Determining Physical Properties of the Cell Cortex

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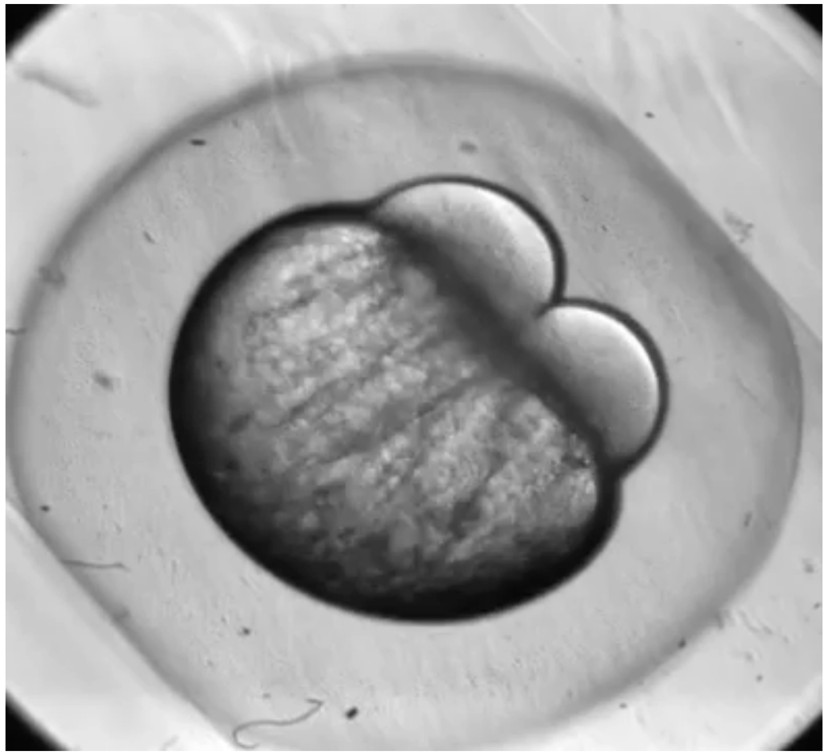
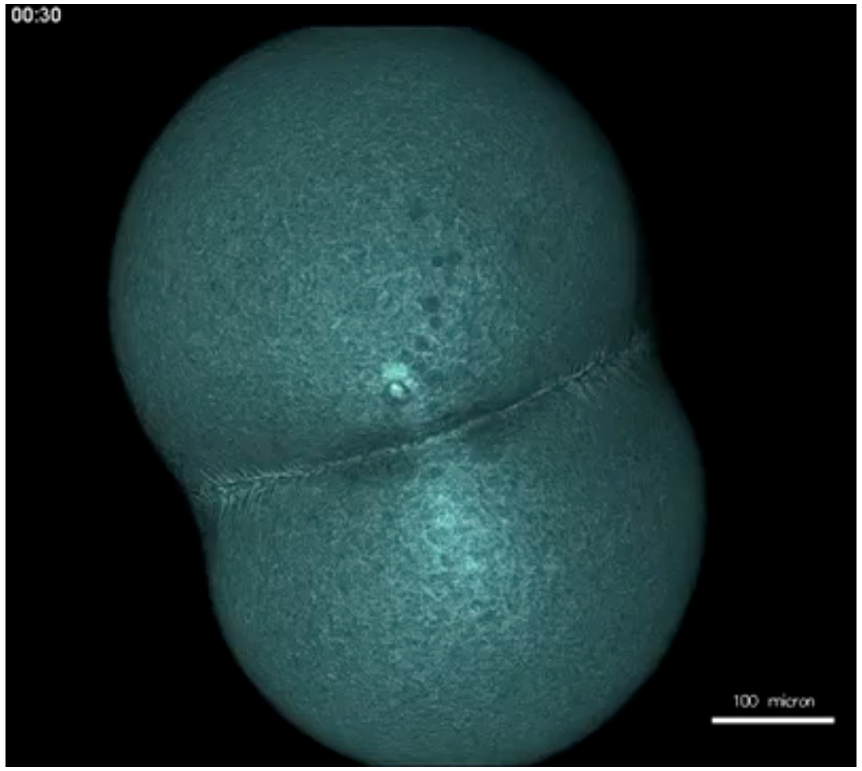
DCS 2017

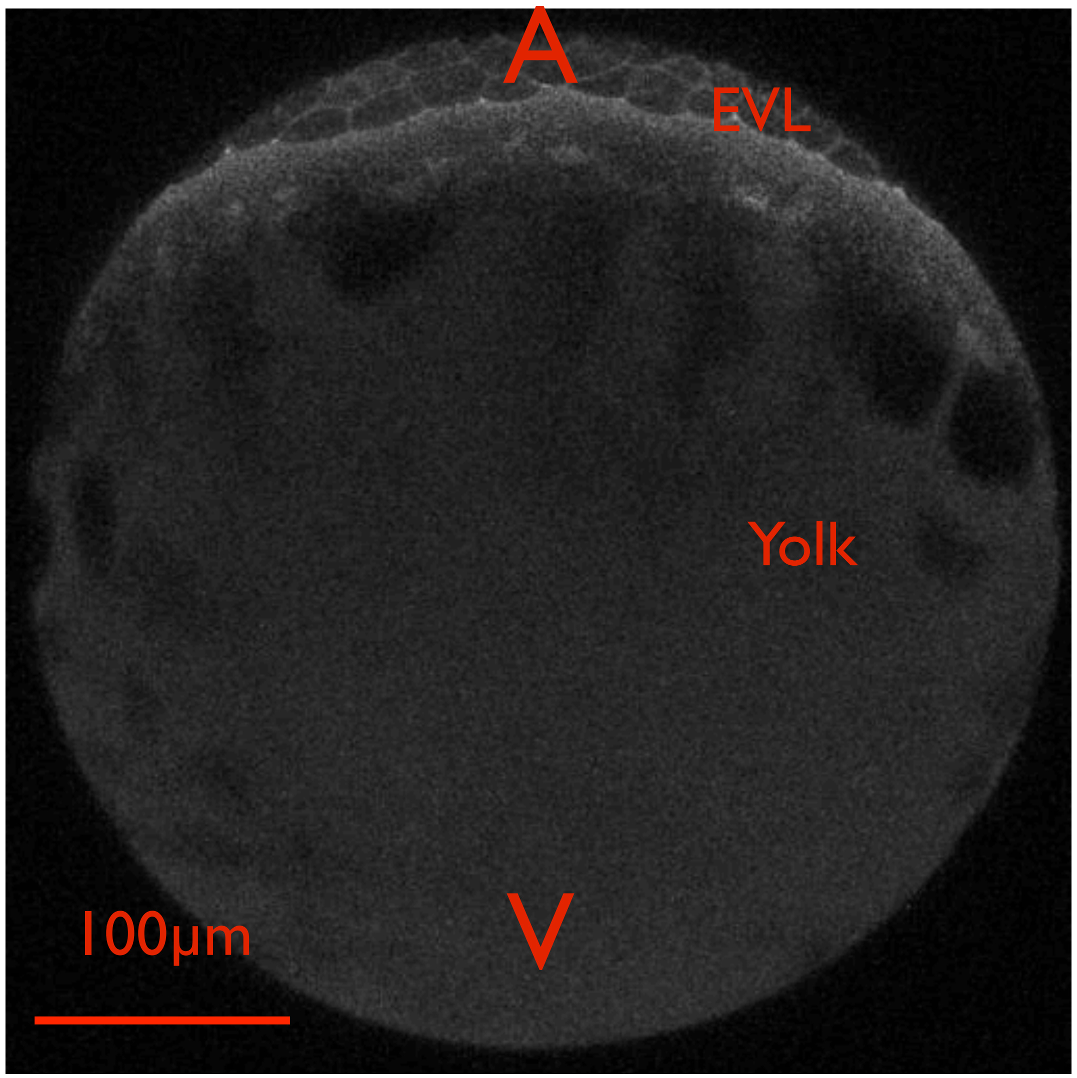
Zebrafish : Embryonic Development





Fengzhu Xiong, Sean Megason (Harvard Medical School)

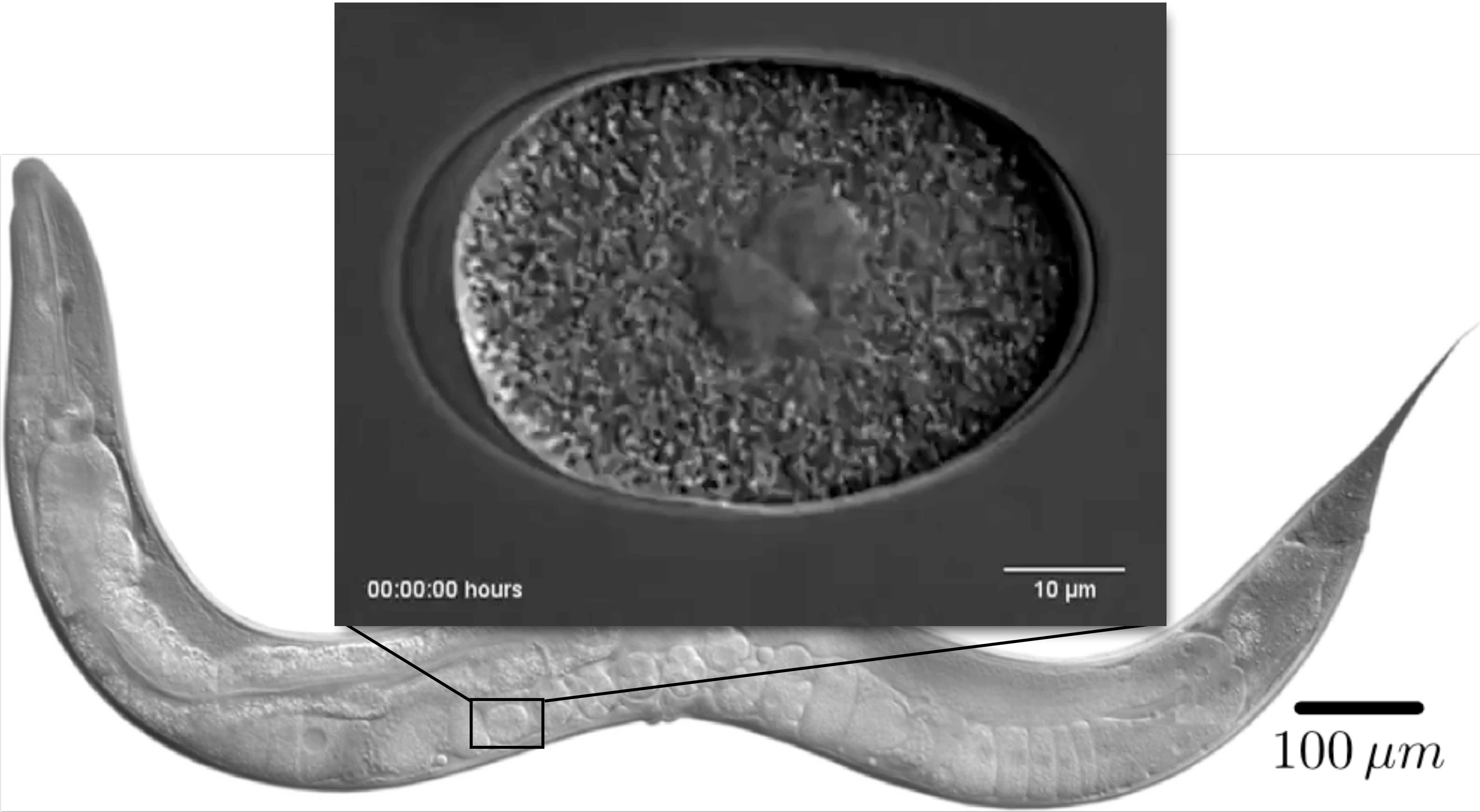
Zebrafish Epiboly



From: Kimmel et al. Stages of embryonic development of the zebrafish Dev. Dyn. 203:253-310, 1995

M. Behrndt et. al.
Science 338, 257 (2012)

C. elegans : Embryonic Development

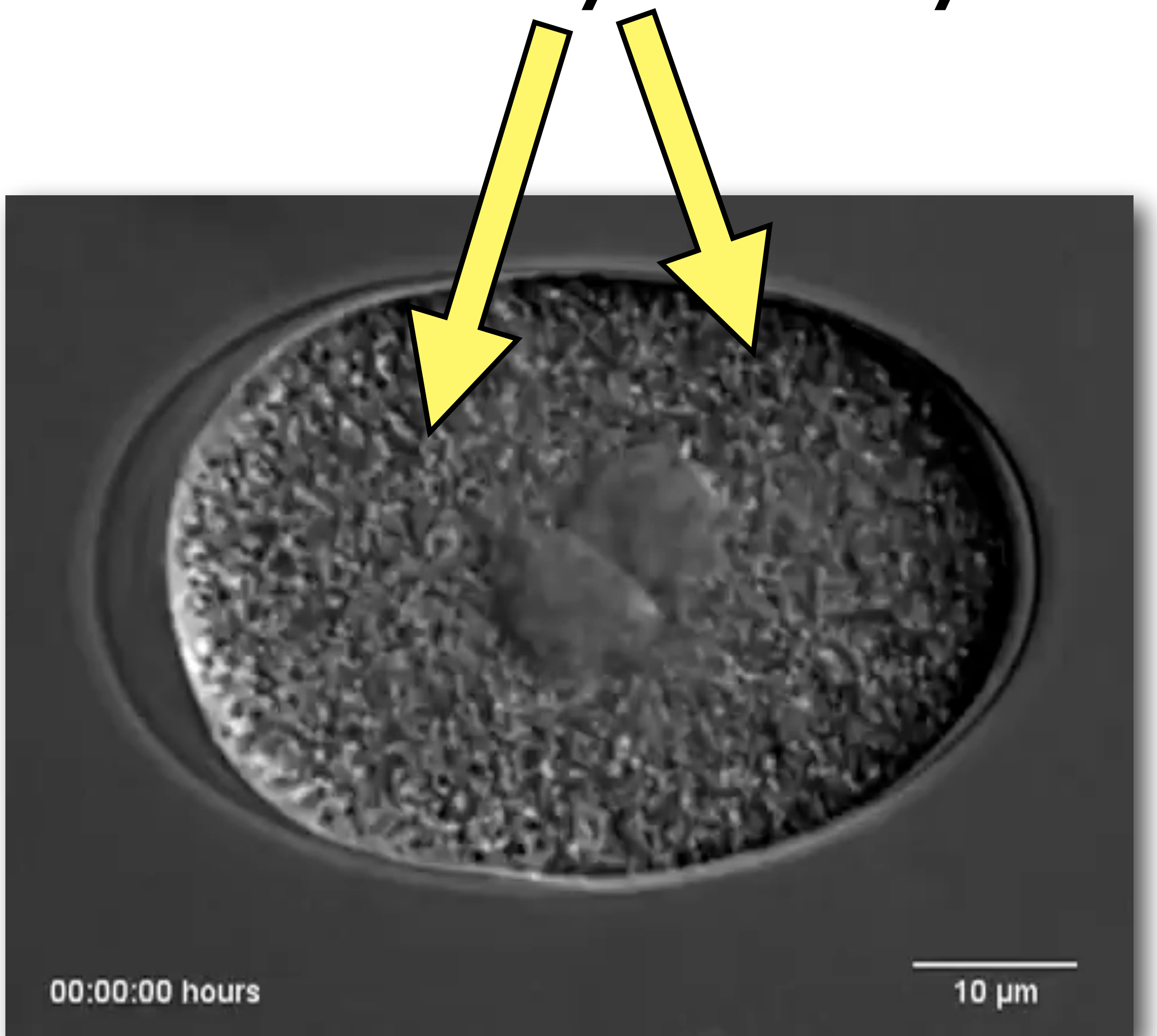


Chin Sang Lab

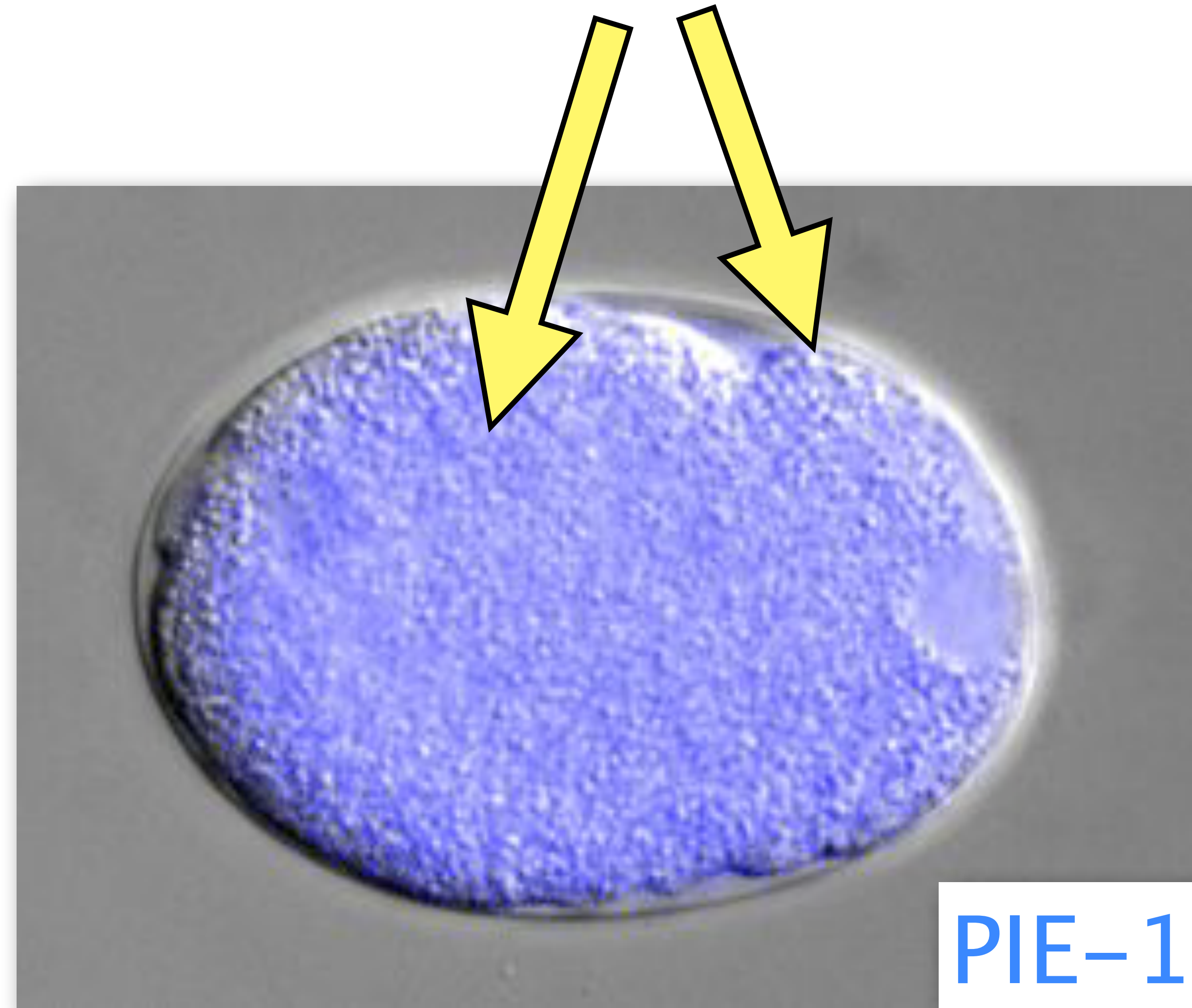
C. elegans : Embryonic Development

Size asymmetry

Composition asymmetry



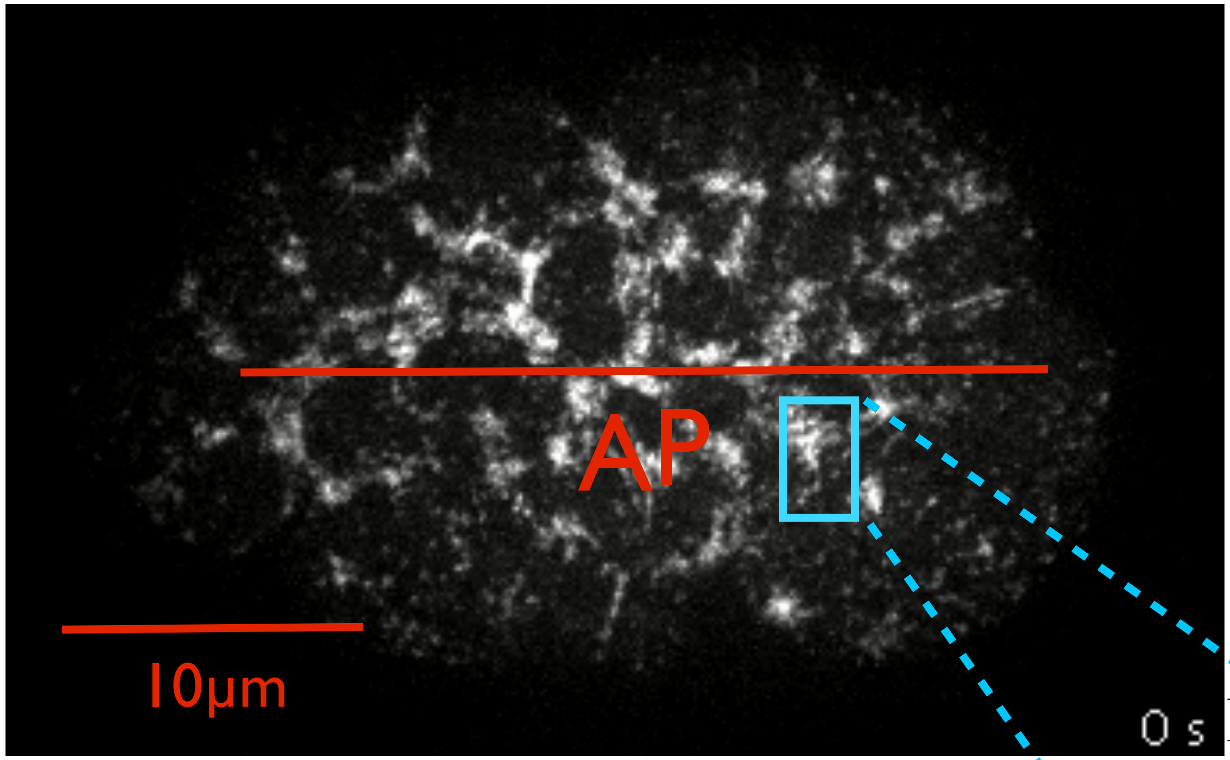
Hyman Lab, MPICBG



Gönczy and Rose, Wormbook (2005)

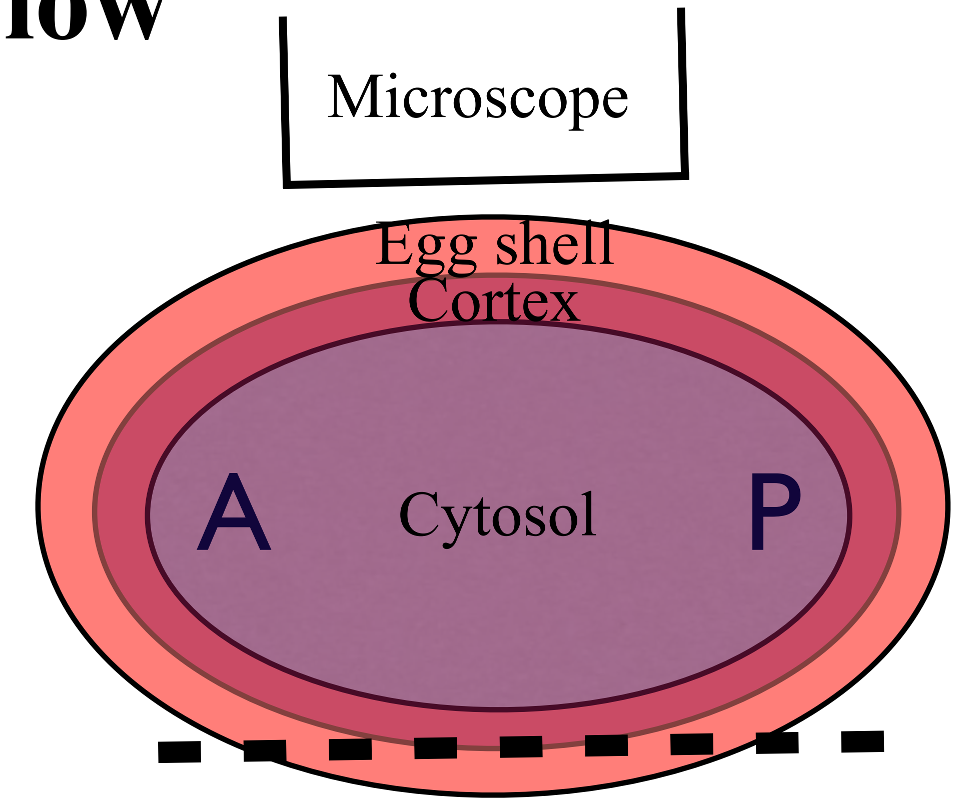
Embryonic Development : Inter-twined Dynamics of Force & Flow

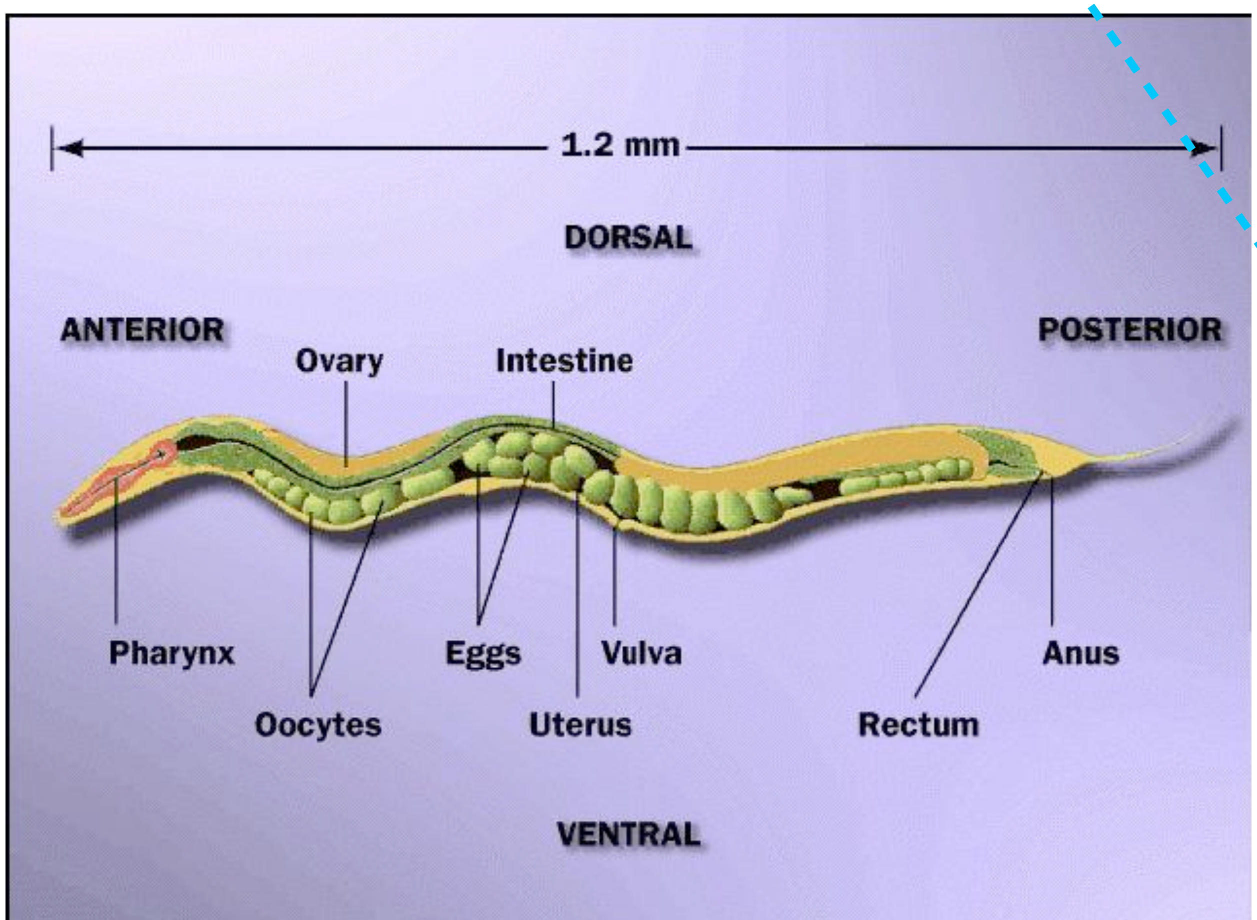
C. elegans A-P flow



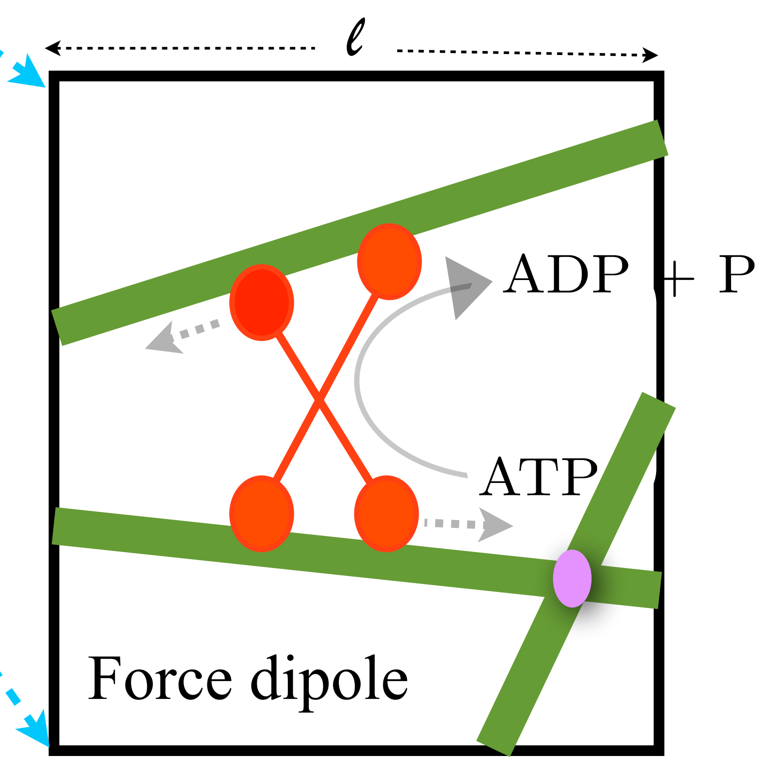
Myosin GFP

Mayer *et. al*, Nature, 2010.



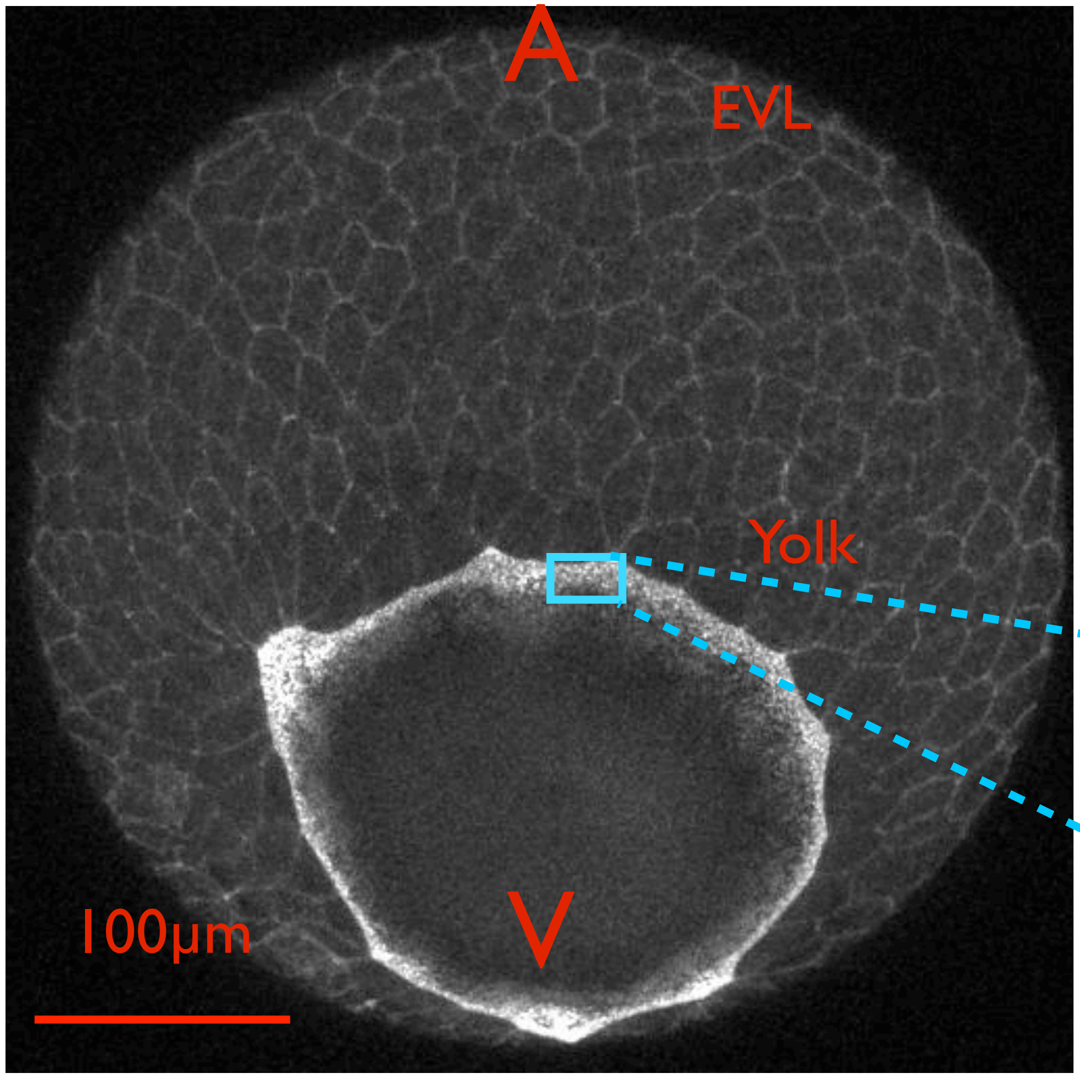


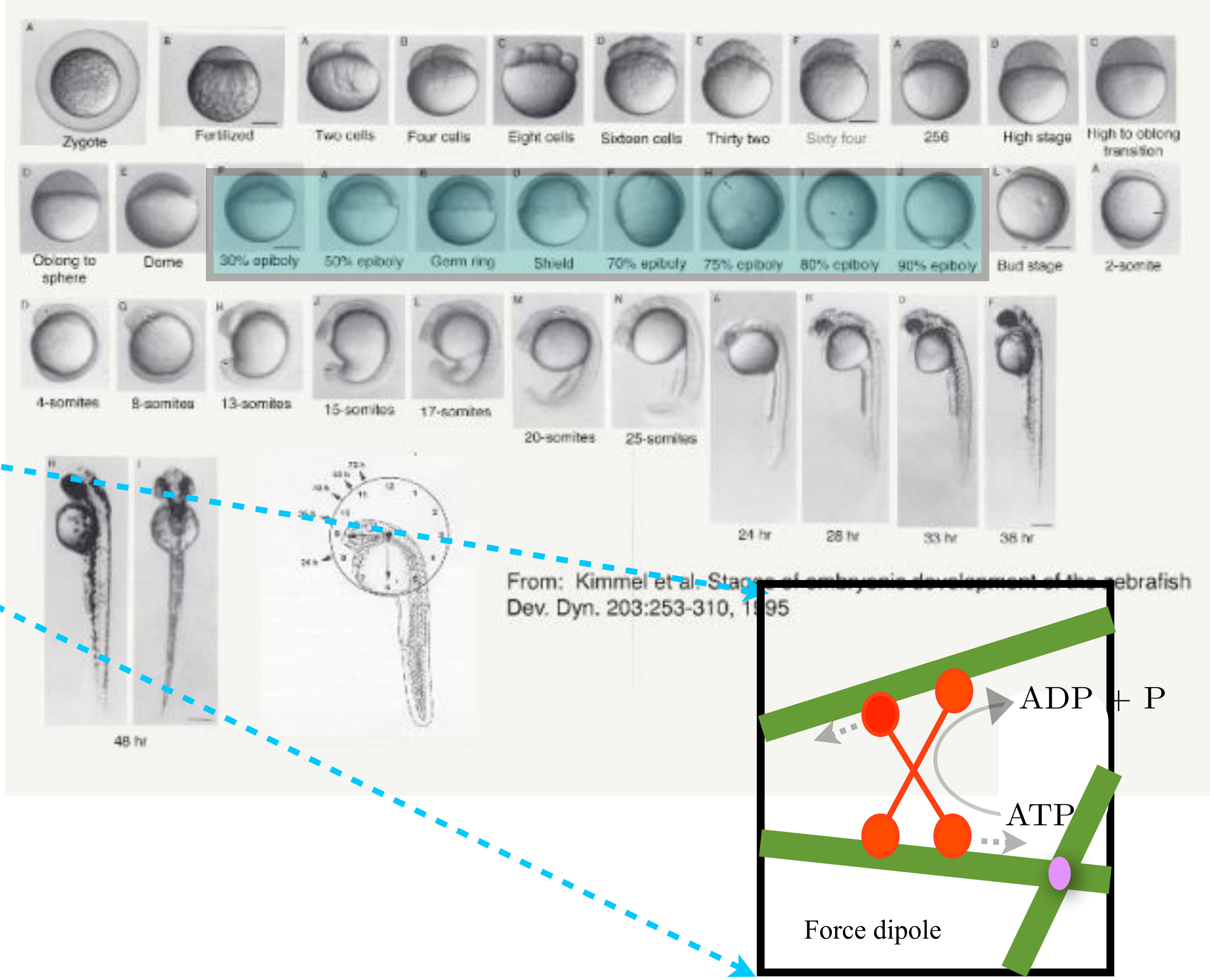
C.elegans http://www.imsc.res.in/~sitabhra/research/neural/celegans/



Smallest 'unit of cell' cortex from molecular scales: **Actin**, **Myosin**, **Actin Binding Proteins,** ATP

Zebrafish epiboly





M. Behrndt et. al.
Science 338, 257 (2012)

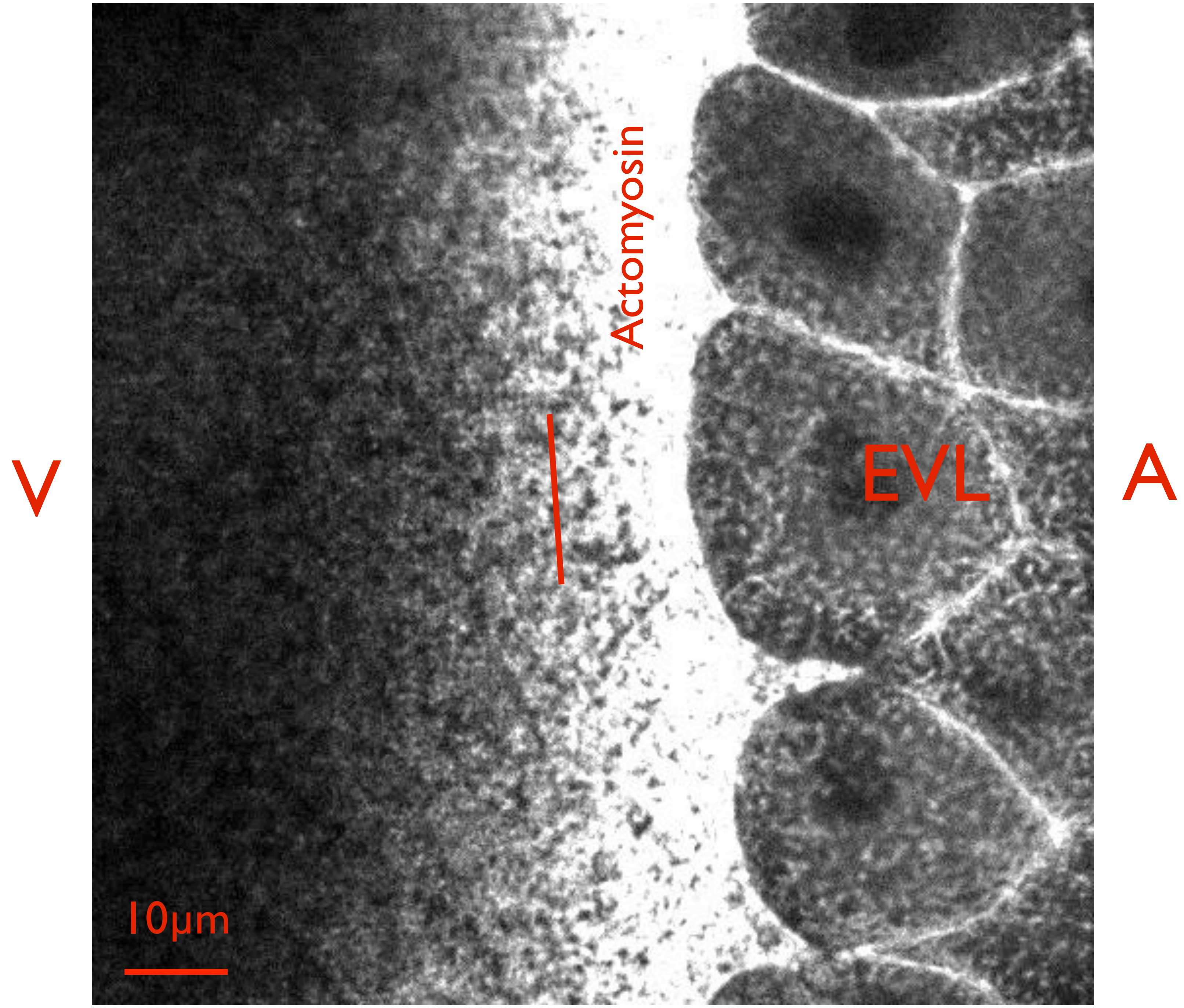
Material Properties of a Fluid Regulate Flow

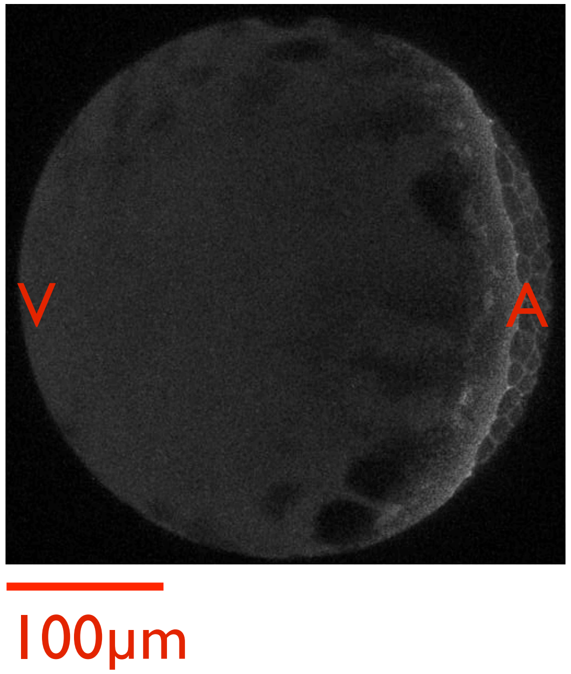

To understand the flow → **Need to estimate the relevant material properties of the concerned fluid**

Perturbation to the fluid to estimate the material properties:

Laser ablation

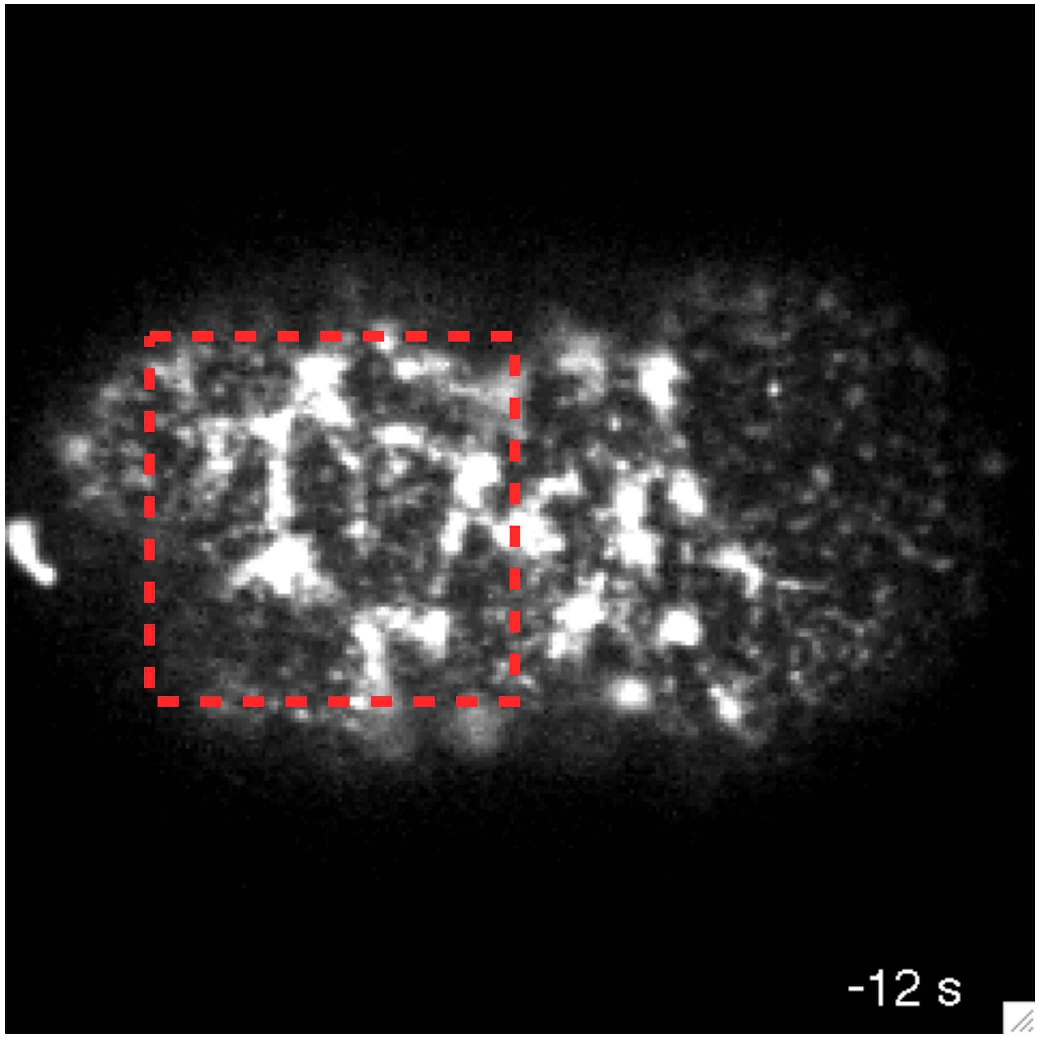
Laser Ablation : Zebrafish





M. Behrndt et. al.

Laser Ablation : *C.elegans*

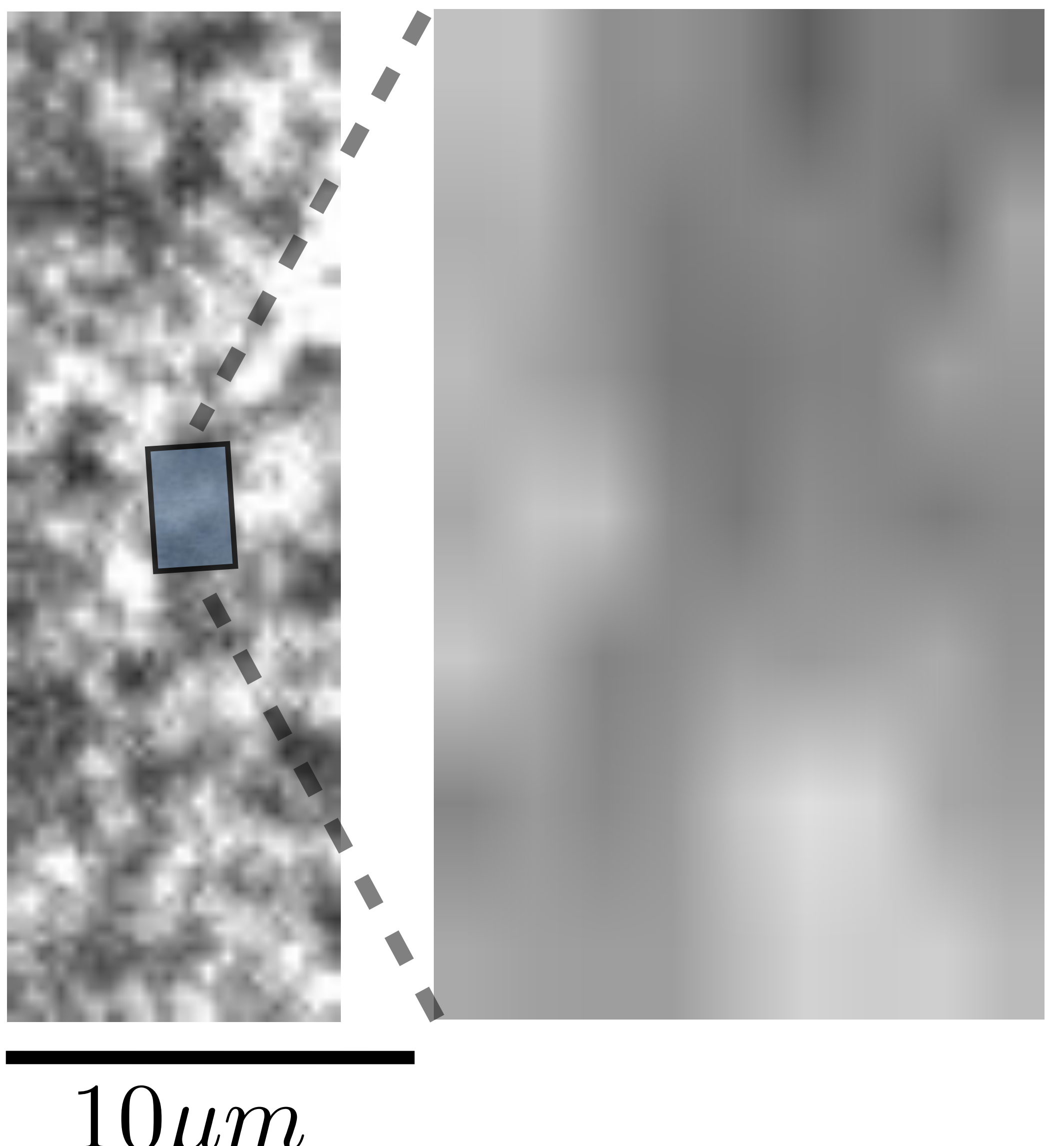


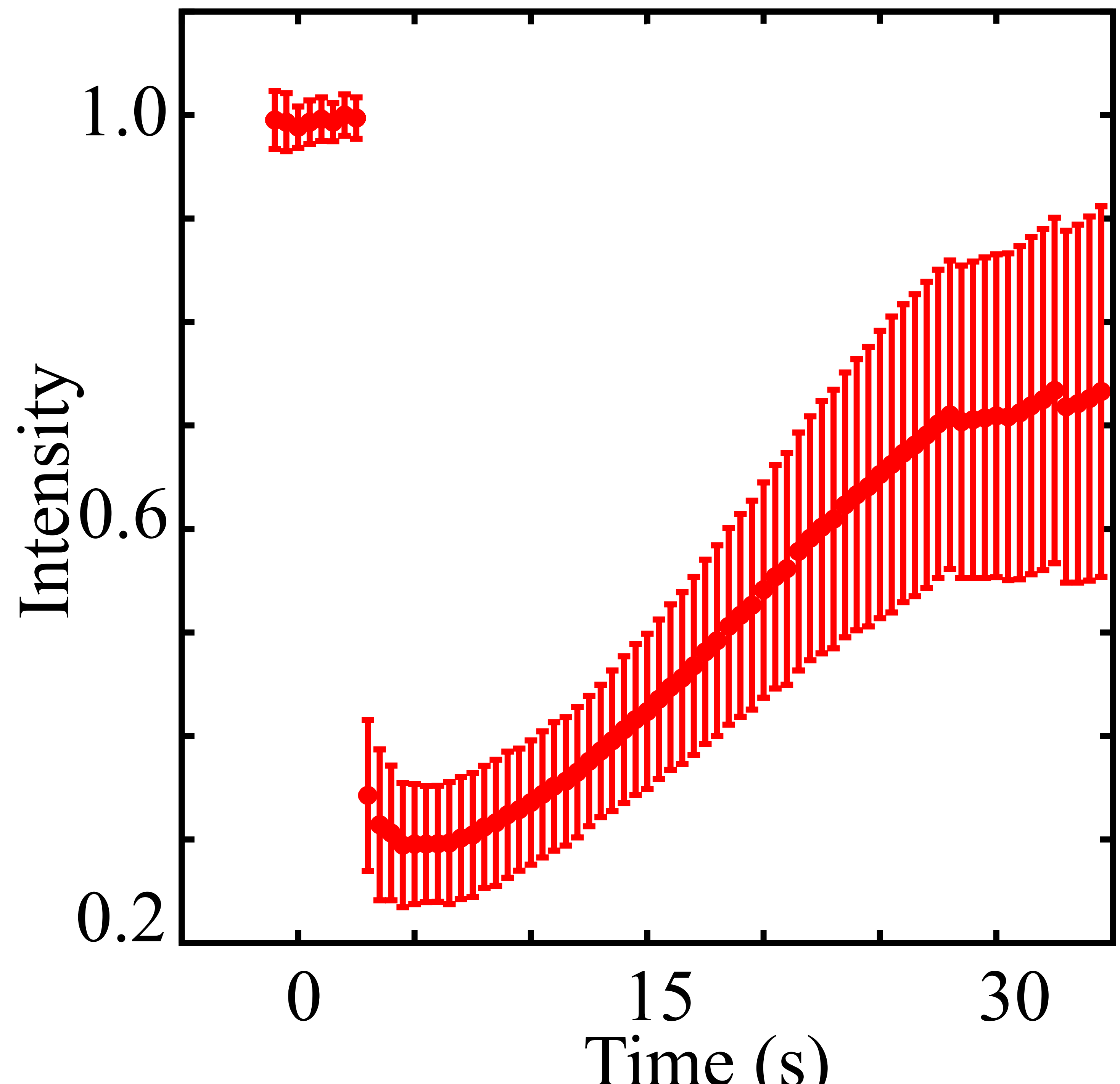
Mayer *et. al*, Nature, 2010.

Analysis of the cortical flow by laser ablation

Cortical Flow by Laser Ablation

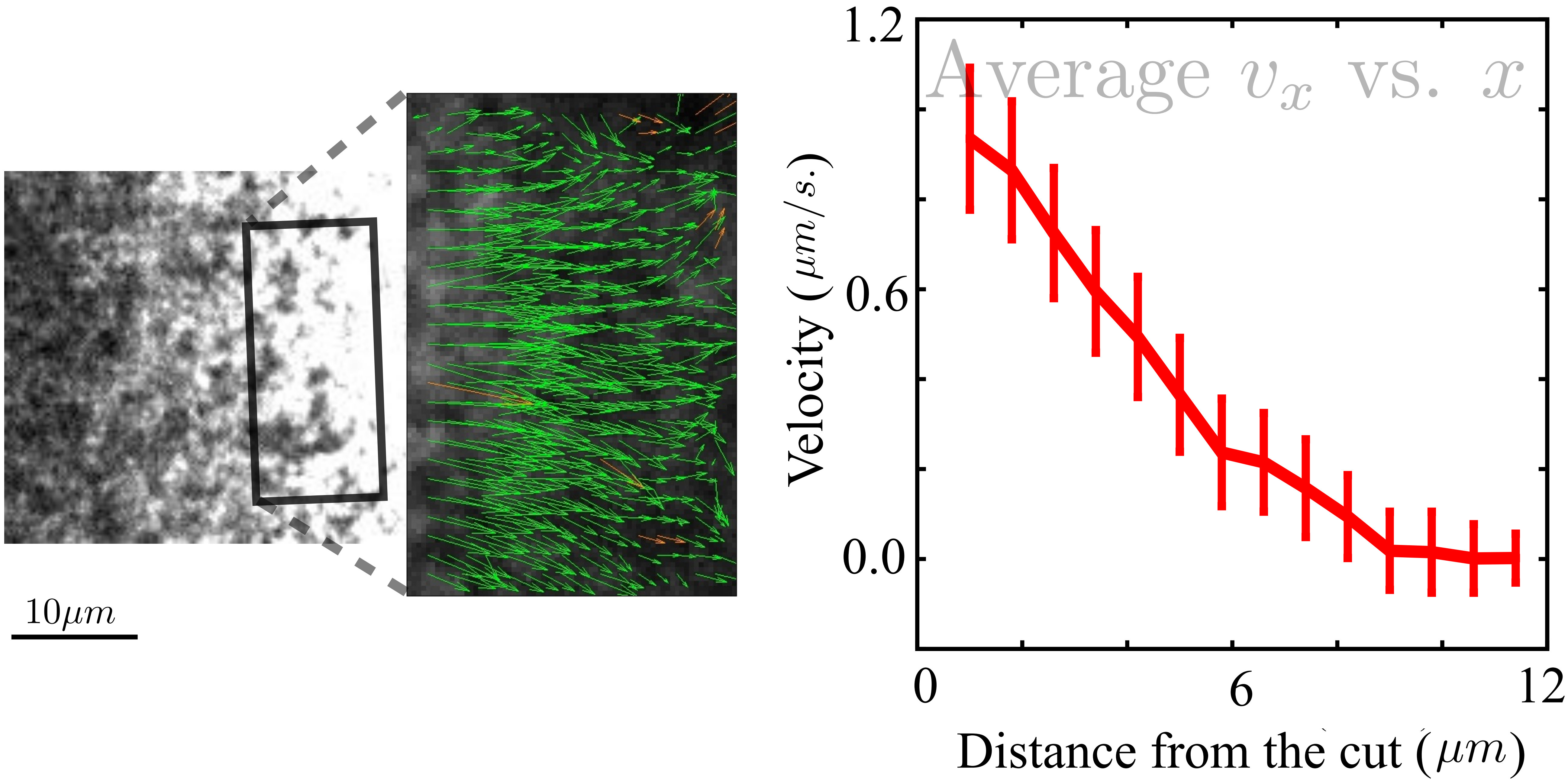
Turn-over & on rate





Cortical Flow by Laser Ablation

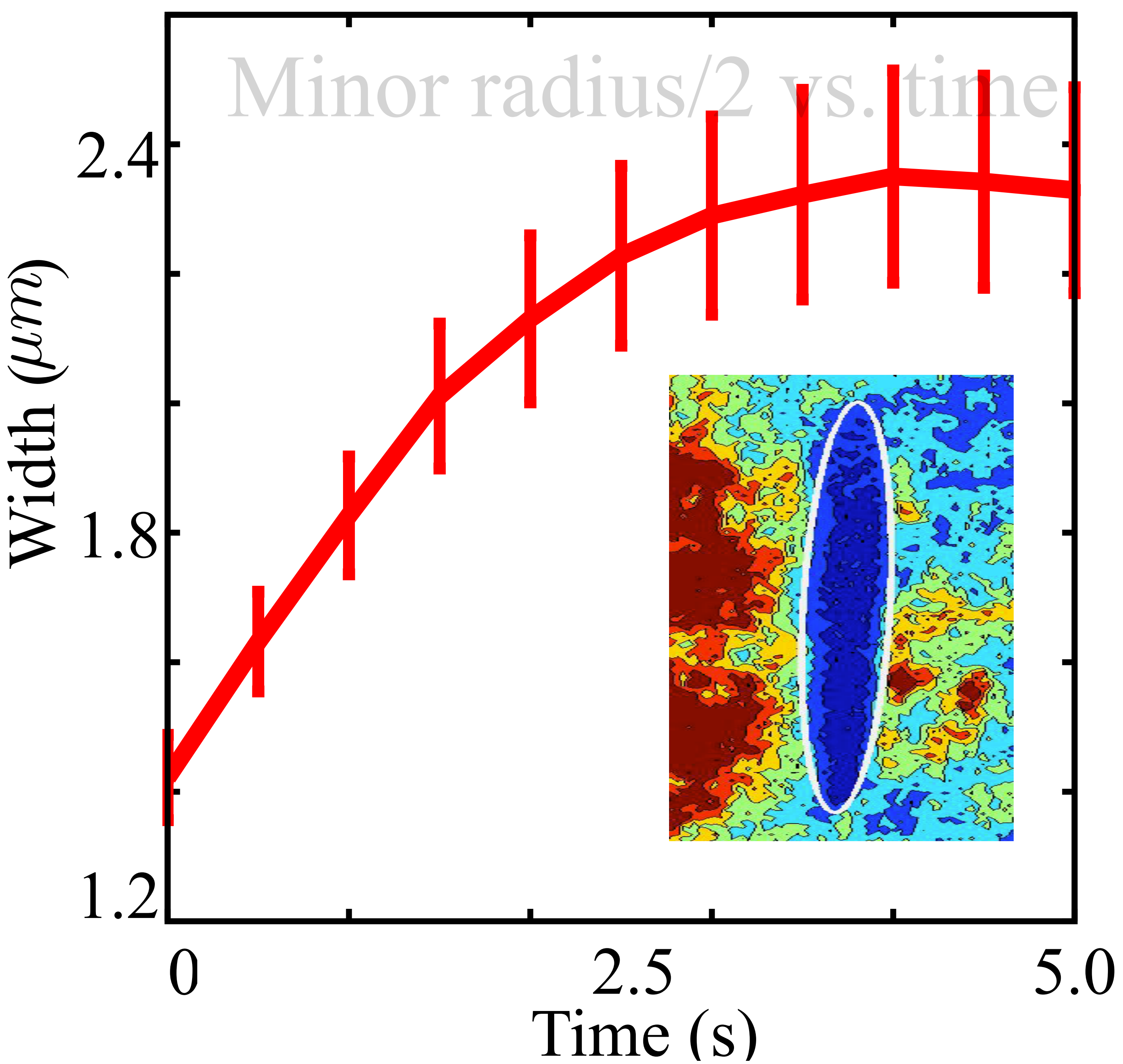
Velocity profile over space



PIV flow field between 1st and 2nd frame (0 to 0.5s)

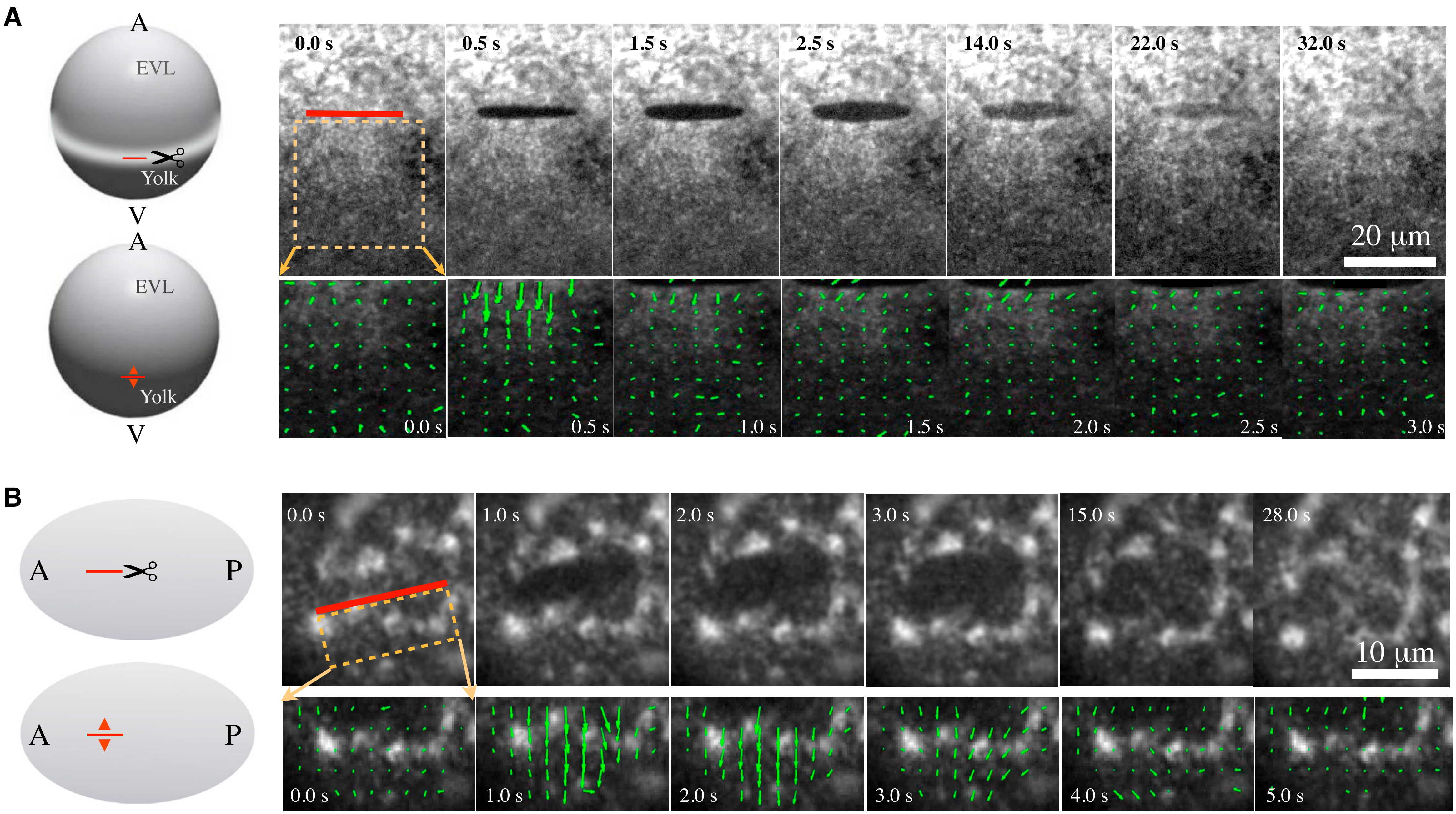
Cortical Flow by Laser Ablation

Width of the hole vs. time



Determine shape of hole as a function of time by thresholding

Cortical Flow by Laser Ablation



A. Saha et. al.
BJ, 2016

Analysis of cortical flow → **Material Properties?**

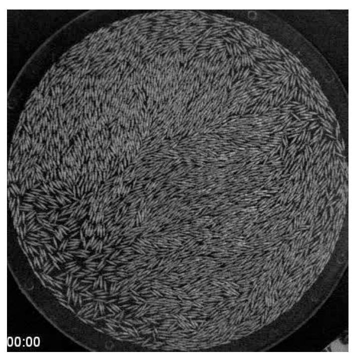
Need a Theory that couples Flow Variables to the Material Properties

A theoretical description of the general properties of living matter is not currently achievable because of its overall complexity, with the detailed state of a cell determined by a large number of variables.

- Marchetti *et. al*. RMP (2013)

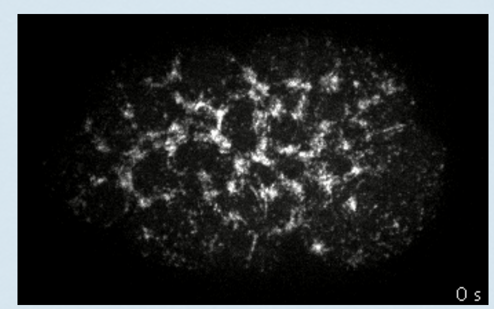
'Active' Matters

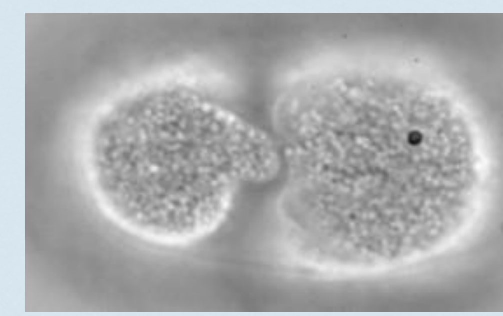
dry (small) η/γ (large) Wet



Vijay Narayan,[1]* Sriram Ramaswamy,[1,2] Narayanan Menon[3]

viscous (small) τ (large) viscoelastic





*'Wet' A*ctive Matters o*r* 'Active Gel'

(description of *slightly* active *polar* gel)

$$T\dot{\mathcal{S}} = \int d\mathbf{r}\left\{-\frac{\partial}{\partial t}\left(\frac{1}{2}\rho m \mathbf{v}^2\right) - \mu\frac{\partial \rho}{\partial t} + h_\alpha \dot{p}_\alpha + r\Delta\mu\right\}.$$

$$\frac{\partial g_\alpha}{\partial t} + \partial_\beta \Pi_{\alpha\beta} = 0,$$

$$(\Pi_{\alpha\beta} = \rho m v_\alpha v_\beta - \sigma^t_{\alpha\beta})$$

$$\frac{\partial \rho}{\partial t} + \nabla\cdot(\rho\mathbf{v}) = 0.$$

$$\longrightarrow T\dot{\mathcal{S}} = \int d\mathbf{r}\{\sigma_{\alpha\beta} v_{\alpha\beta} + P_\alpha h_\alpha + r\Delta\mu\},$$

where

$$\sigma^t_{\alpha\beta} = \sigma_{\alpha\beta} + \sigma^A_{\alpha\beta} - \delta_{\alpha\beta} P,$$

$$P_\alpha = \frac{Dp_\alpha}{Dt} = \frac{\partial p_\alpha}{\partial t} + v_\beta \partial_\beta p_\alpha + \omega_{\alpha\beta} p_\beta$$

$$v_{\alpha\beta} = \tfrac{1}{2}(\partial_\alpha v_\beta + \partial_\beta v_\alpha),$$

$$\omega_{\alpha\beta} = \tfrac{1}{2}(\partial_\alpha v_\beta - \partial_\beta v_\alpha).$$

(d) : same sig. under time reversal
(r) : opposite sig. under time reversal

Flux	Force	
$\sigma_{\alpha\beta} = \sigma^r_{\alpha\beta} + \sigma^d_{\alpha\beta},$	$v_{\alpha\beta}$	(r)
$P_\alpha = P^r_\alpha + P^d_\alpha,$	h_α	(d)
$r = r^r + r^d.$	$\Delta\mu$	(d)

K. Kruse et. al.
Eur. Phys. J. E (2005)

How to couple thermodynamic forces and fluxes?

* Linear Onsager expansion
* Respect symmetries of the system

K. Kruse et. al.
Eur. Phys. J. E (2005)

How to couple thermodynamic forces and fluxes?

1. **Spatial symmetry** : The tensorial character of the Onsager expansion should be conserved.

2. **Time-reversal symmetry** :

a. Dissipative flux : fluxes and forces with same time signature couples.
b. Reactive flux : fluxes and forces with opposite time signature couples.

K. Kruse et. al.
Eur. Phys. J. E (2005)

*'Wet' A*ctive Matters *or* 'Active Gel'

(description of *slightly* active *polar* gel)

Linear Onsager expansion..

Dissipative flux (flux and force with same time sig.)

$$P^d_\alpha = \frac{h_\alpha}{\gamma_1} + \epsilon p_\alpha \Delta\mu,$$

$$r^d = \Lambda\Delta\mu + \epsilon p_\alpha h_\alpha.$$

$$\sigma^d = \bar{\eta} u,$$
$$\tilde{\sigma}^d_{\alpha\beta} = 2\eta\tilde{v}_{\alpha\beta}.$$

Reactive flux (flux and force with opposite time sig.)

$$\sigma^r = -\bar{\zeta}\Delta\mu + \bar{\nu}_1 p_\alpha h_\alpha,$$
$$\tilde{\sigma}^r_{\alpha\beta} = -\zeta\Delta\mu q_{\alpha\beta} + \frac{\nu_1}{2}\left(p_\alpha h_\beta + p_\beta h_\alpha - \frac{2}{3} p_\gamma h_\gamma \delta_{\alpha\beta}\right),$$
$$P^r_\alpha = -\bar{\nu}_1 p_\alpha \frac{u}{3} - \nu_1 p_\beta \tilde{v}_{\alpha\beta},$$
$$r^r = \bar{\zeta}\frac{u}{3} + \zeta q_{\alpha\beta}\tilde{v}_{\alpha\beta}.$$

$$q_{\alpha\beta} = p_\alpha p_\beta - \tfrac{1}{3}\delta_{\alpha\beta}$$

K. Kruse et. al.
Eur. Phys. J. E (2005)

*‘Wet’ A*ctive Matters *or* ‘Active Gel’

(description of *slightly* active *polar* gel)

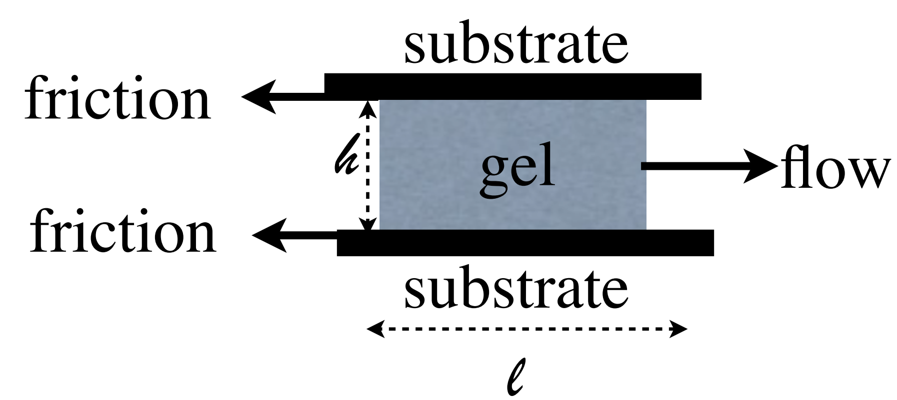
Viscoelastic constitutive eq.
(compressible, apolar, isotropic active gel)

$$\left(1+\tau\frac{D}{Dt}\right)(\sigma_{\alpha\beta}-\zeta\Delta\mu\delta_{\alpha\beta})=\eta(\partial_\alpha v_\beta+\partial_\beta v_\alpha)+\eta_b\partial_\gamma v_\gamma\delta_{\alpha\beta}$$

Active Gel with Substrate

(momentum balance)

$$\nabla . \sigma = \gamma \mathbf{v}$$



$h/\ell << 1$

dry ←(small)— η/γ —(large)→ Wet

G. Salbreux et. al.

Phys. Rev. Lett.(2009).

Dynamics of Myosin Density

rate of change of density profile = advection of the density profile with flow + source term

$$\frac{\partial c}{\partial t} = D\nabla^2 c - \nabla.(\vec{v}c) + \frac{c_0 - c}{\tau_a}$$

Physical Principles

1. stress ~ viscous strain rate
2. stress ~ elastic strain
3. total strain = viscous strain + elastic strain
4. total stress = passive stress + active stress

<u>Constitutive Eq.</u>

1. rate of change of height profile = advection of the density profile with flow + wound healing

<u>Dynamics of density</u>

1. cortex - a ‘thin film’
2. gradient of stress ~ flow velocity

<u>Force balance</u>

Theoretical Model

Material properties:

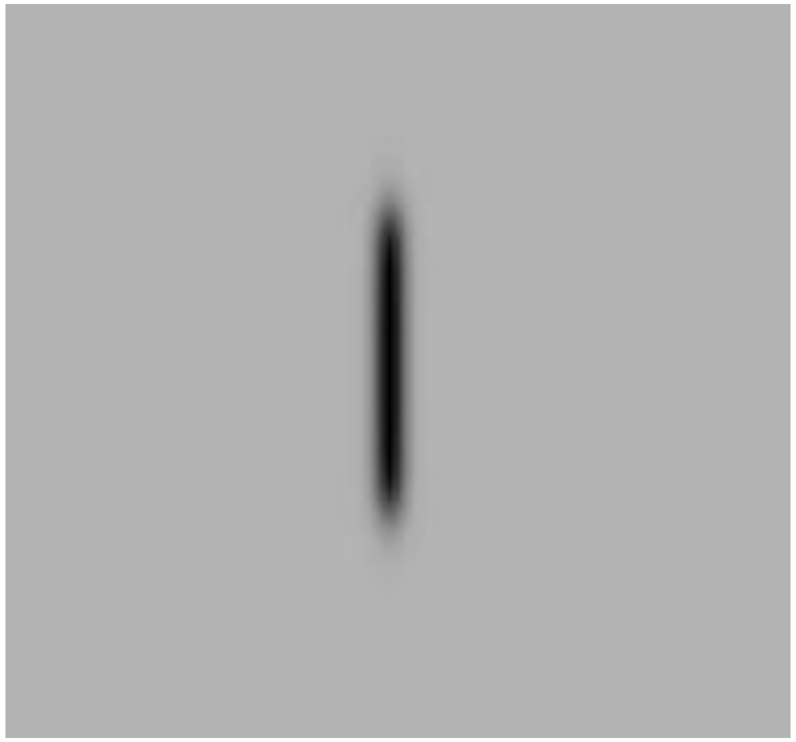
Shear viscosity η
Bulk viscosity η_b
Time constant for viscoelastic relaxation τ
Time constant for turning over of cortex τ_a
Friction coefficient γ
Active contractility ξ

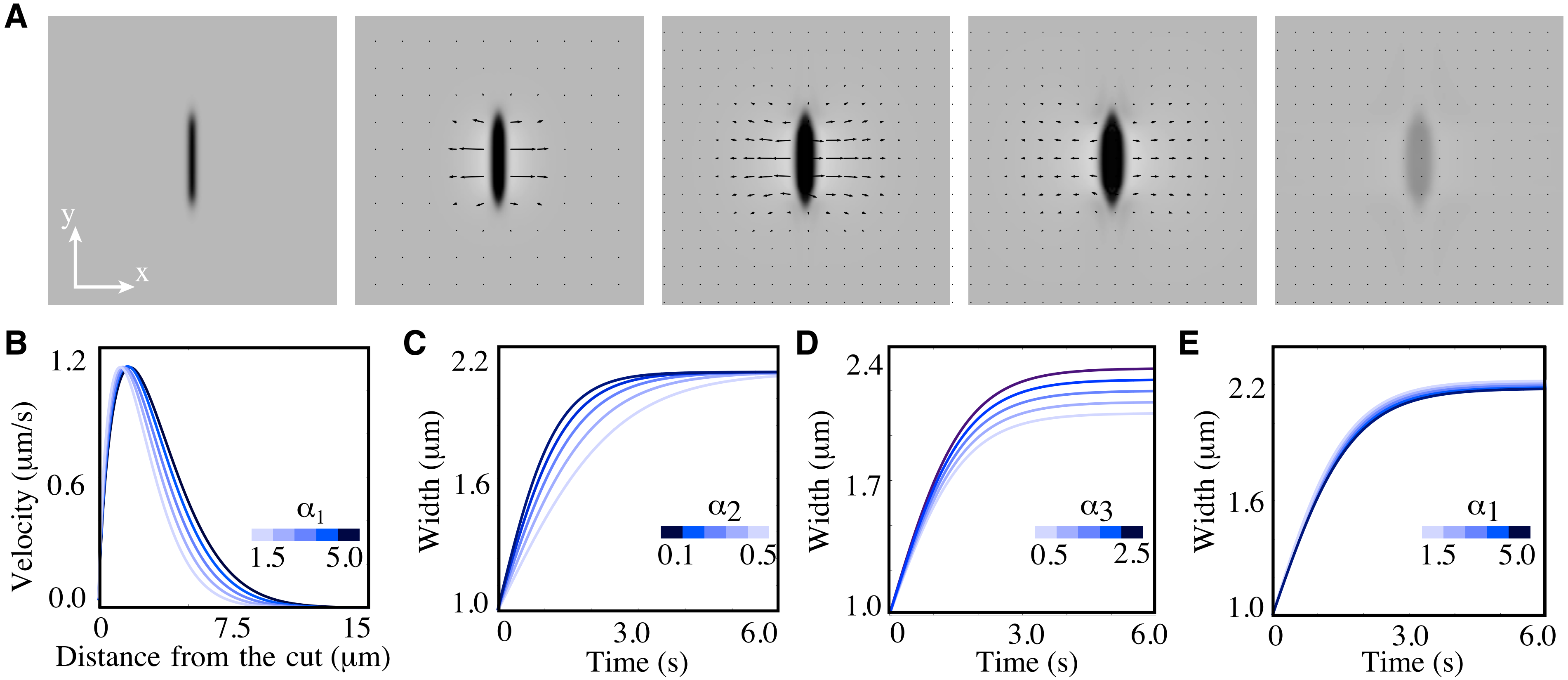
Dynamical variables

Density
Velocity v_α
Stress (active and passive) $\sigma_{\alpha\beta}, \sigma^a\delta_{\alpha\beta}$

Perturbation to the Fluid to Estimate the Material Properties

Laser ablation : Theory





To Estimate Material Properties....

Find Independent Parameters of the theory.

↓

Solve the model equations with laser ablation as initial condition to have the cut responses as in experiment.

↓

Minimize the difference between all the experimental and theoretical cut responses simultaneously with the independent parameters. Note the values of the parameters where the difference is minimum.

↓

From these values, find the material parameters.

Dimensionless Free Parameters of the Model

$$\alpha_1 = \frac{\lambda_c}{\lambda}$$

$\lambda_c = \text{cut length}$

$$\alpha_2 = \frac{\tau}{\tau_a}$$

$(\lambda = \text{hydrodynamic length} = \sqrt{\frac{\eta}{\gamma}})$

$$\alpha_3 = \frac{\xi^a \tau_a}{\gamma \lambda_c^2}$$

Global Fitting of Response Curves

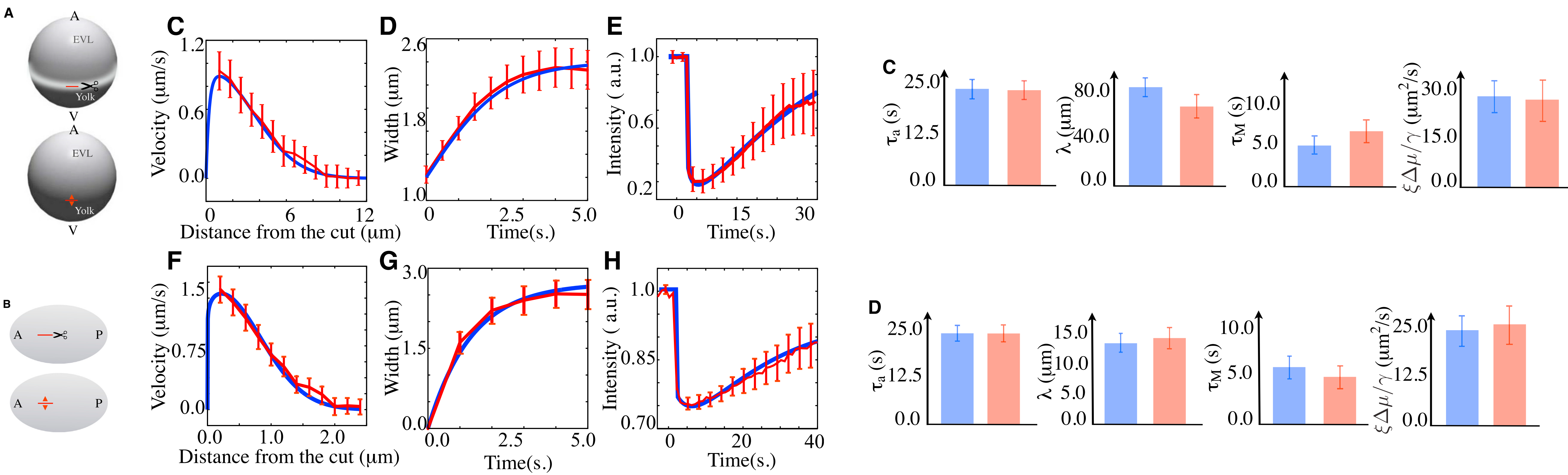
Squared distance between theory (t) and experimental (e) responses of ablation:

$$\Delta(\alpha_i) = \sum_l \left(\frac{I_e^l - I_t}{\sigma_I^l} \right)^2 + \sum_m \left(\frac{V_e^m - V_t}{\sigma_V^m} \right)^2 + \sum_n \left(\frac{W_e^n - W_t}{\sigma_W^n} \right)^2$$

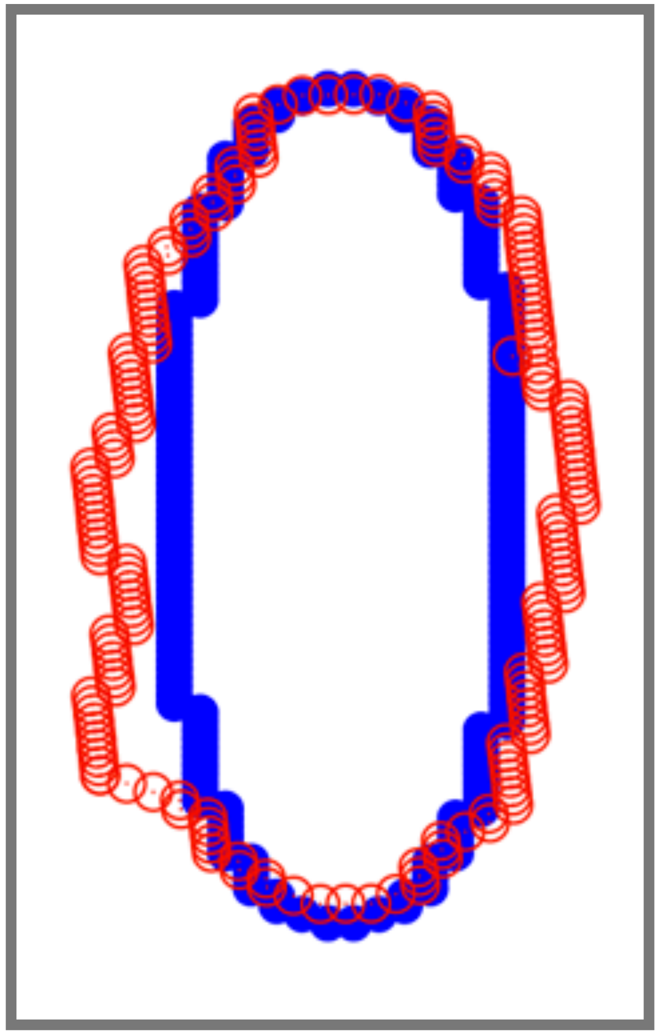
Intensity / density difference　　Velocity profile difference　　Width of the cut difference

$$\{\alpha_i\} \to (\alpha_1, \alpha_2, \alpha_3, \tau_a)$$

Material Parameters



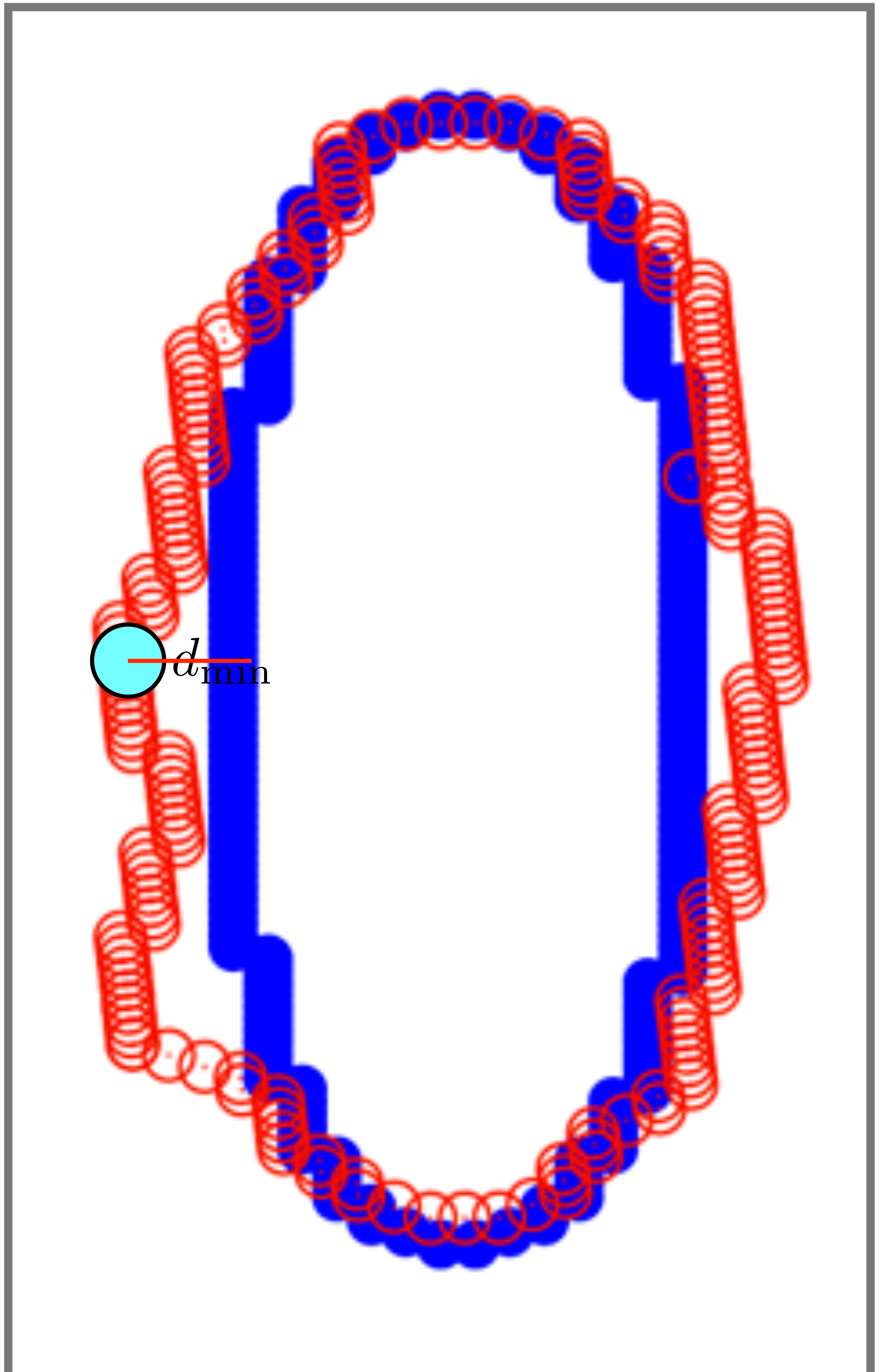
Evolution of the Shape of the Hole



Shape: Experiment

Shape: Theory

‘Distance’ Between Shapes from Experiment and Theory



Boundary points: Experiment

Boundary points: Theory

$$S = \sum d^e_{min}$$

Minimization of the 'Distance'

- $\dfrac{\partial S}{\partial \alpha_i} = 0$
- $S(\{\alpha_i\} = \{\alpha_i^*\}) = S_{\min}$
- At $\{\alpha_i\} = \{\alpha_i^*\}$

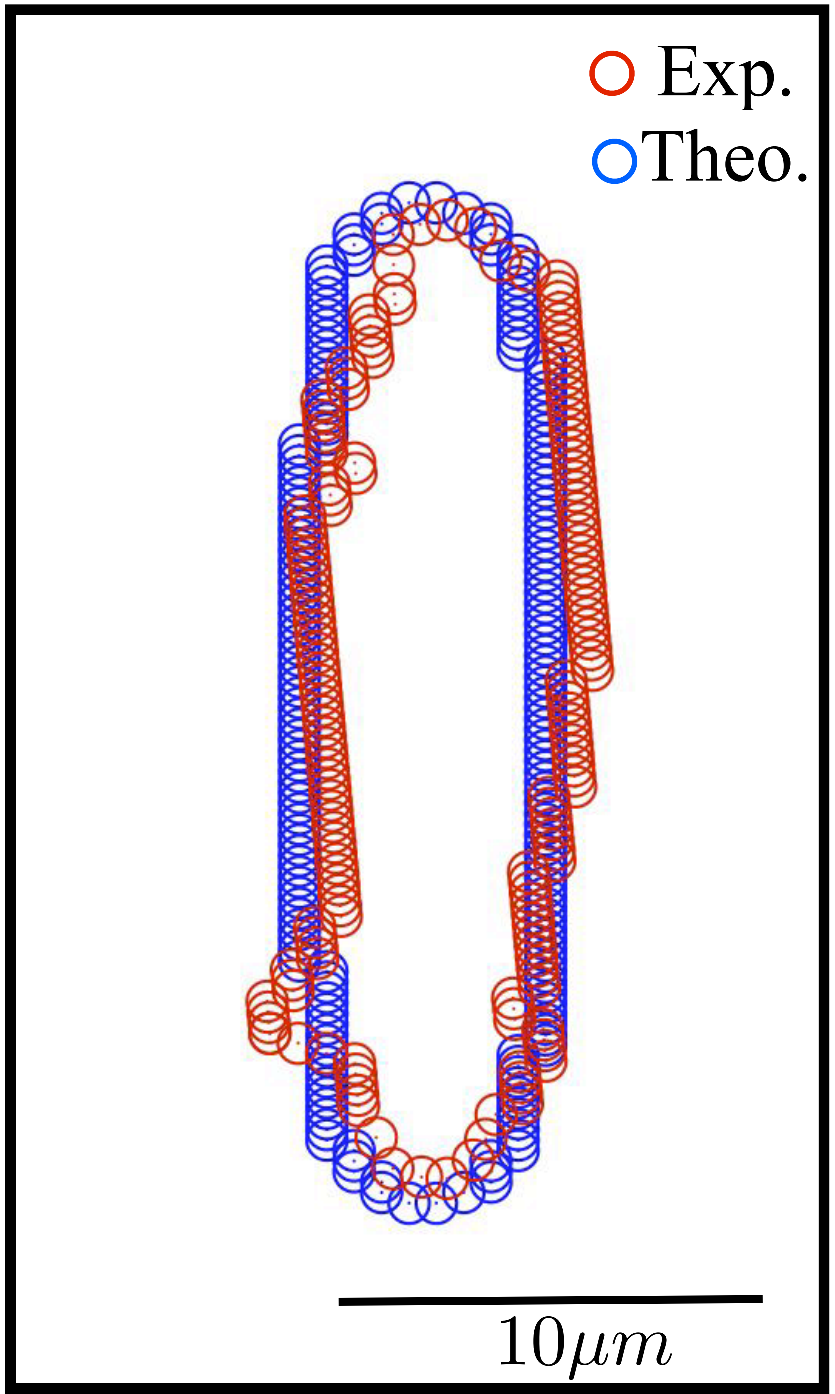
$$\alpha_1 = \frac{\lambda_c}{\lambda} = \alpha_1^*$$

$$\alpha_2 = \frac{\tau}{\tau_a} = \alpha_2^*$$

$$\alpha_3 = \frac{\xi^a \tau_a}{\gamma \lambda_c^2} = \alpha_3^*$$

Boundary points: Experiment

Boundary points: Theory



Conclusion

Acknowledgements

Division Biological Physics

Grill-lab

Heisenberg-group