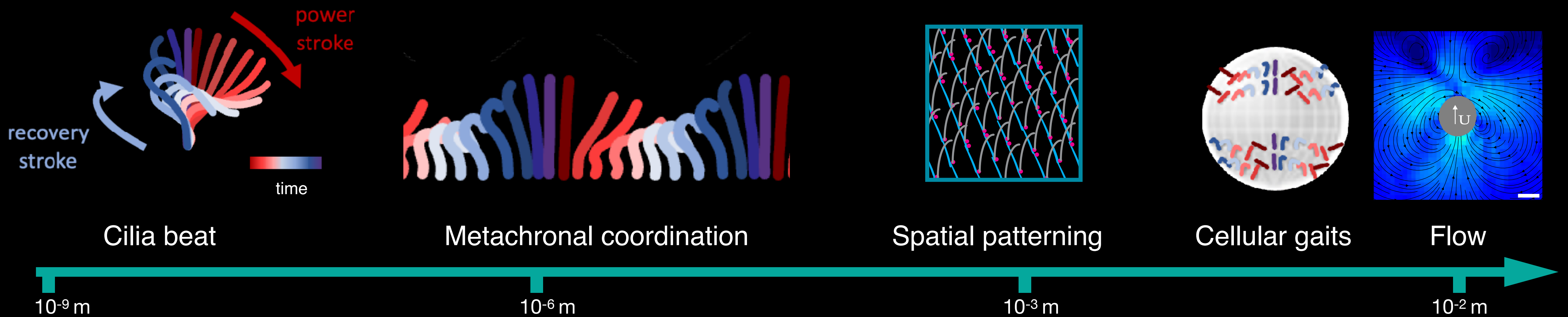
$10^{-9}$  m

$10^{-6}$  m

$10^{-3}$  m

$10^{-2}$  m

# Function emerges from the spatio-temporal coordination of cilia across length scales



# Function emerges from the spatio-temporal coordination of cilia across length scales

## Cellular function

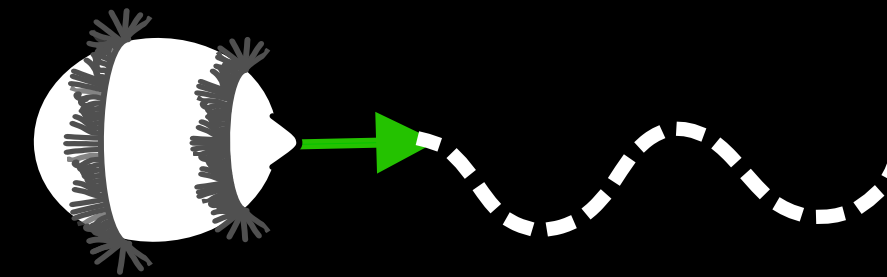
Temporal Patterning

+

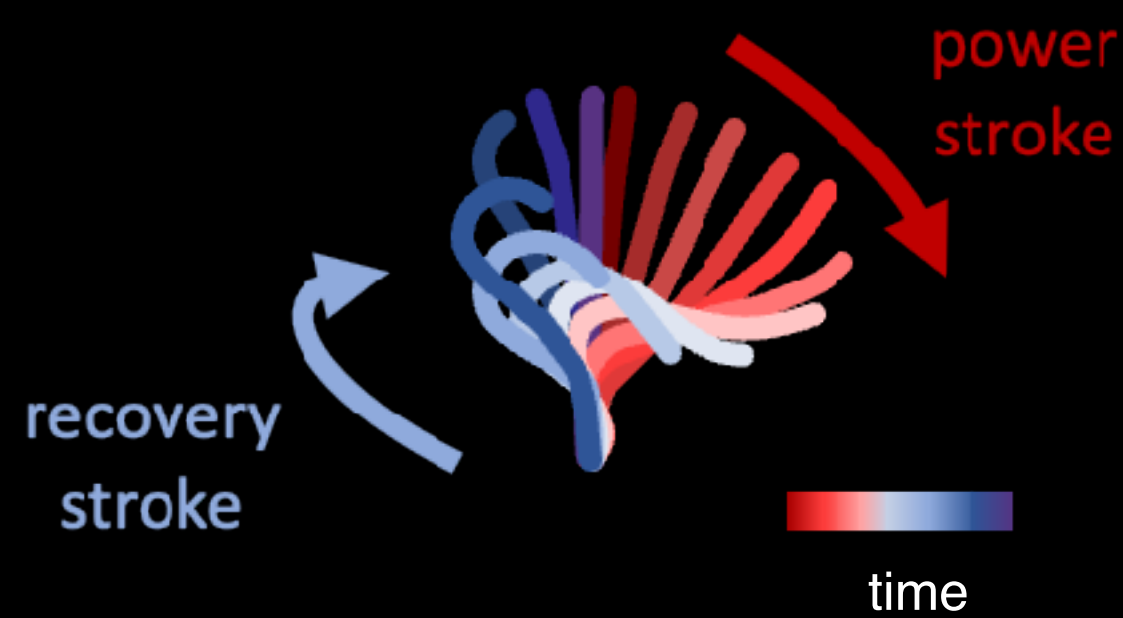
Spatial Patterning

=

Swimming



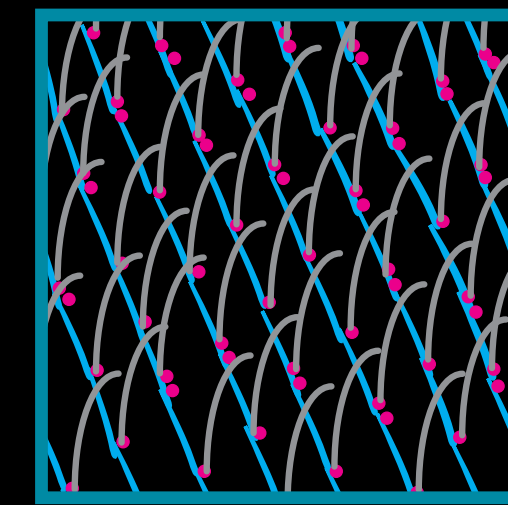
Feeding



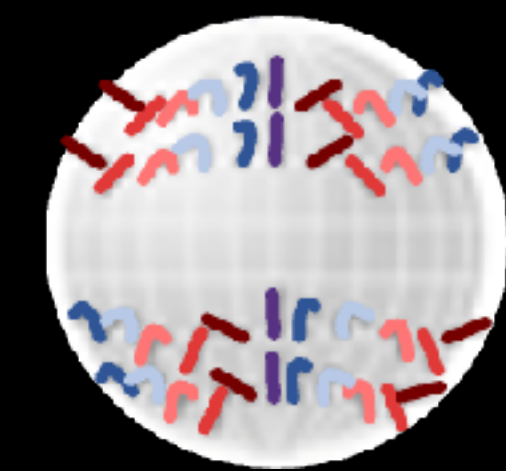
Cilia beat



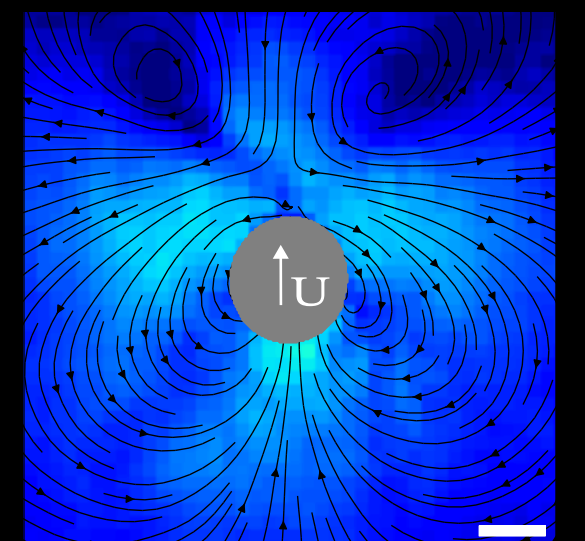
Metachronal coordination



Spatial patterning



Cellular gaits



Flow

$10^{-9}$  m

$10^{-6}$  m

$10^{-3}$  m

$10^{-2}$  m

# Function emerges from the spatio-temporal coordination of cilia across length scales

## Cellular function

Swimming

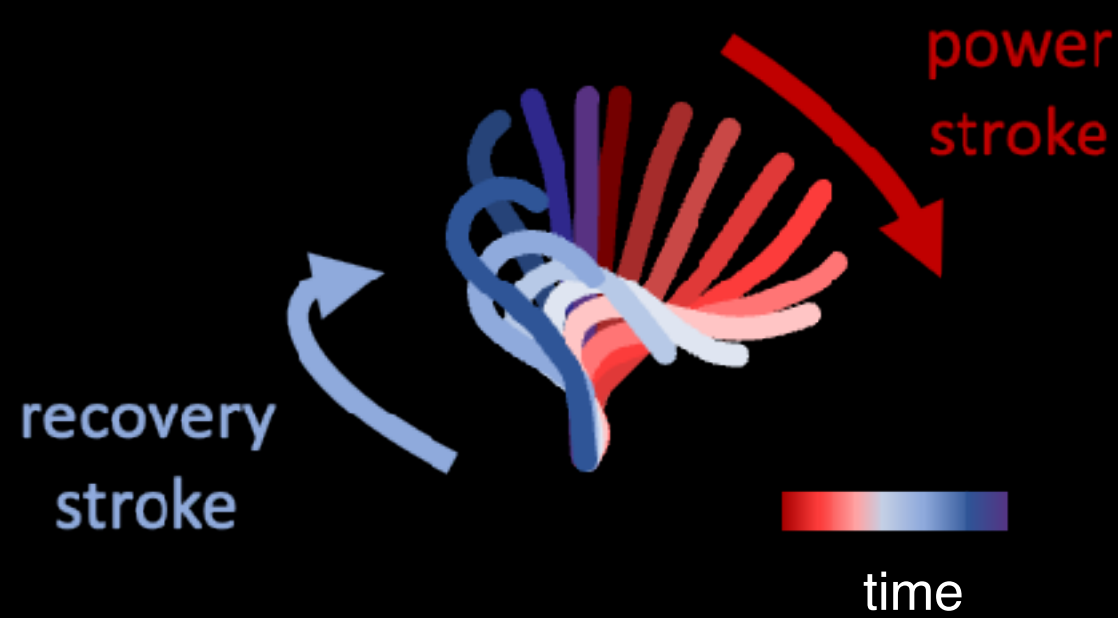
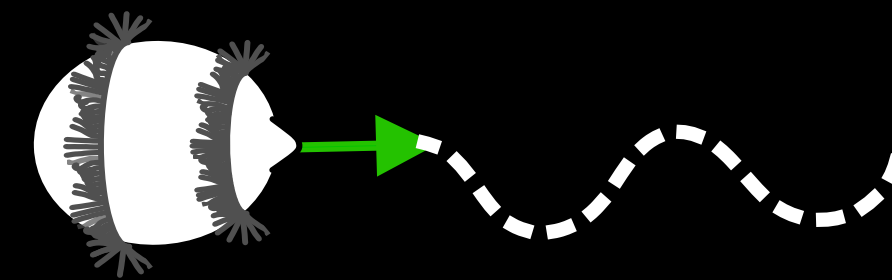
Feeding

Temporal Patterning

+

Spatial Patterning

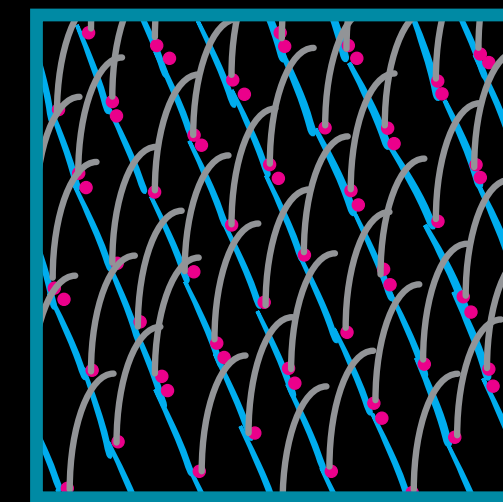
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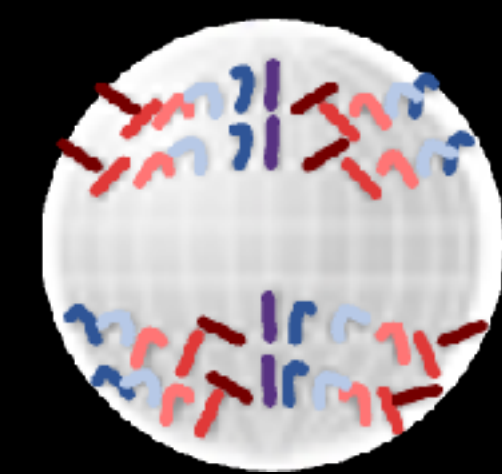
Cilia beat



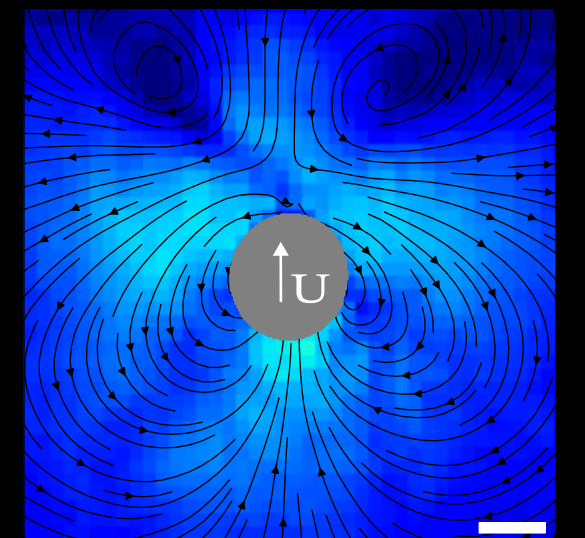
Metachronal coordination



Spatial patterning



Cellular gaits



Flow

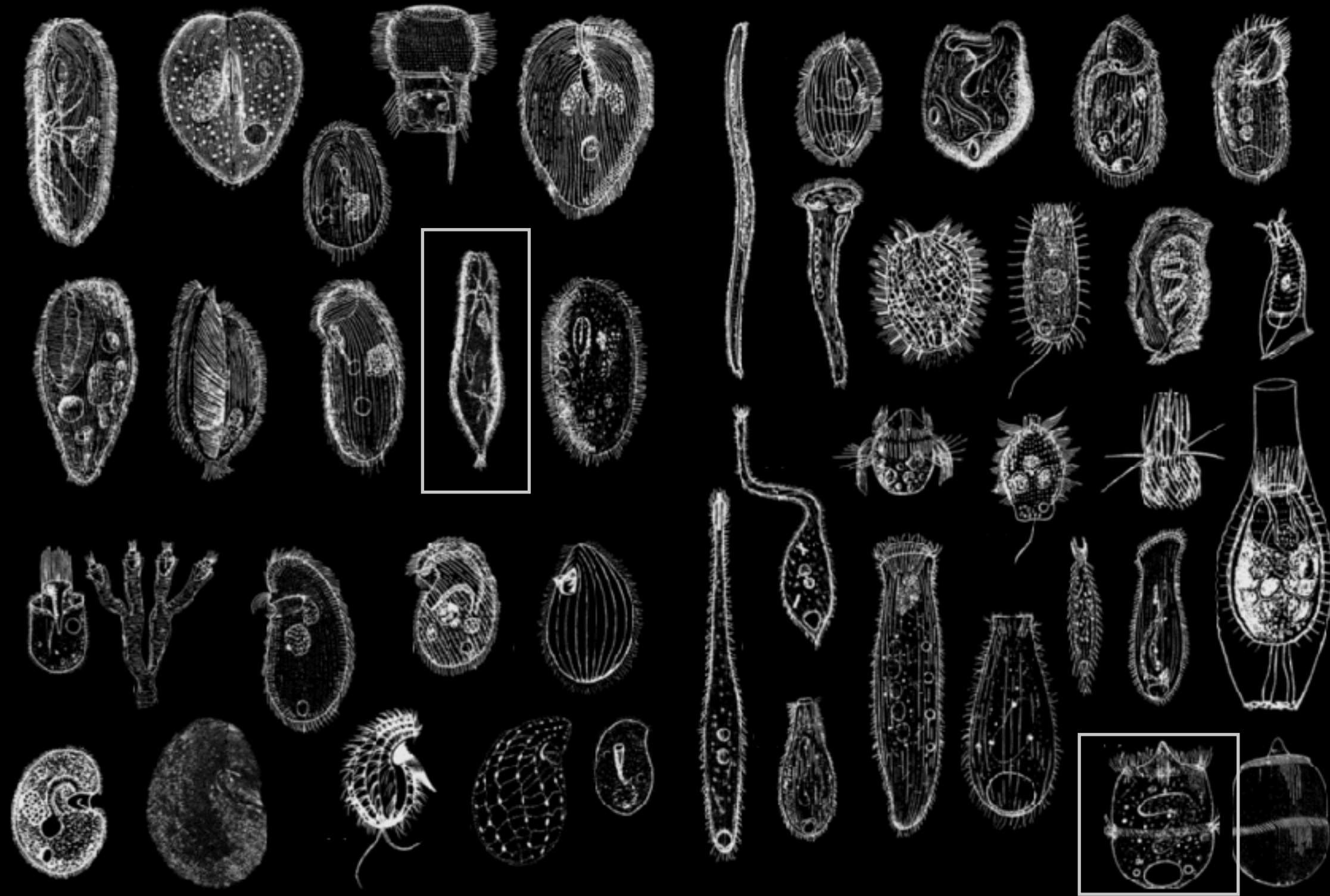
$10^{-9}$  m

$10^{-6}$  m

$10^{-3}$  m

$10^{-2}$  m

# Ciliates are free-living unicellular eukaryotes with a wide diversity of shapes

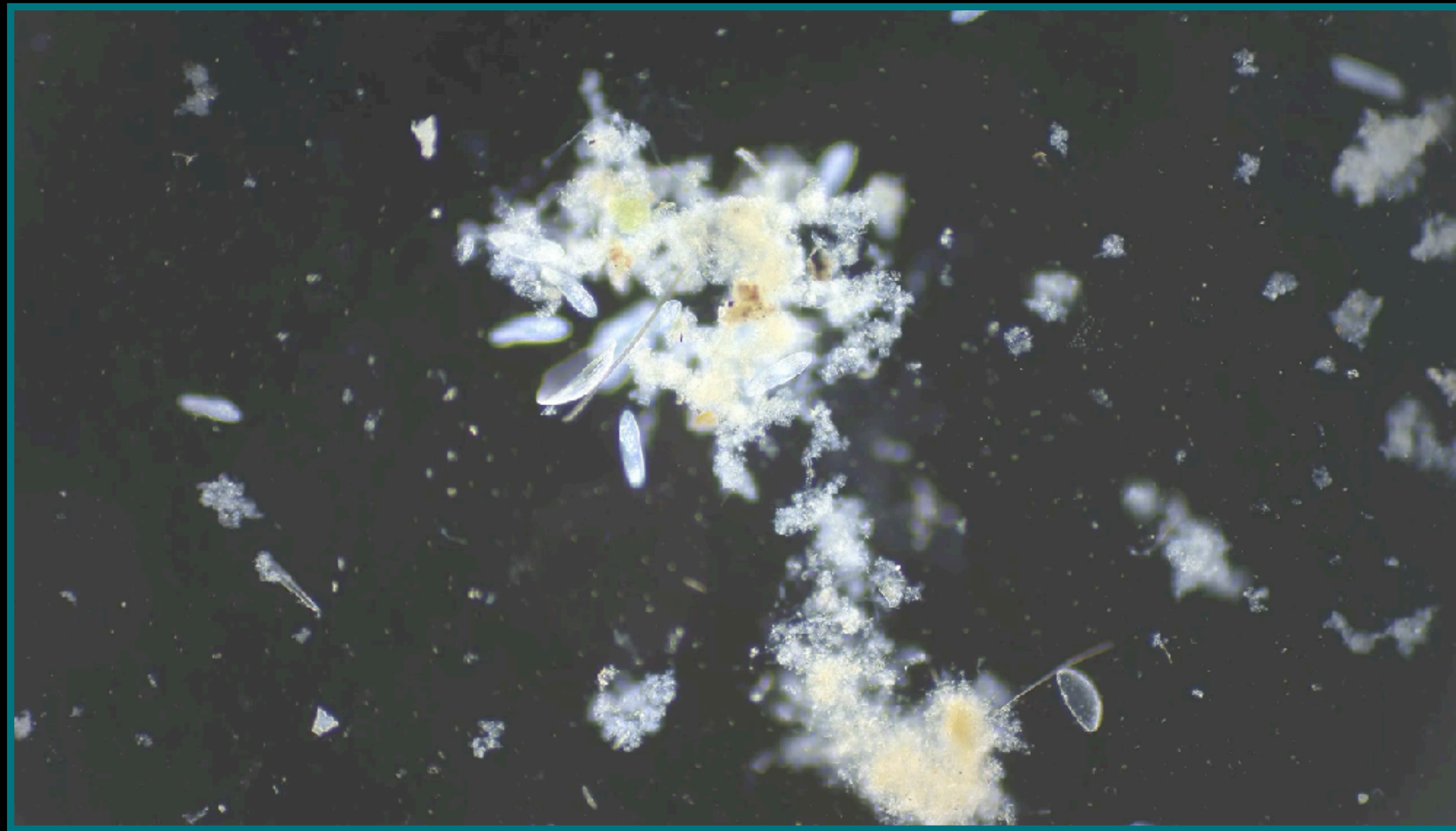


A. Warren, et al., "Chapter 2 protozoa," in *Thorp and Covich's Freshwater Invertebrates (Fourth Edition)*.



Lake Geneva

# Ciliates display remarkable behavioral sophistication



Coyle S. *MboC*. 2020.

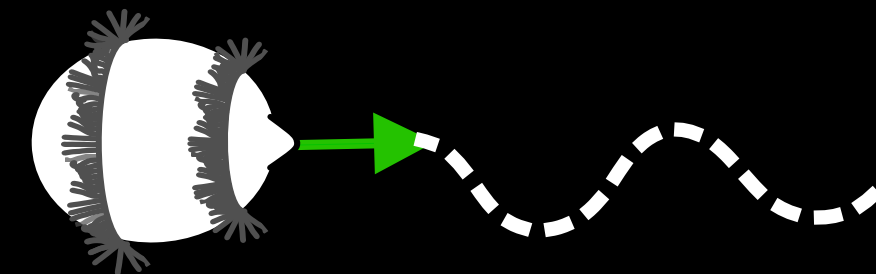
Hunting



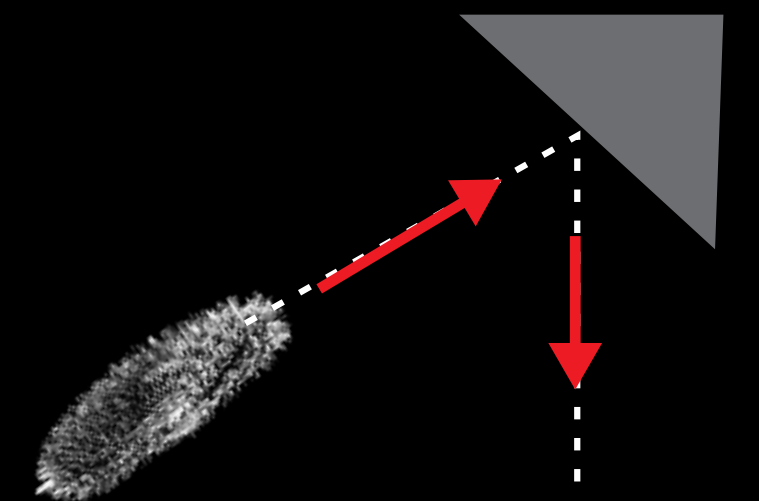
Feeding



Swimming



Navigation

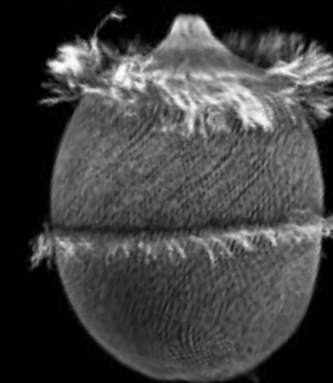


These functions require the generation of **fluid flow** driven by cilia

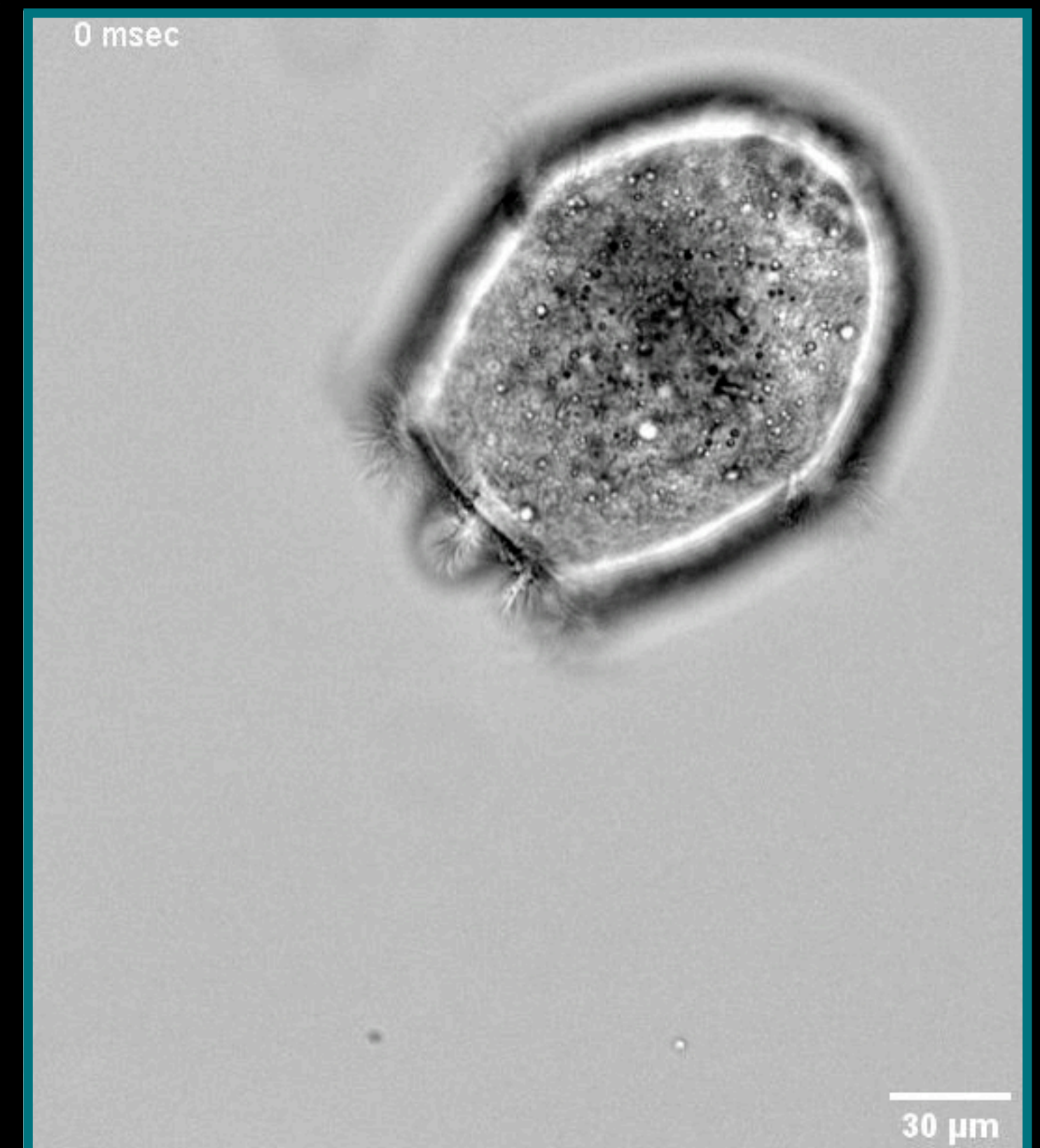
# Flow emerges from the spatio-temporal coordination of cilia



*Paramecium tetraurelia*

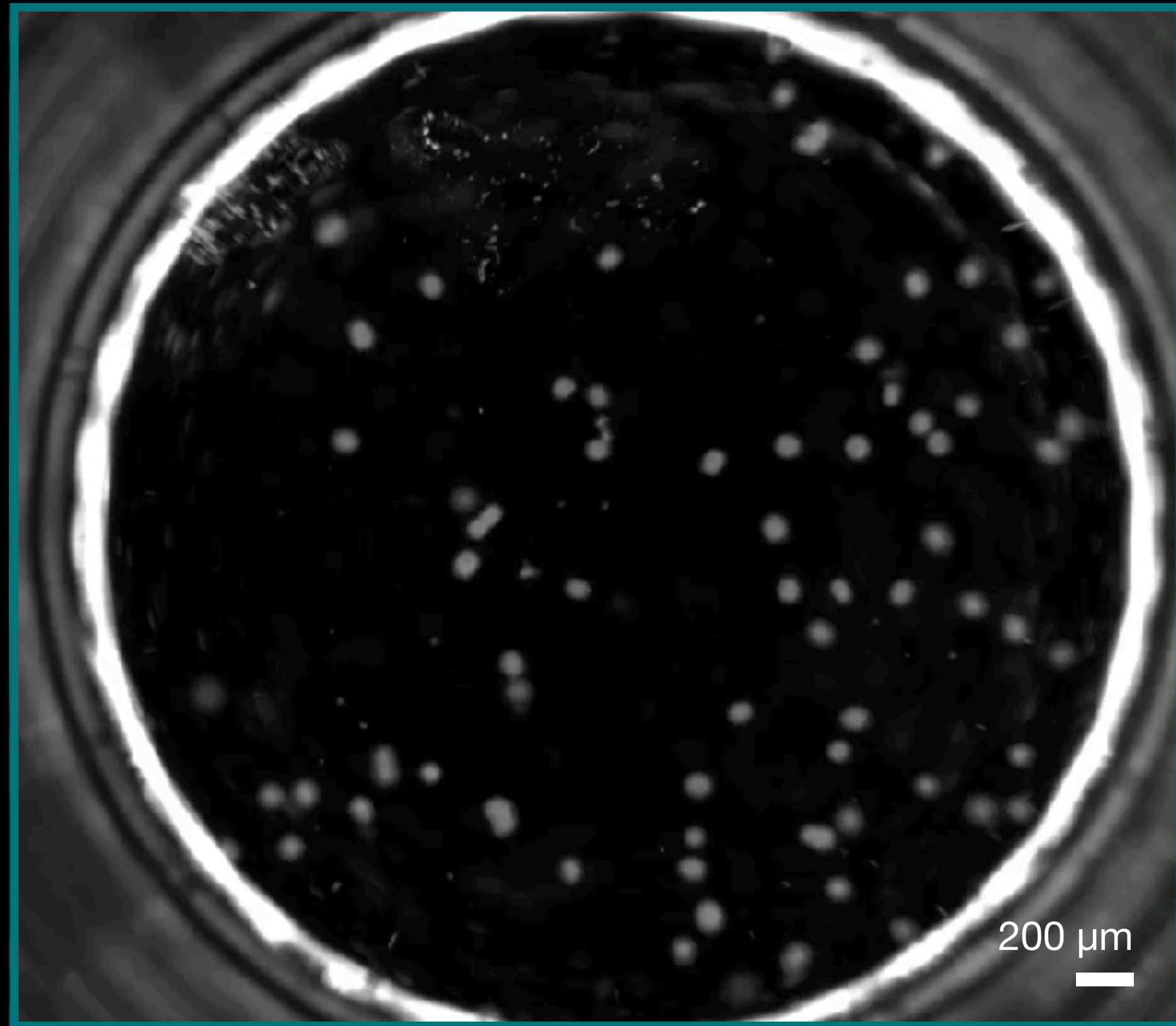


*Didinium nasutum*

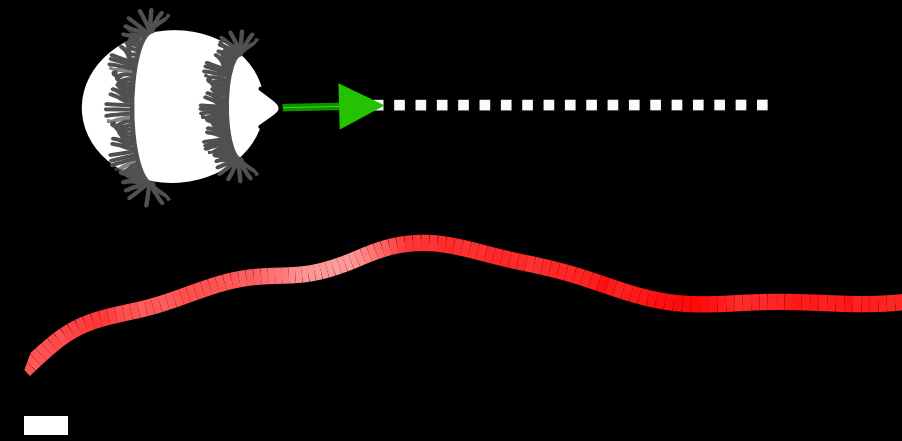


Surface of ciliates is covered by highly structured arrays of thousands of cilia organised in rows/bands. Cilia beat with periodic stroke (~20-50 Hz) and coordinate temporally forming metachronal waves

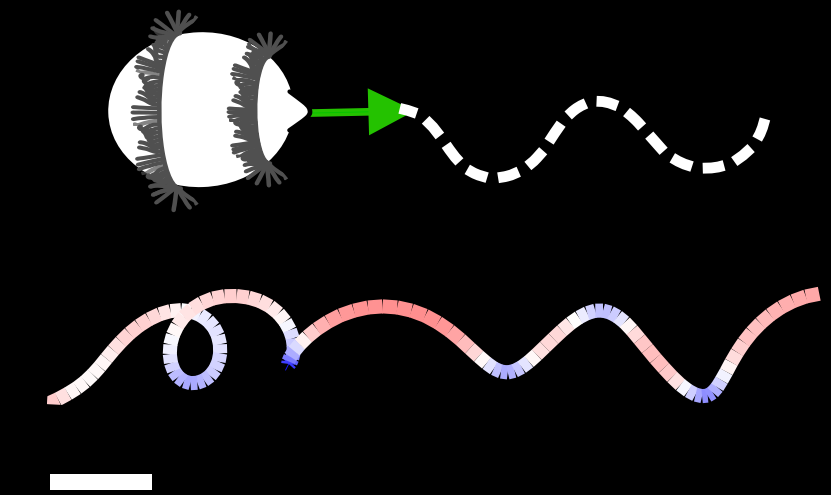
# Didinium exhibits remarkable diversity in its motility



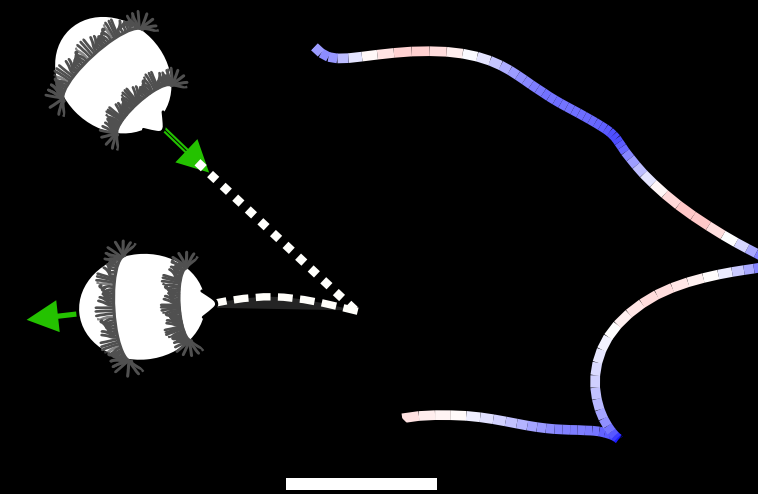
i. Directed swimming  
(Straight)



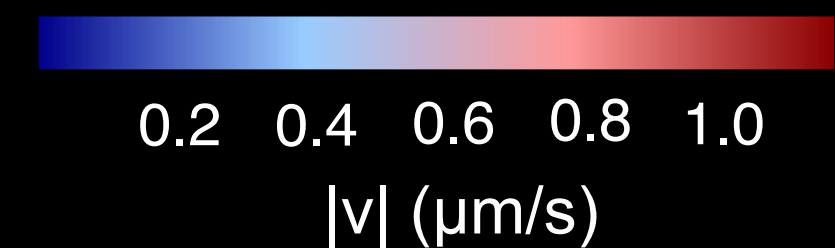
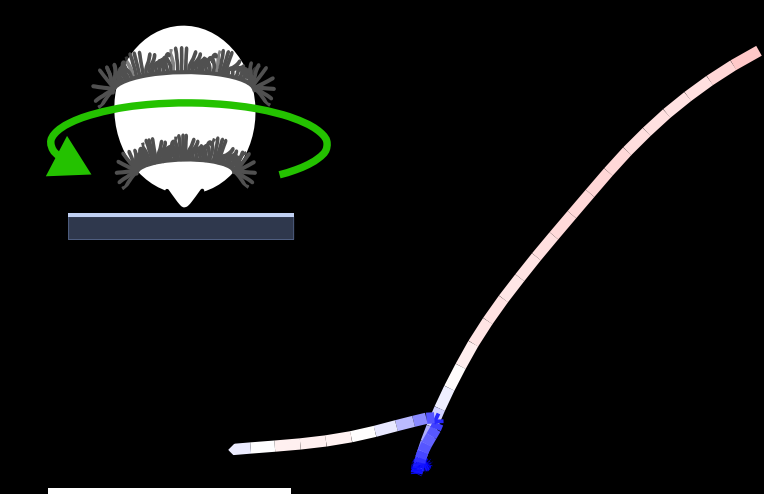
ii. Directed swimming  
(Curved)



iii. Direction reversal

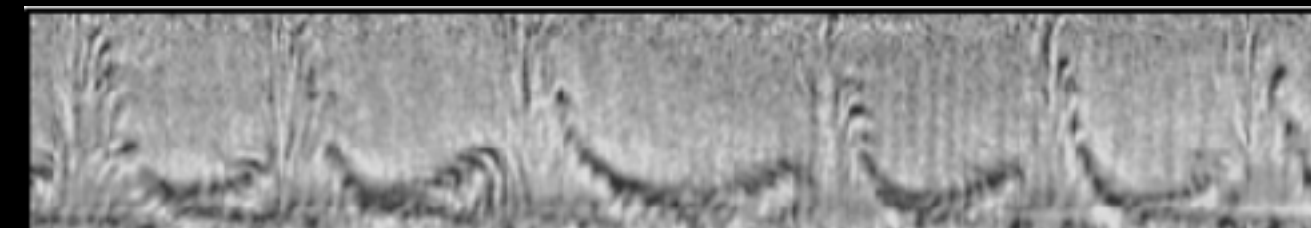
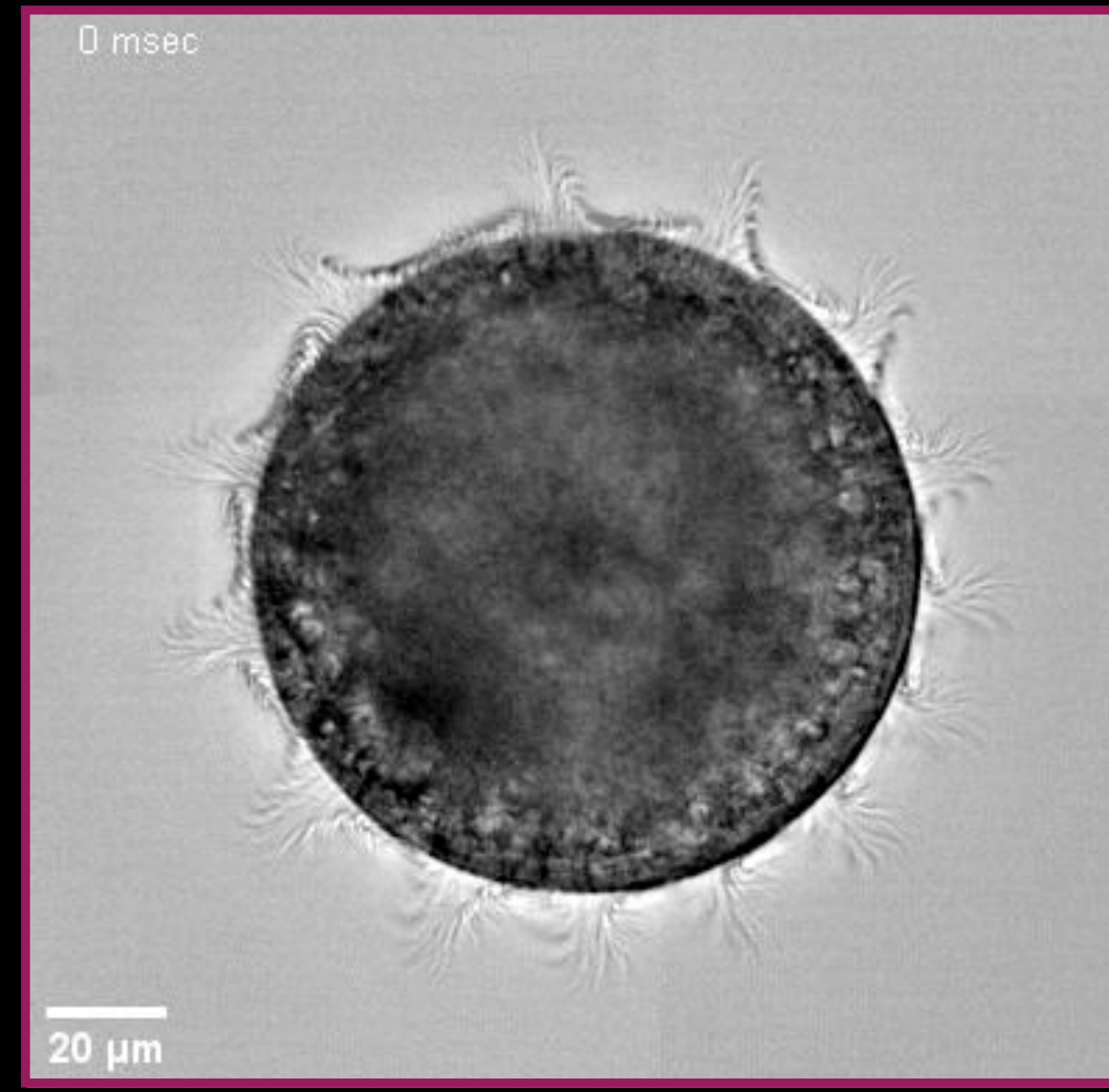
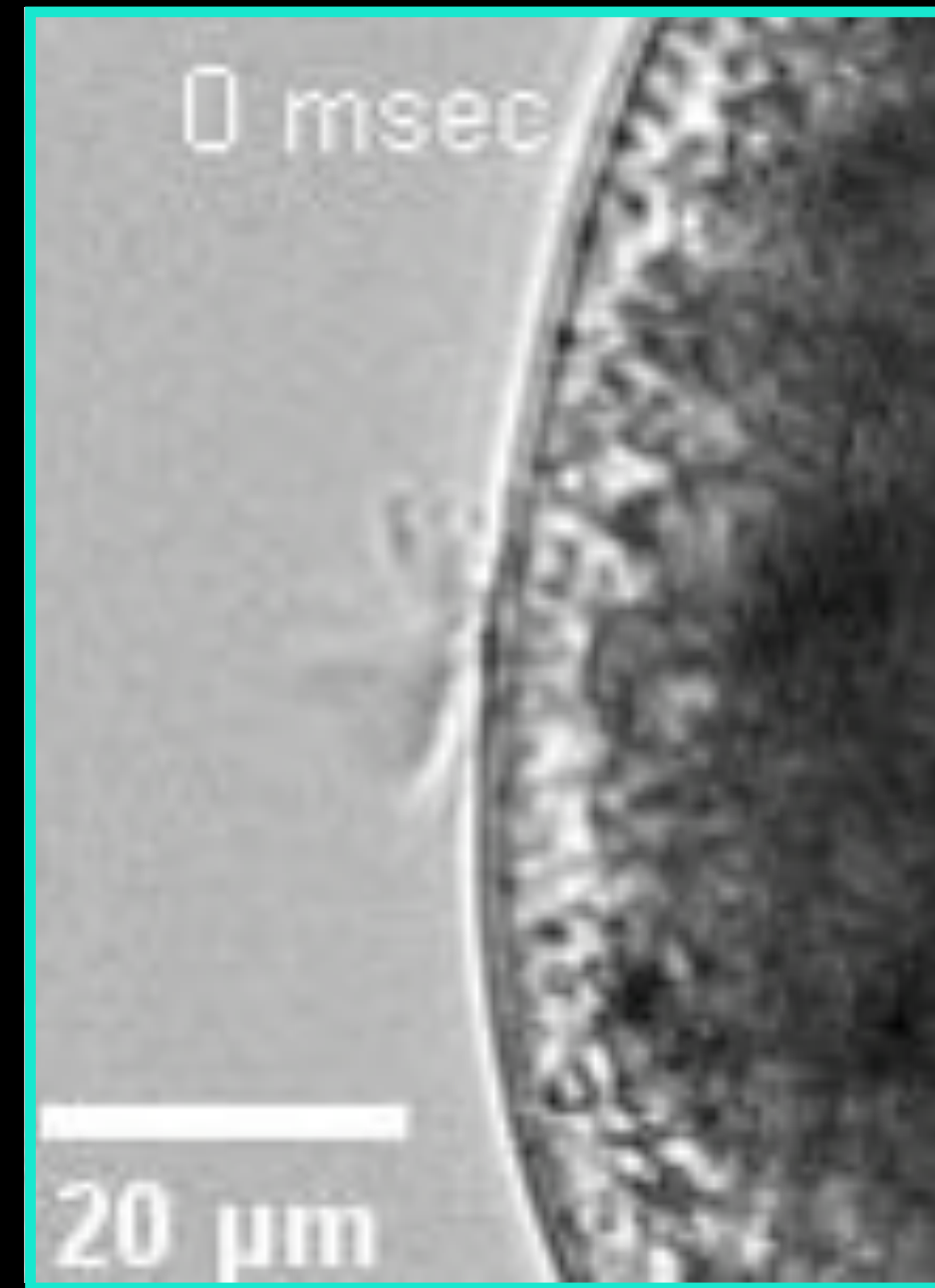
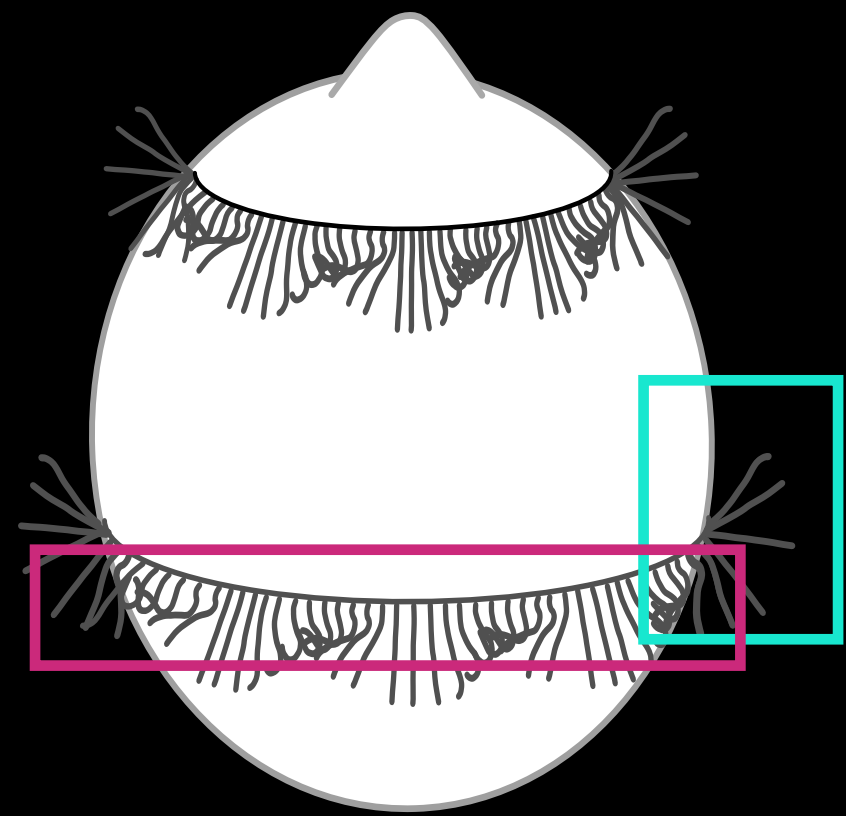


iv. Surface spinning

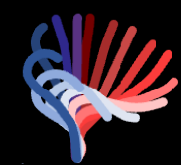


How are swimming gaits encoded by cilia array patterns?

# Steady metachronal wave dynamics give rise to robust swimming direction



Cilia beat



Metachronal wave



Cellular gait



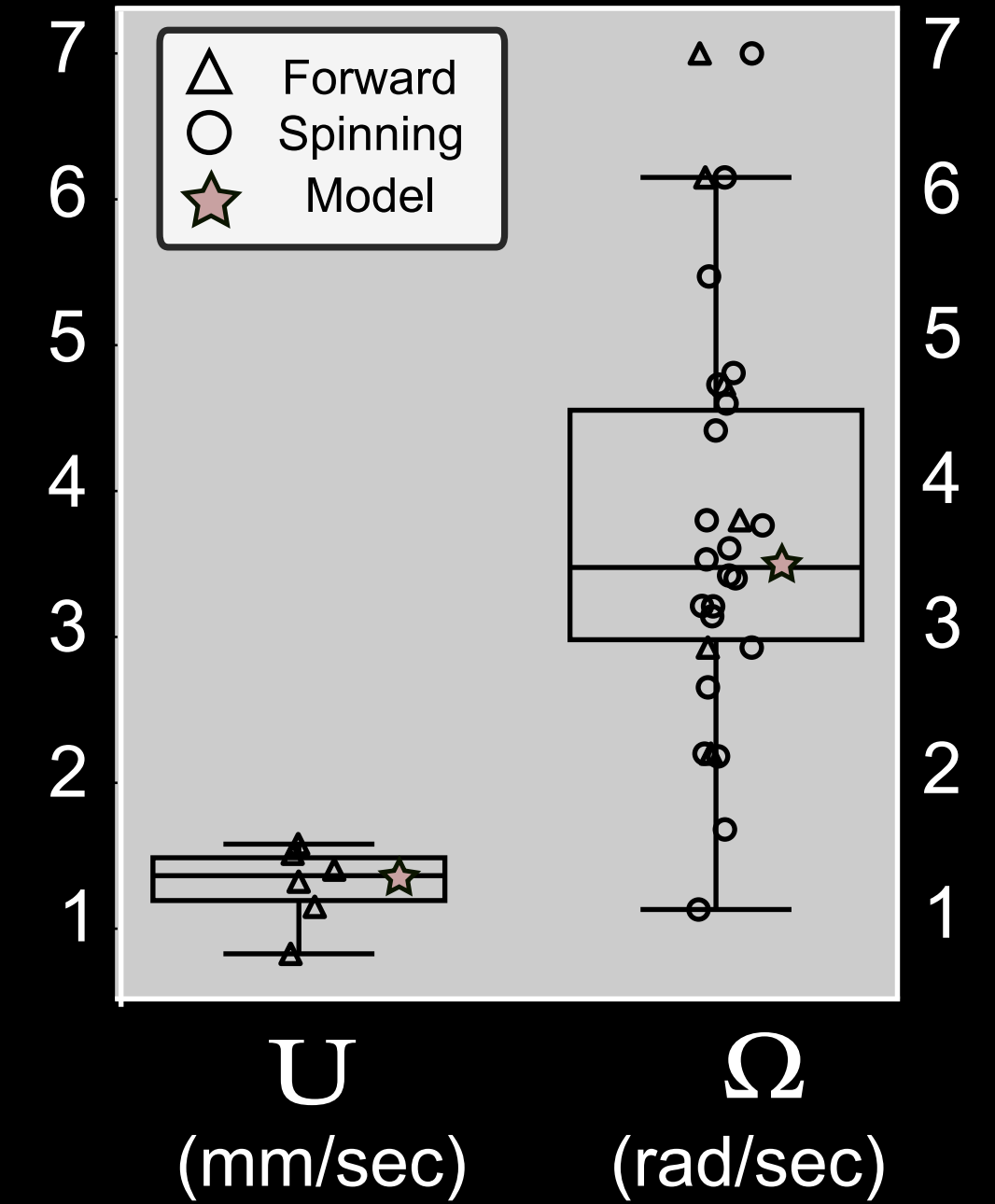
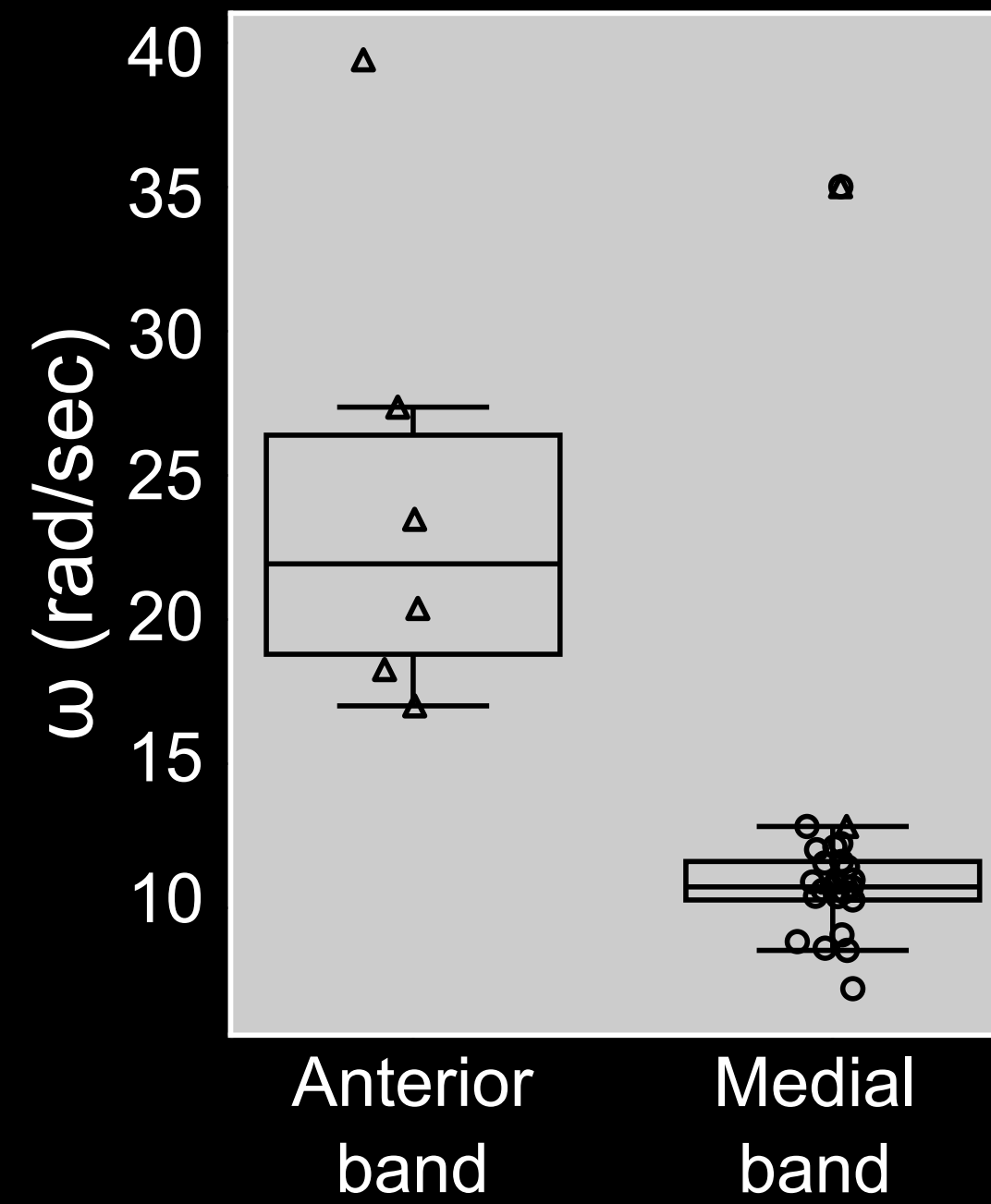
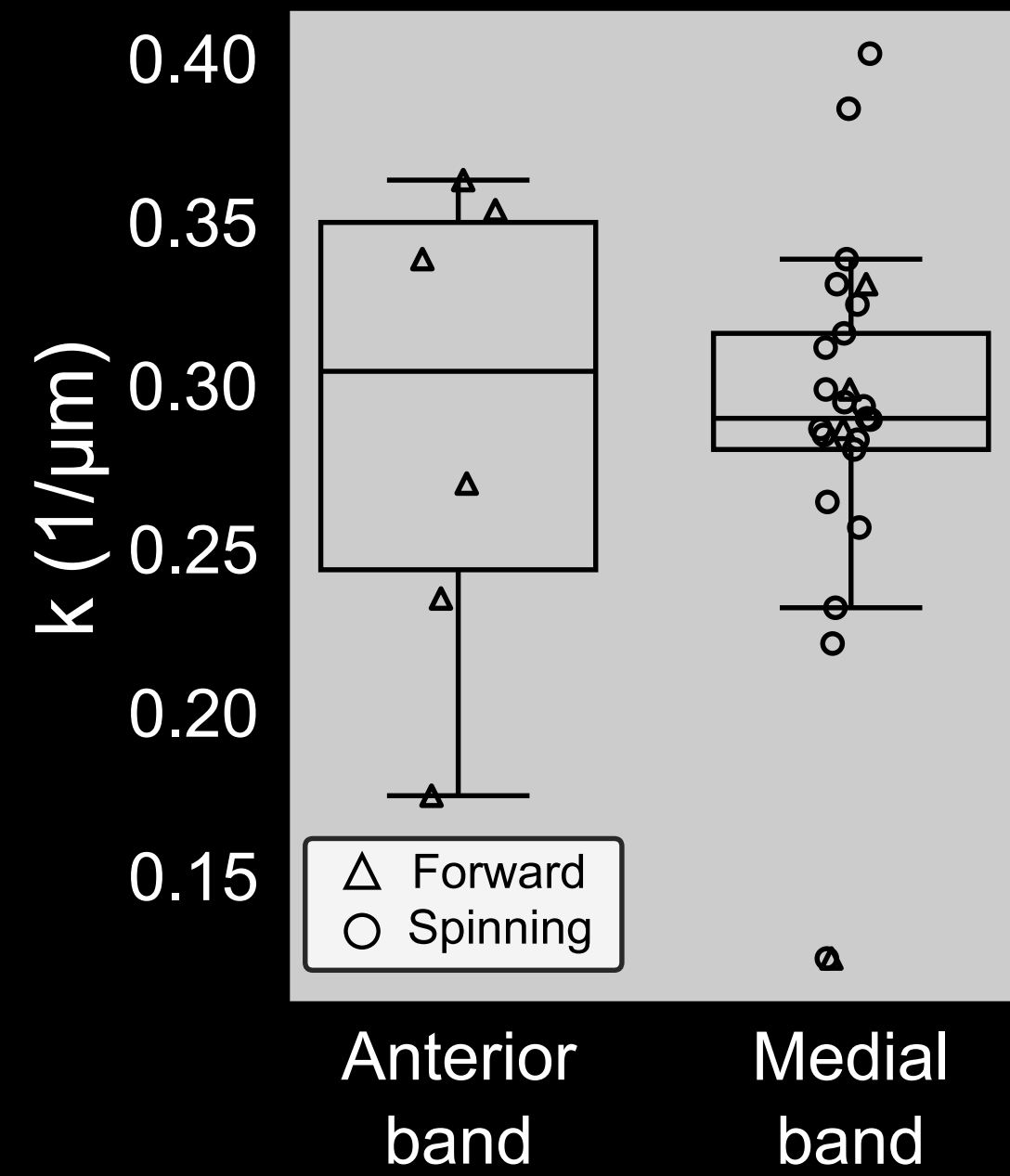
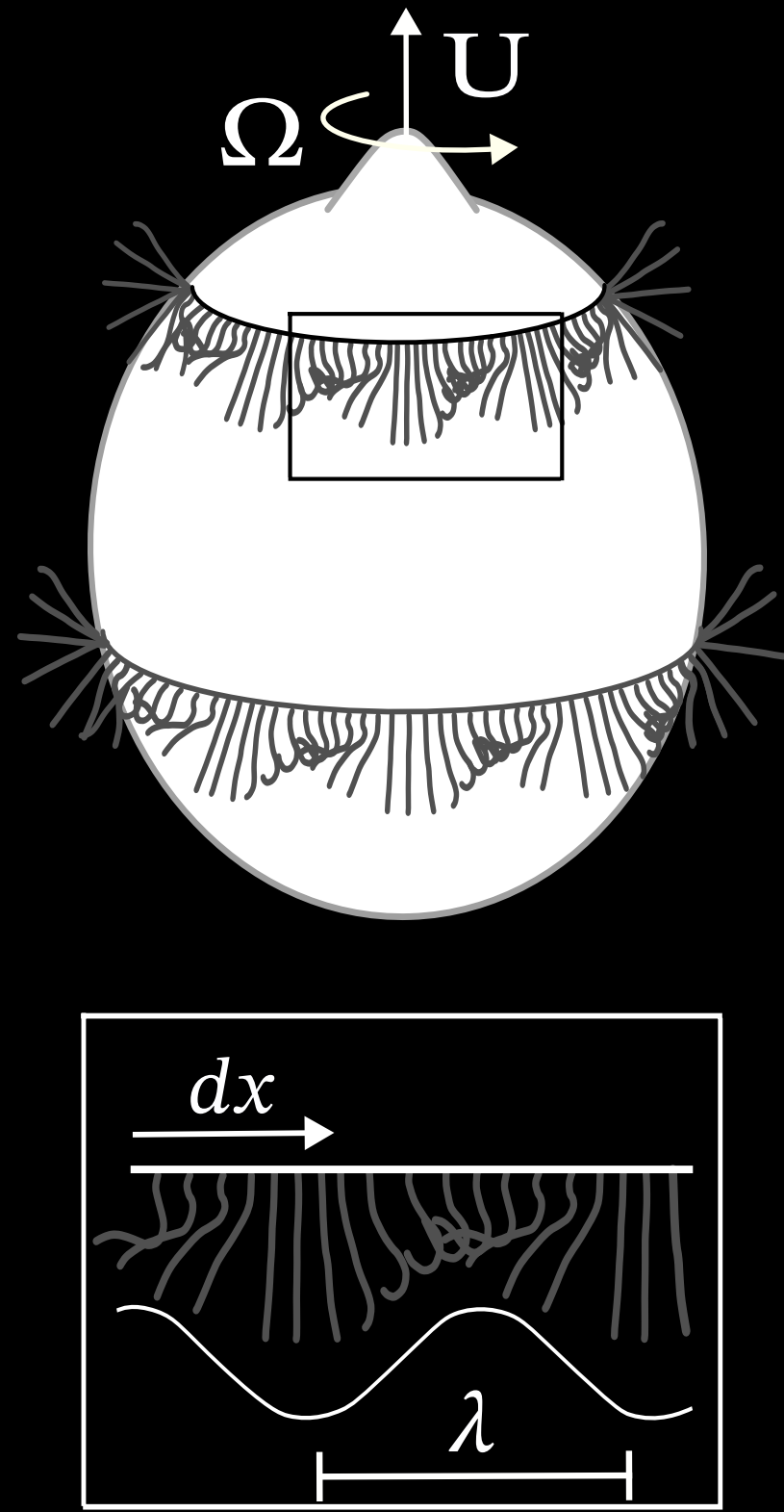
$10^{-9}$  m

$10^{-6}$  m

$10^{-3}$  m

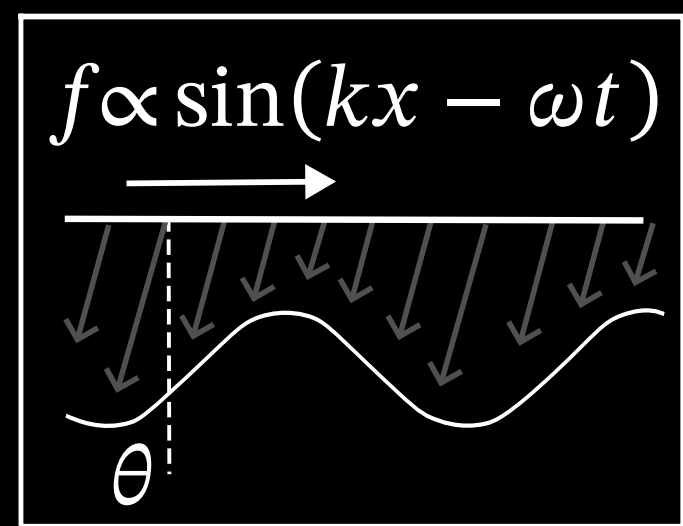
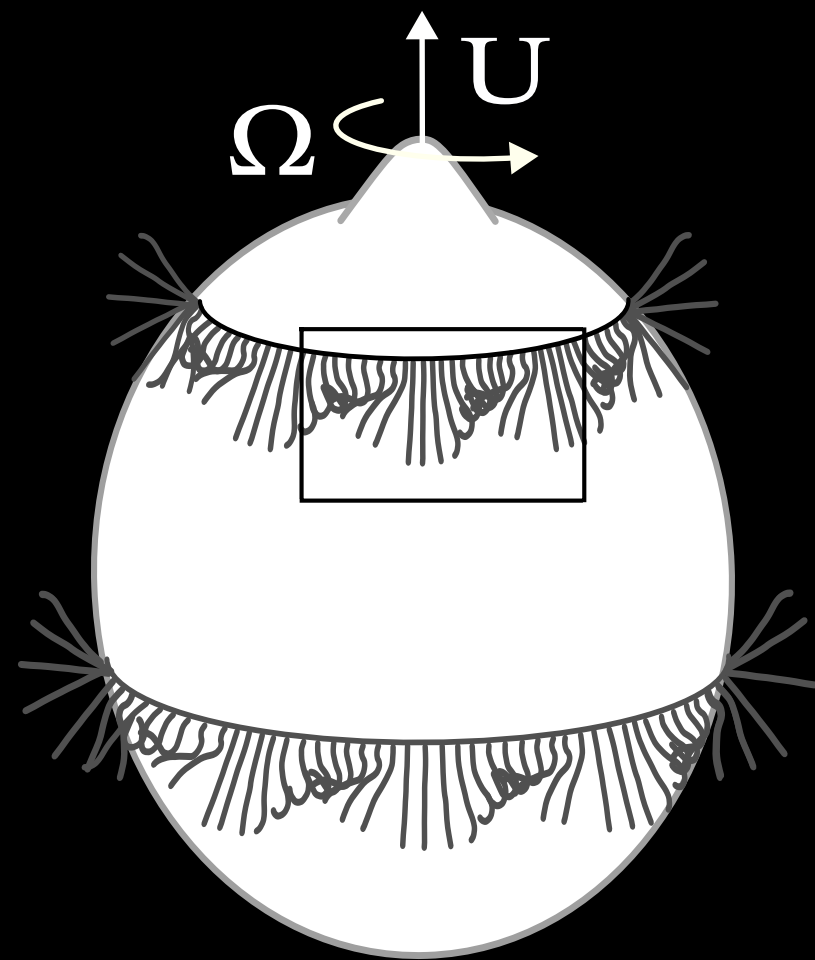
$10^{-2}$  m

# Steady metachronal wave dynamics give rise to robust swimming direction



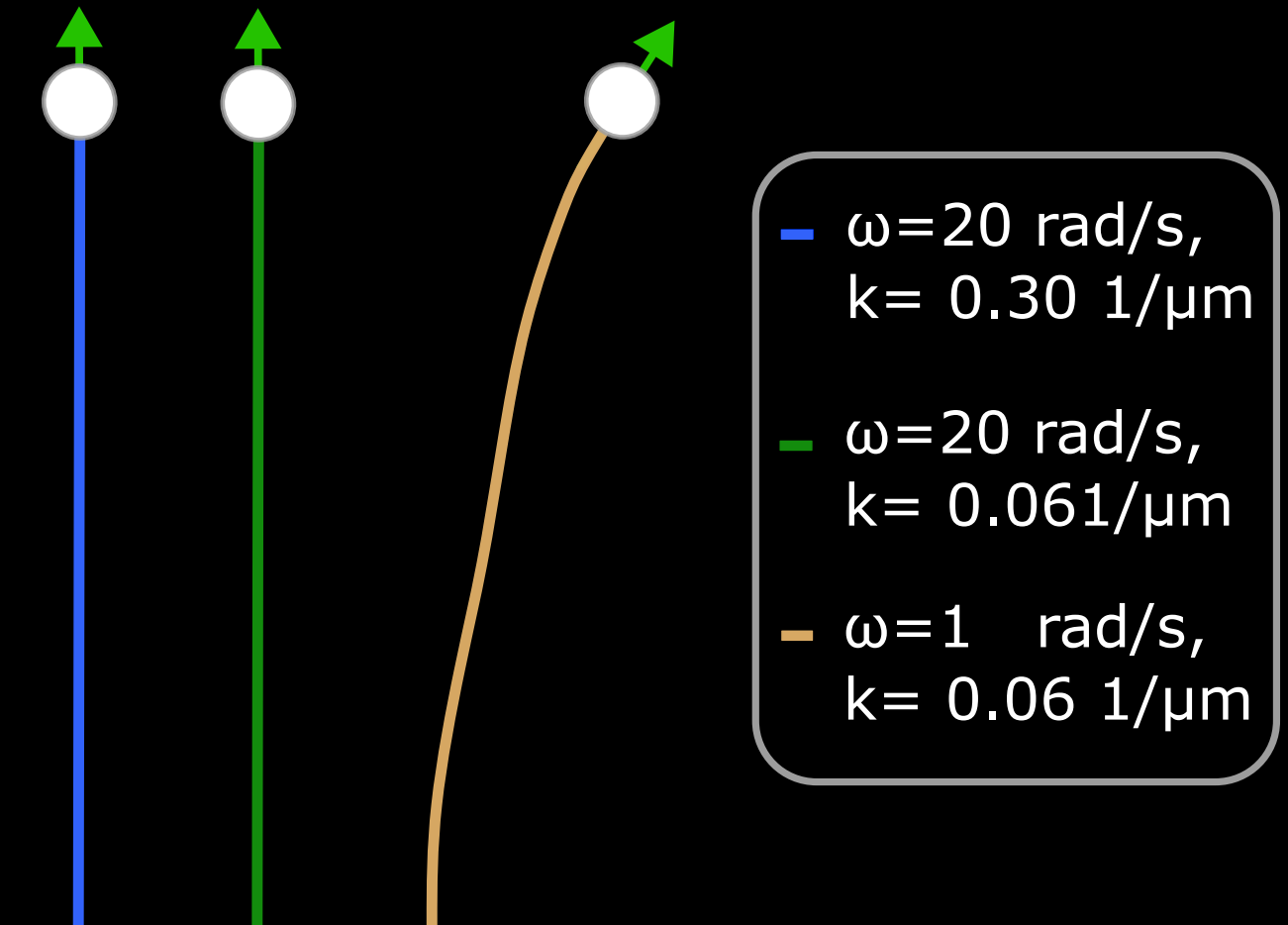
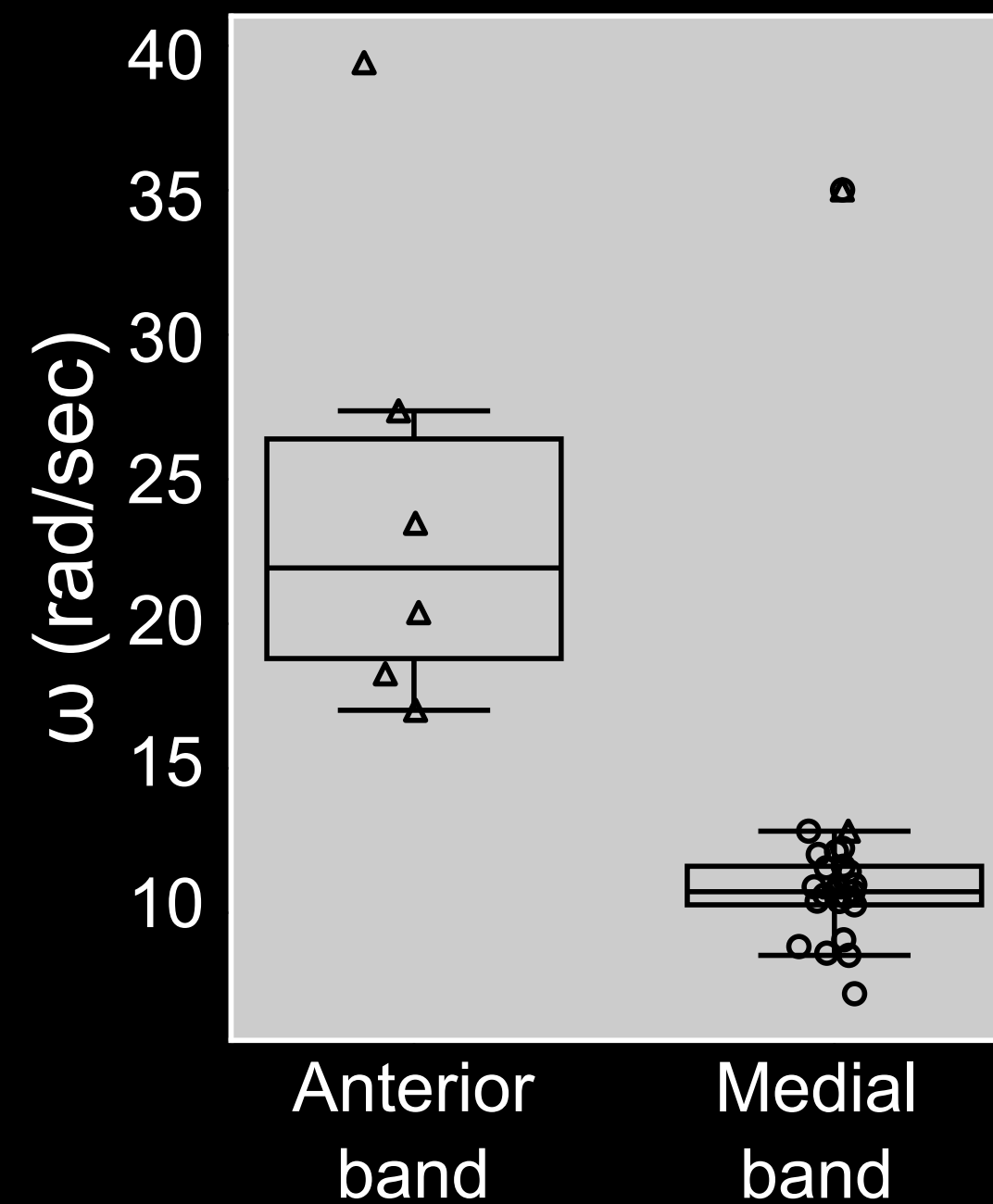
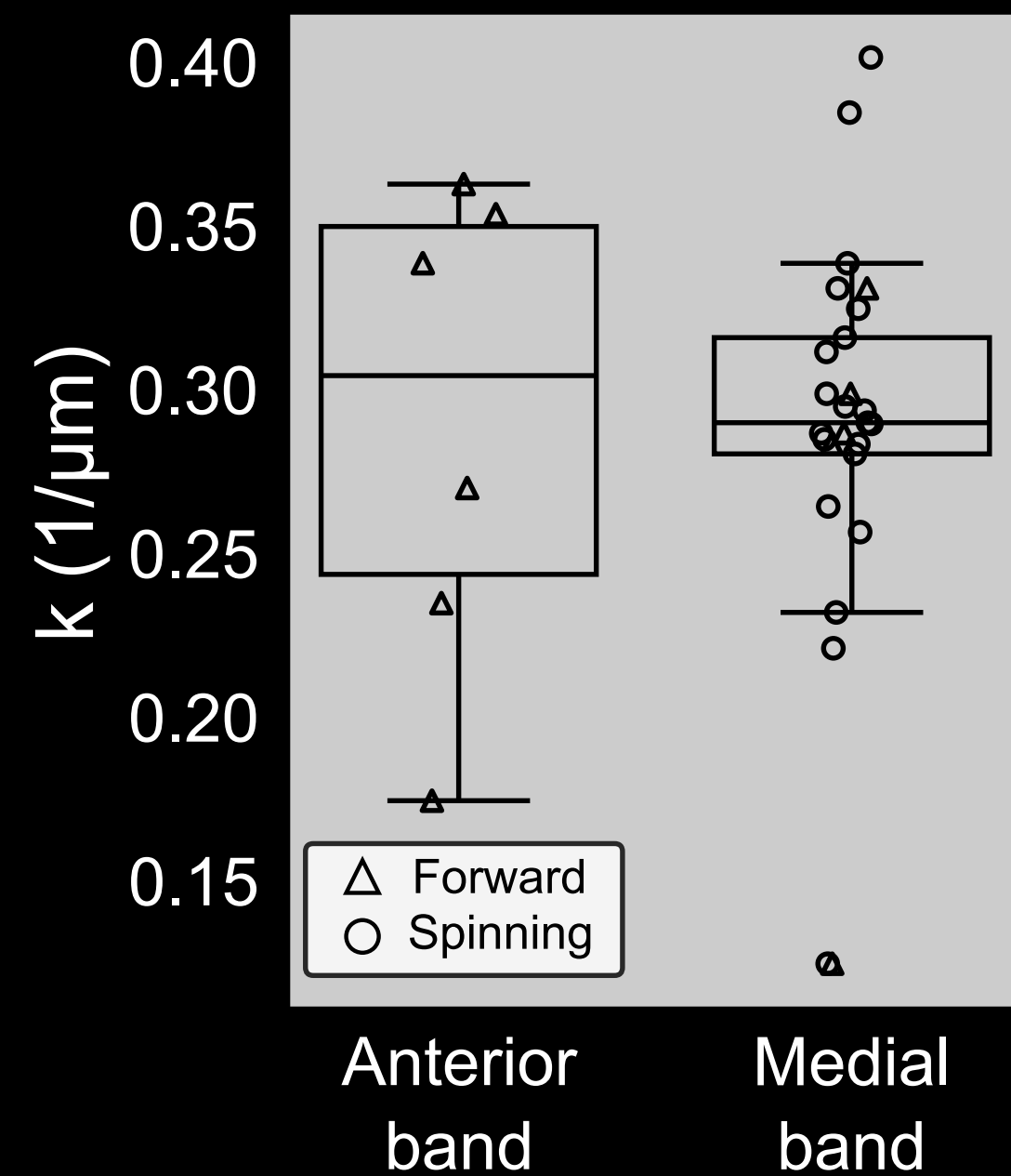
$$k = \frac{2\pi}{\lambda} \quad \omega = \frac{1}{R} \frac{dx}{dt}$$

# Steady metachronal wave dynamics give rise to robust swimming direction

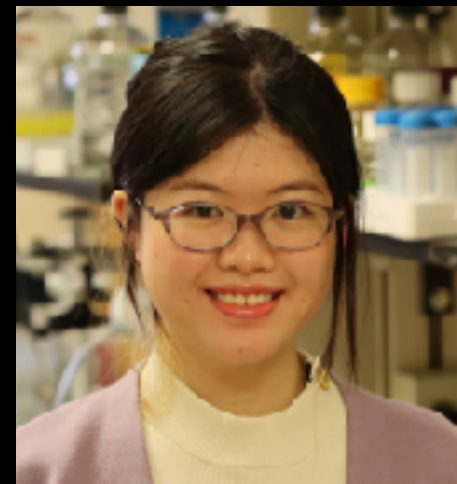


$$F \sin \theta = 8\pi\mu R^2 \Omega$$

$$F \cos \theta = 6\pi\mu R U$$



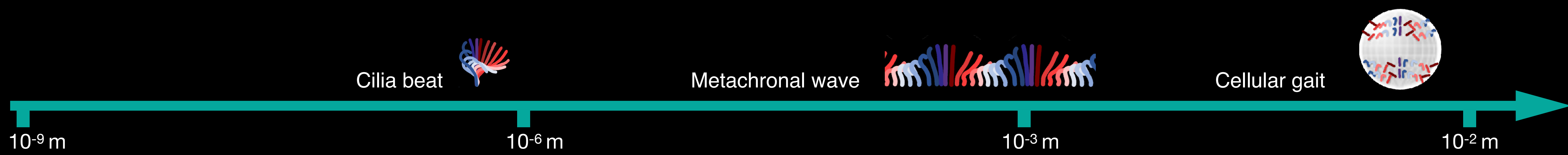
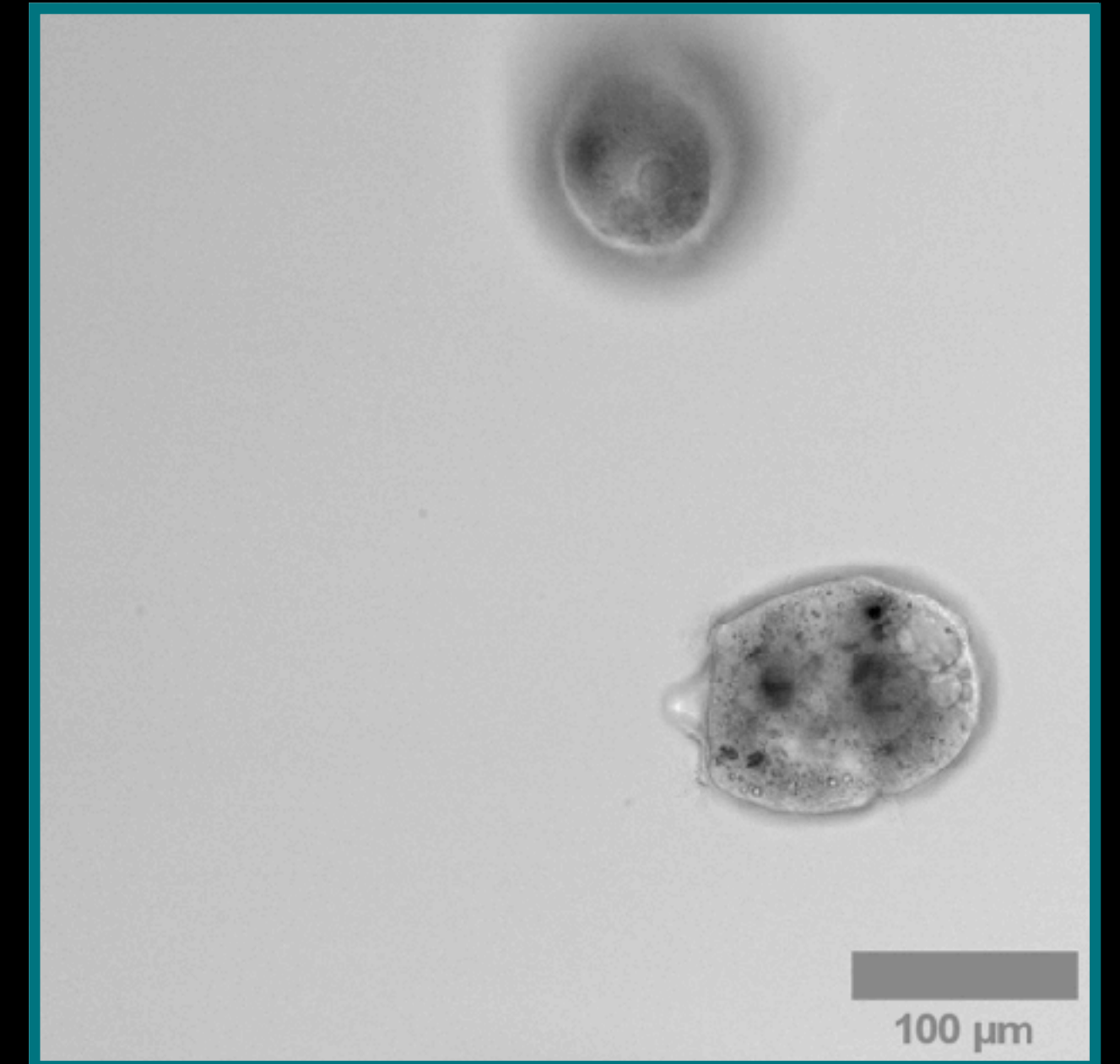
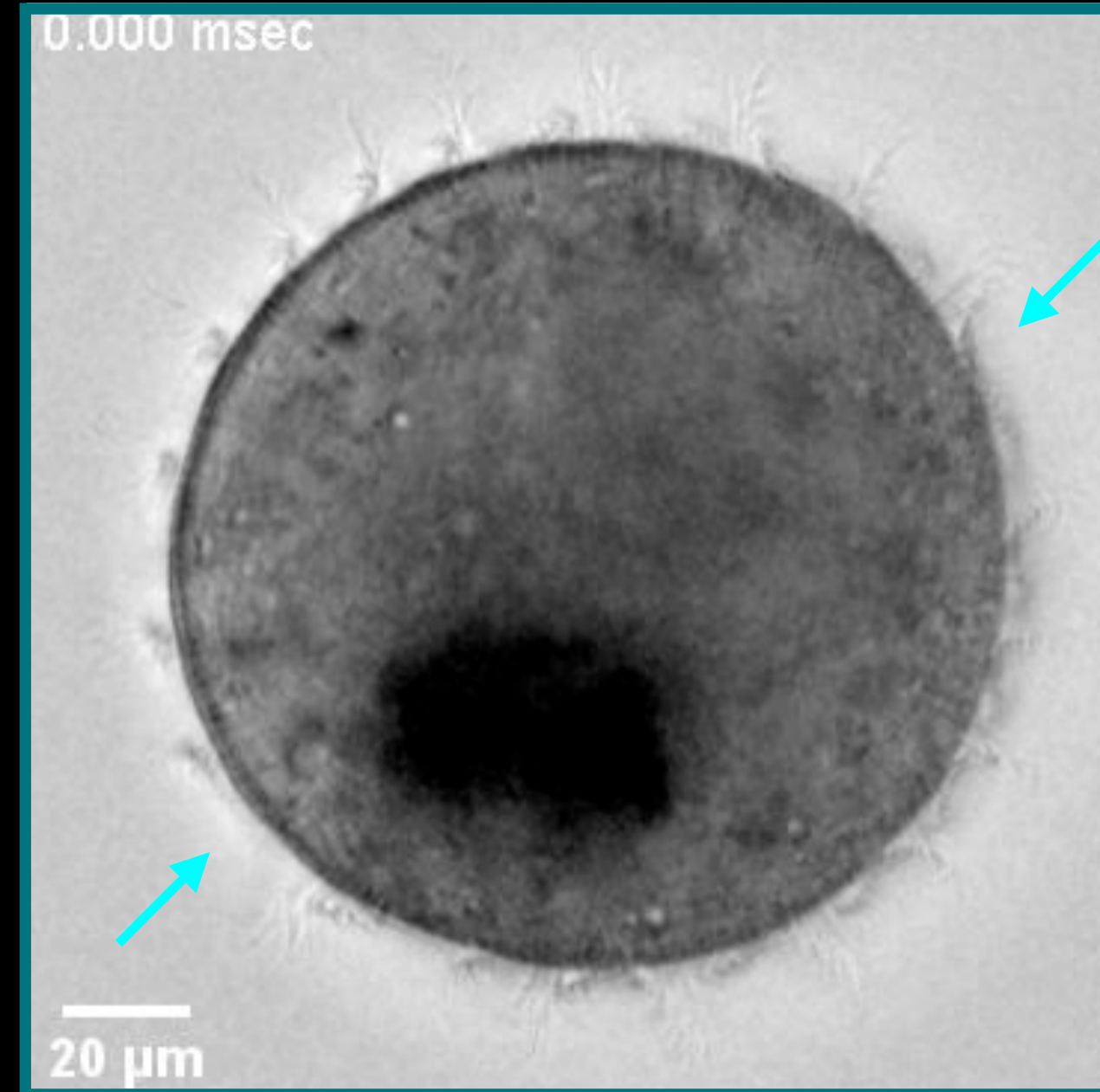
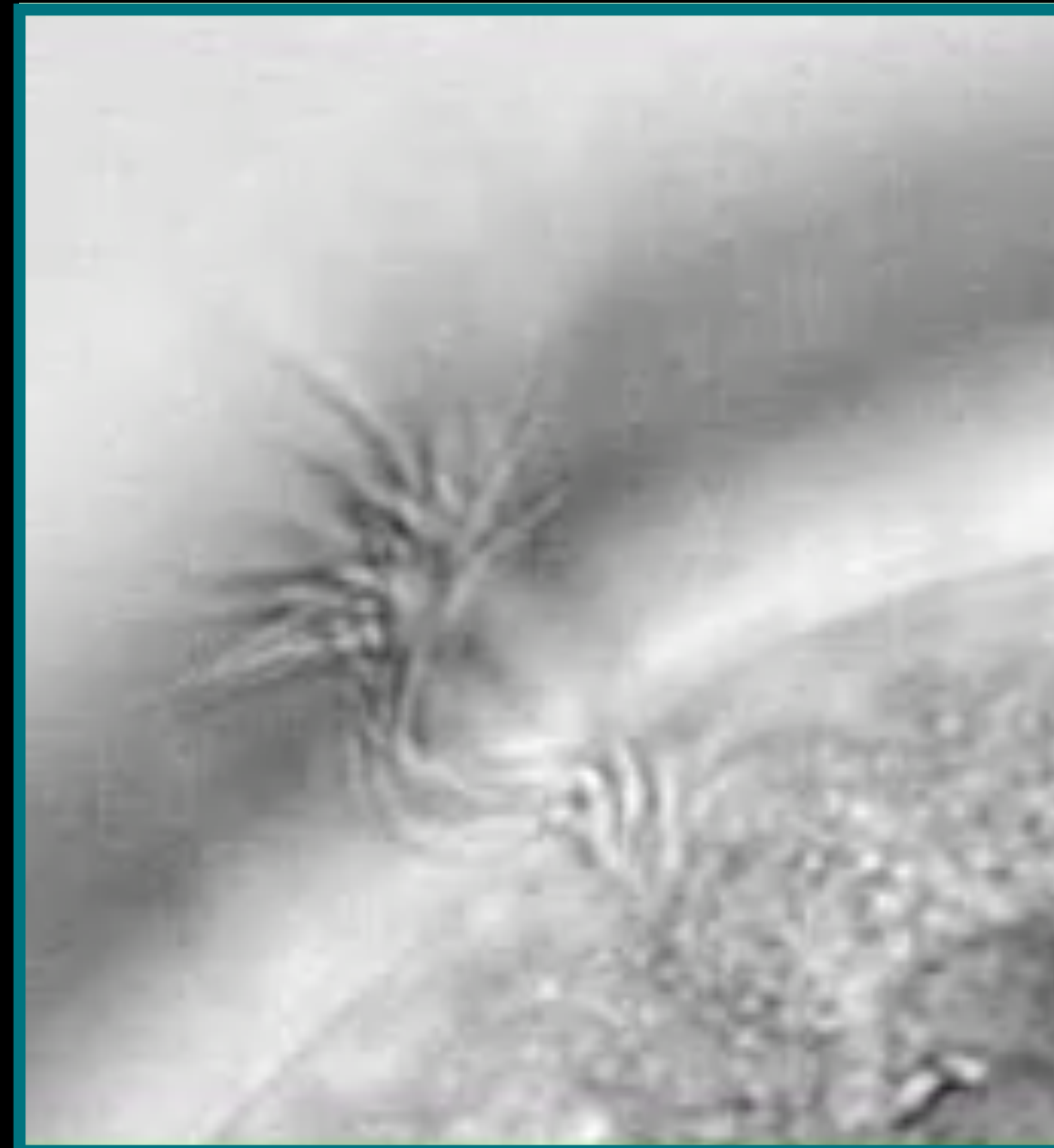
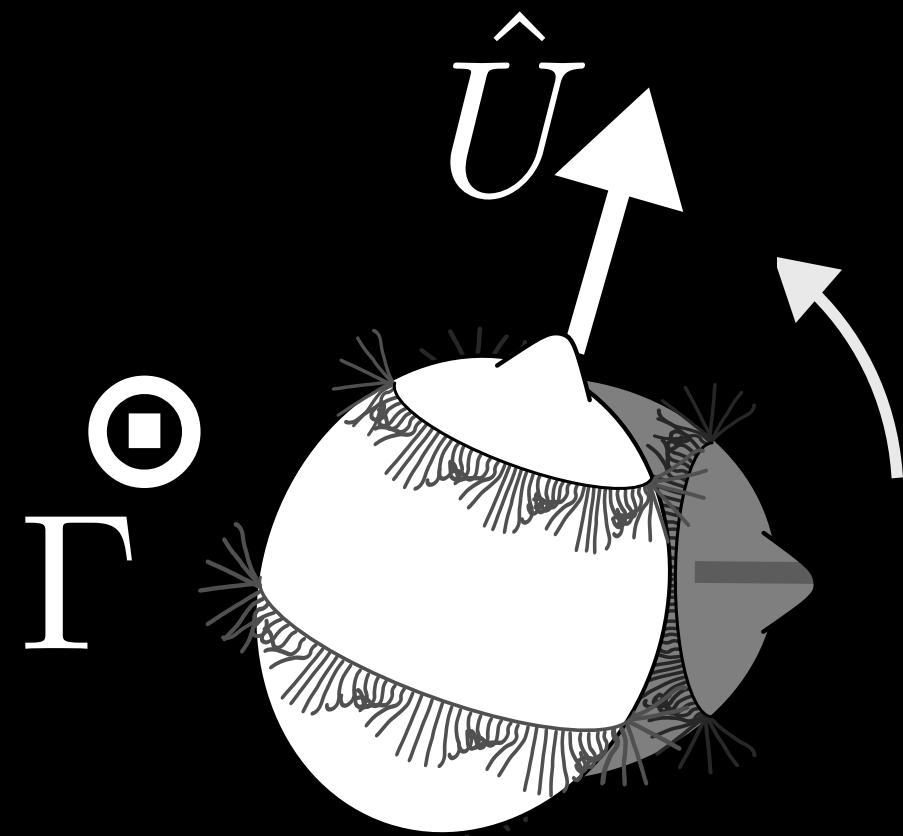
Arnold Mathijssen



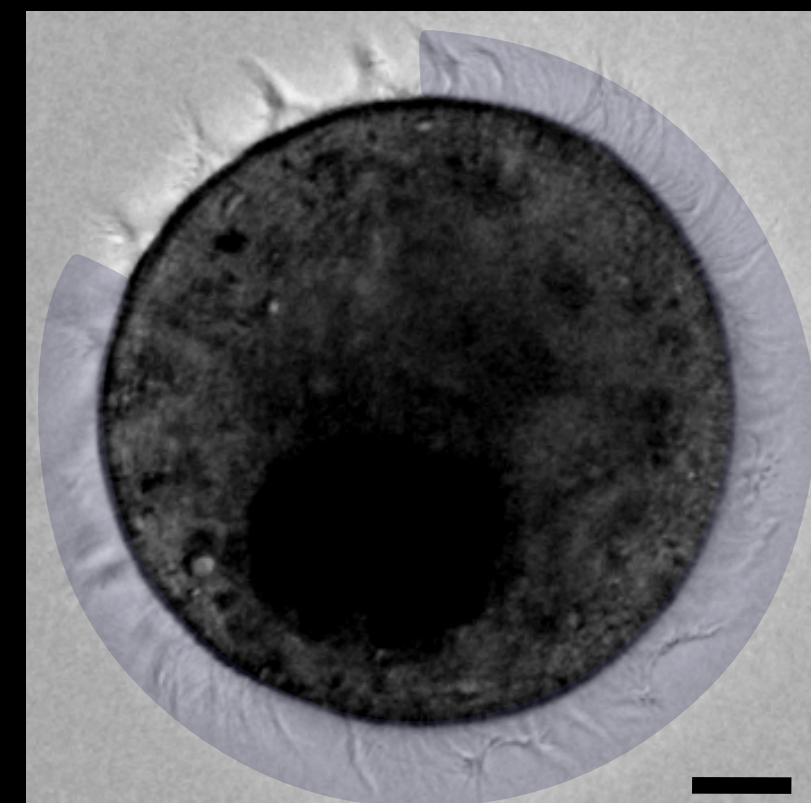
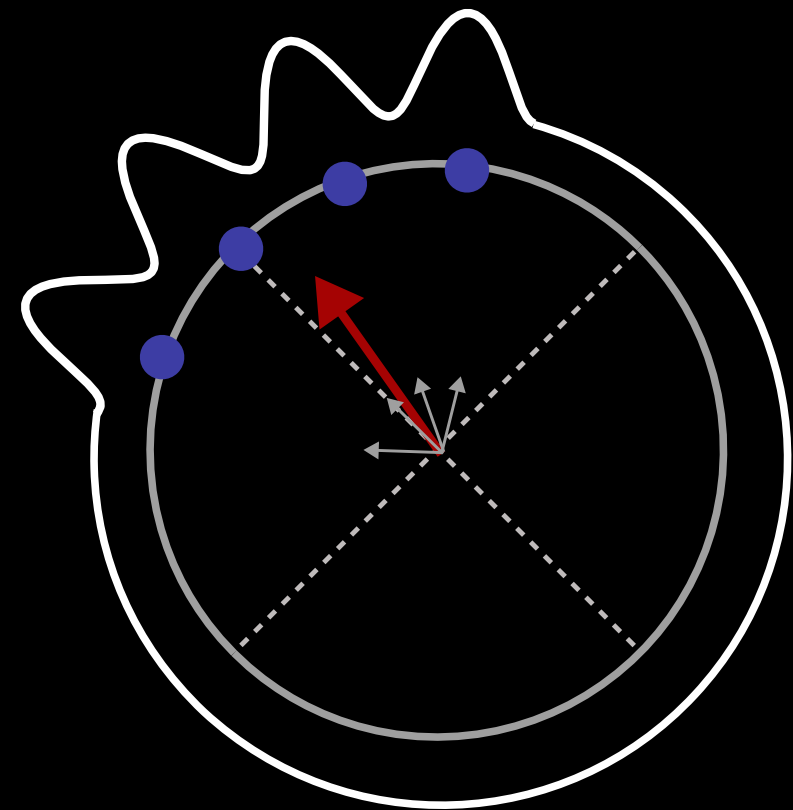
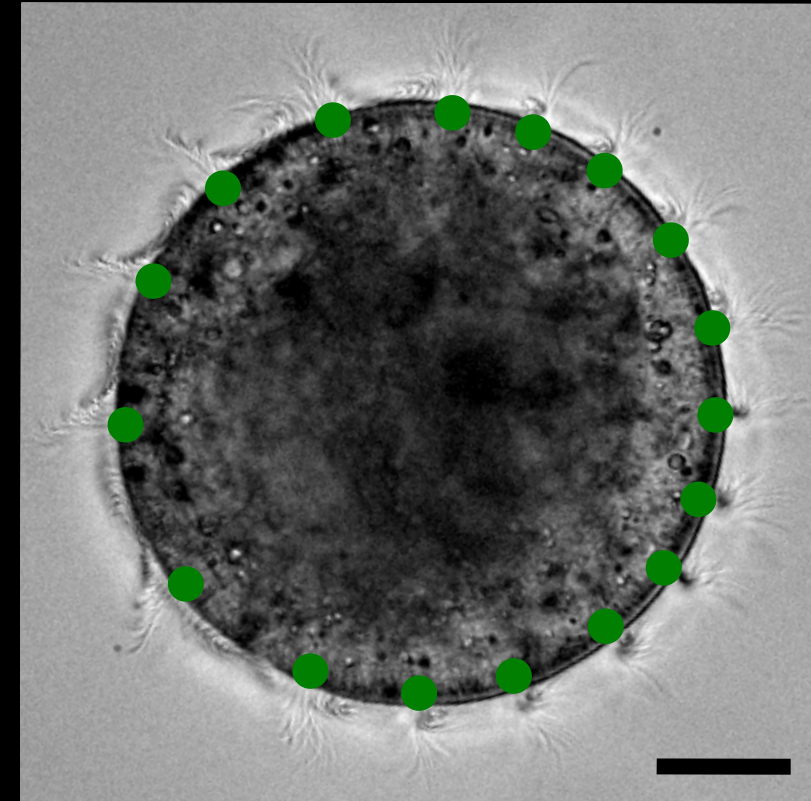
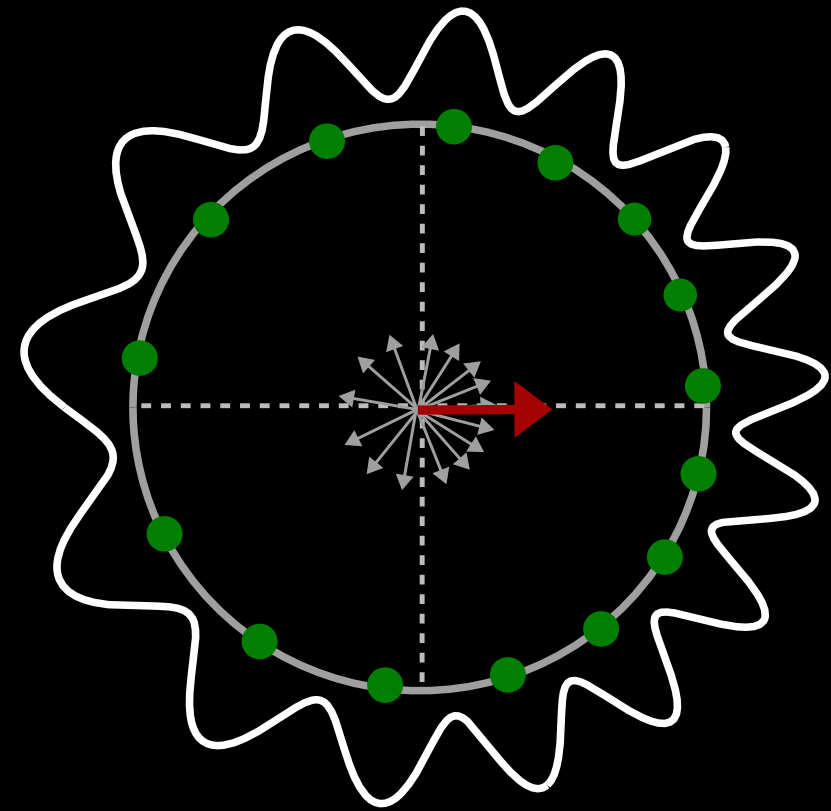
Maggie Liu

Global metachronal coordination gives rise to robust swimming independent of wave parameters

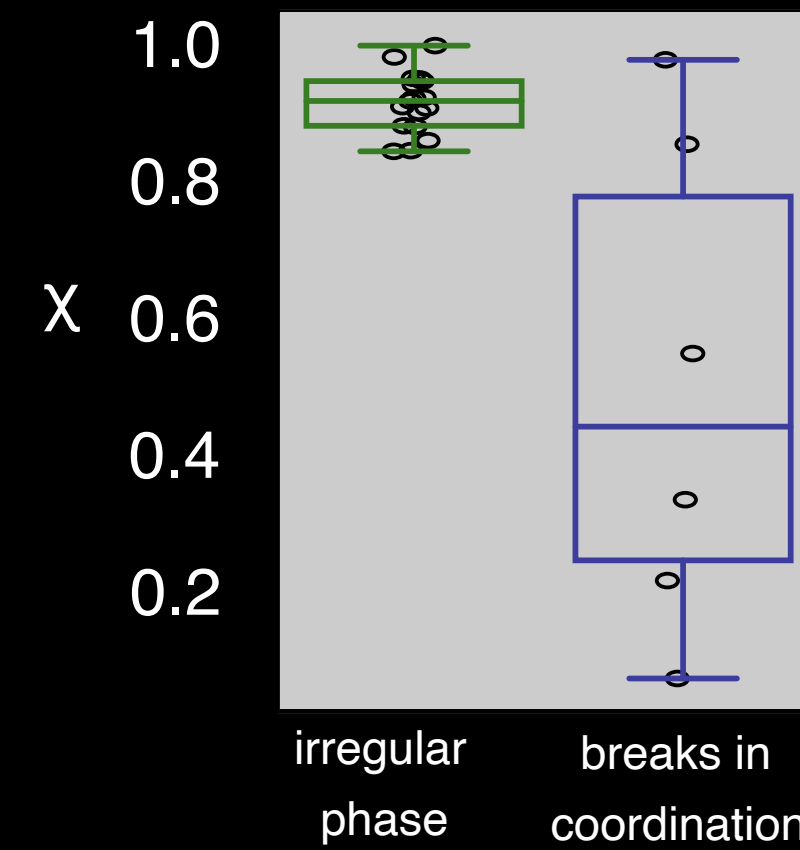
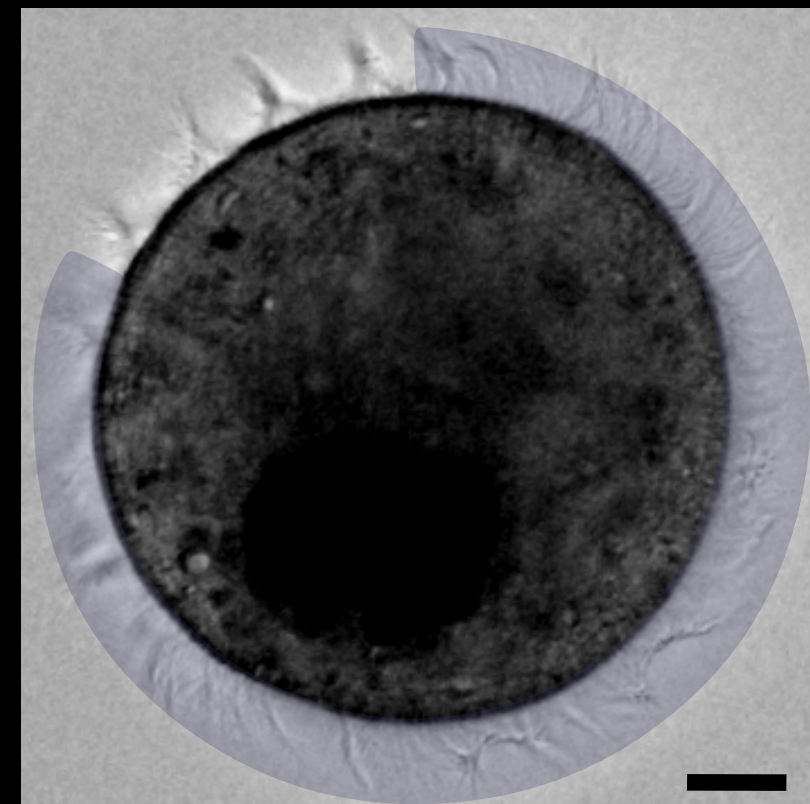
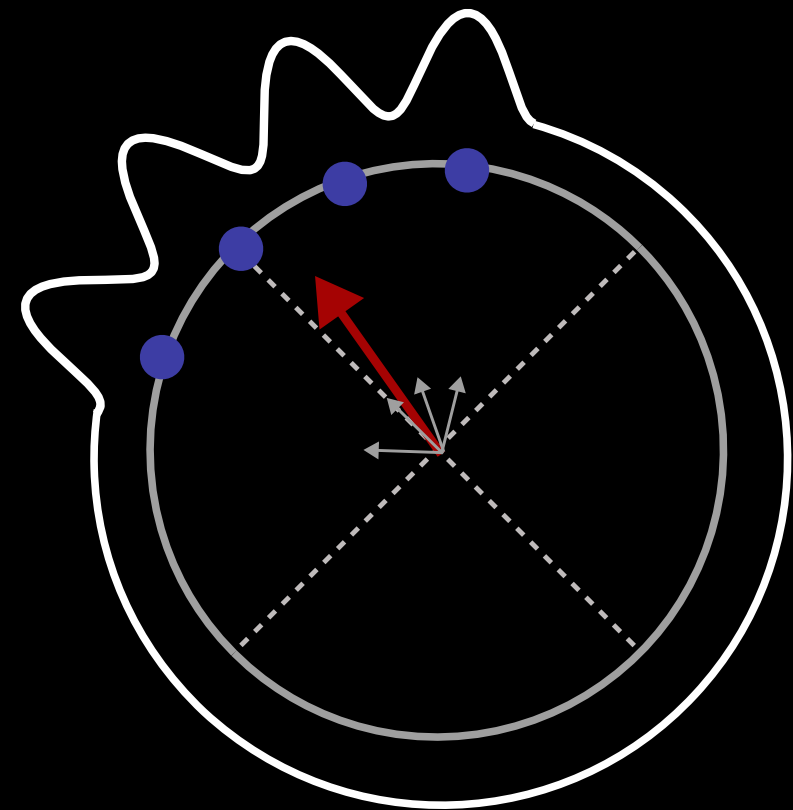
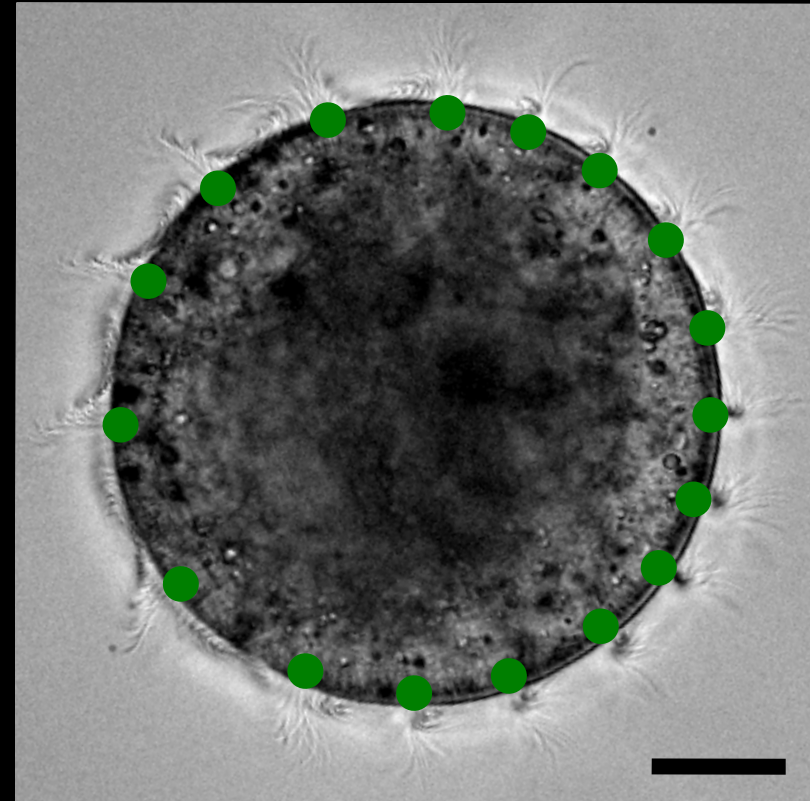
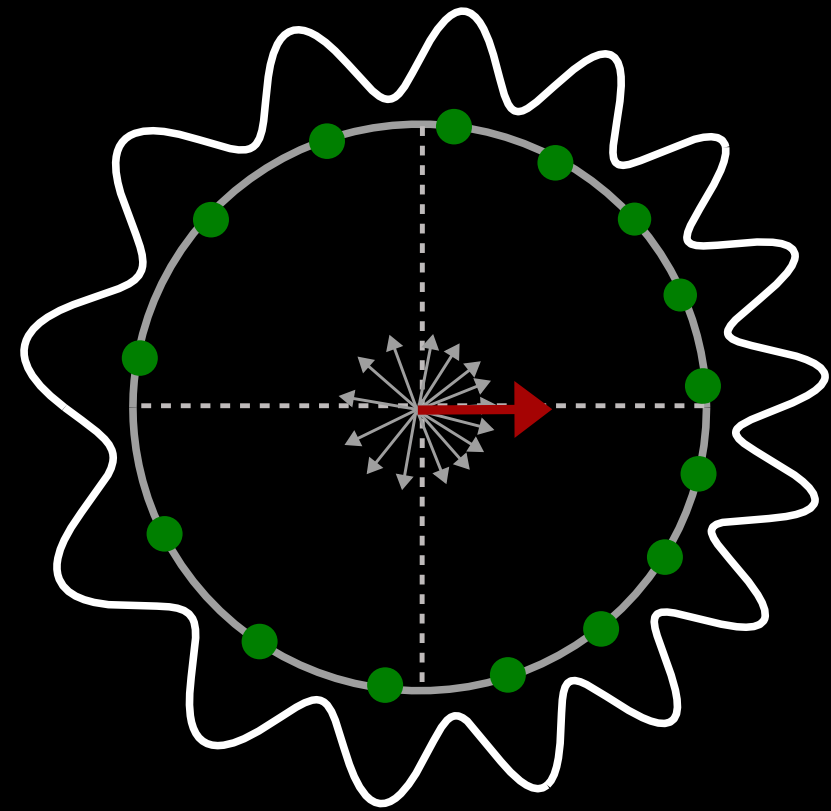
# Temporal coordination of cilia across length scales is highly dynamic



# Inhomogeneities in metachronal wave patterning encode diverse swimming gaits

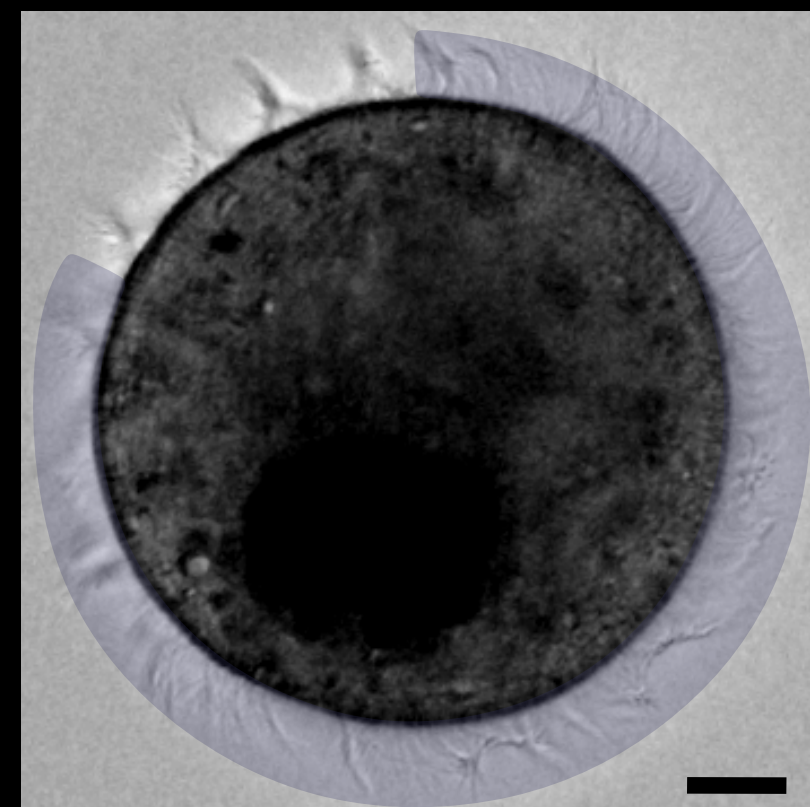
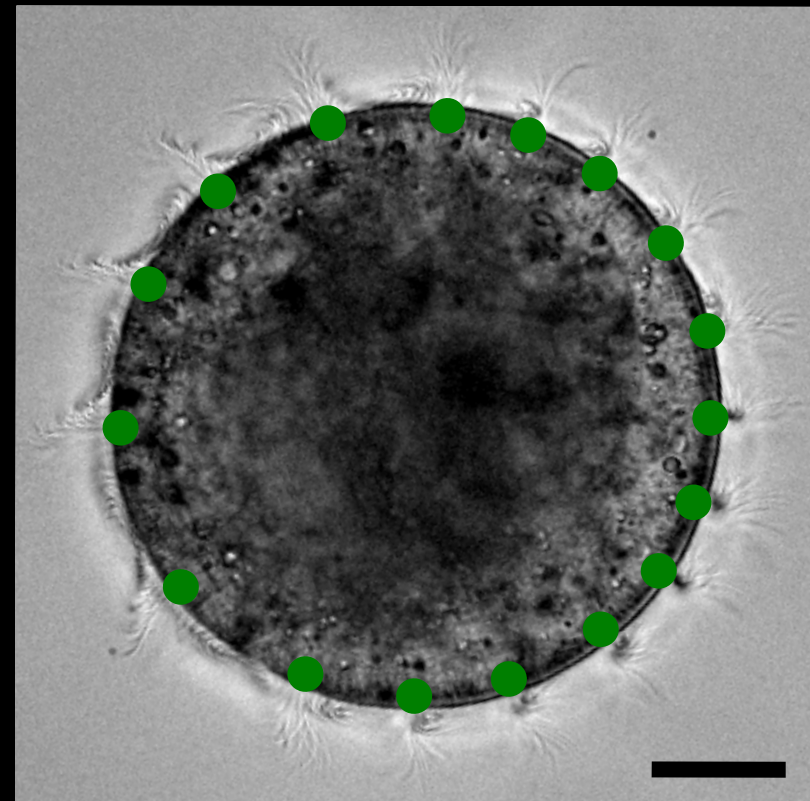
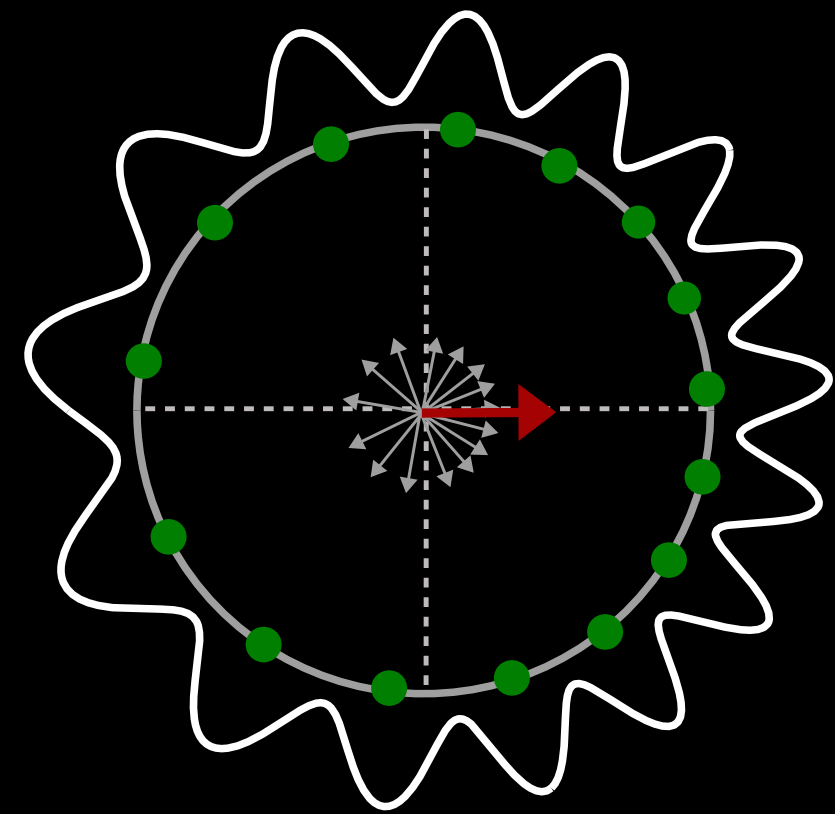


# Inhomogeneities in metachronal wave patterning encode diverse swimming gaits

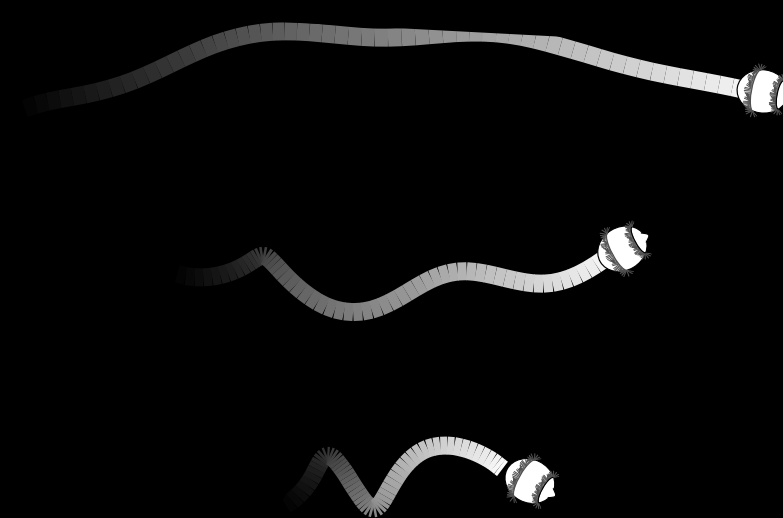


$$Z = \left| \frac{1}{N} \sum_{j=1}^N e^{i\theta_j} \right| \quad \chi = 1 - Z$$

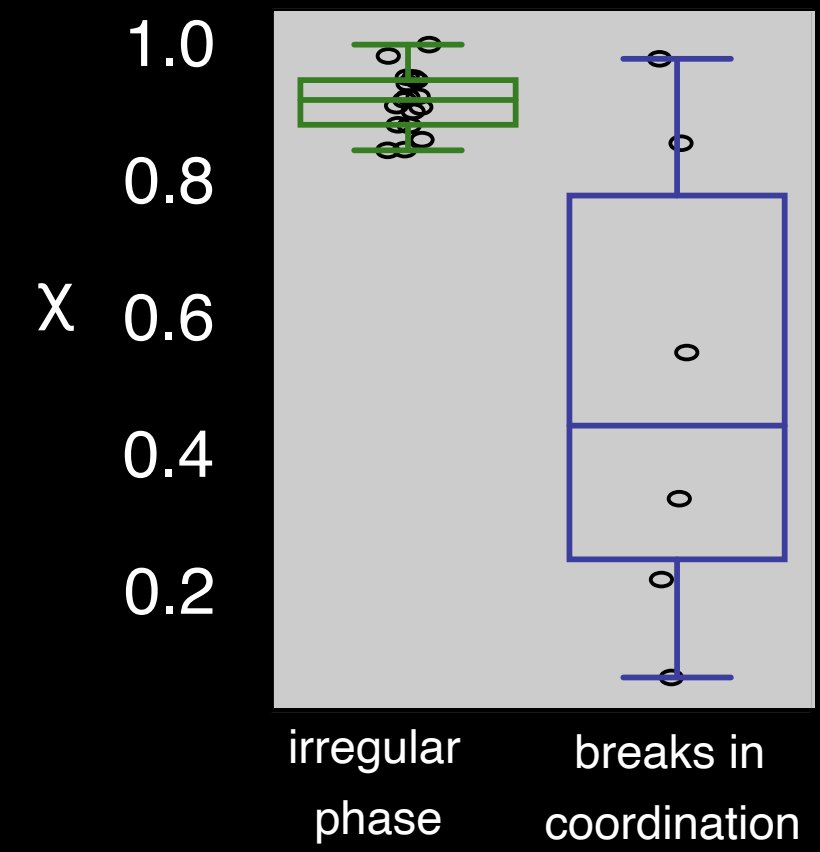
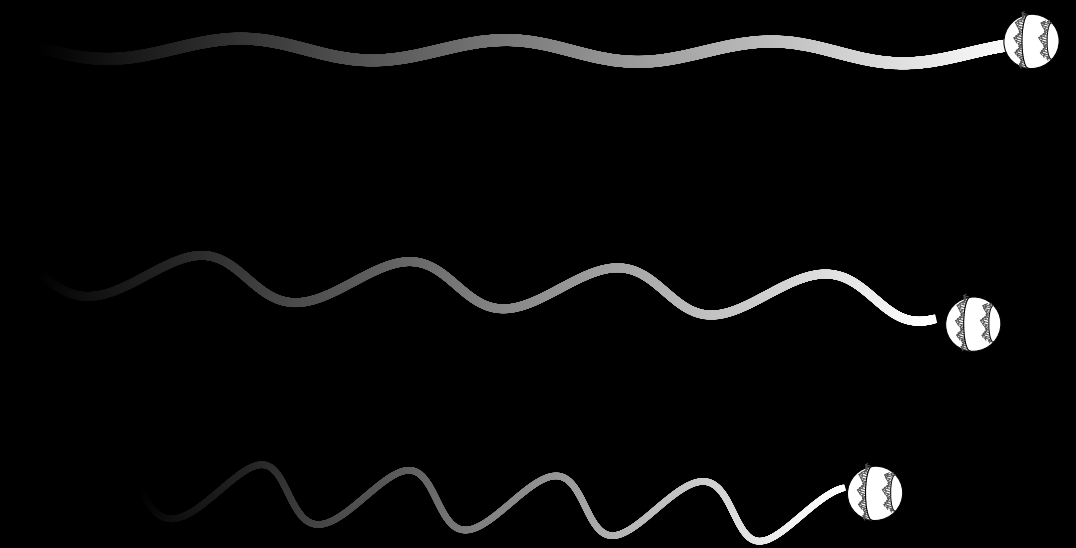
# Inhomogeneities in metachronal wave patterning encode diverse swimming gaits



Experiment

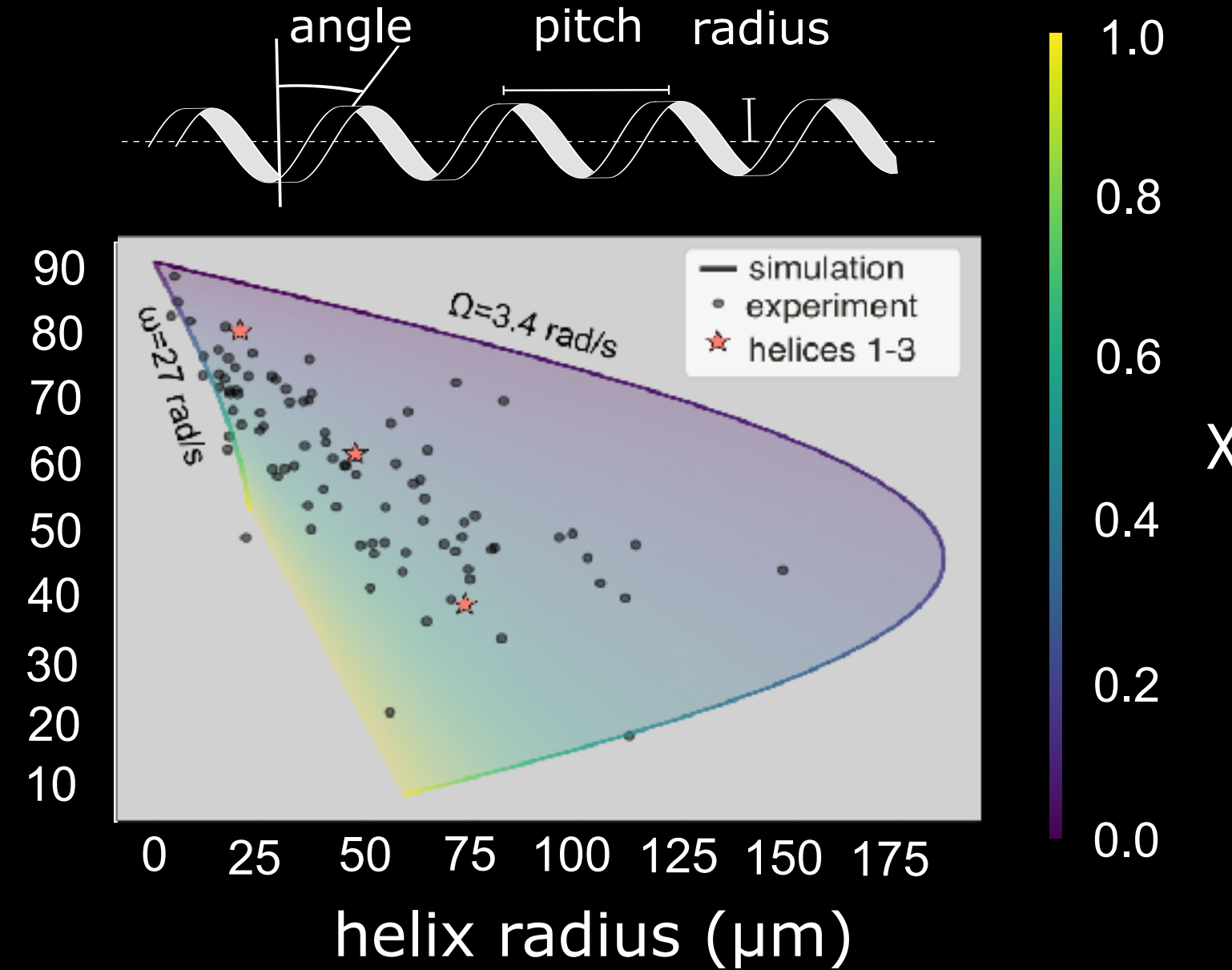


Simulation

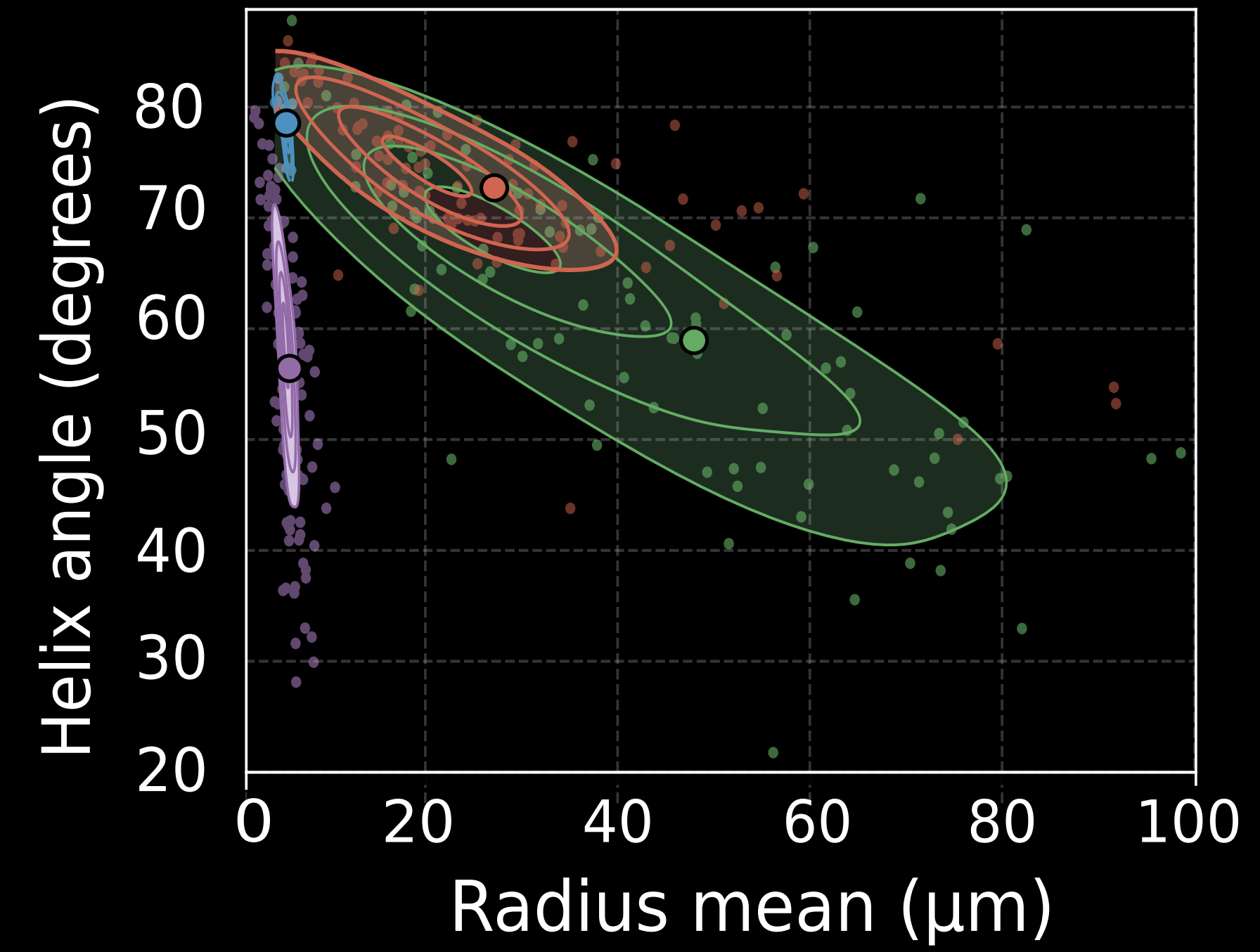
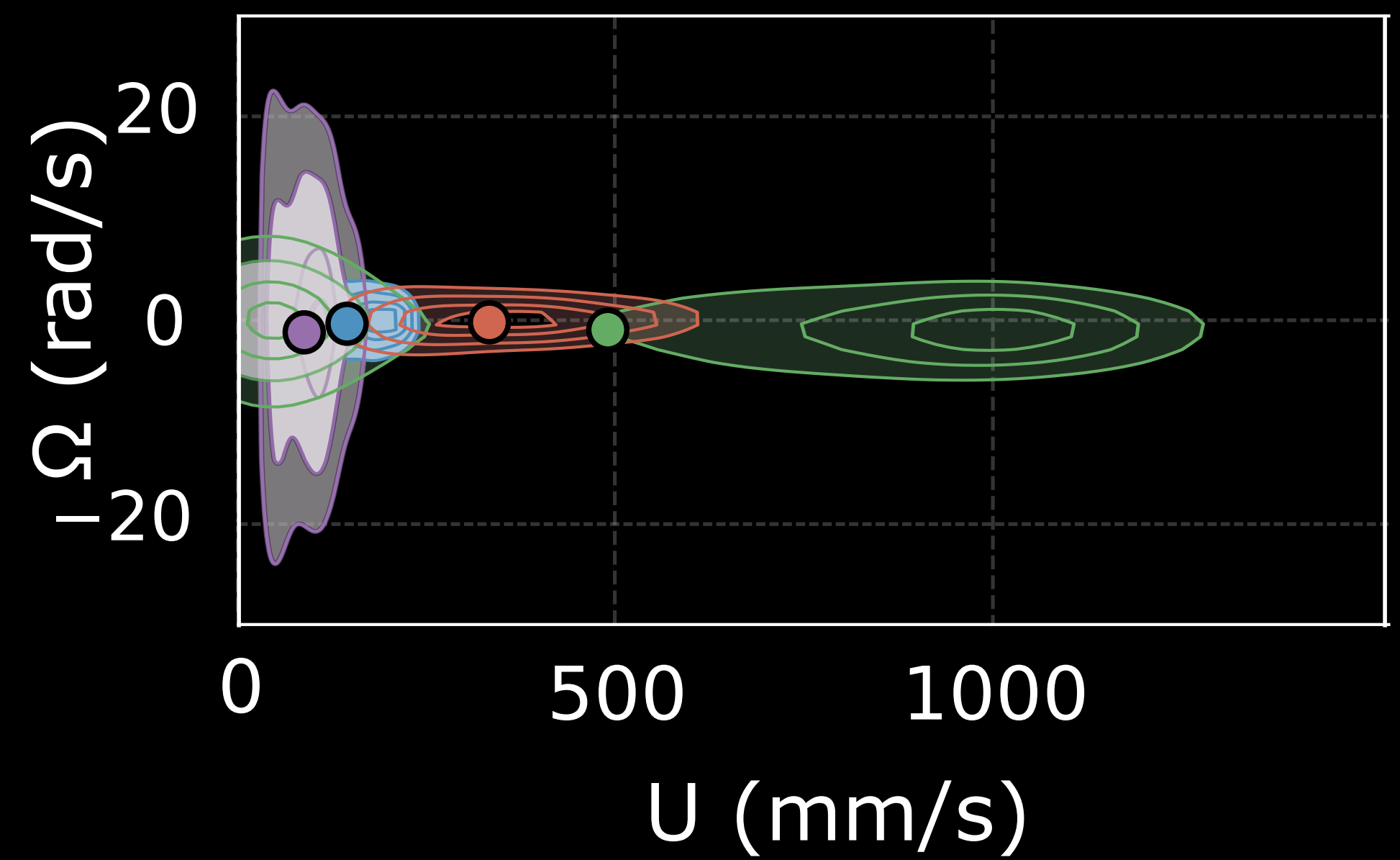
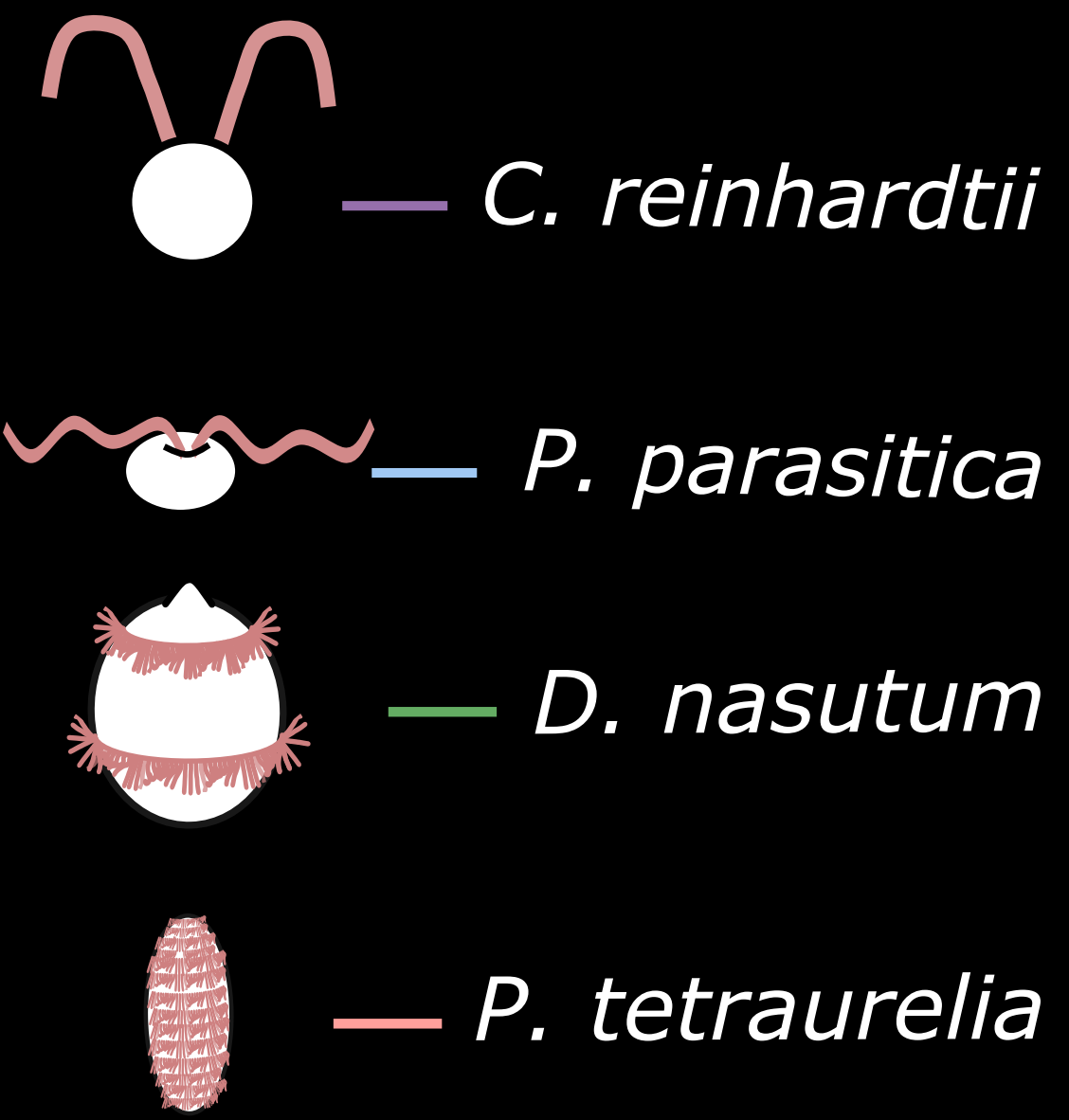


$$Z = \left| \frac{1}{N} \sum_{j=1}^N e^{i\theta_j} \right| \quad \chi = 1 - Z$$

helix angle (degrees)



# Cilia spatiotemporal dynamics encode the motility behavioral space of cells



Didinium exhibits remarkable versatility of gaits

# Function emerges from the spatio-temporal coordination of cilia across length scales

## Cellular behavior

Swimming

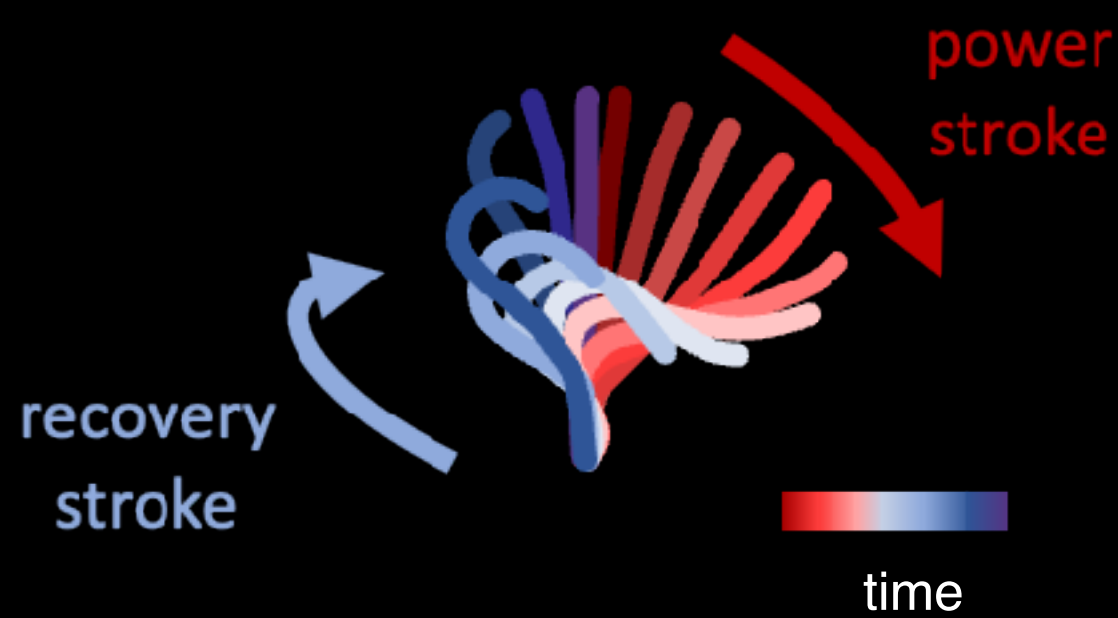
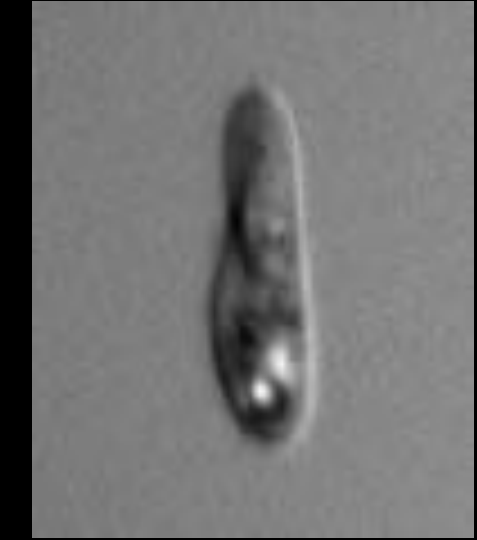
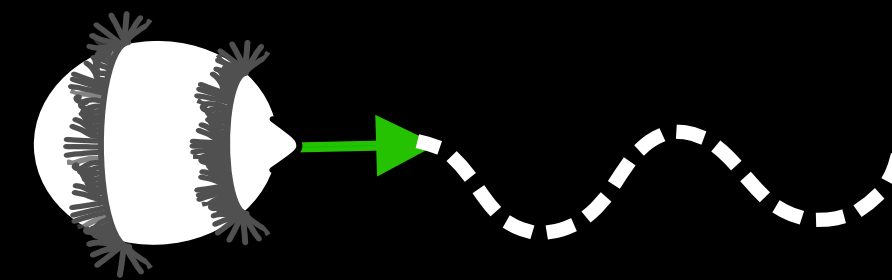
Feeding

Temporal Patterning

+

Spatial Patterning

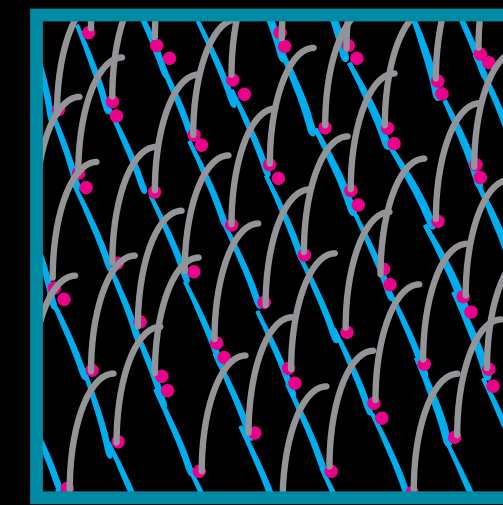
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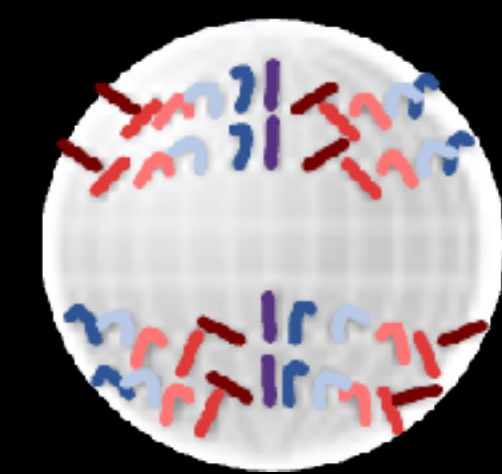
Cilia beat



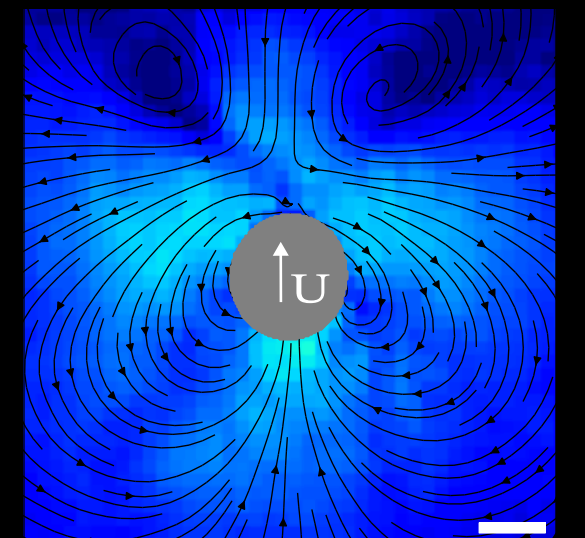
Metachronal coordination



Spatial patterning



Cellular gaits



Flow

$10^{-9}$  m

$10^{-6}$  m

$10^{-3}$  m

$10^{-2}$  m

# Function emerges from the spatio-temporal coordination of cilia across length scales

## Cellular behavior

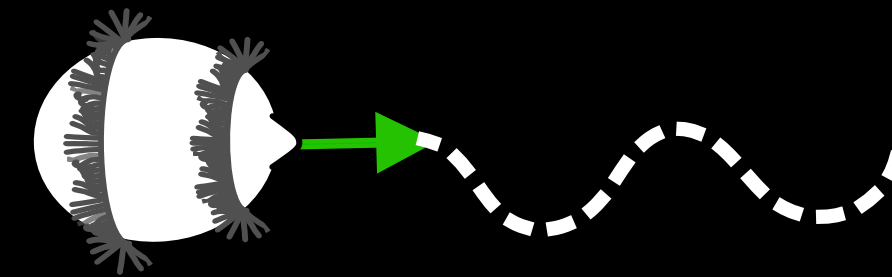
Temporal Patterning

+

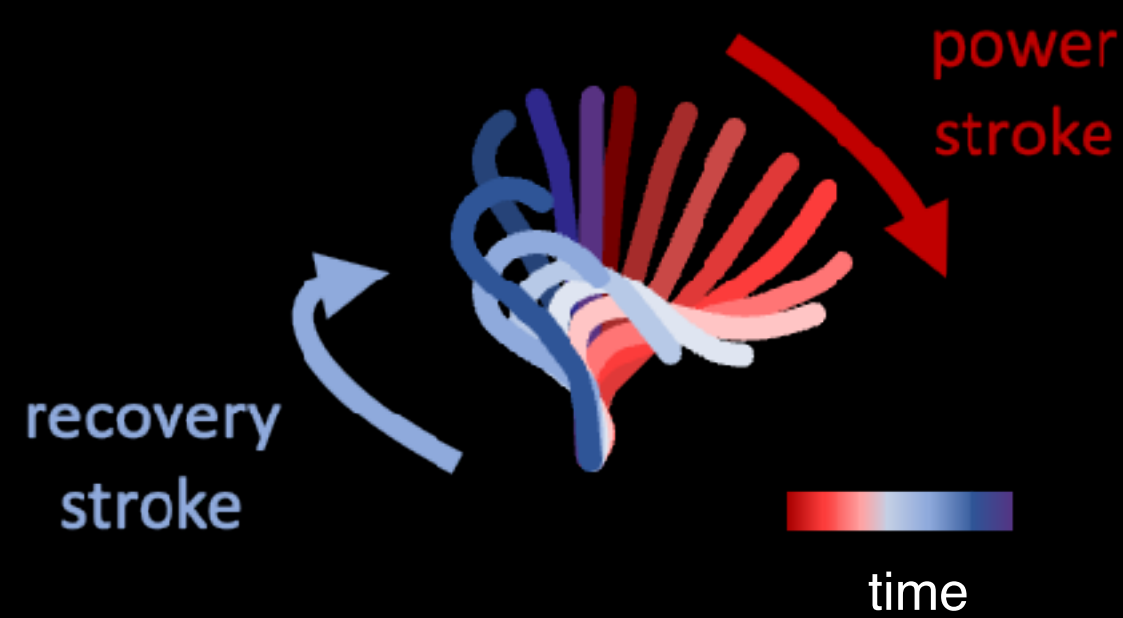
Spatial Patterning

=

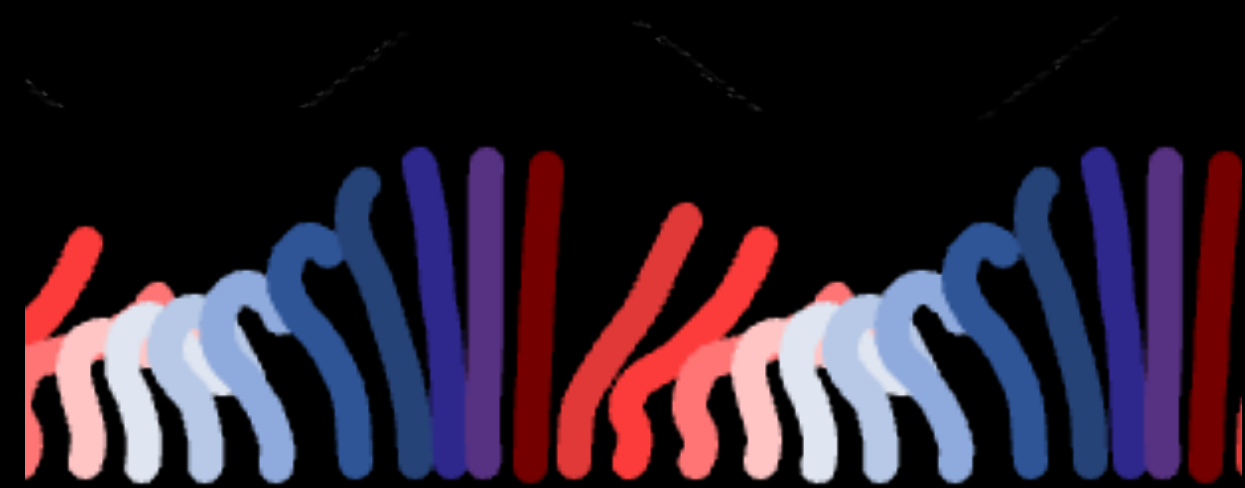
Swimming



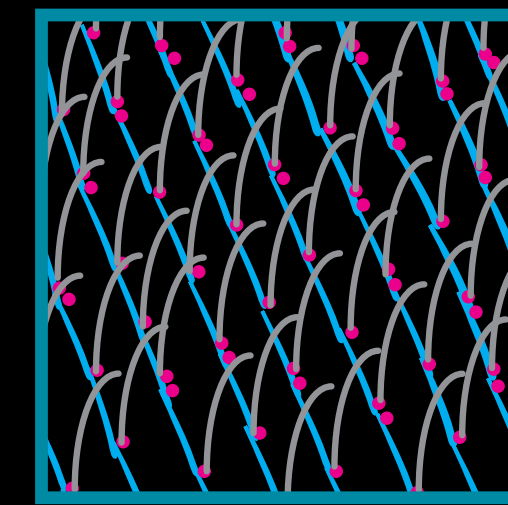
Feeding



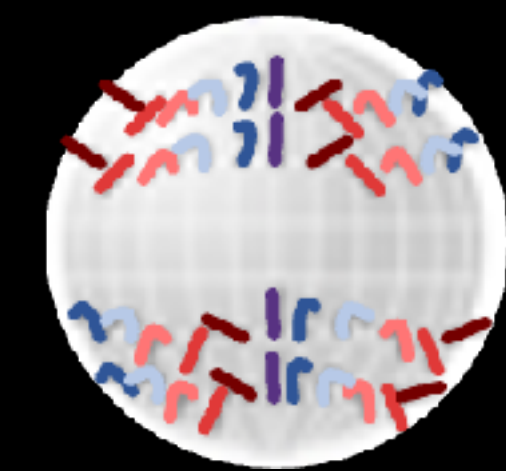
Cilia beat



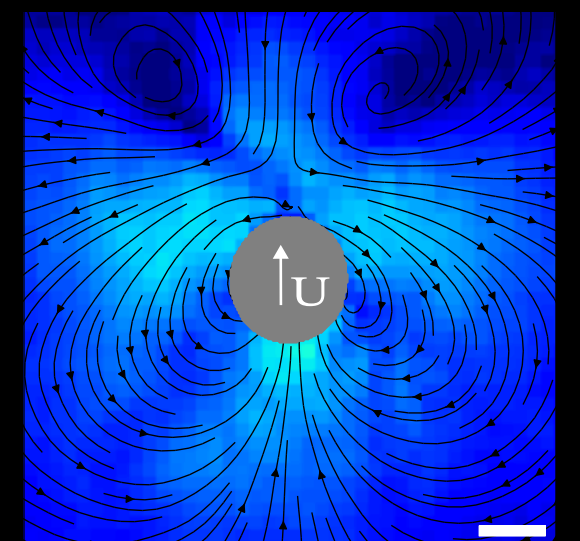
Metachronal coordination



Spatial patterning



Cellular gaits



Flow

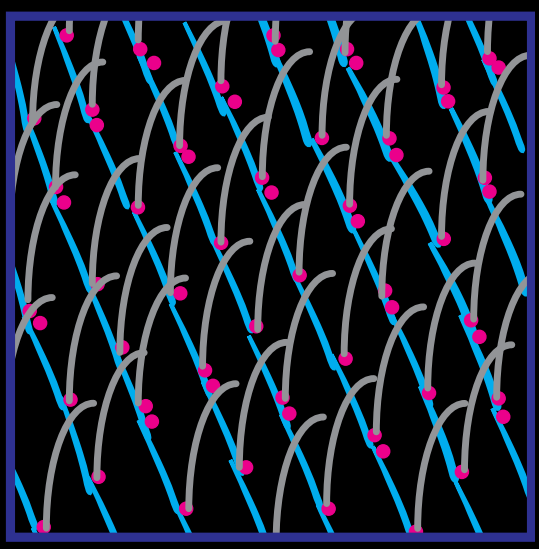
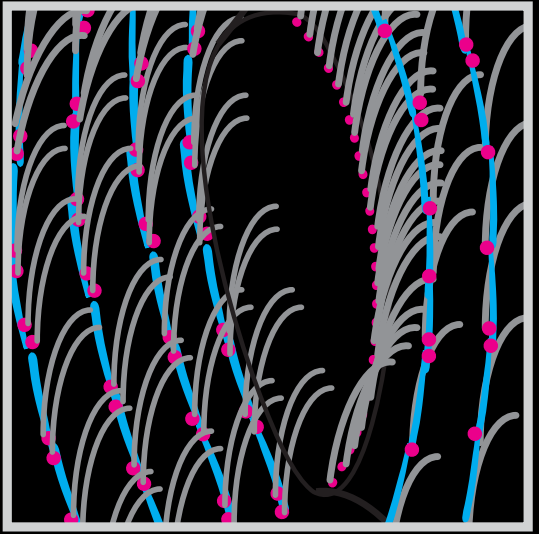
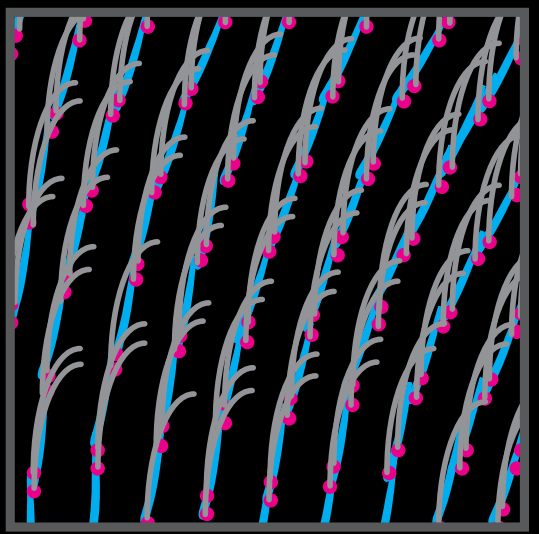
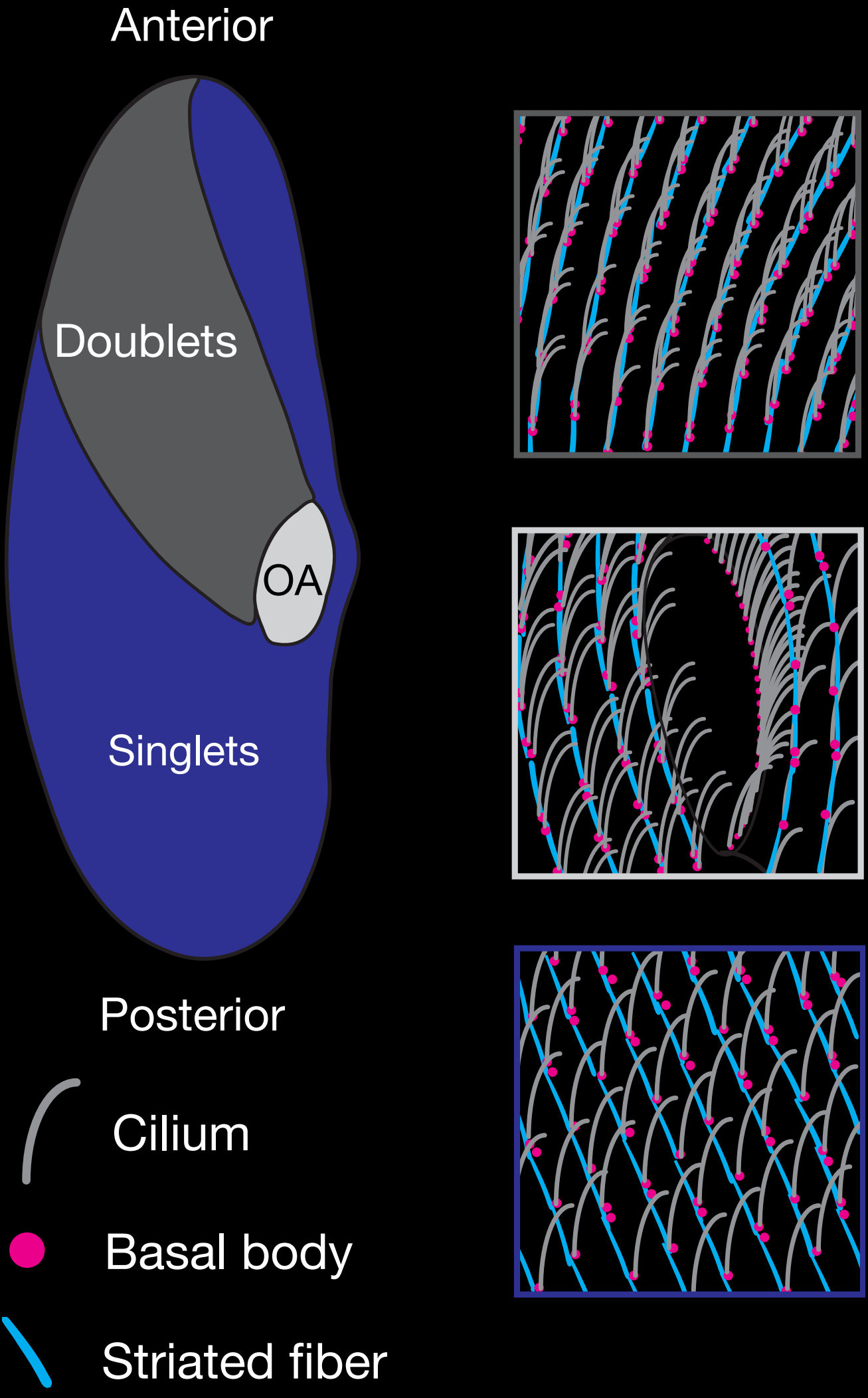
$10^{-9}$  m

$10^{-6}$  m

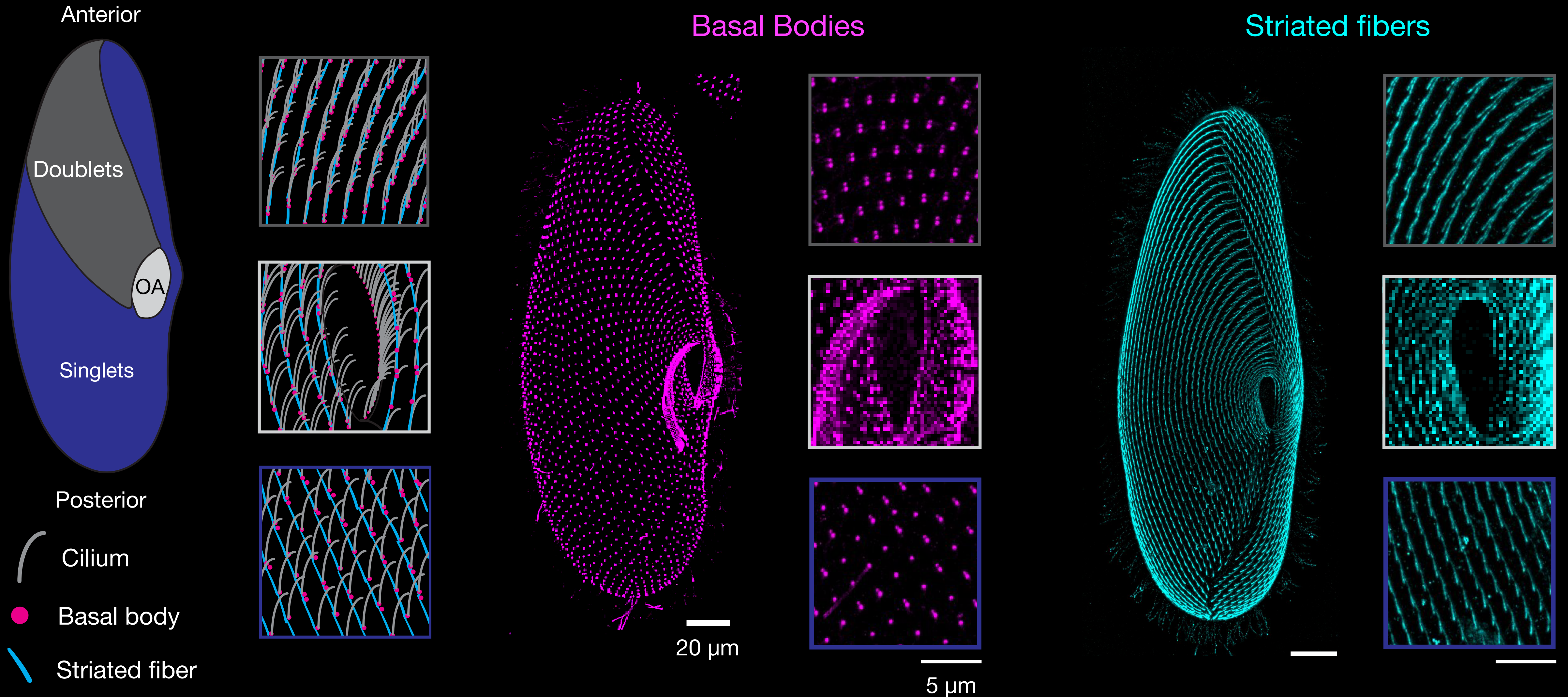
$10^{-3}$  m

$10^{-2}$  m

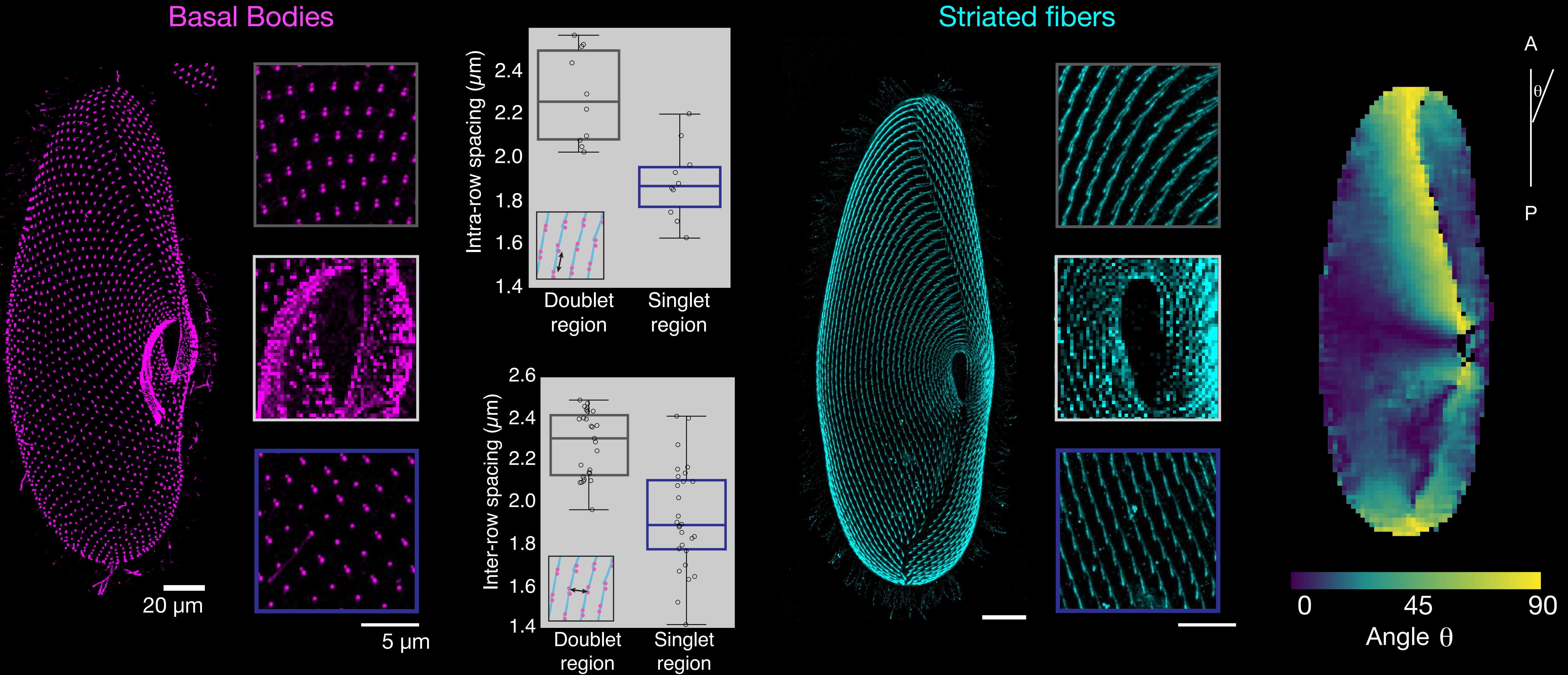
# Paramecium is partitioned into cilia arrays with distinct spatial patterning



# Paramecium is partitioned into cilia arrays with distinct spatial patterning



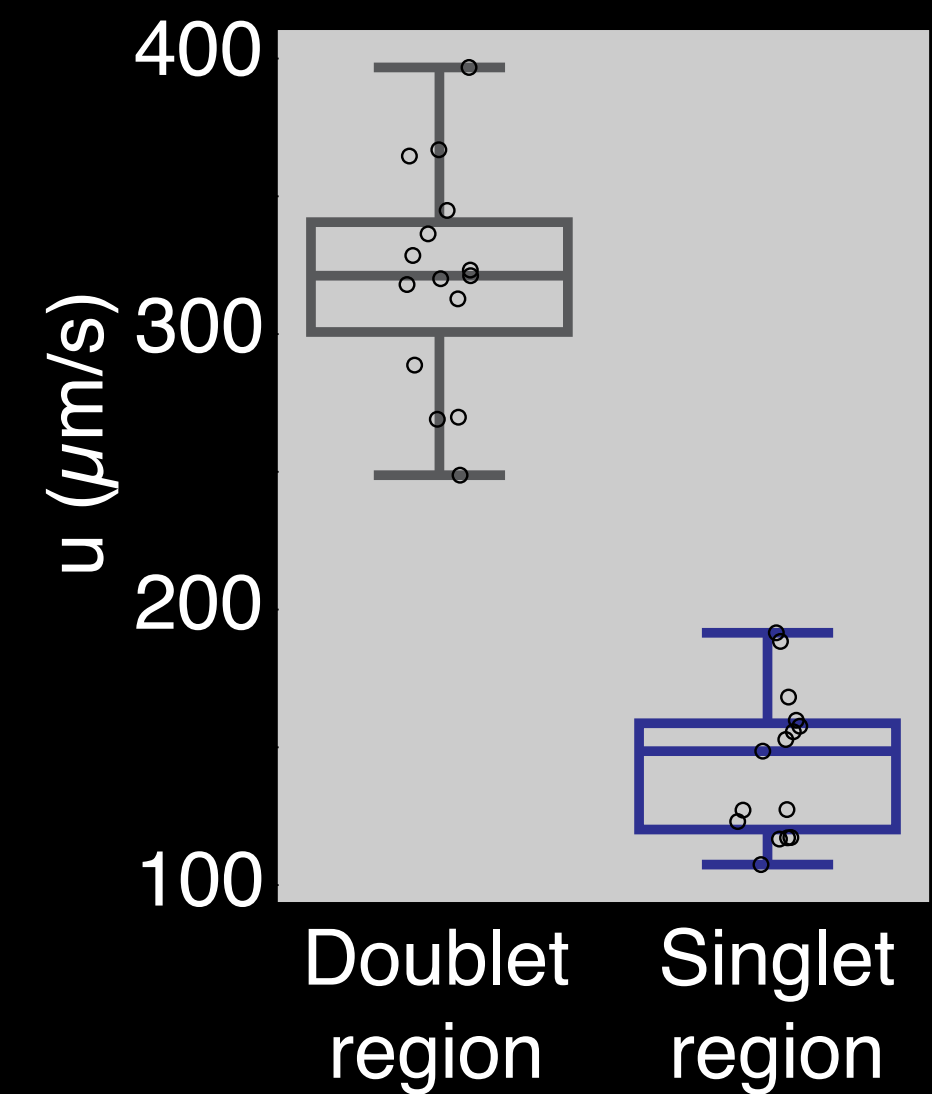
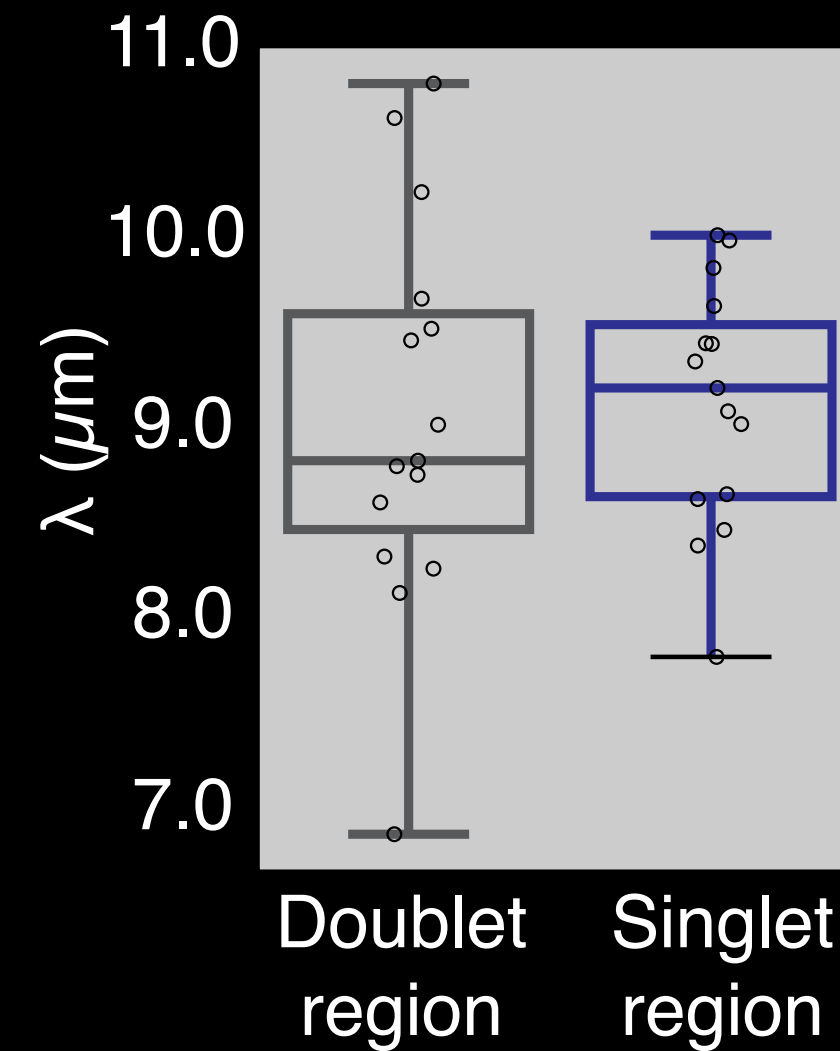
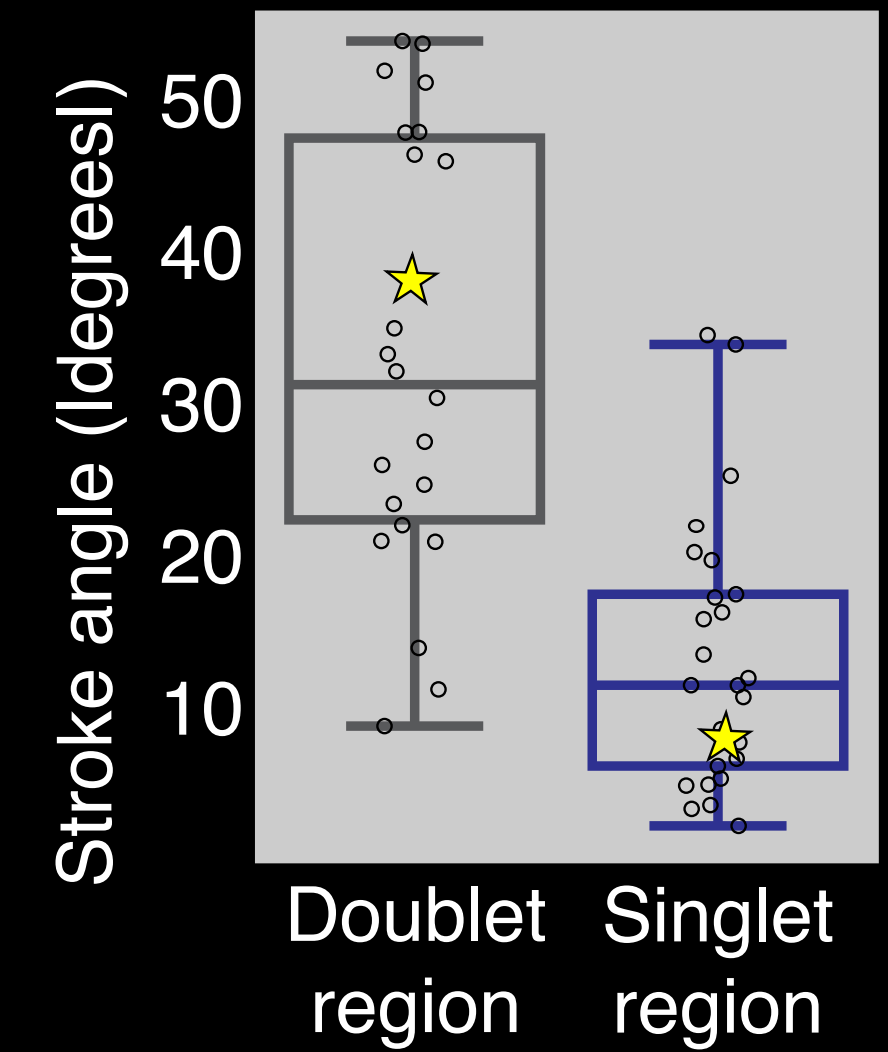
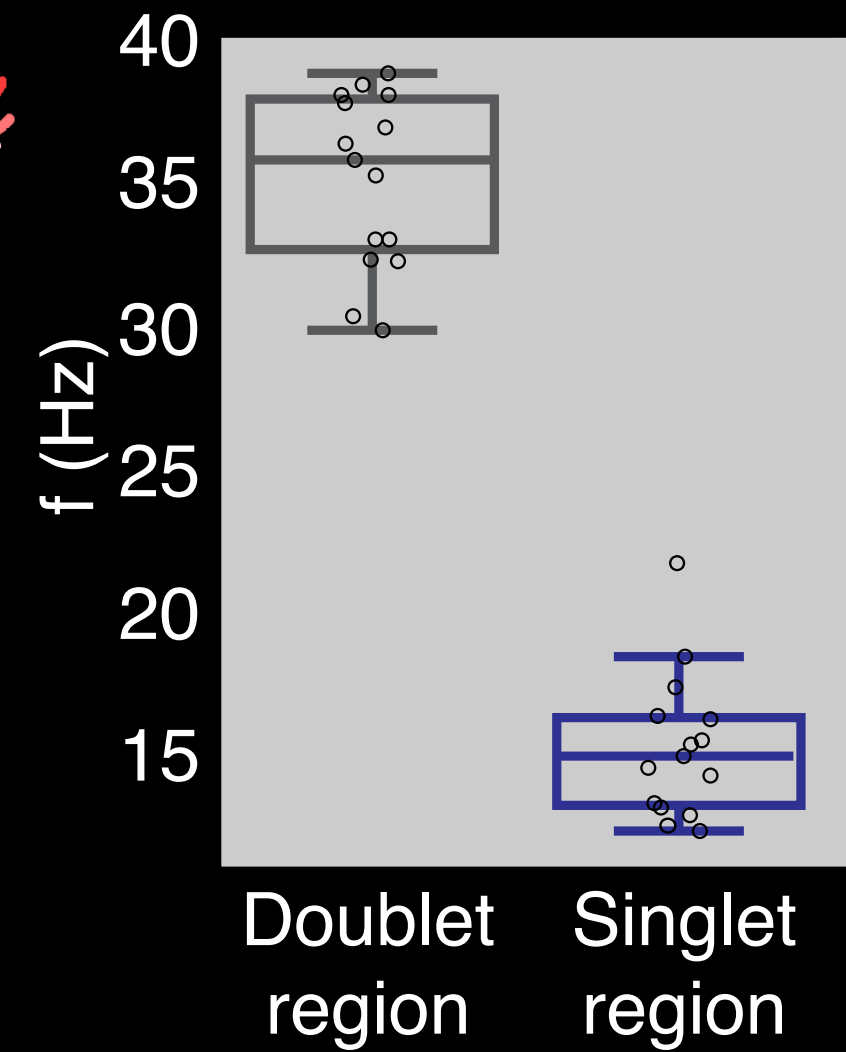
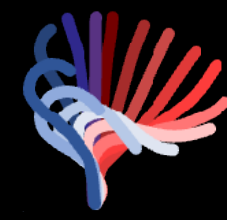
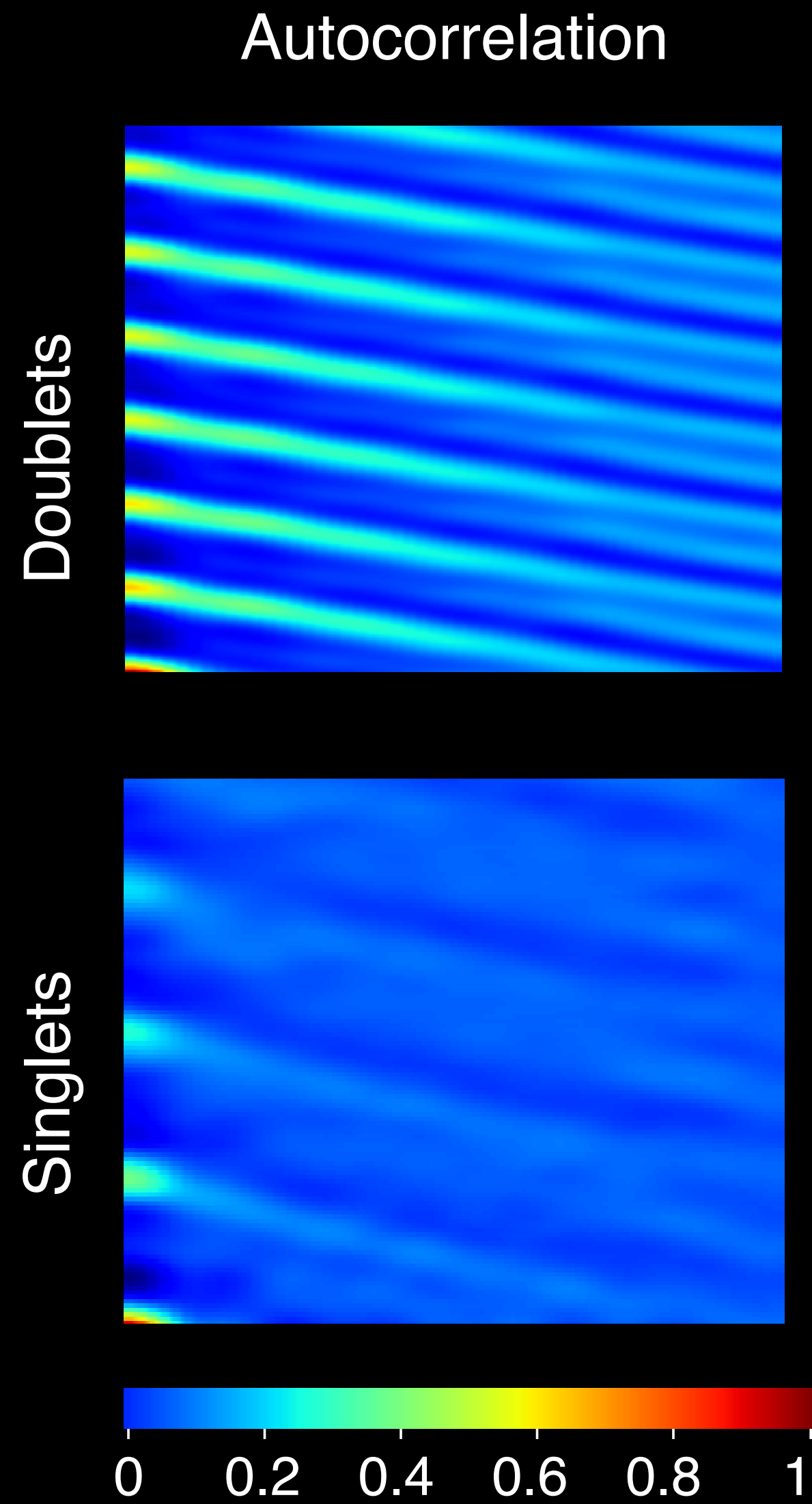
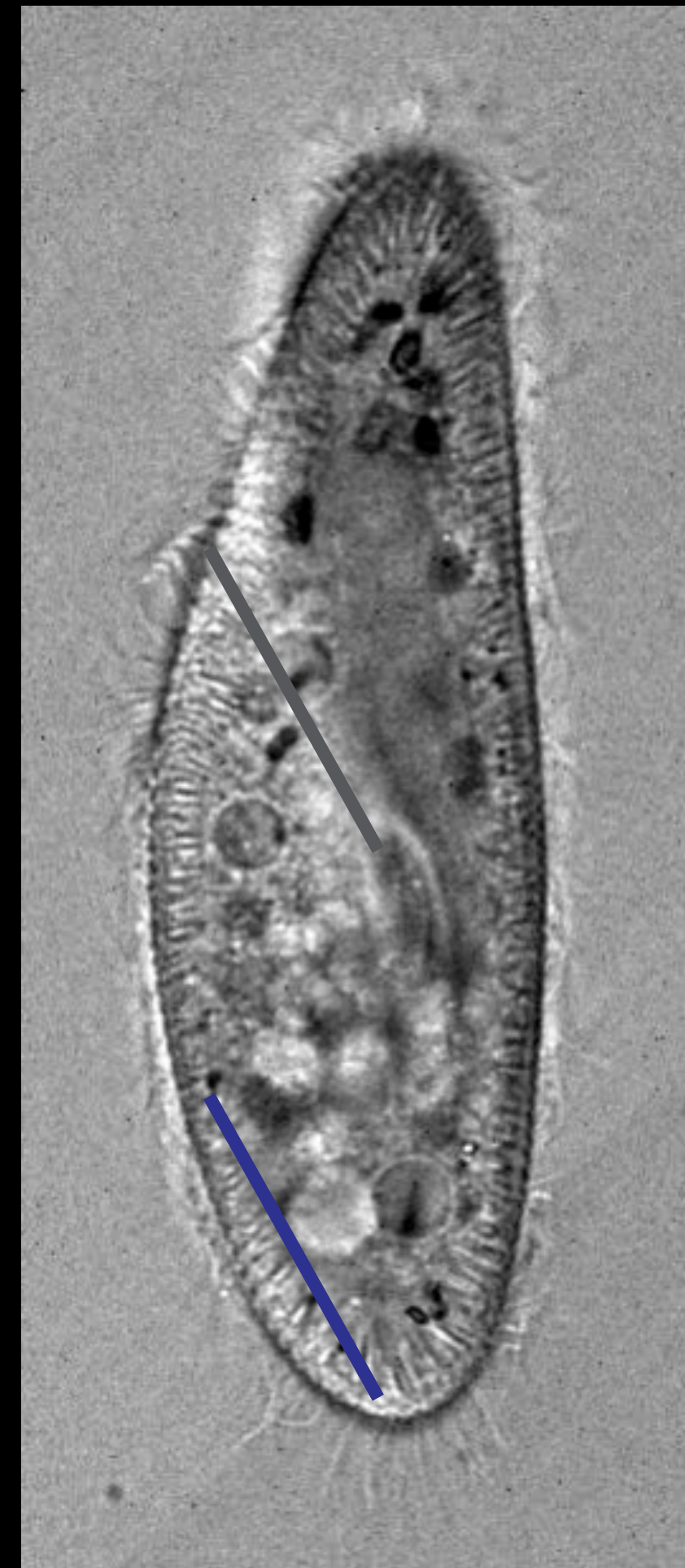
# Paramecium is partitioned into cilia arrays with distinct spatial patterning



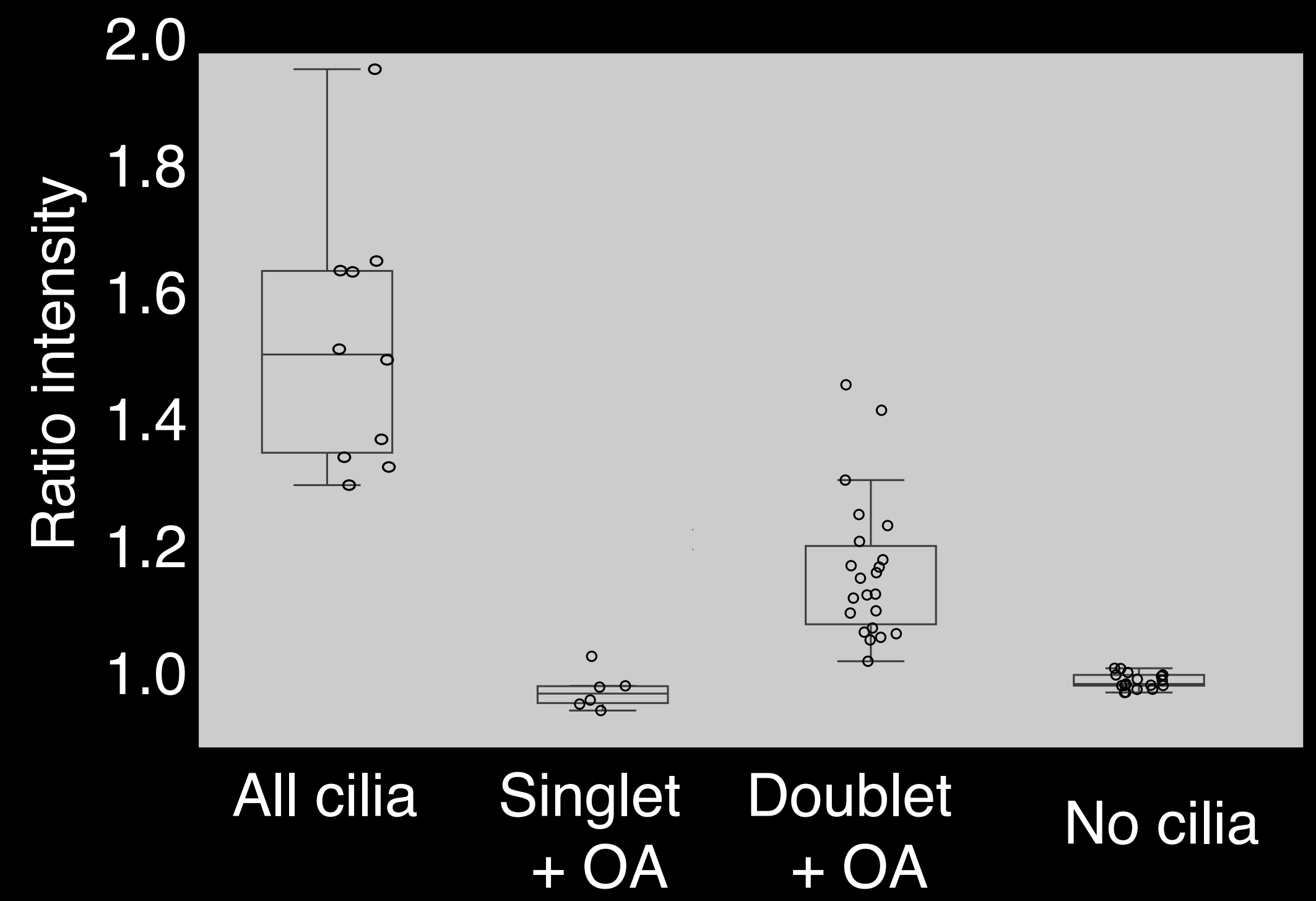
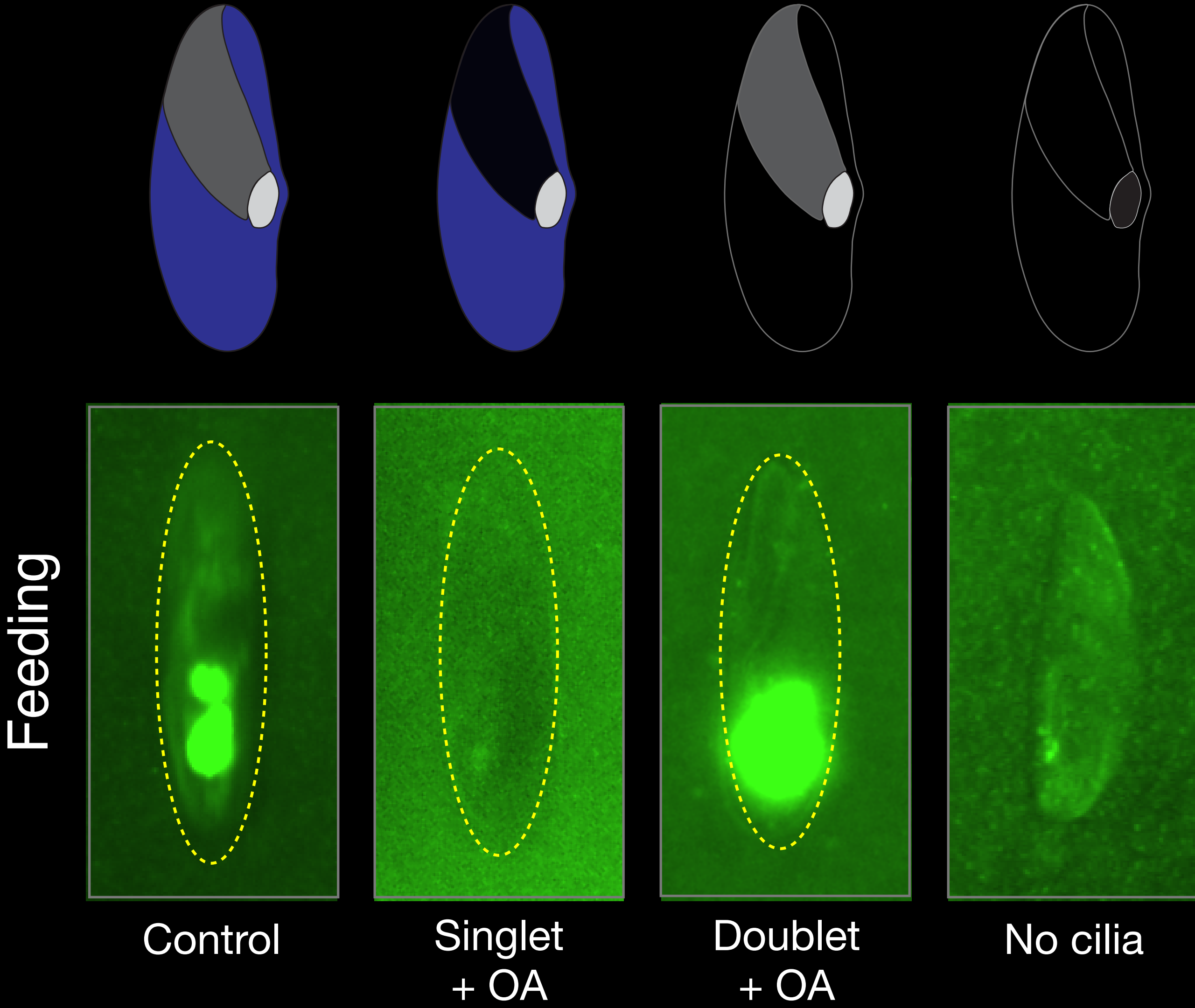
# Cilia temporal patterning is distinct in singlet and doublet regions



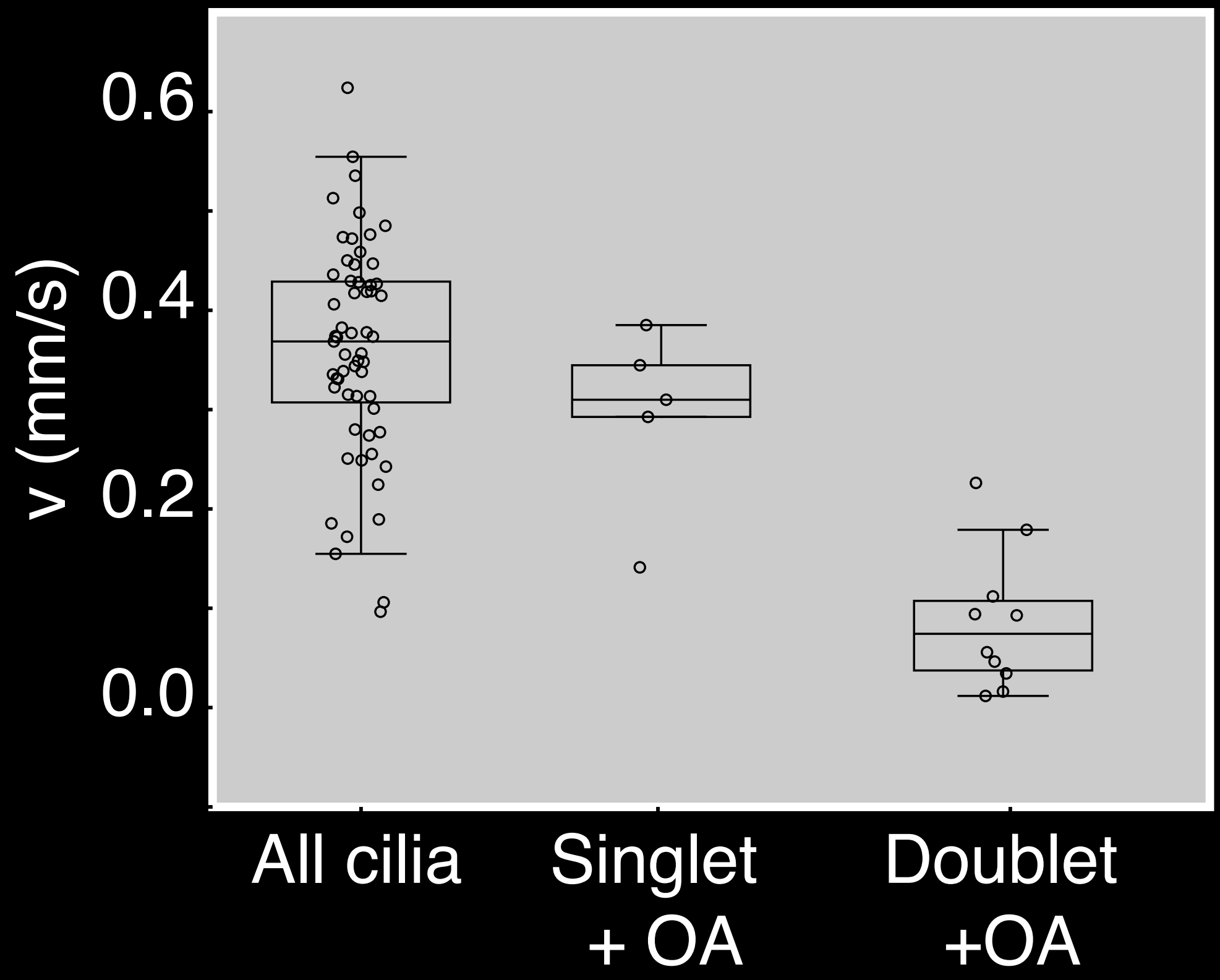
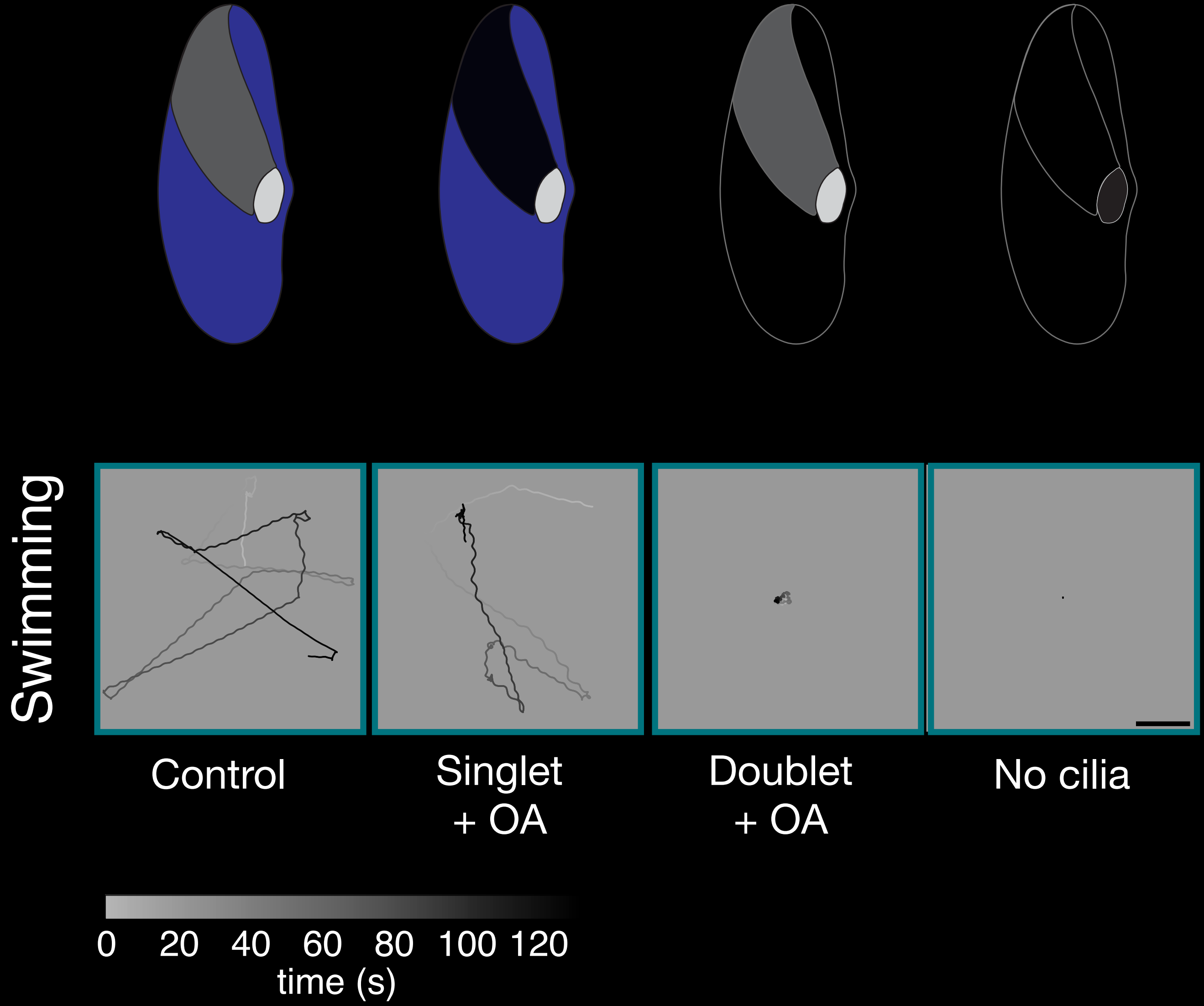
# Cilia temporal patterning is distinct in singlet and doublet regions



# Spatial patterning encoded in different regions underlies feeding or swimming



# Spatial patterning encoded in different regions underlies feeding or swimming



# Function emerges from the spatio-temporal coordination of cilia across length scales

## Cellular behavior

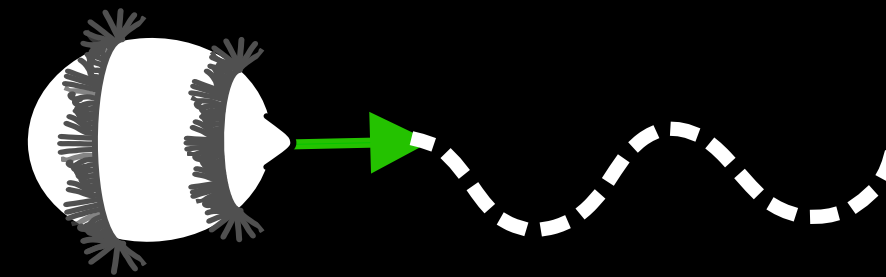
Temporal Patterning

+

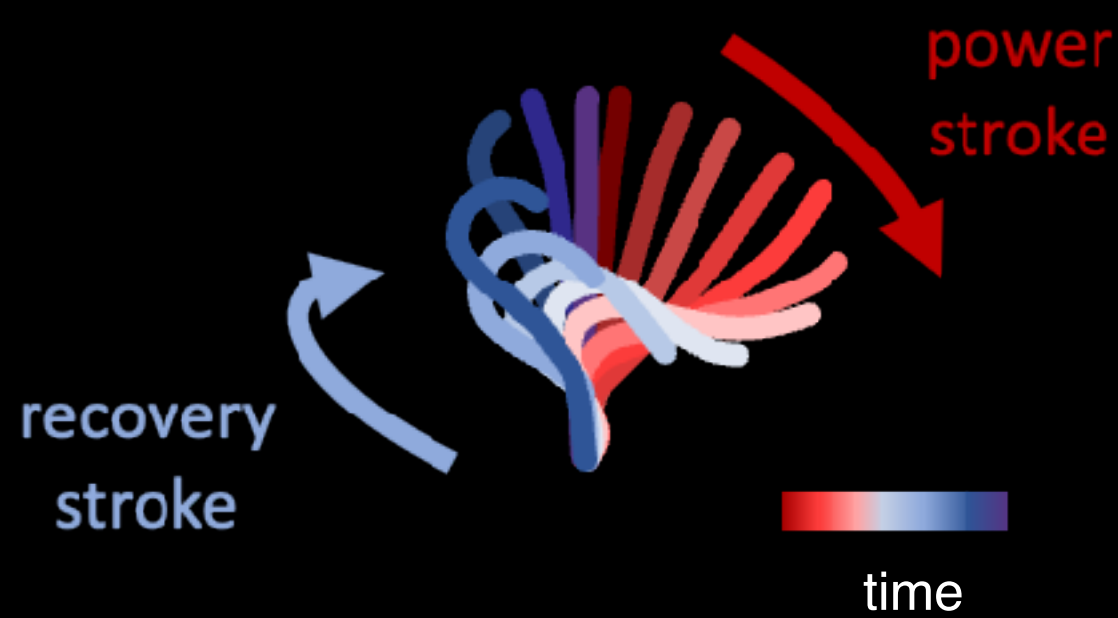
Spatial Patterning

=

Swimming



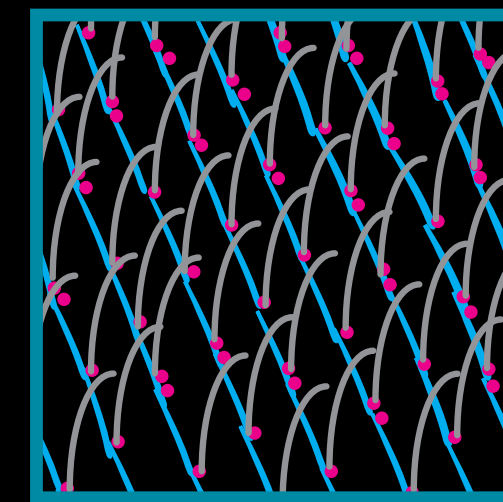
Feeding



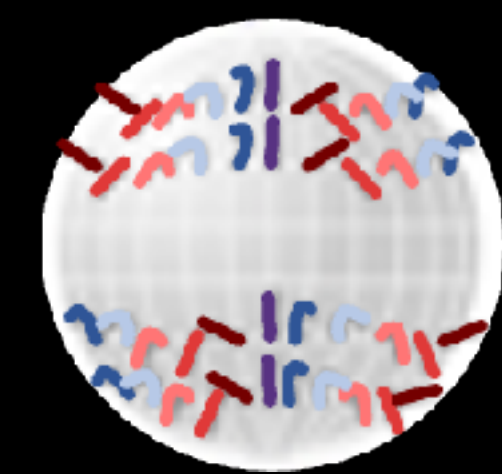
Cilia beat



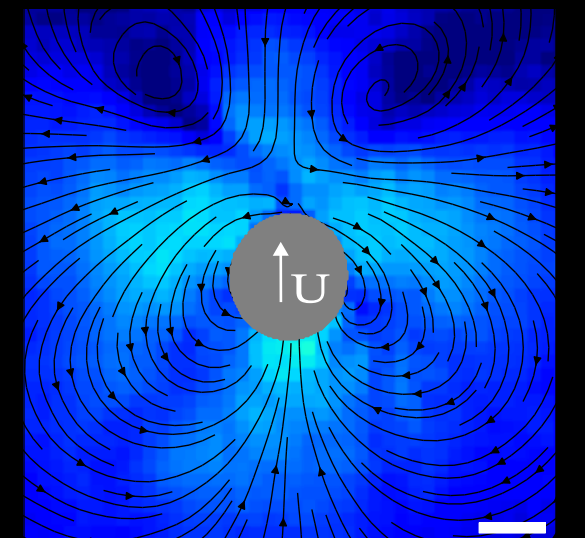
Metachronal coordination



Spatial patterning



Cellular gaits



Flow

$10^{-9}$  m

$10^{-6}$  m

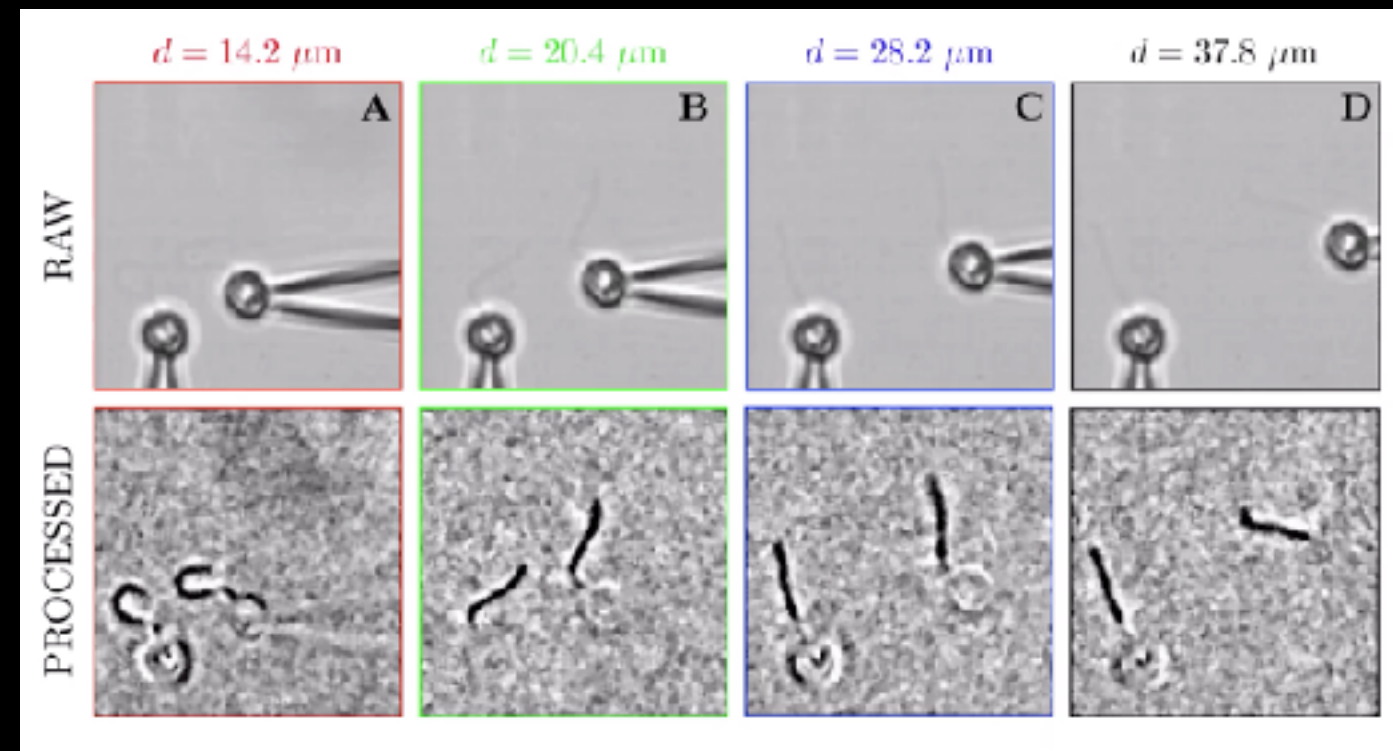
$10^{-3}$  m

$10^{-2}$  m

# Function emerges from the spatio-temporal coordination of cilia across length scales

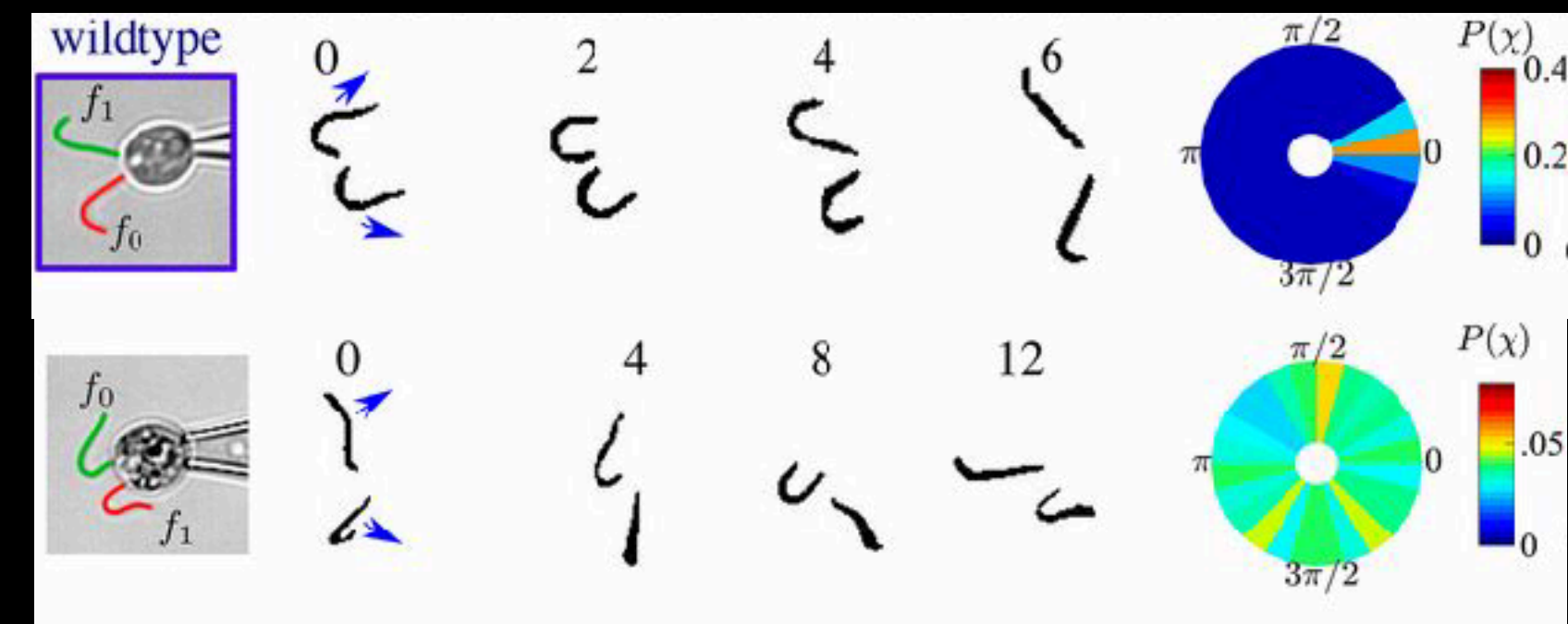
## Temporal Patterning

### Hydrodynamic coupling

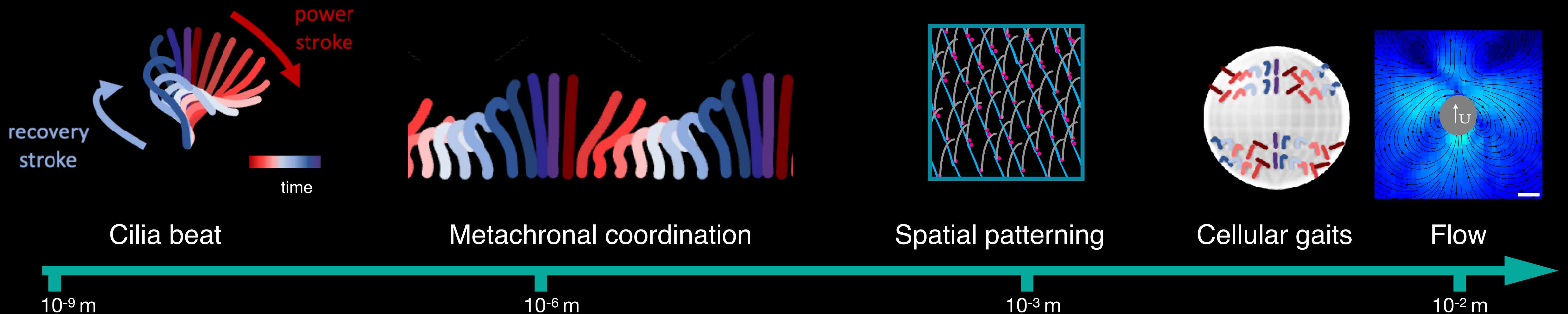


Brumley D et al. *eLife*. 2014.

### Mechanical coupling

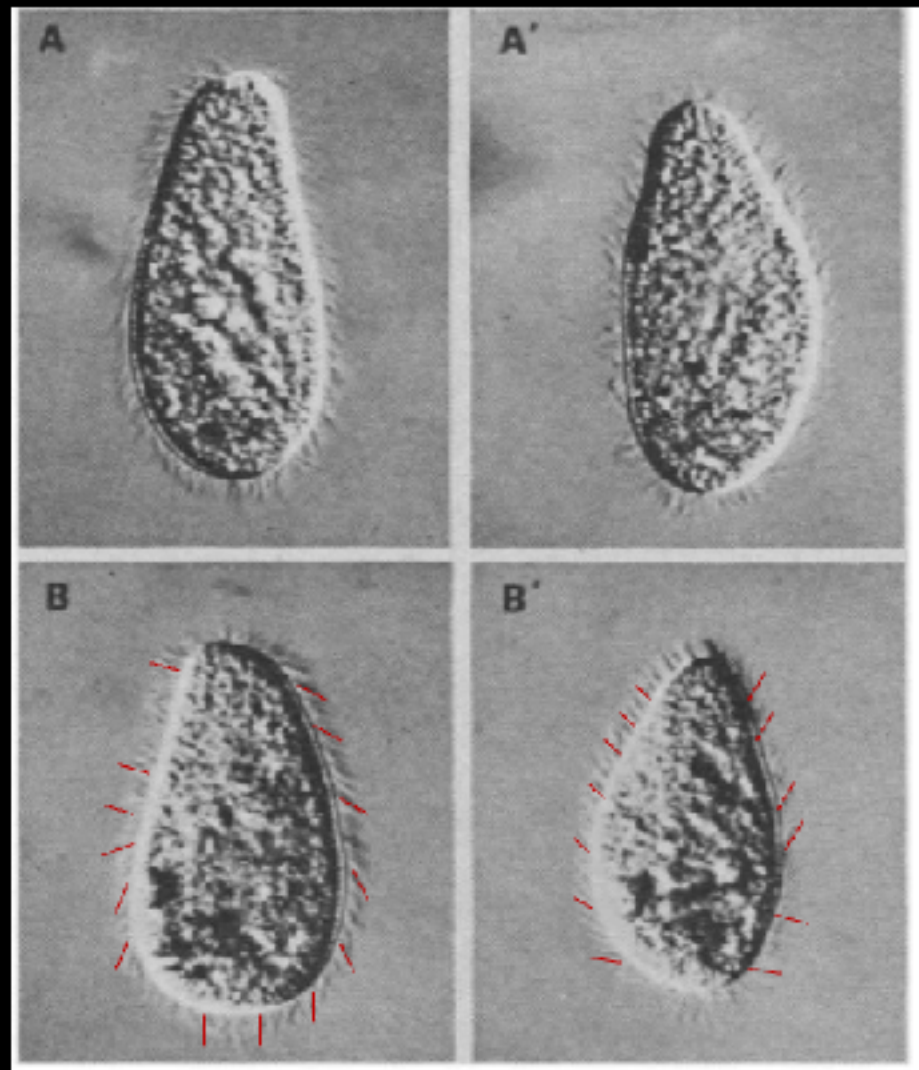


Wan K and Goldstein R. *PNAS*. 2016.

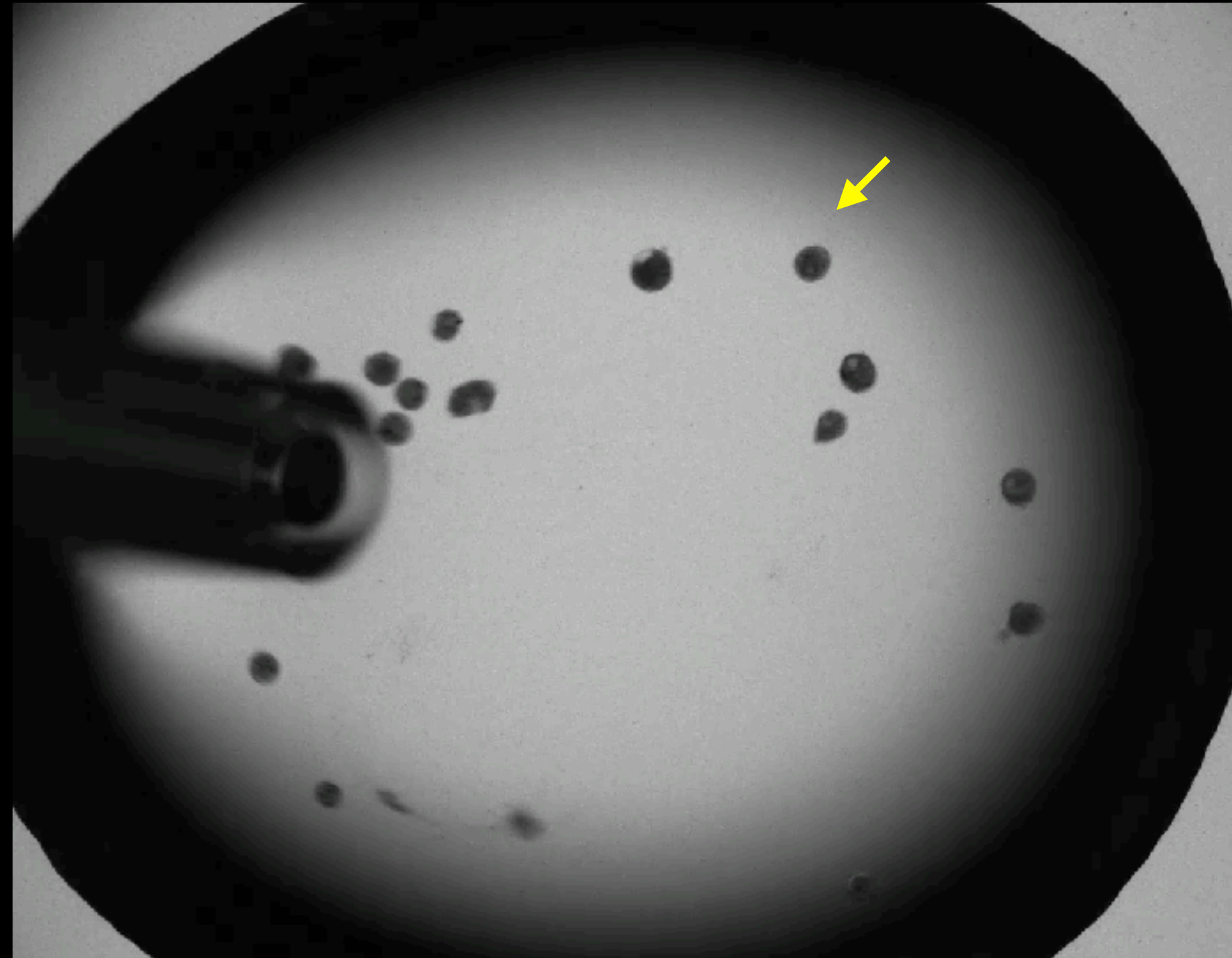


# Complex integrated regulation of cilia limits our mechanistic understanding

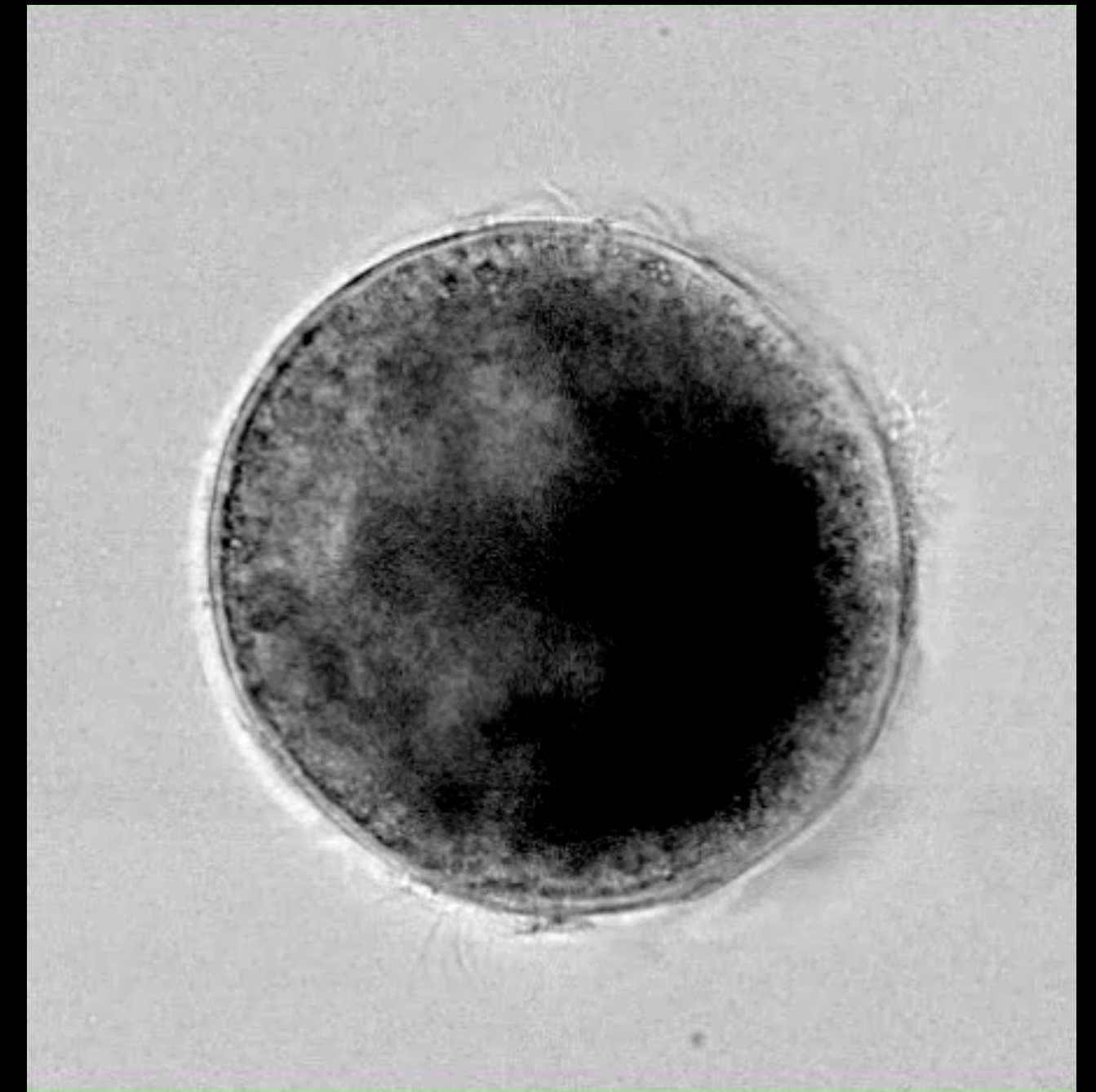
## Ciliate “ghosts”



Kung et al. *Science* 1973.



## Didinium “ghosts”



Detergent extracted cell cortices “ghosts” can help us gain mechanistic understanding of MW formation.

# Centrin forms a mesh-like anisotropic cellular-scale network in Paramecium

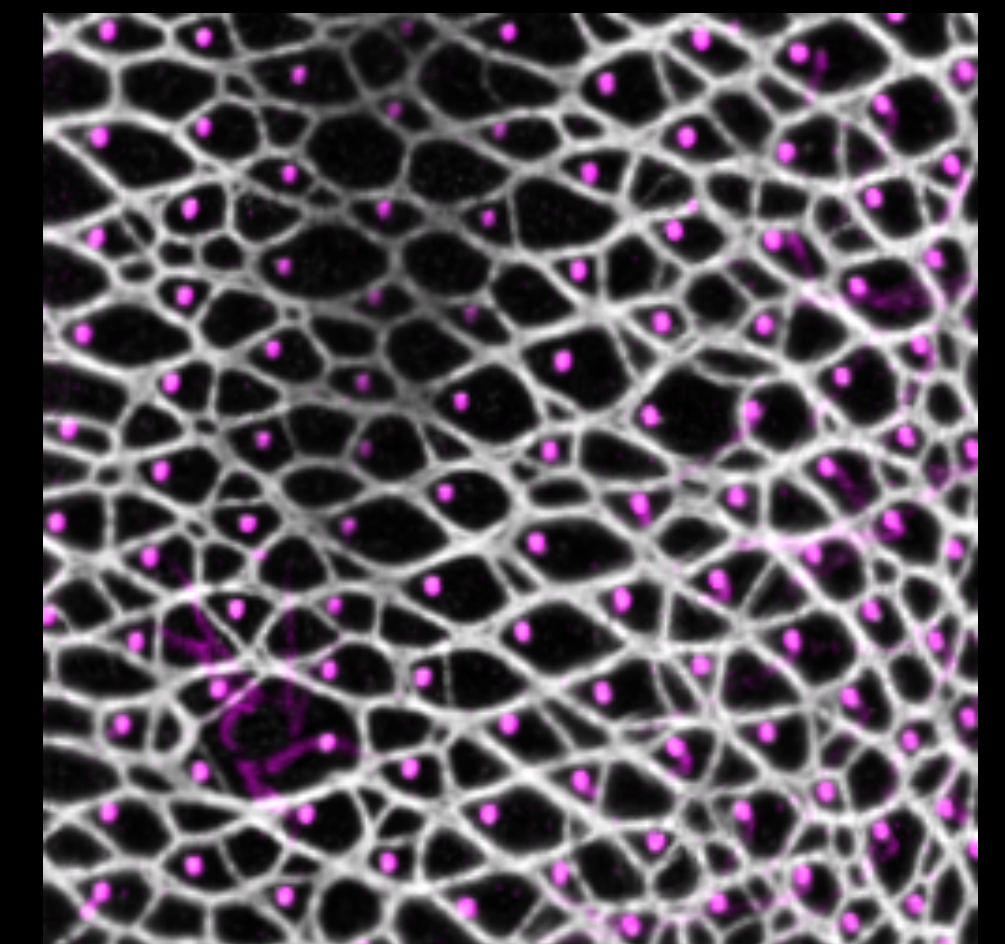
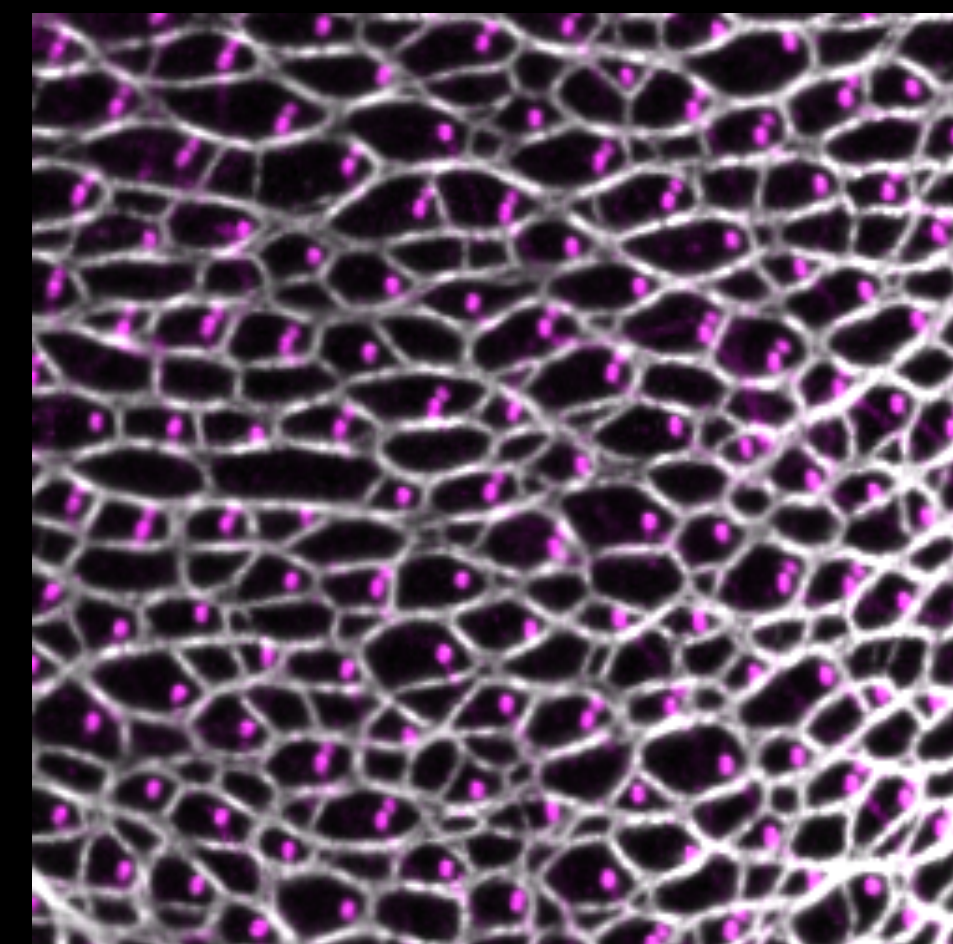
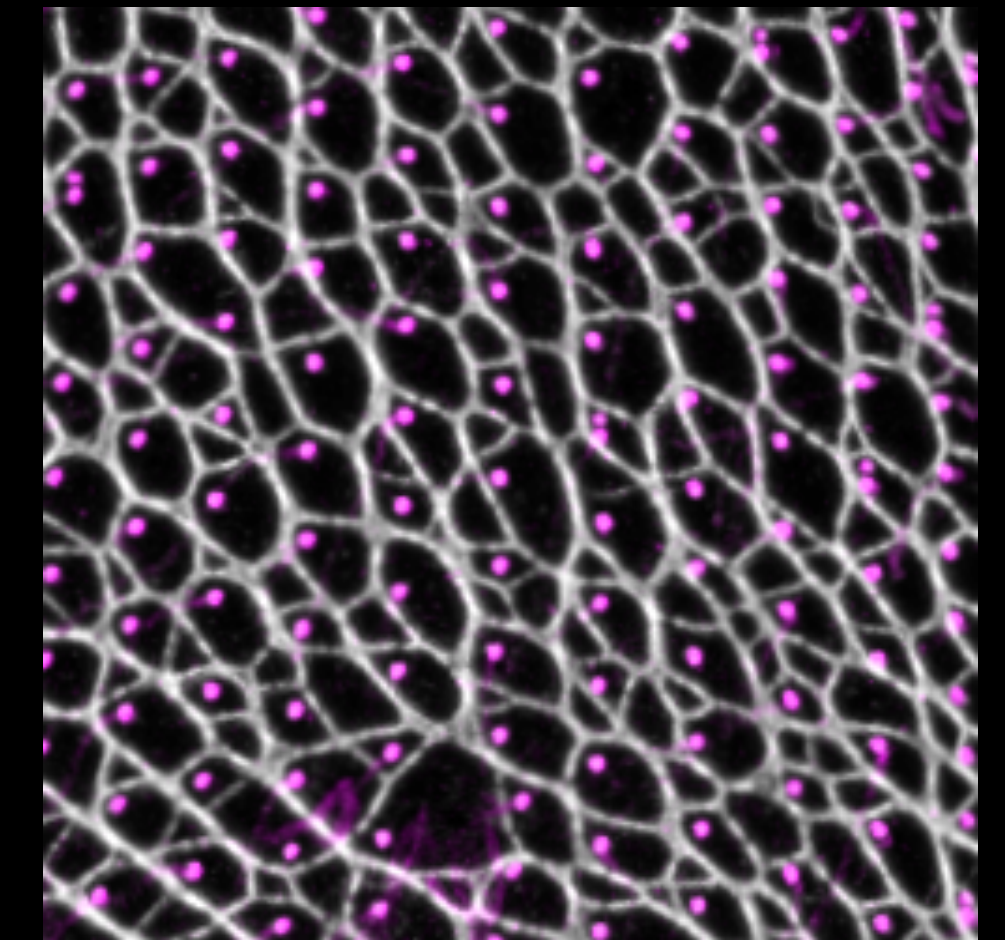
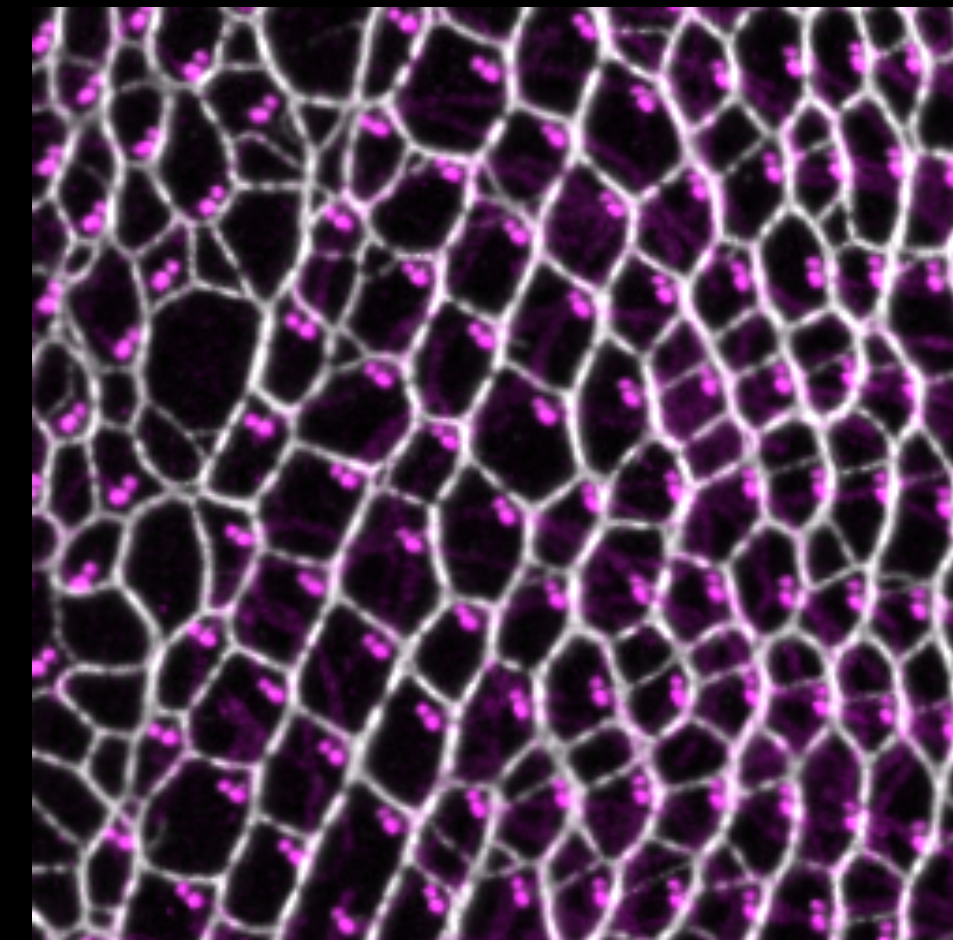
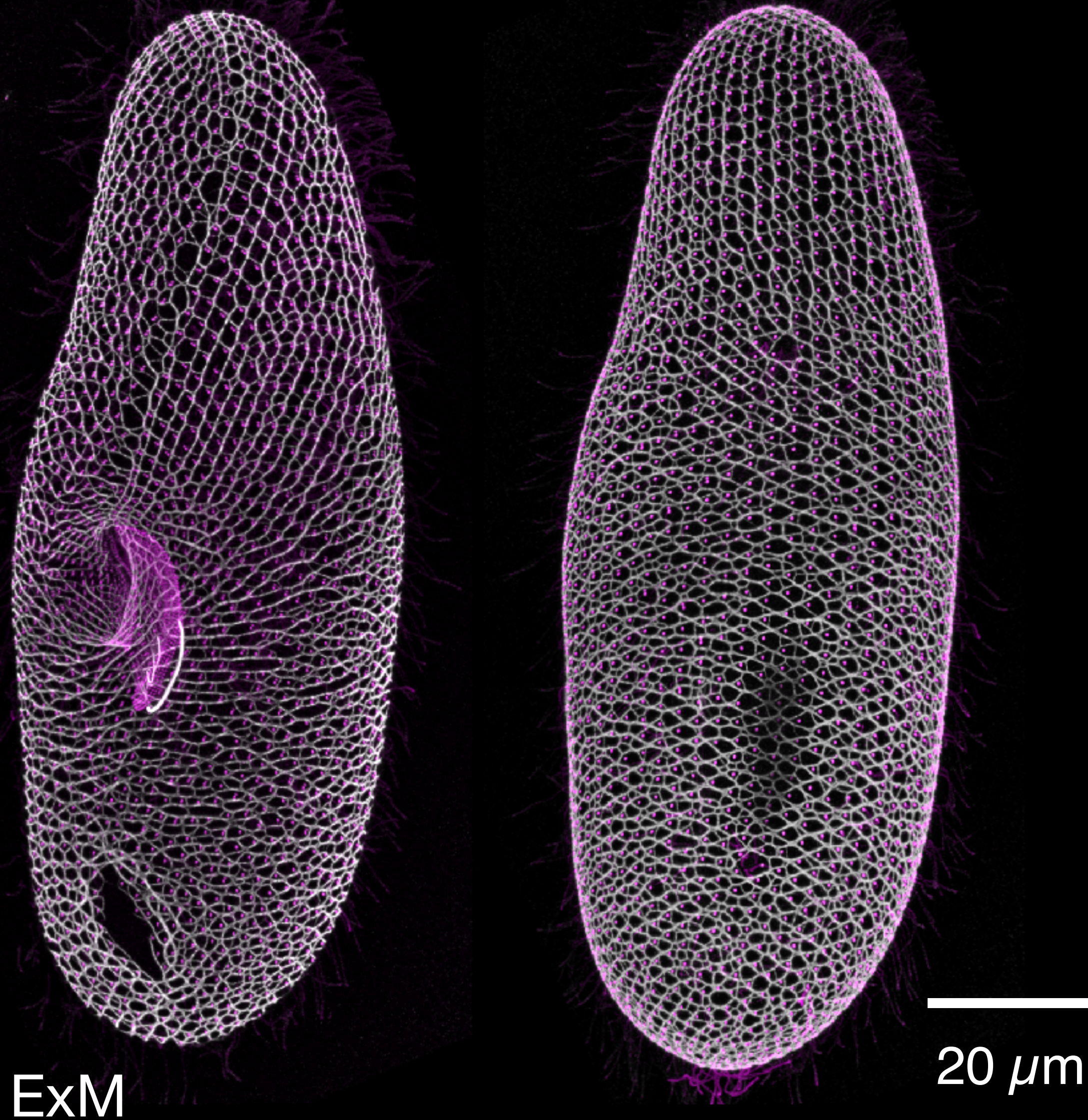
Centrin Basal Bodies

Ventral

Dorsal

Ventral

Dorsal



5  $\mu\text{m}$

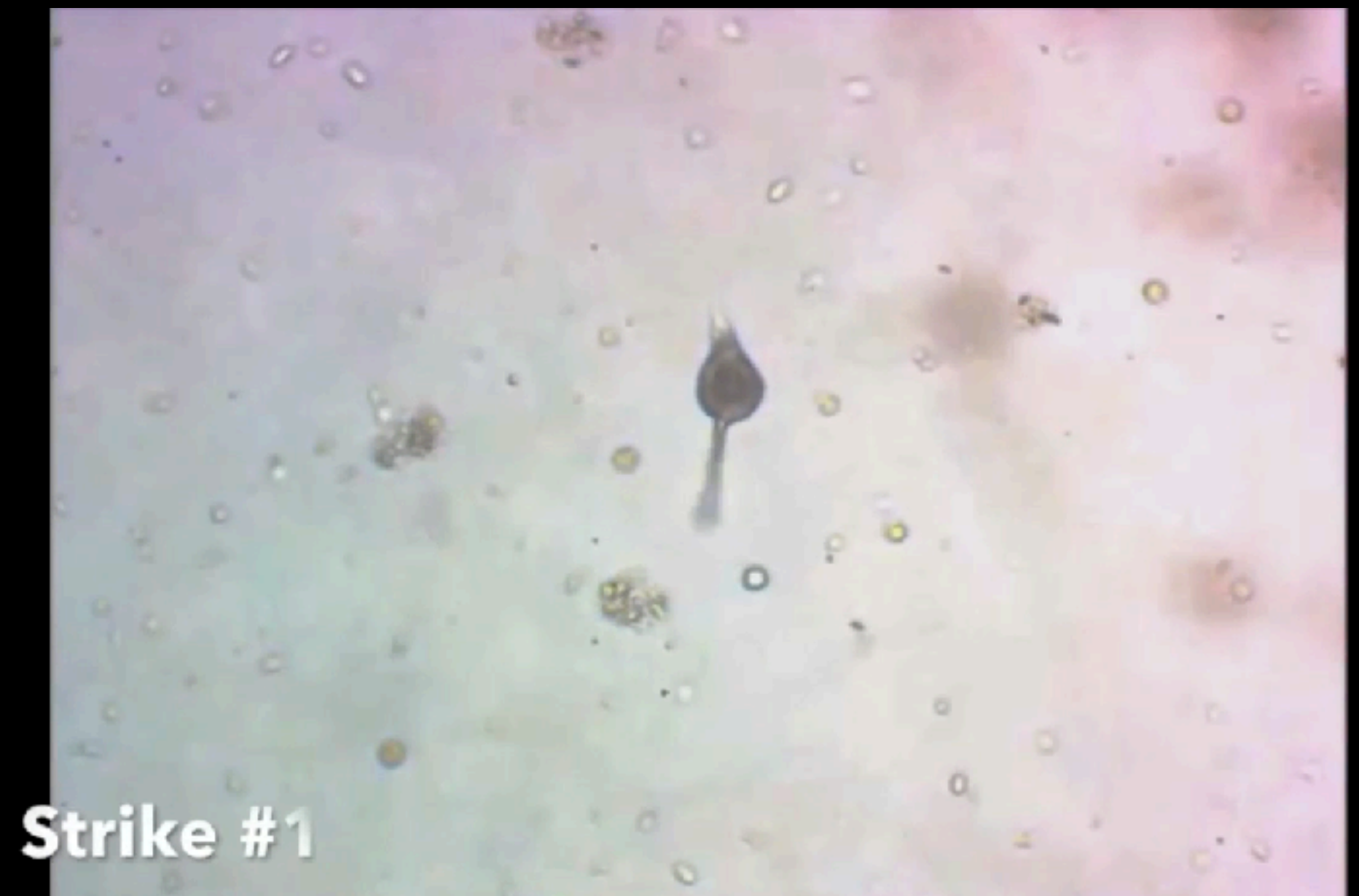
# Large scale ultrafast cellular deformations are driven by centrin

Spirostomum



Mathijssen et al. *Nature* 2019.

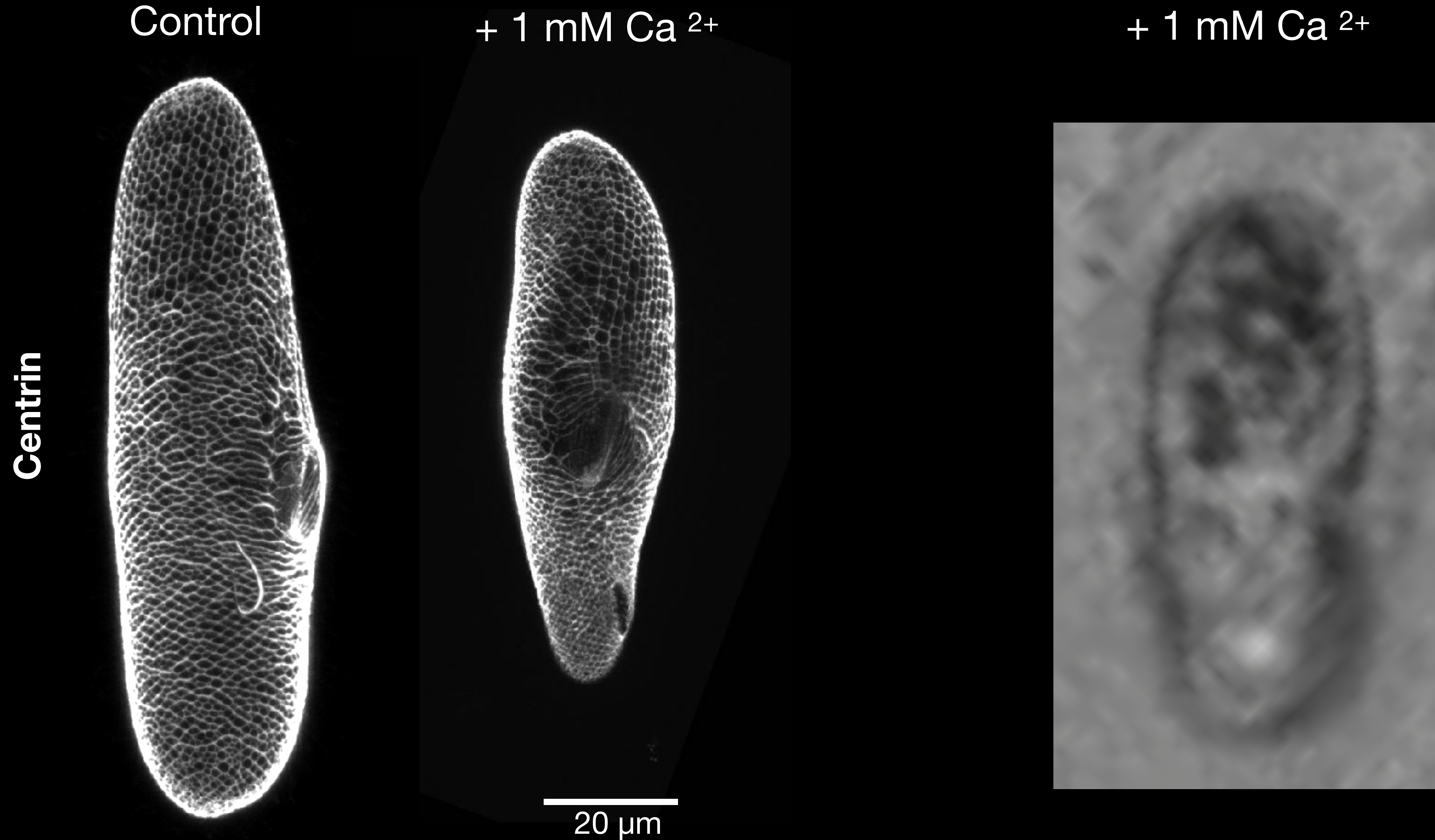
Lacrymaria



Coyle et al. *Curr. Biol.* 2008.

Free living unicellular protists undergo large scale ultrafast deformations in response to diverse environmental stimuli. These deformations underlie the behavioral responses necessary for survival of these organisms.

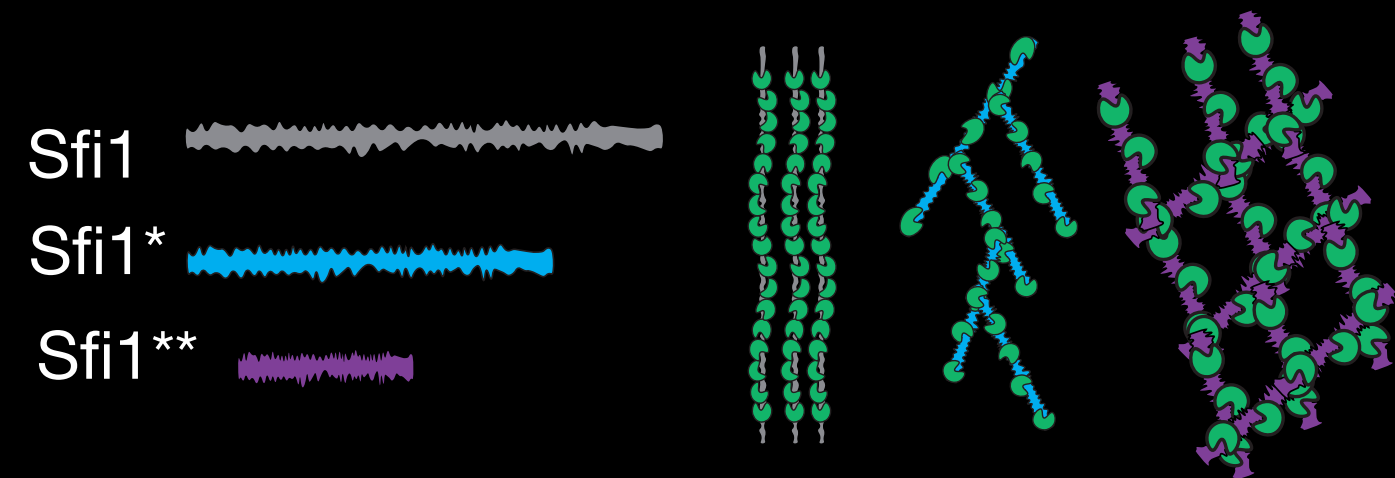
# Paramecium undergoes an anisotropic cellular-scale deformation triggered by calcium



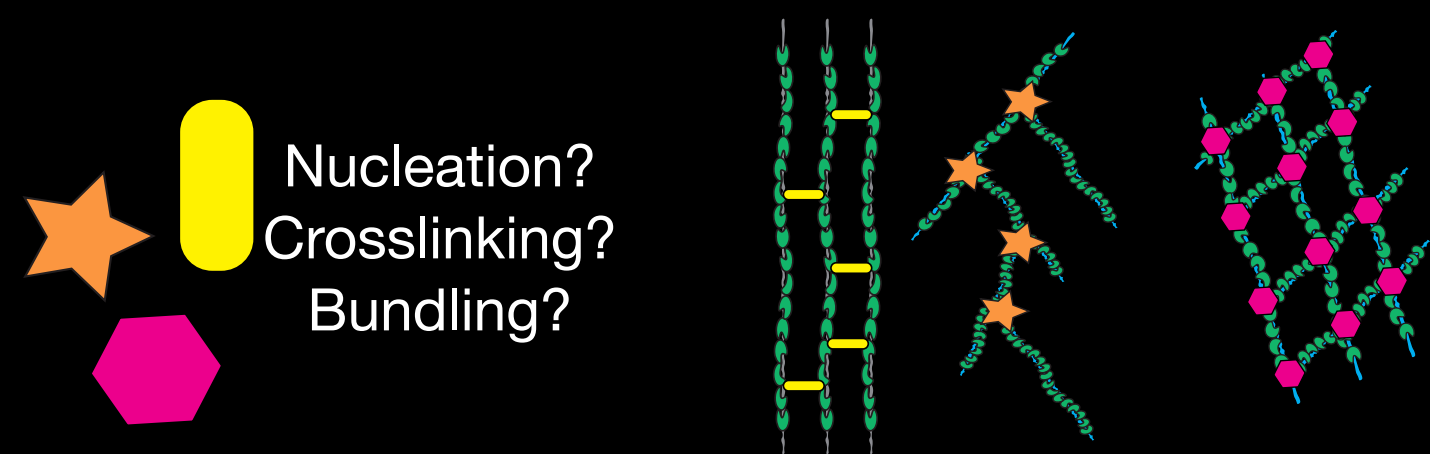
# Understanding centrin driven cellular deformation is a multiscale problem

How are centrin networks assembled?

Geometry specified by Sfi1 length

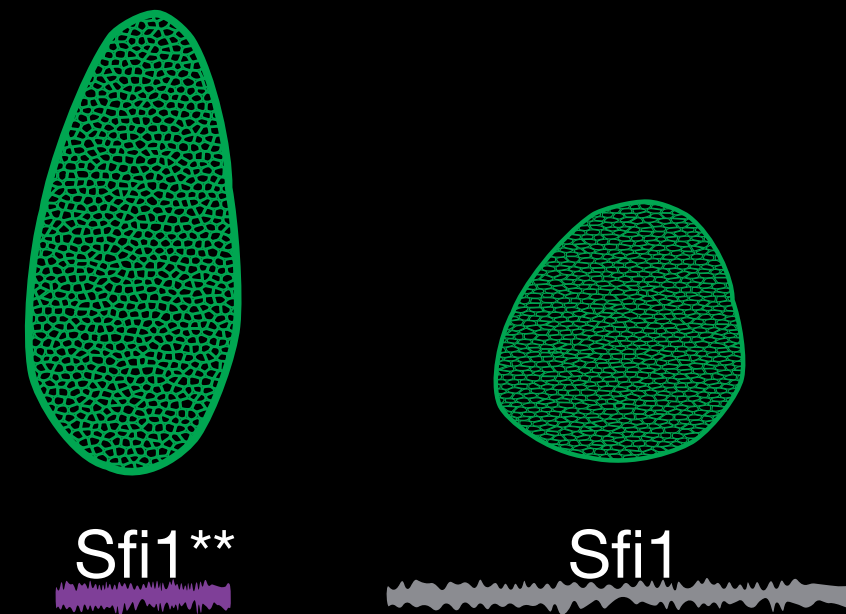


Geometry modulated by accessory proteins

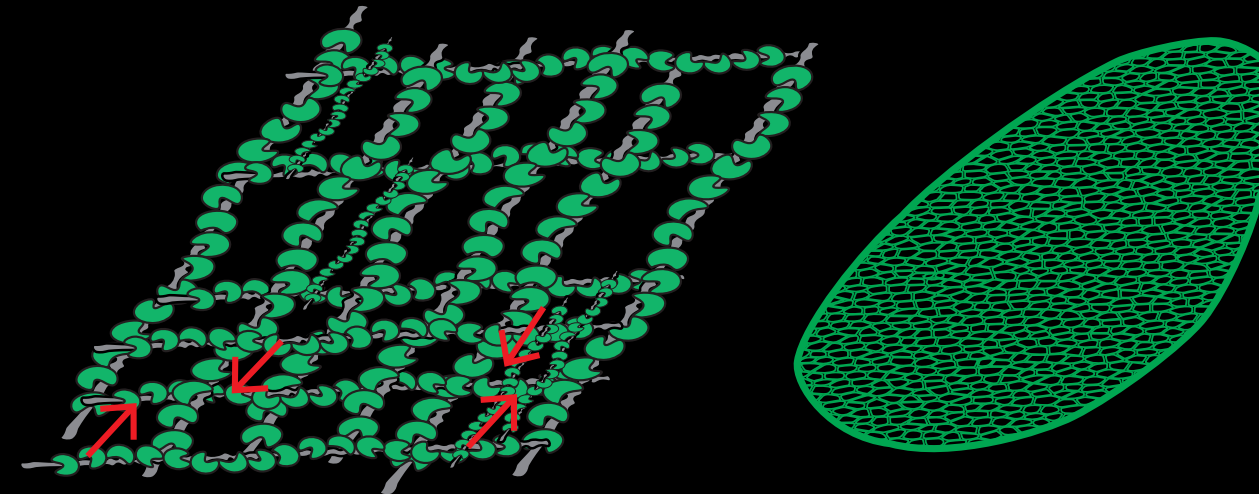


How do network deformations lead to cellular shape changes?

Network deforms homogeneously  
Sfi1 length determines cell deformation

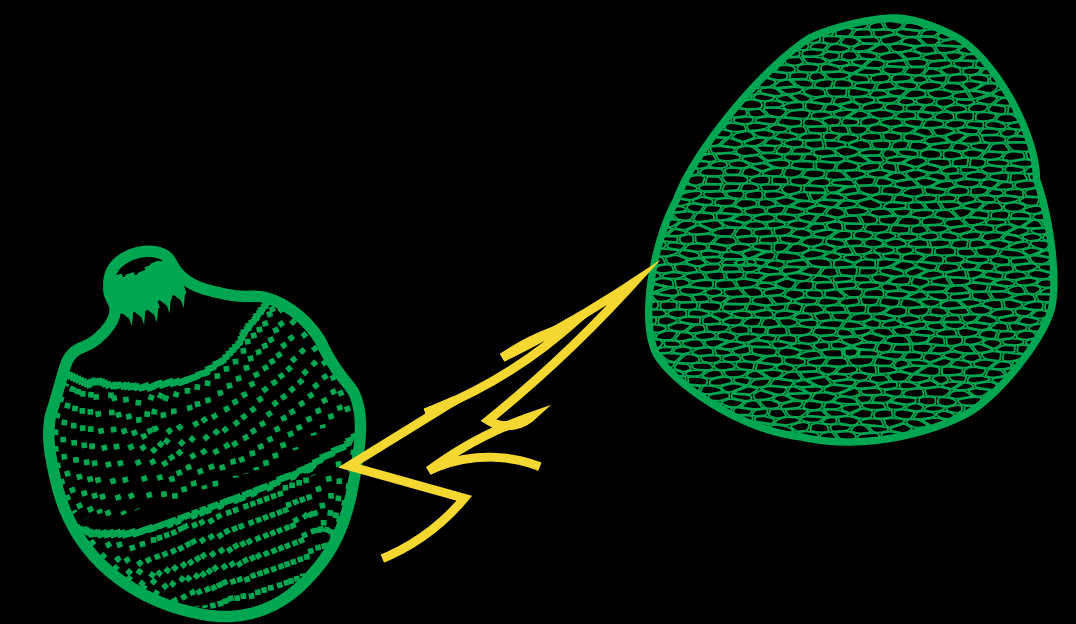


Strain varies across network  
Local geometry governs cell deformation



How does centrin encode the behavioral responses of cells?

Cell escape requires contraction



# Acknowledgements



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