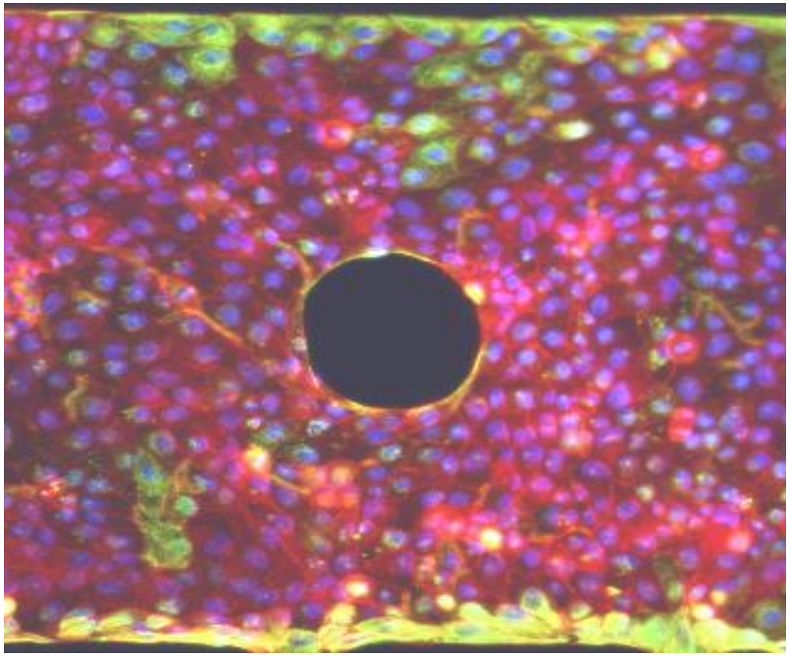
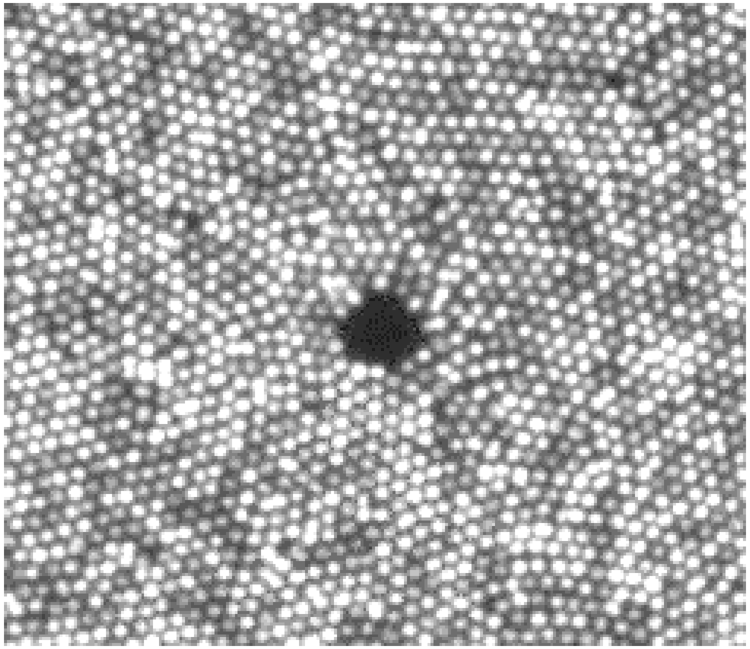




Stokes flow experiment in biological tissues: comparison with an active abiotic system

Helene Delanoë-Ayari (Université de Lyon, France)

Outline

- Motivations

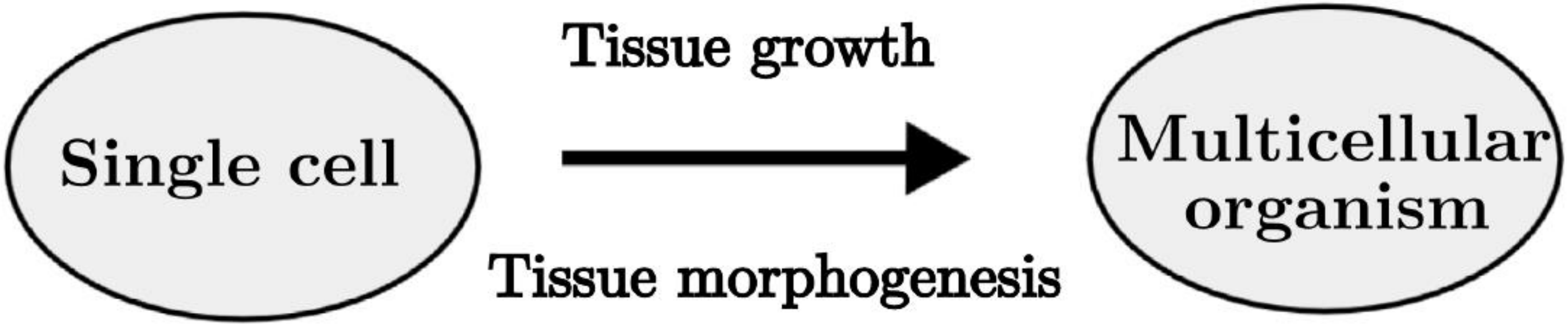
- 2D cellular systems
- 3D cellular systems

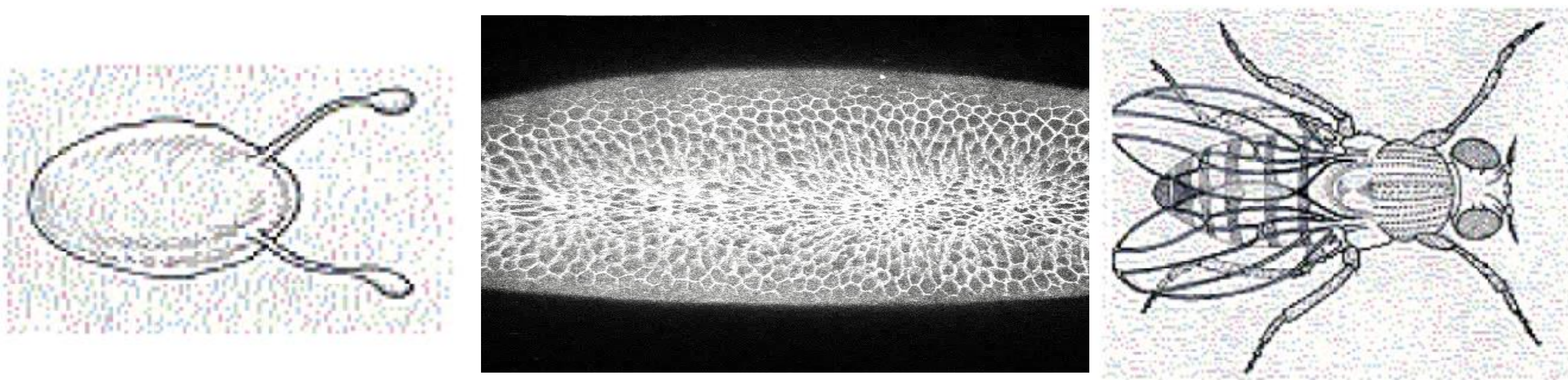
- Active colloids

- Conclusion and perspectives

Biological motivations:

Morphogenesis= morphe (shape) + genesis (creation)





Fertilized egg   Developing embryo   Adult drosophila

25 µm

B. Sanson, University of Cambridge

Questions for a physicist:

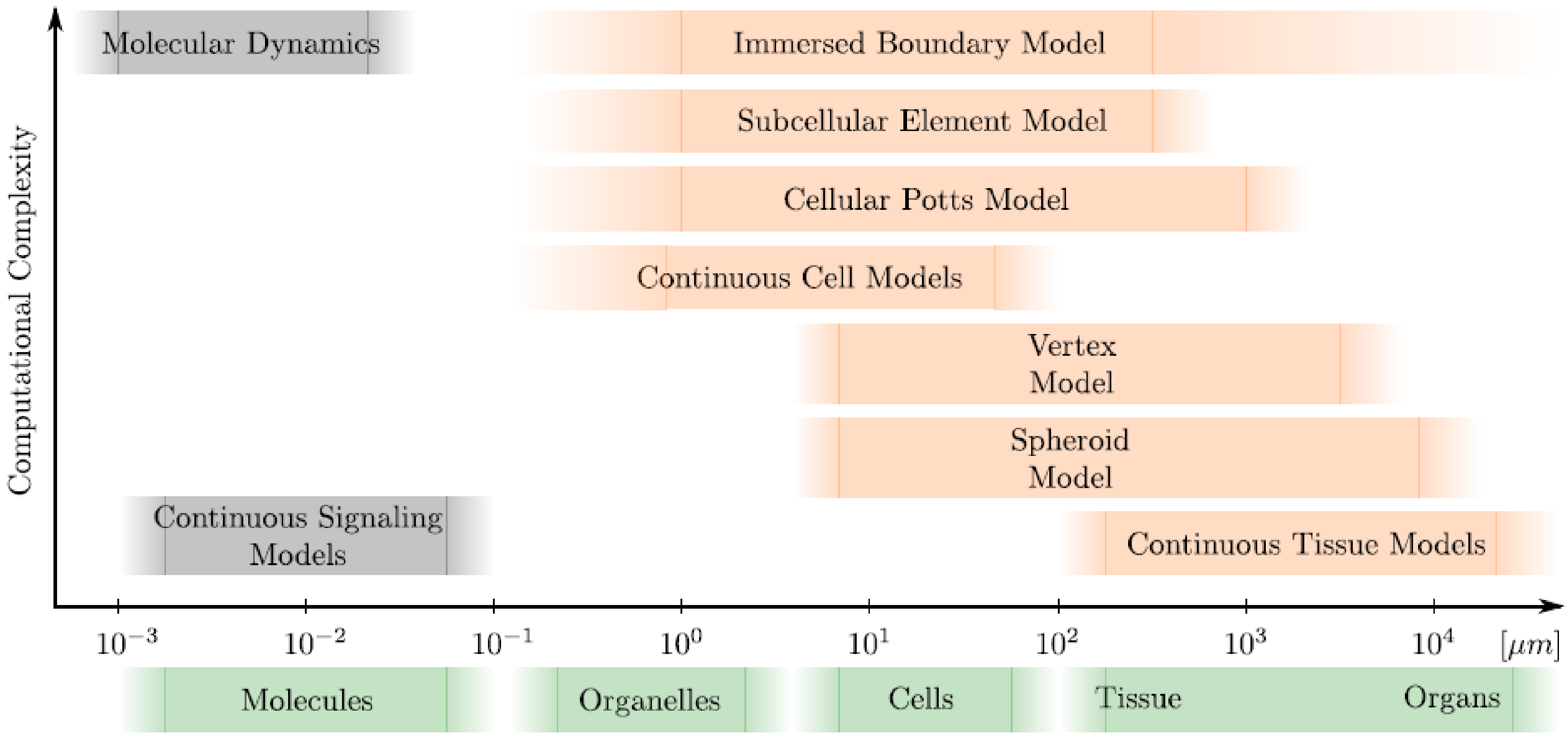
What are the tissue mechanical properties?

- How does a tissue respond to an impose force?
- Respective intercellular and intracellular contributions to tissues mechanical properties?
- Differences with a passive cellular material like a foam?
- Differences with active particles?

Underlying question: what is the best way of Modeling Tissues?

- Continuum mechanics
  - Solid mechanics (elastic & plastic)
  - Visco-elastic materials
  - Fluid mechanics
- Discrete Tissue Models
  - Subcellular elements
  - Cellular elements
  - Coarse-grained discrete models

Cell-based Modelling



Tanaka, Simulation Frameworks for Morphogenetic Problems, MDPI Computation, 2015

Centroid based model (ex: Viszek) versus Contour based models (ex: Vertex)?

Beatrici et al., Soft Matter 2023

Outline

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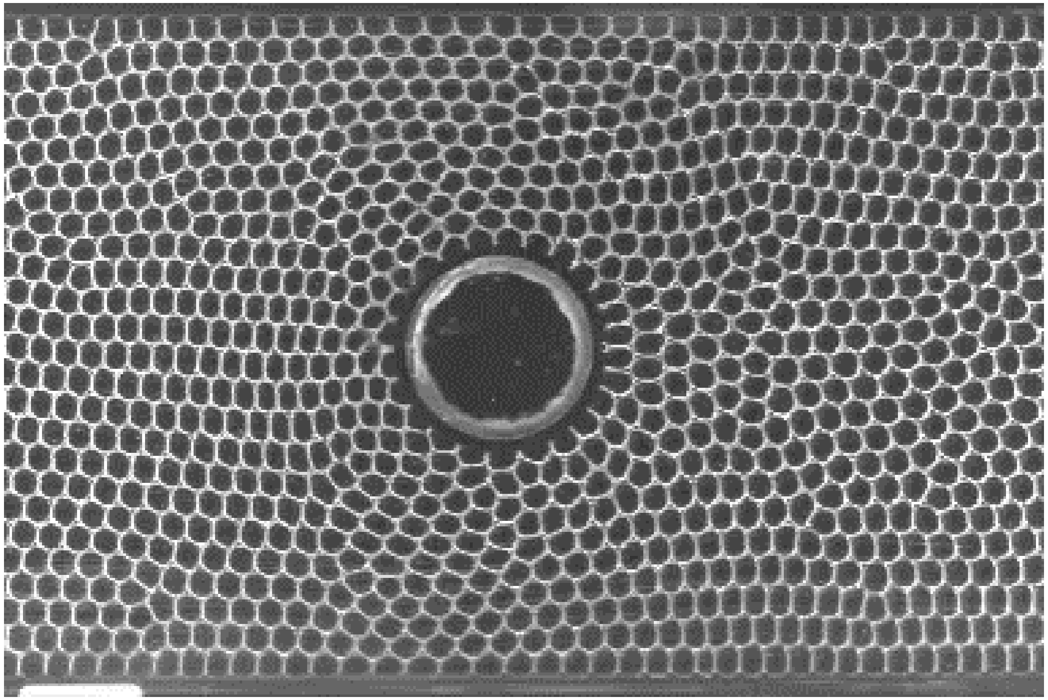
- 3D cellular systems
- Active colloids
- Conclusion and perspectives

The stokes' Experiment: methodology from foams

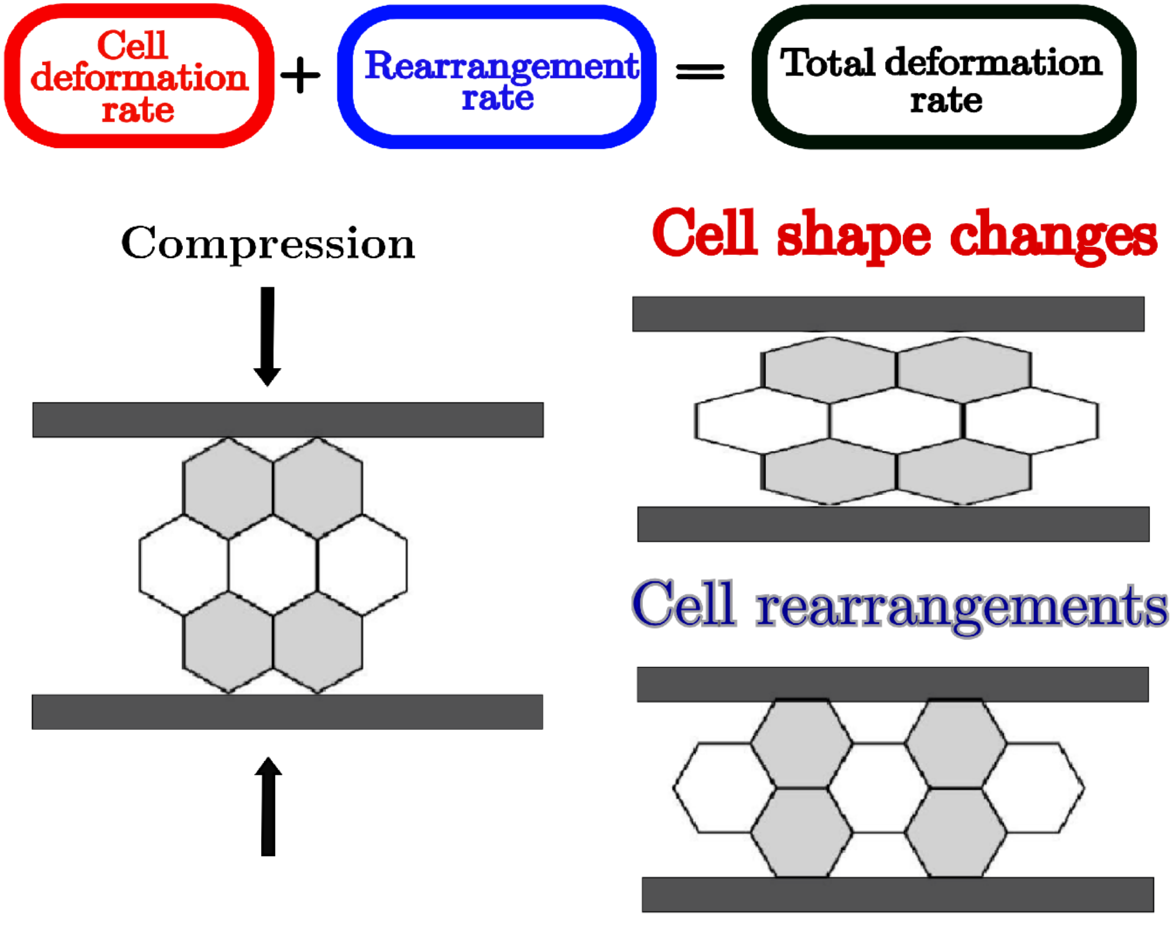


B.Dollet, F. Graner

+Bidimensionnal foam

+Heteregeous flow in:
- velocity
- deformation
- gradient of velocity

Individual cell deformation versus cell rearrangements



The actors :

Sham Tlili

Melina Durande

François Graner

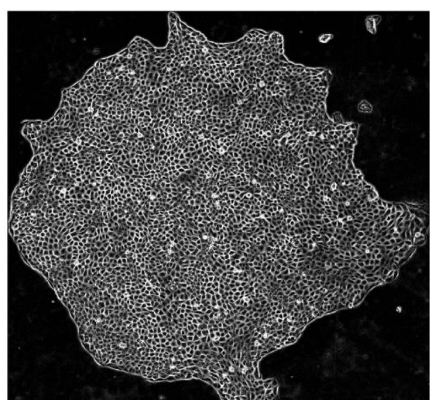
MDCK: (Madin-Darby Canine Kidney) epithelial tissue

Cell monolayers

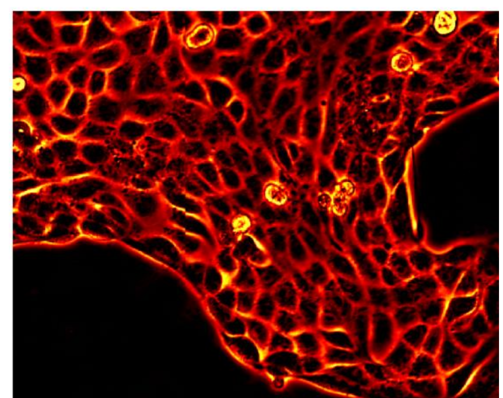
One cell thick layer

Cells adhere :
to the substrate
to each other

$1000 \mu m$

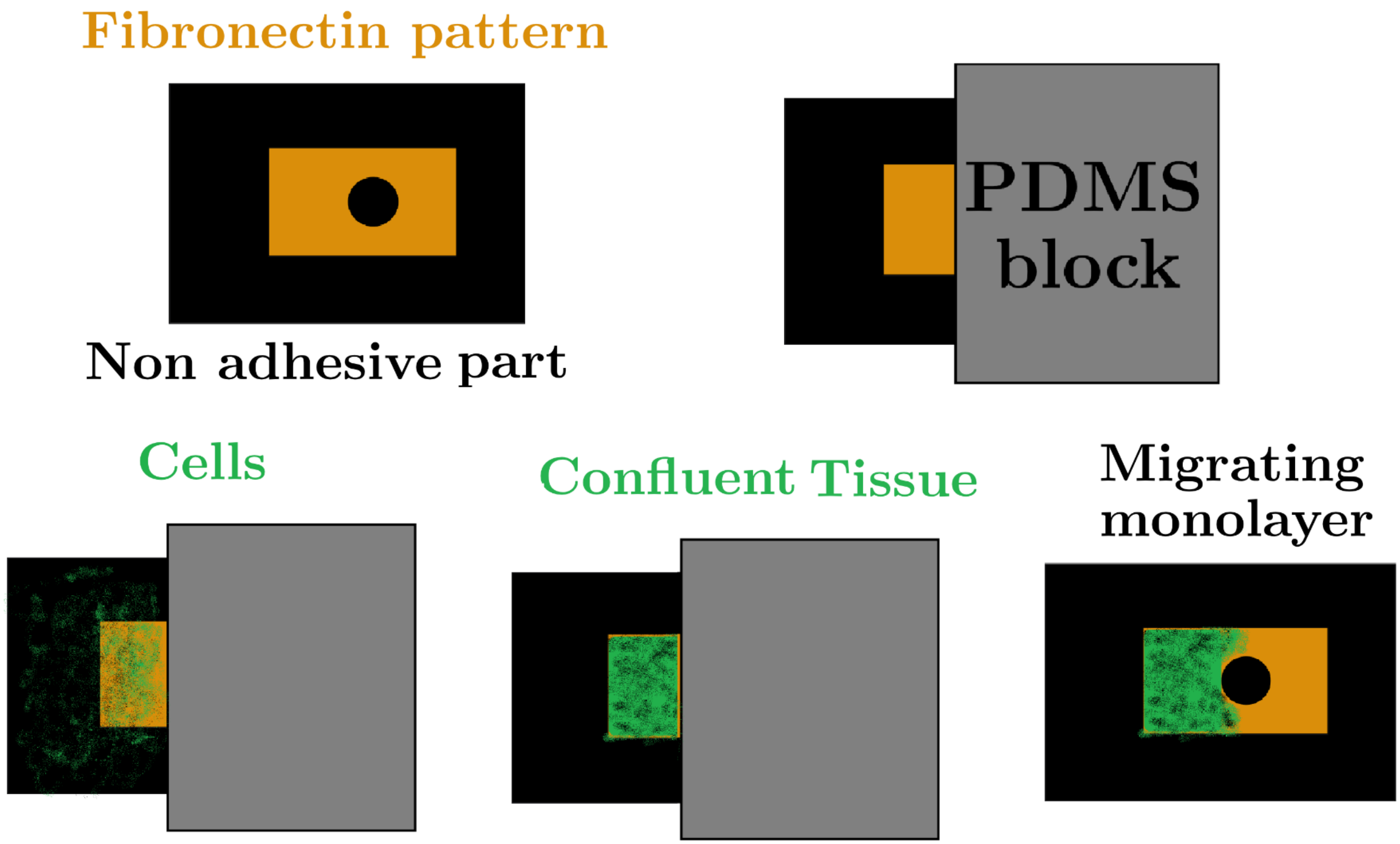


$50 \mu m$



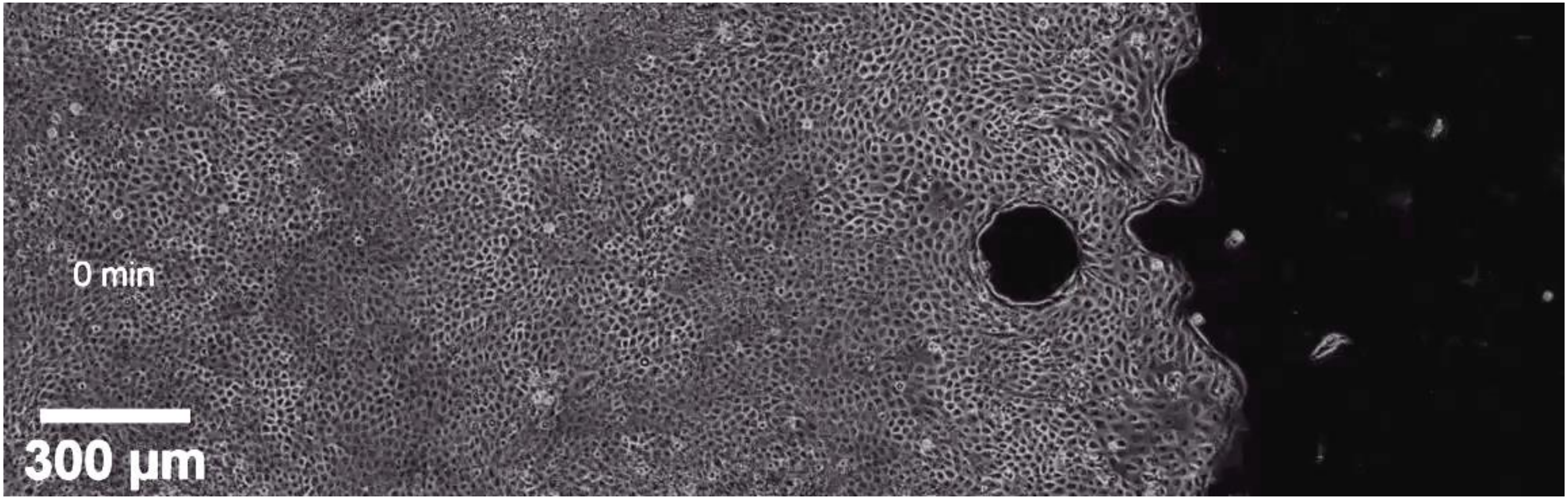
Making cell monolayers collectively migrate

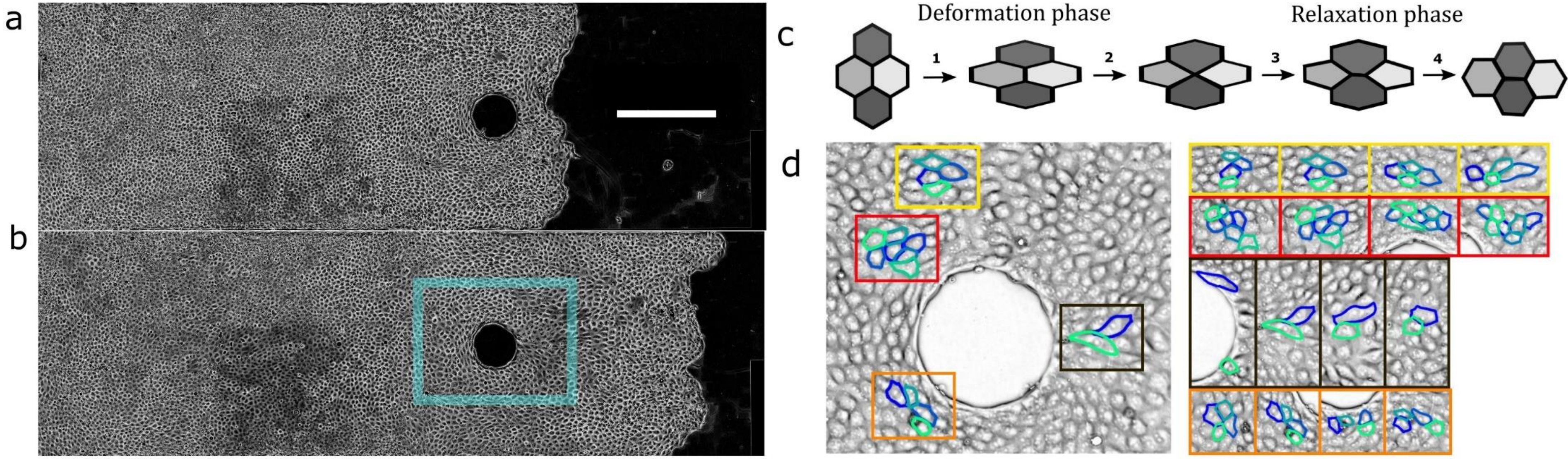
PDMS +



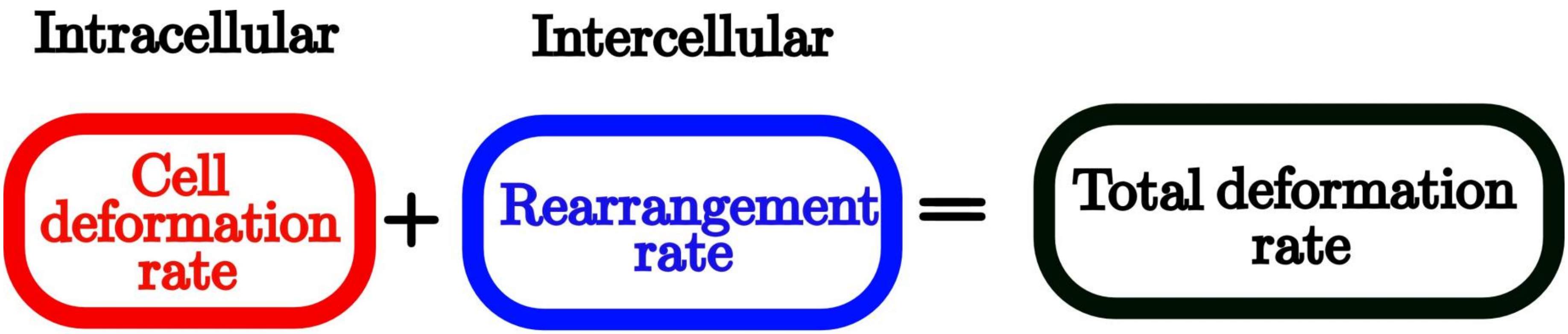
=chemical obstacle

Now the Stokes experiment



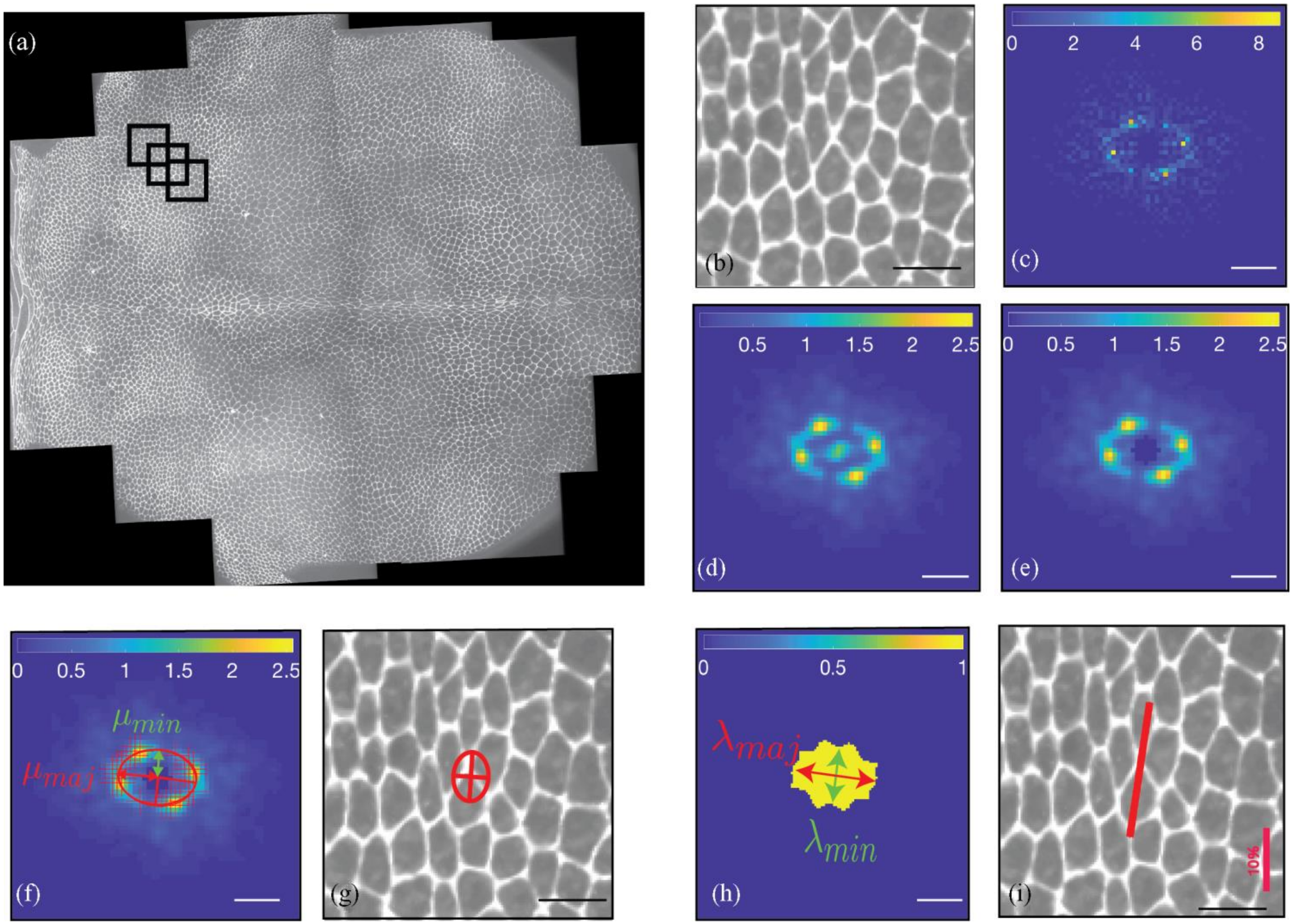


The idea…



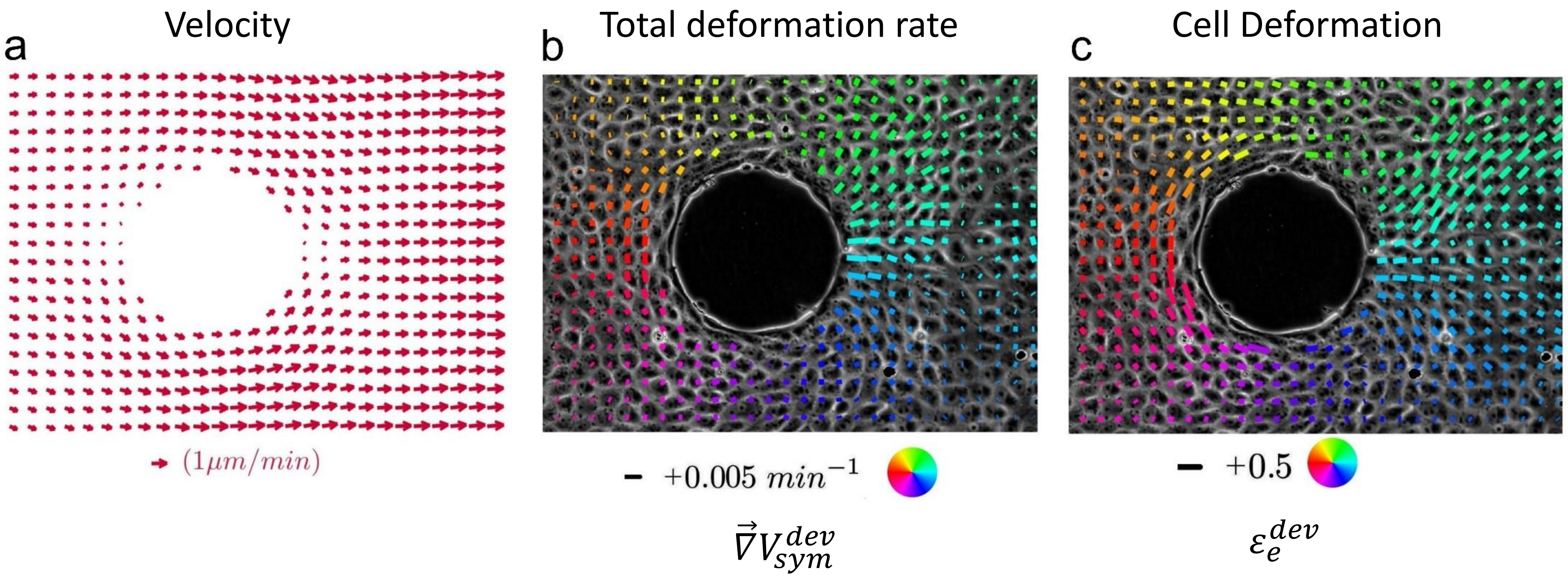
$$\dot{\varepsilon}_{intra} + \dot{\varepsilon}_{inter} = \vec{\nabla}\vec{v}$$

Measuring average local cell anisotropy and size using FFT



Durande, M., Tlili, S., Homan, T., Guirao, B., Graner, F., & Delanoë-Ayari, H. (2019). Fast determination of coarse-grained cell anisotropy and size in epithelial tissue images using Fourier transform. *Physical Review E*, *99*(6), 062401.

Image analysis: Tensors calculation

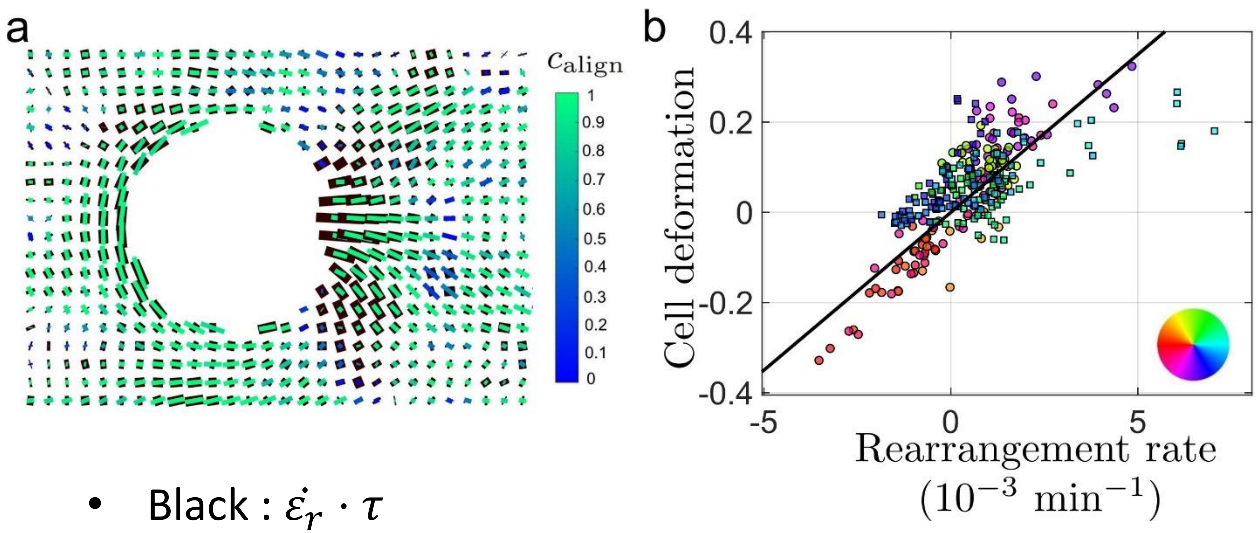


$$\langle \dot{\varepsilon}_{\mathrm{r}} \rangle = \langle \nabla v_{\mathrm{sym}} - \frac{\partial \varepsilon_{\mathrm{e}}}{\partial t} - \vec{v} \cdot \nabla \varepsilon_{\mathrm{e}} \rangle$$

MDCK cell monolayers=Maxwell liquid

$$\sigma = E\varepsilon = \eta\dot{\varepsilon_r}$$

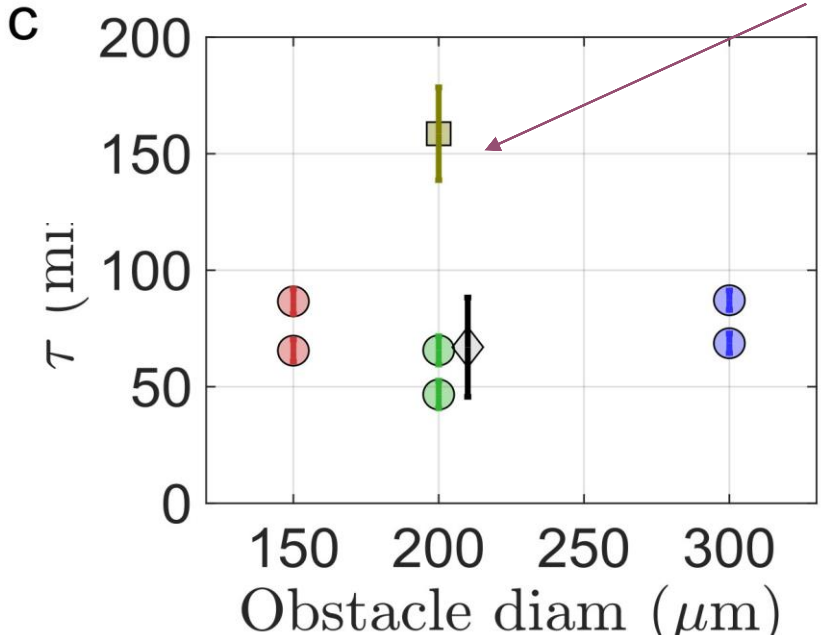
$$\varepsilon = \frac{\eta\dot{\varepsilon_r}}{E} = \tau\dot{\varepsilon_r}$$



- Black : $\dot{\varepsilon_r} \cdot \tau$
- Green/blue: ε

What about activity?

Blebbistatin: kill myosin II activity



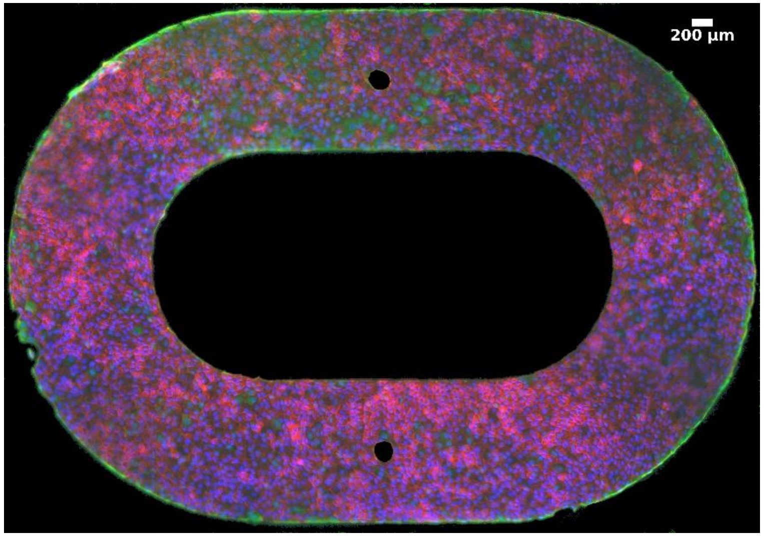
This would be coherent with recent works showing that activity is at
The origin of a shear-thining property of the tissue.

Oriola, D., Alert, R., & Casademunt, J. (2017). Fluidization and Active Thinning by Molecular Kinetics in Active Gels. *Physical Review Letters*, *118*(8), 1–6.

Other questions and measurements:

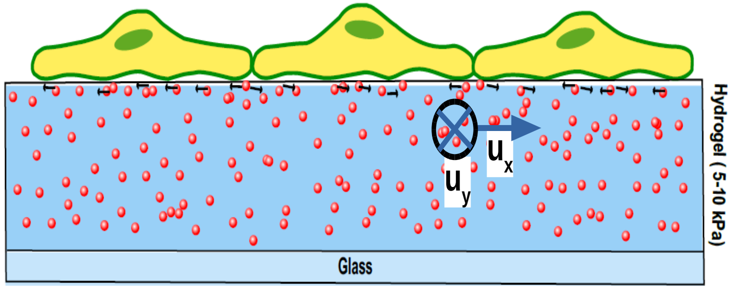
Influence boundary conditions

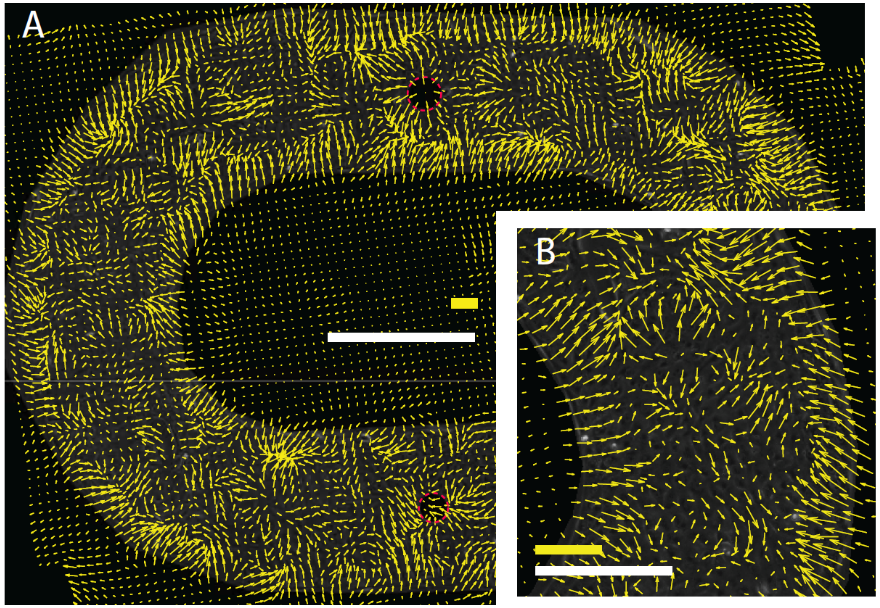
Racetrack: no free front



Flows and standing waves

Measure forces and stresses





Outline

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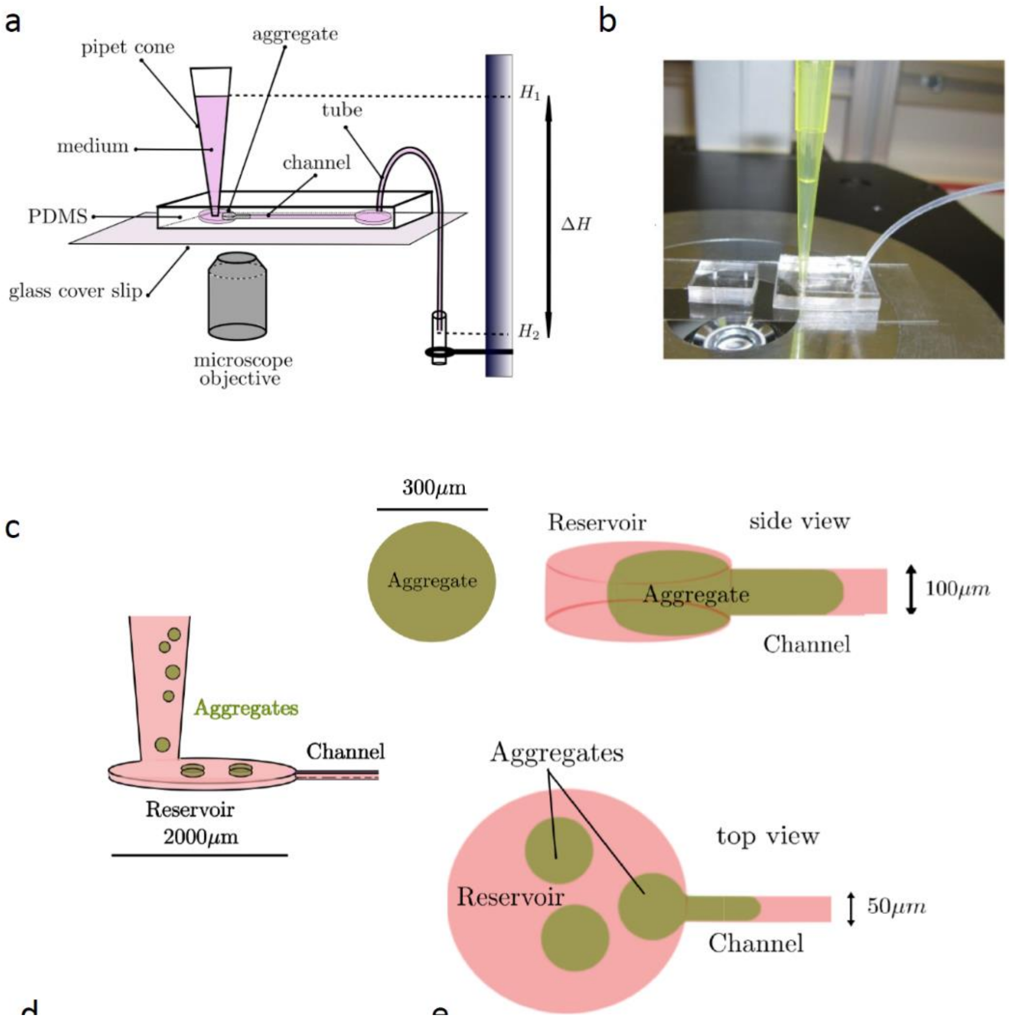
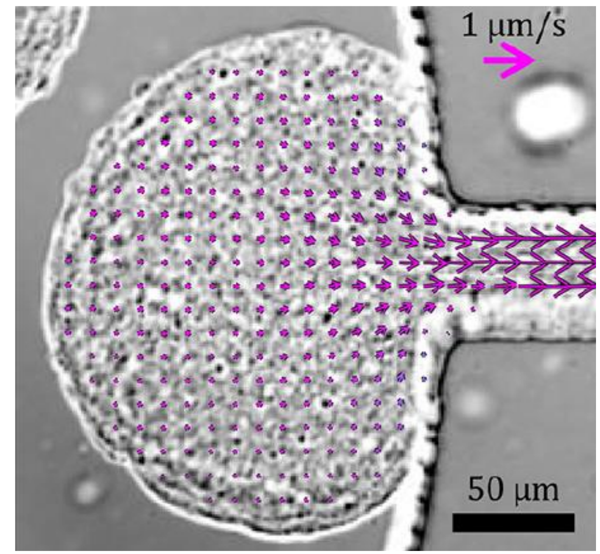
- Active colloids
- Conclusion and perspectives

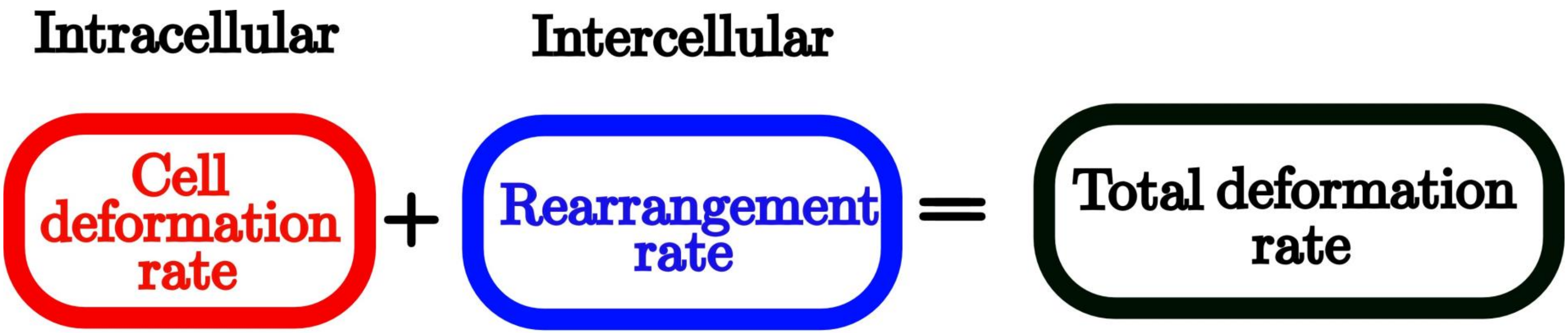
Very same idea in 3D experiments in a constriction (no motility)





Tlili S, Graner F, Delanoë-Ayari H. **A microfluidic platform to investigate the role of mechanical constraints on tissue reorganization.** *To appear in Development 2022.*

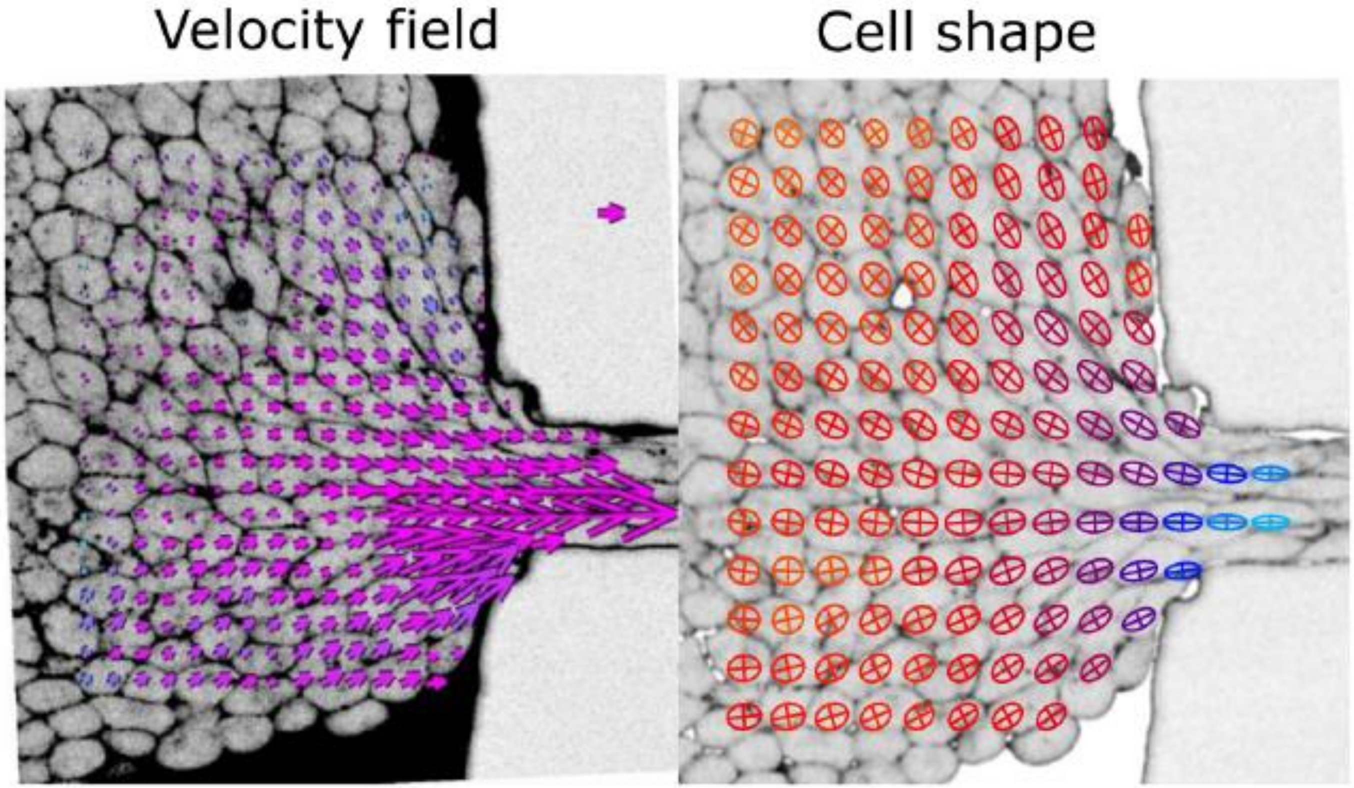
Same idea with a Lagrangian approach



$$\dot{\varepsilon}_{intra} \quad + \quad \dot{\varepsilon}_{inter} \quad = \quad \vec{\nabla}\vec{v}$$

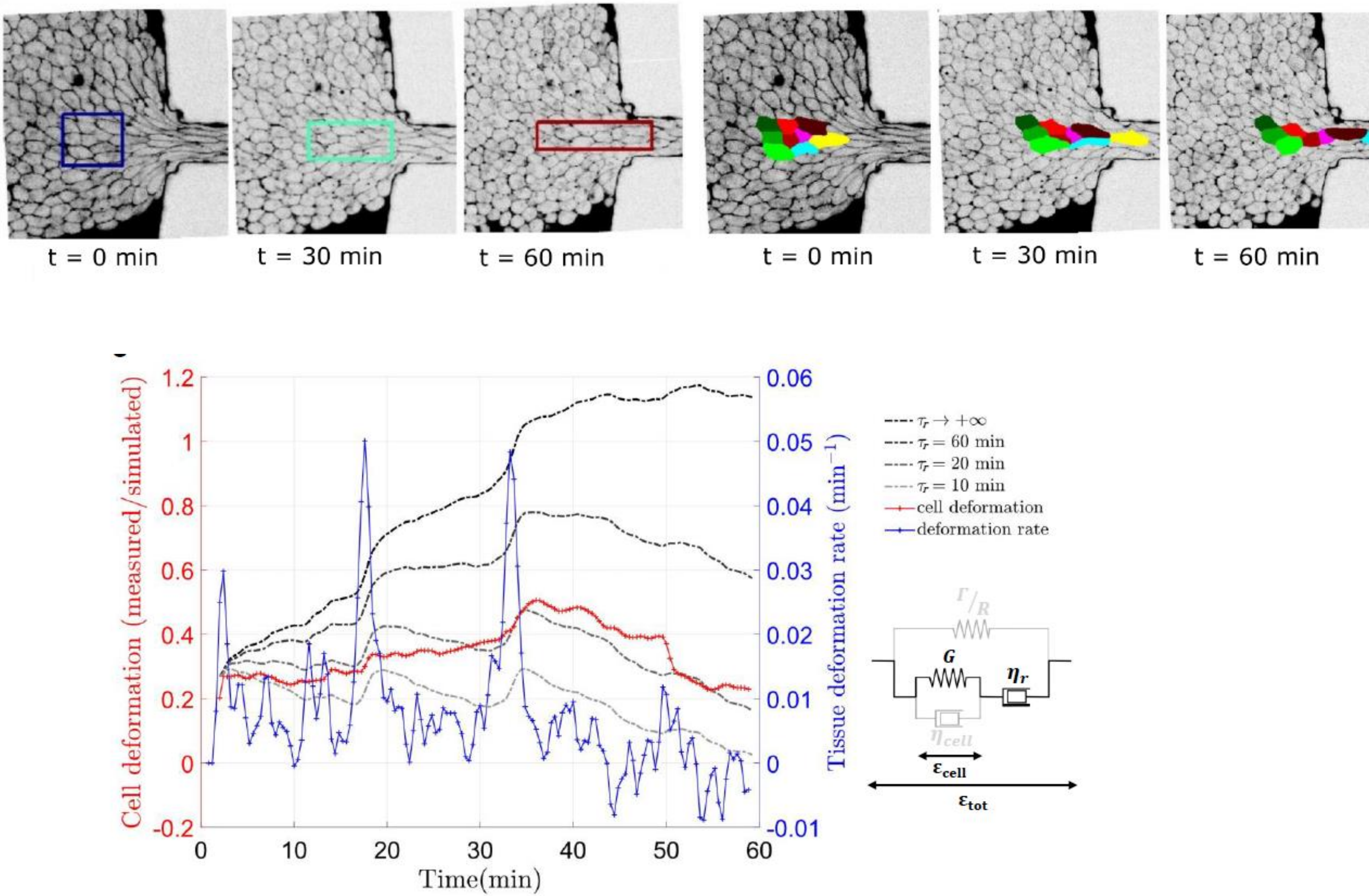
Output: $\tau_{viscoelastic}$

Same tools for Quantification as in 2D

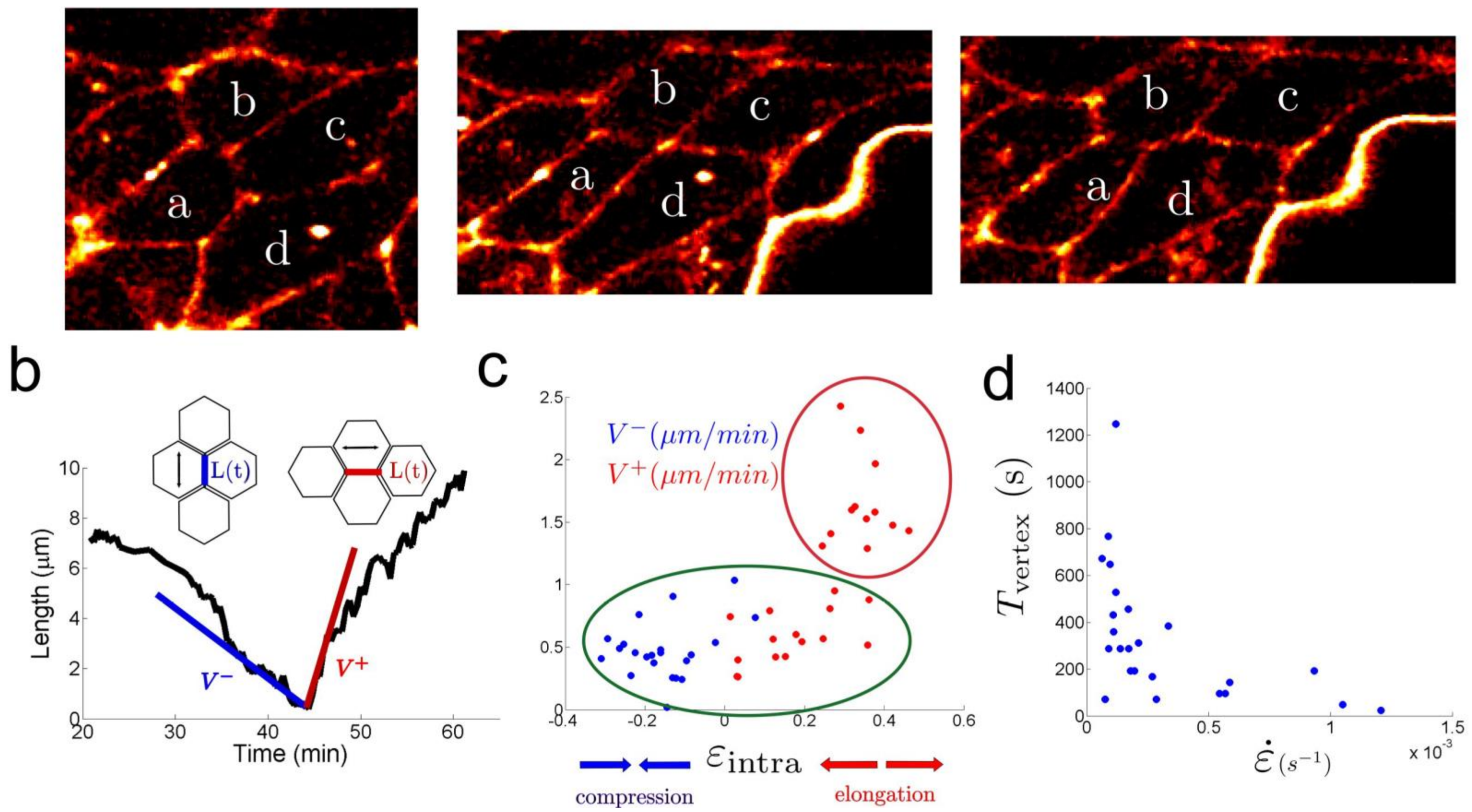


Kanade-Lucas-Tomasi

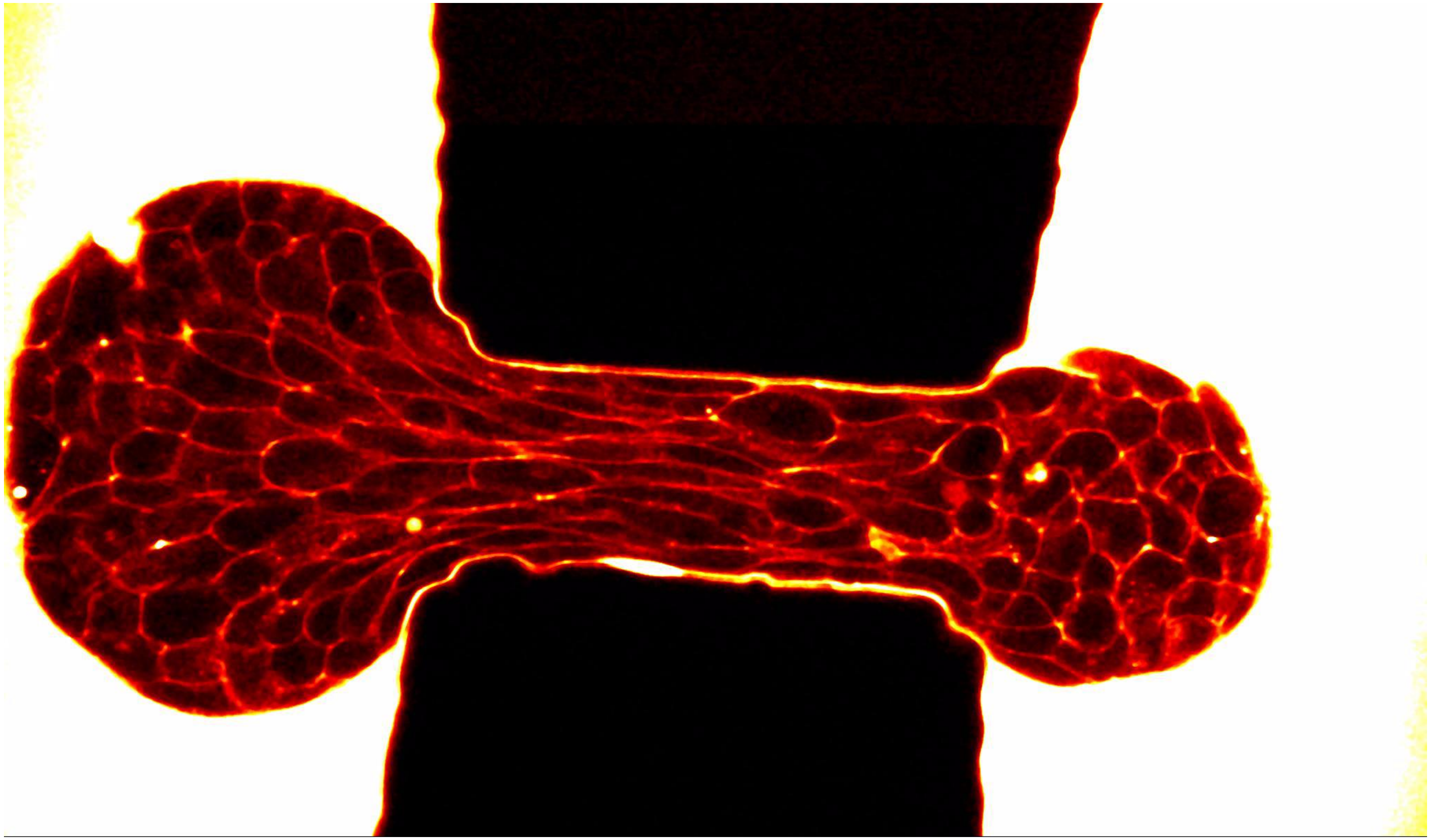
Fourier, segmentation

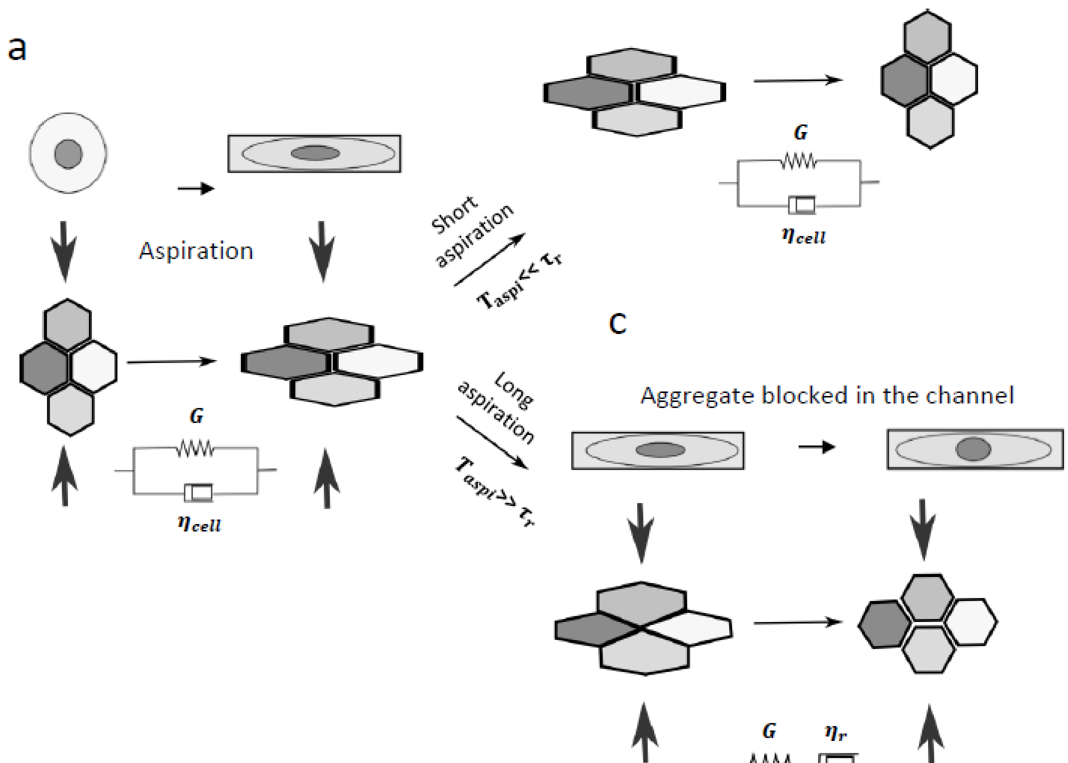

t = 0 min
t = 30 min
t = 60 min
t = 0 min
t = 30 min
t = 60 min
Cell deformation (measured/simulated)
Tissue deformation rate (min^{-1})
Time(min)
$\tau_r \to +\infty$
$\tau_r = 60$ min
$\tau_r = 20$ min
$\tau_r = 10$ min
cell deformation
deformation rate
Γ/R
G
η_r
η_{cell}
ε_{cell}
ε_{tot}

Microscopic Events, microscopic relaxation times



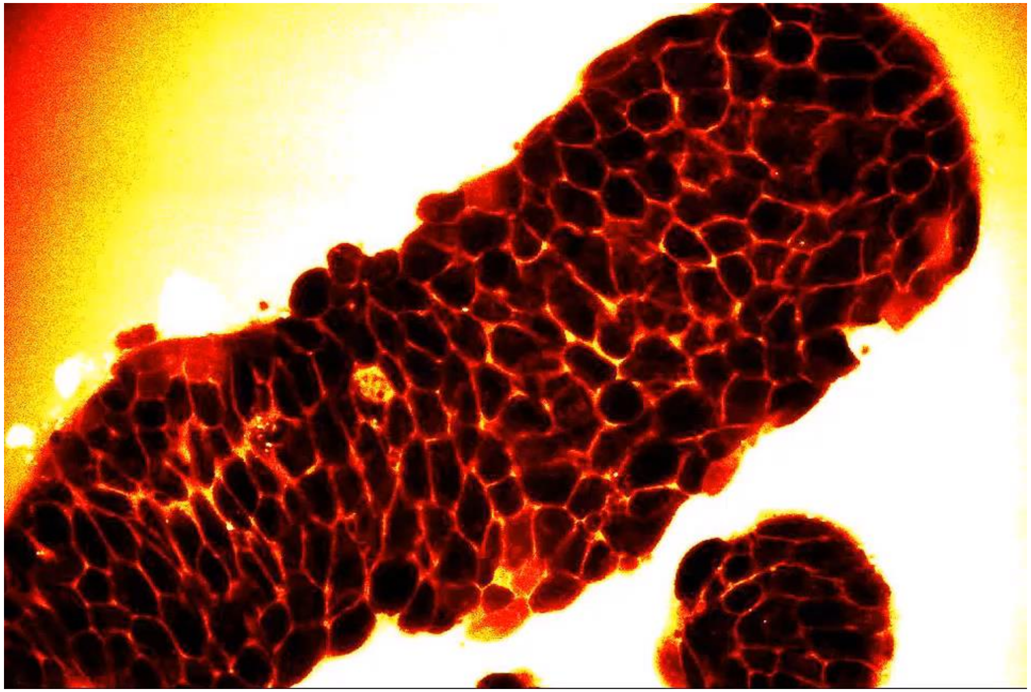
Fast aspiration



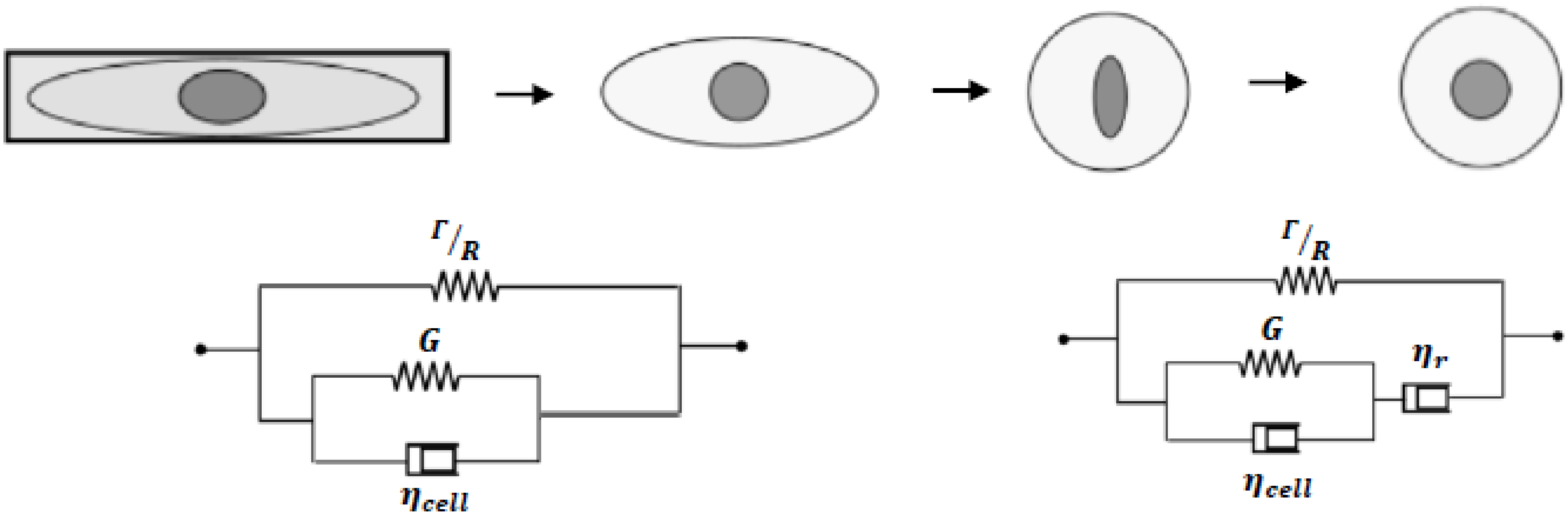


a
Aspiration
G
η_{cell}
Short aspiration
$T_{aspi} << \tau_r$
G
η_{cell}
Long aspiration
$T_{aspi} >> \tau_r$
c
Aggregate blocked in the channel
G
η_r

Relaxation after slow aspiration



Relaxation after a long aspiration $T_{aspi} >> \tau_r$



Extract typical mechanical parameters

quantity	*symbol*	*value*
cell group scale visco-elastic relaxation time	τ_r	10^3 s
cell group scale viscosity	η_r	10^5 Pa.s
elastic modulus	G	10^2 Pa
cell scale visco-elastic relaxation time	$\tau_{\rm cell}$	10^2 s
cell scale viscosity	$\eta_{\rm cell}$	10^4 Pa.s
aggregate scale capillary modulus	(Γ/R)	10^2 Pa

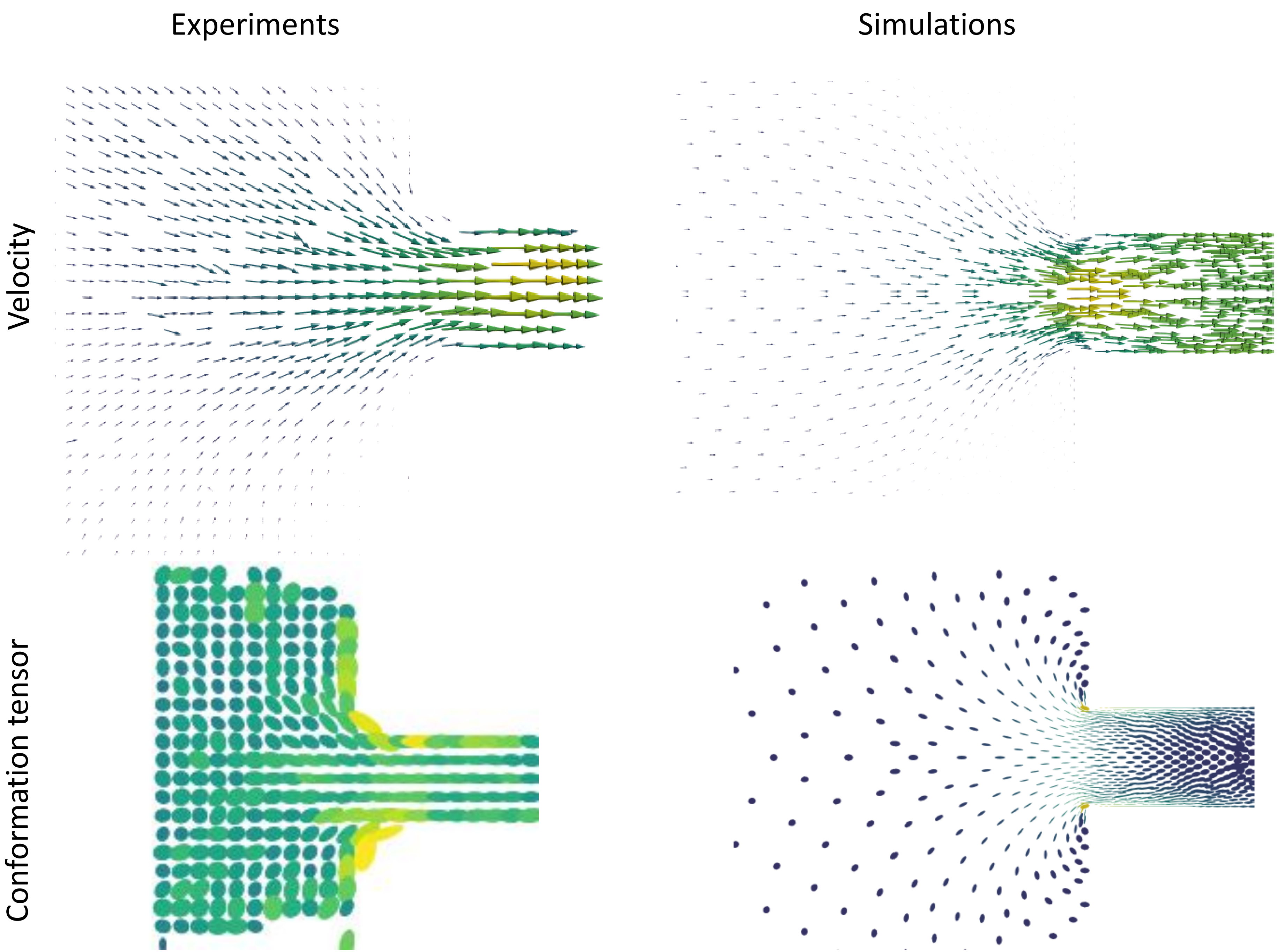
+ Description as a passive material,
+ What is specific to tissue and to activity?
+ Difference between cells and particles?

Perspectives : for more quantitative analysis

+ On the experimental Side: Segmentation using deep learning

+ modeling: Finite Element Modelling of tissues
Collaboration N. Shourick, M.Renard P. Saramito, I. Cheddadi

Oldroyd Model of viscoelastic fluid,
With FENE models (Finitely Extensible Non-Linear Elastic)



Experiments
Simulations
Velocity
Conformation tensor

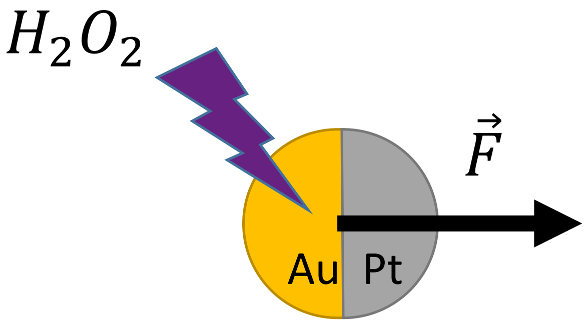
Active abiotic system : Colloïds

Cécile Cottin-Bizonne

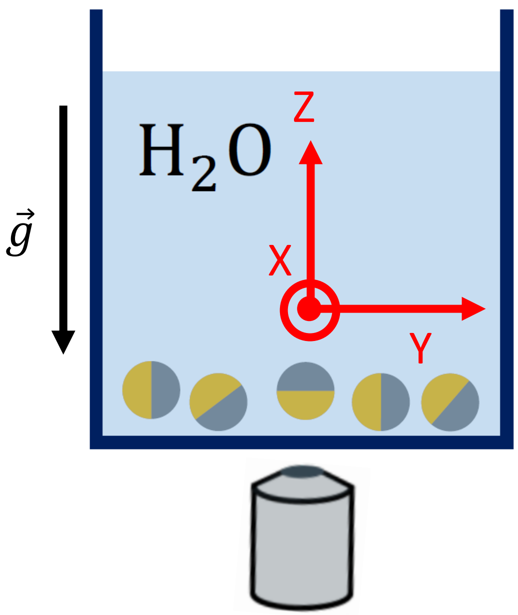
Mathieu Leocmach

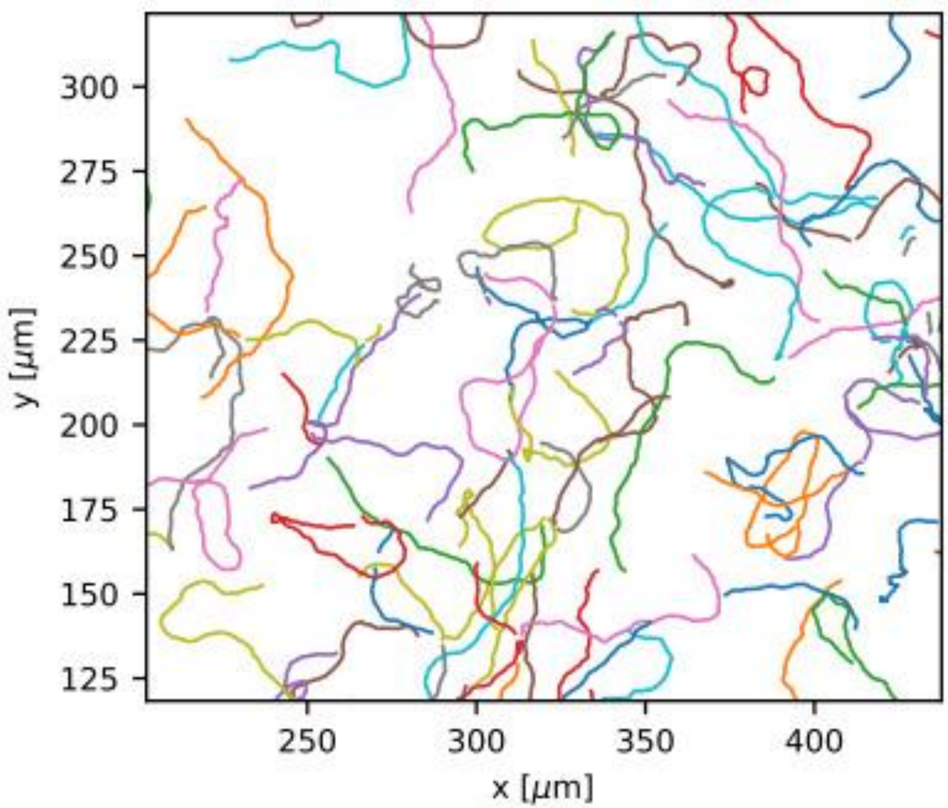
Guillaume Duprez,
PhD student

Our active system: active colloids



H_2O_2 fuel for **self-propulsion**
(I. Theurkauff *et al.* PRL 2012)

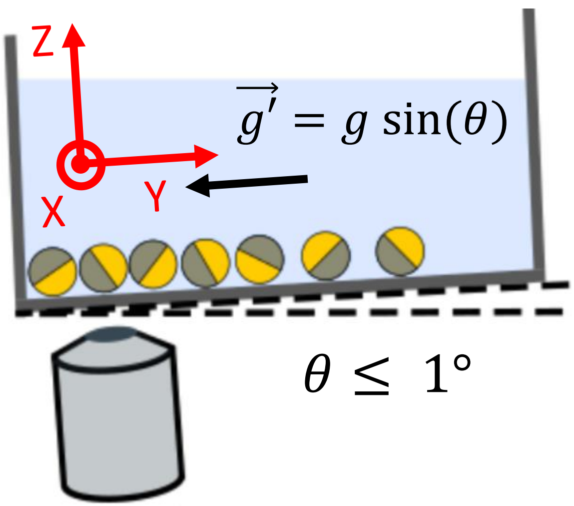




Trajectories of active colloids

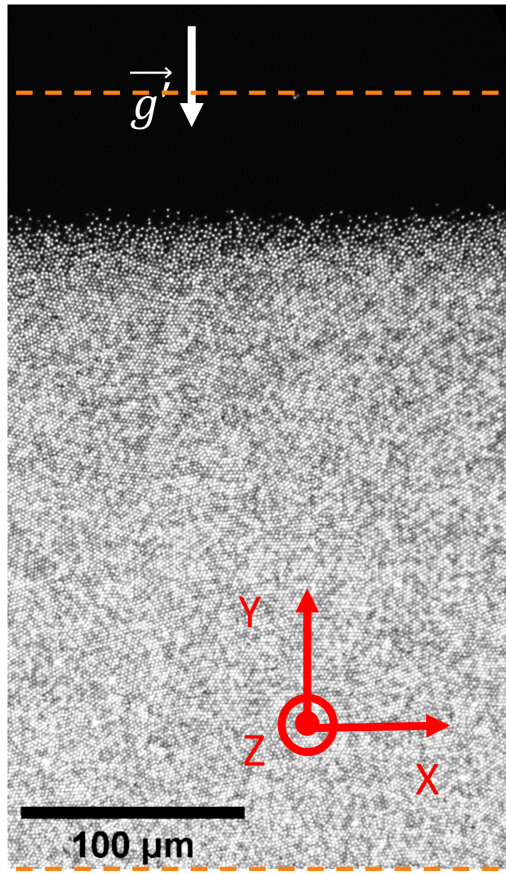
How to make dense assemblies?

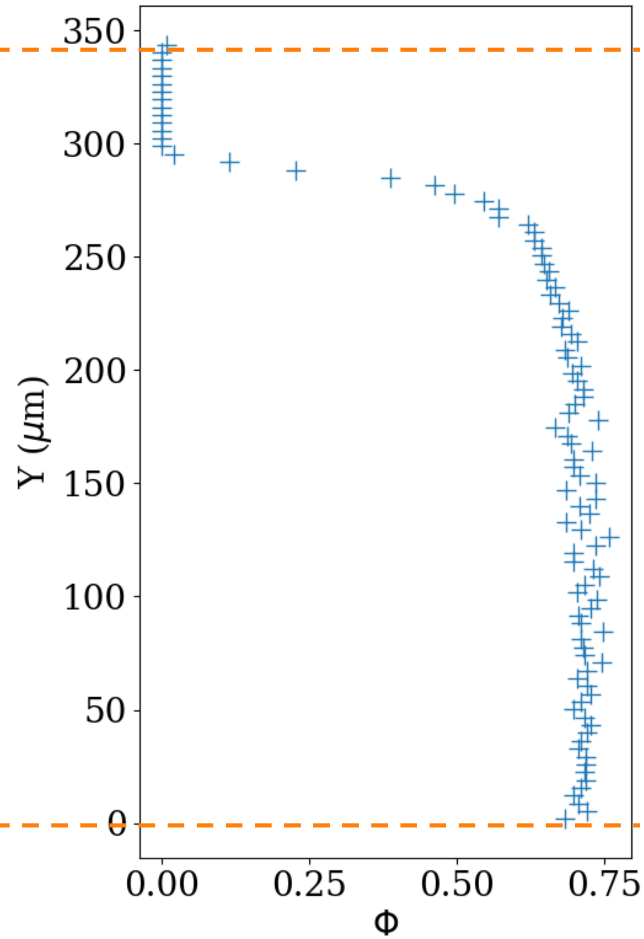
Tilting the container



$\theta \leq 1°$

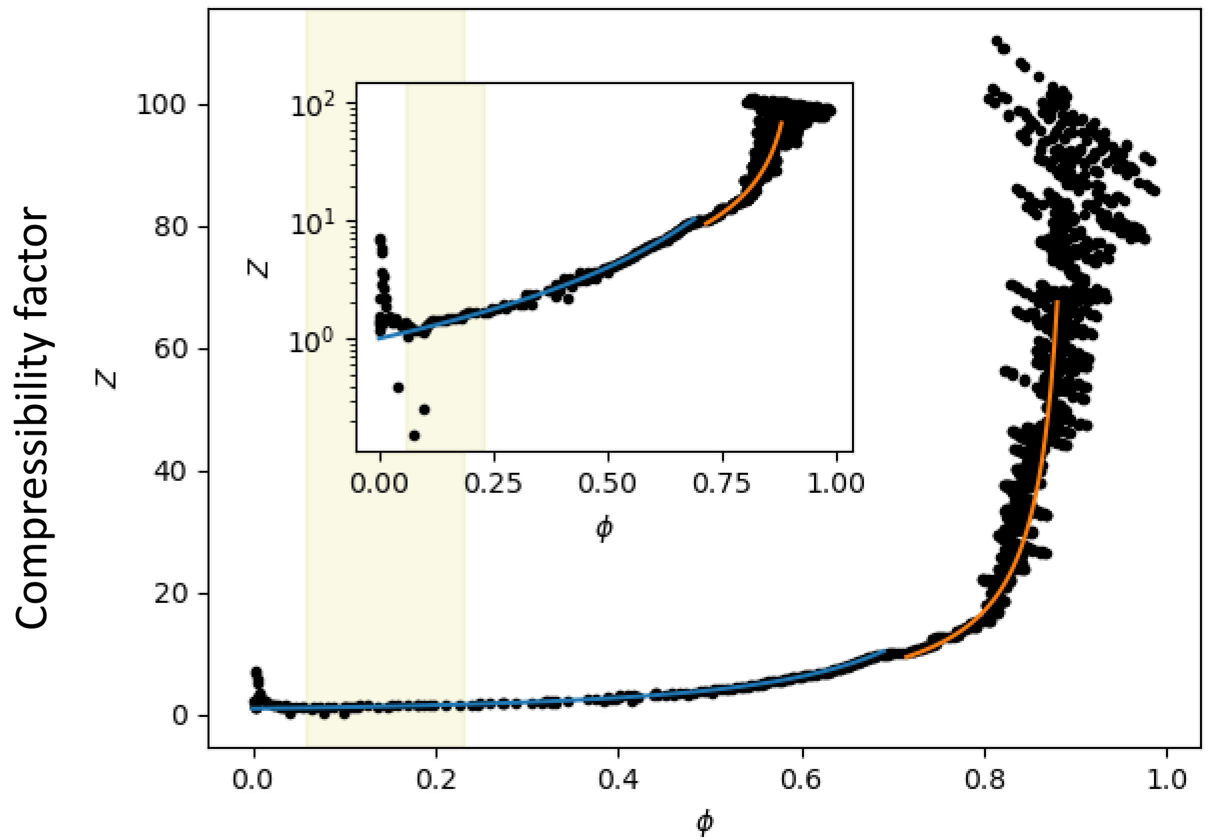
g': in-plane gravity





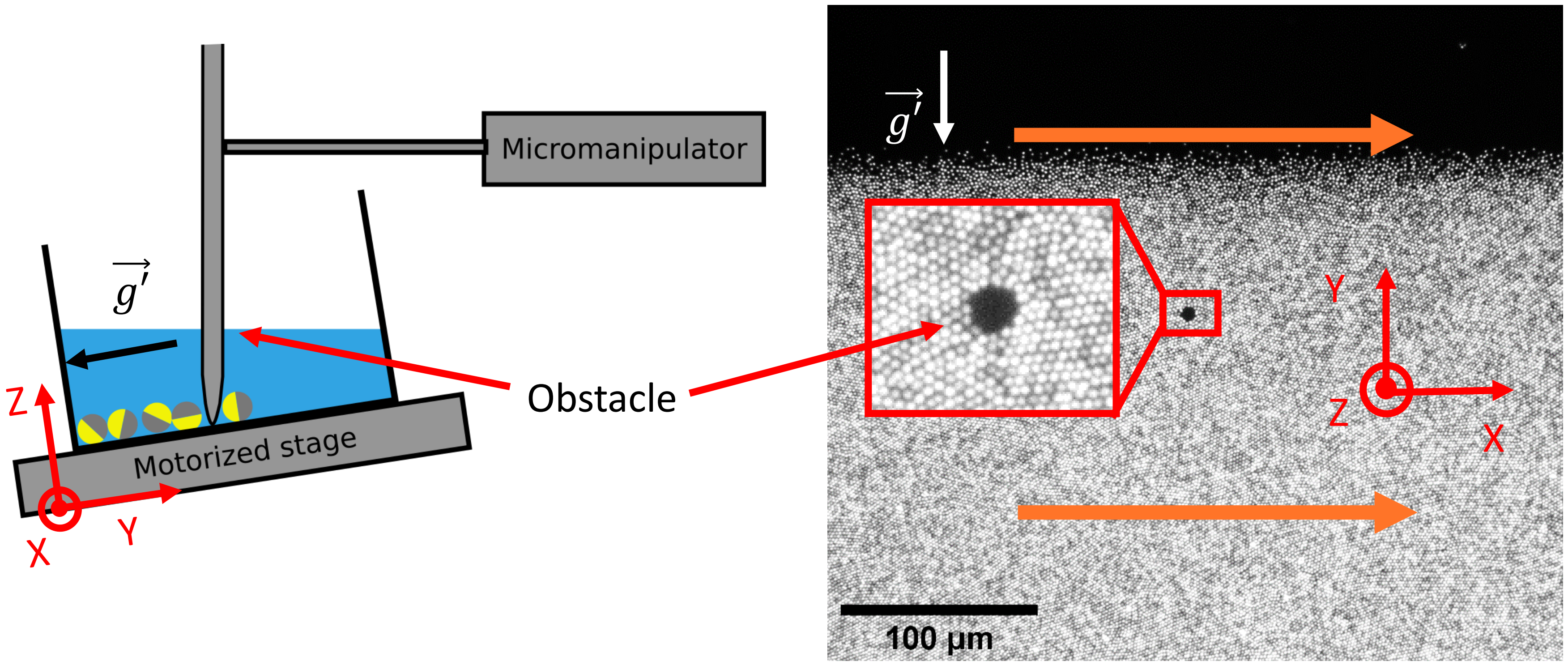
Volume fraction

Equation of states for a gaz of hard sphere (blue gaz, orange liquid)



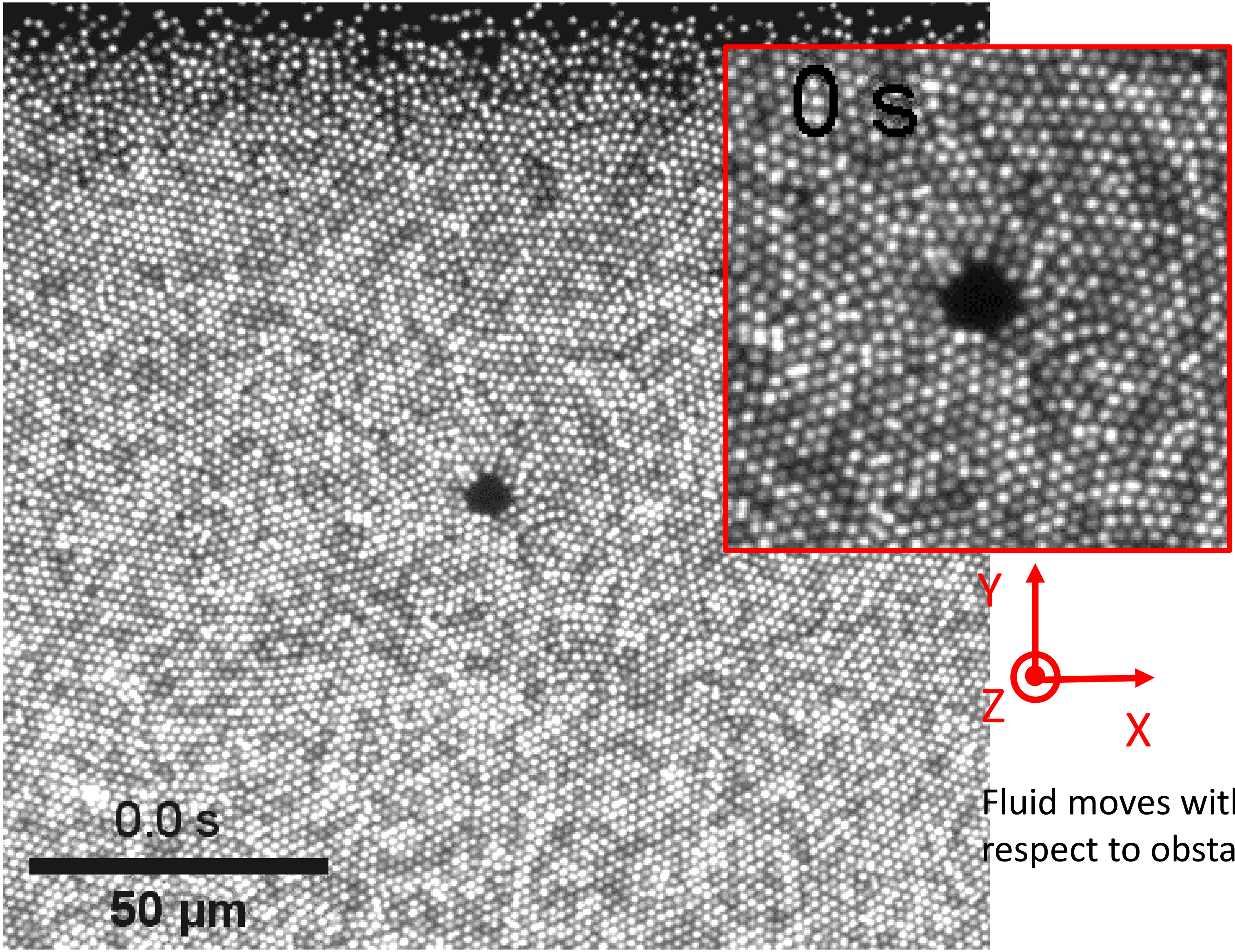
Fit of the blue part, gives access to an effective Temperature
And so to a quantification of activity

Probing the microrheology



- **10** µm obstacle : glass rod approach with the micromanipulator
- Movement : induced by the motorized stage on the whole sediment

It's better to see it !

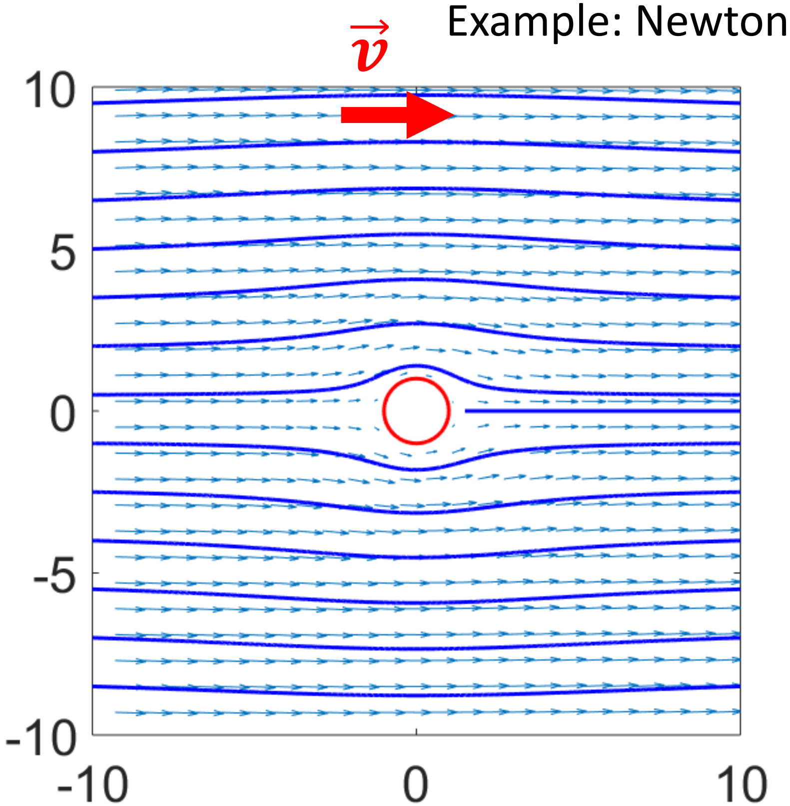


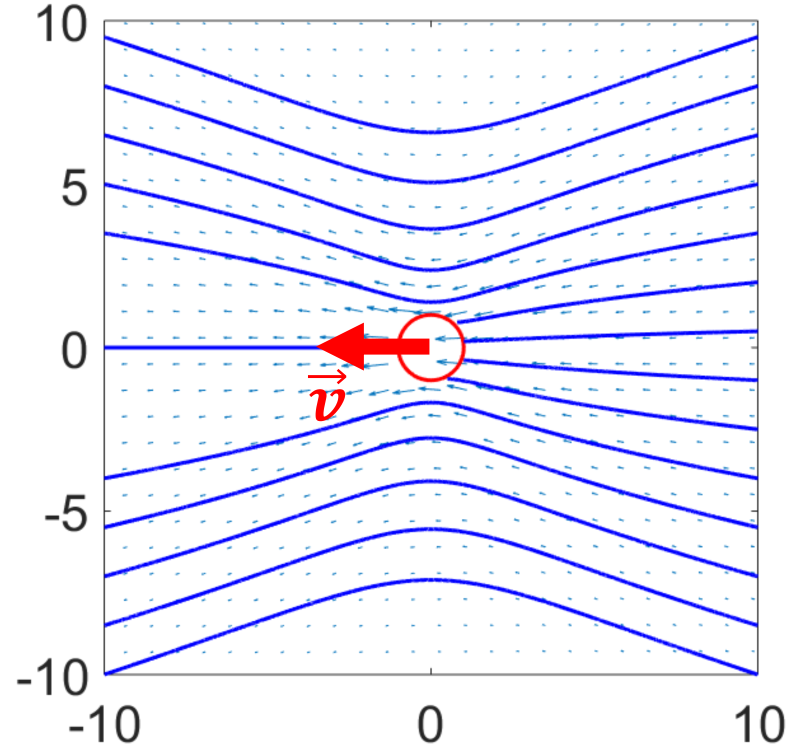
Fluid moves with respect to obstacle

Two different points of view

Obstacle referential | Fluid referential

Example: Newtonian fluid in Stokes flow



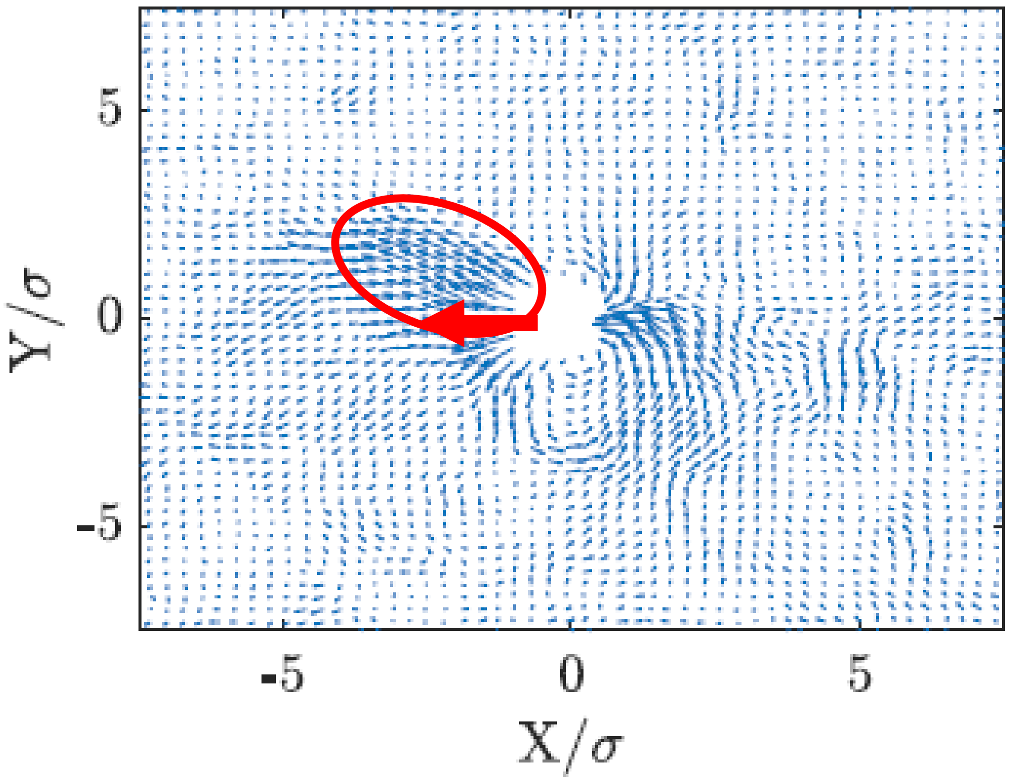


Coordinates in obstacle size units.

Our observables: Velocity field, Density

Our referential: Fluid

First observations: Flow field of passive colloids



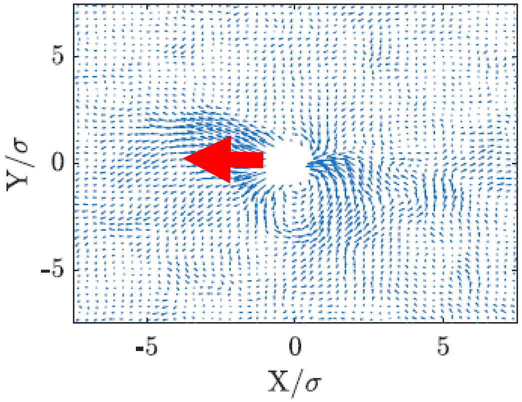
Velocity fields averaged over 4 s. Fluid referential

Observations :

- Heterogeneity
- Block movements
- Fluctuating

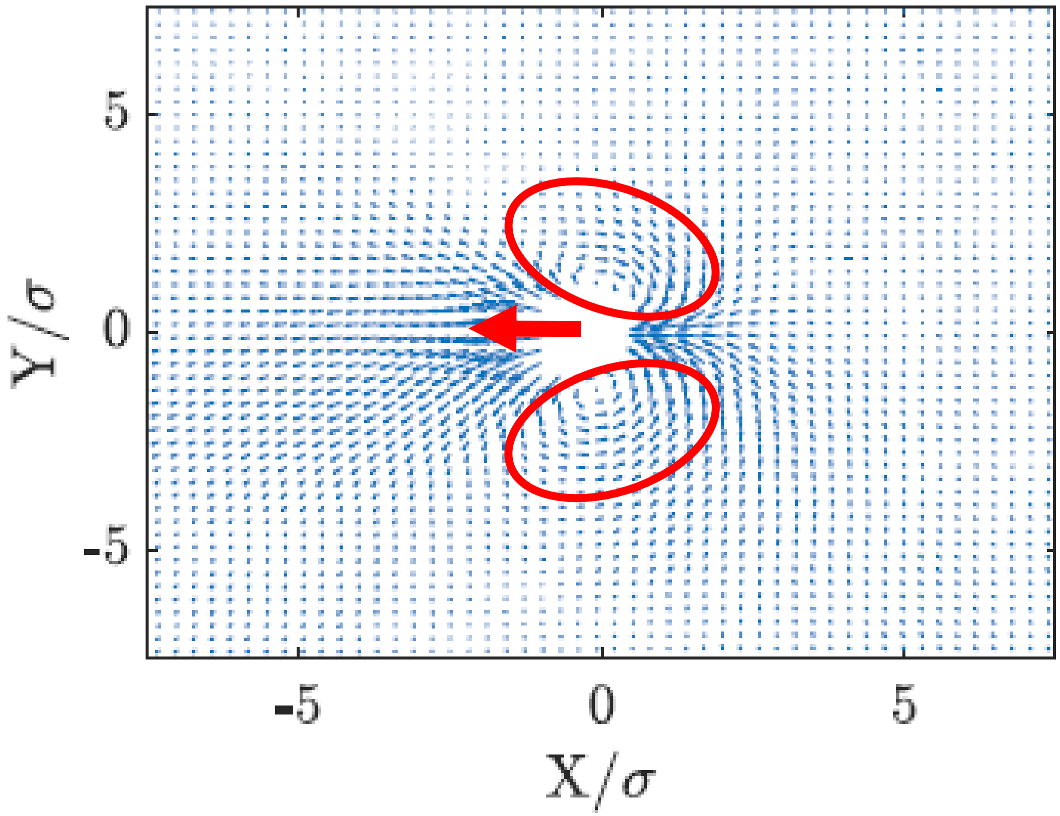
Yield stress fluid behaviour?

Mean flow field of passive colloids



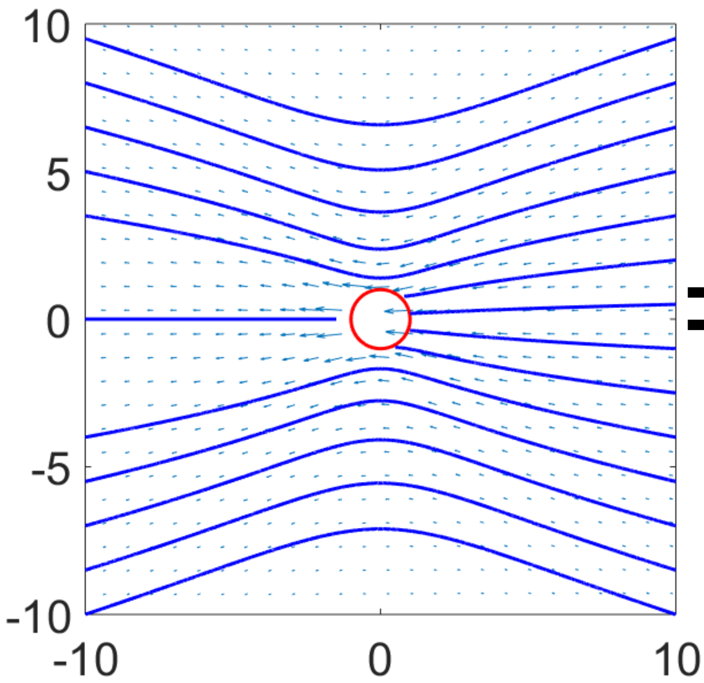
Observations :

- Smoother
- Recirculation



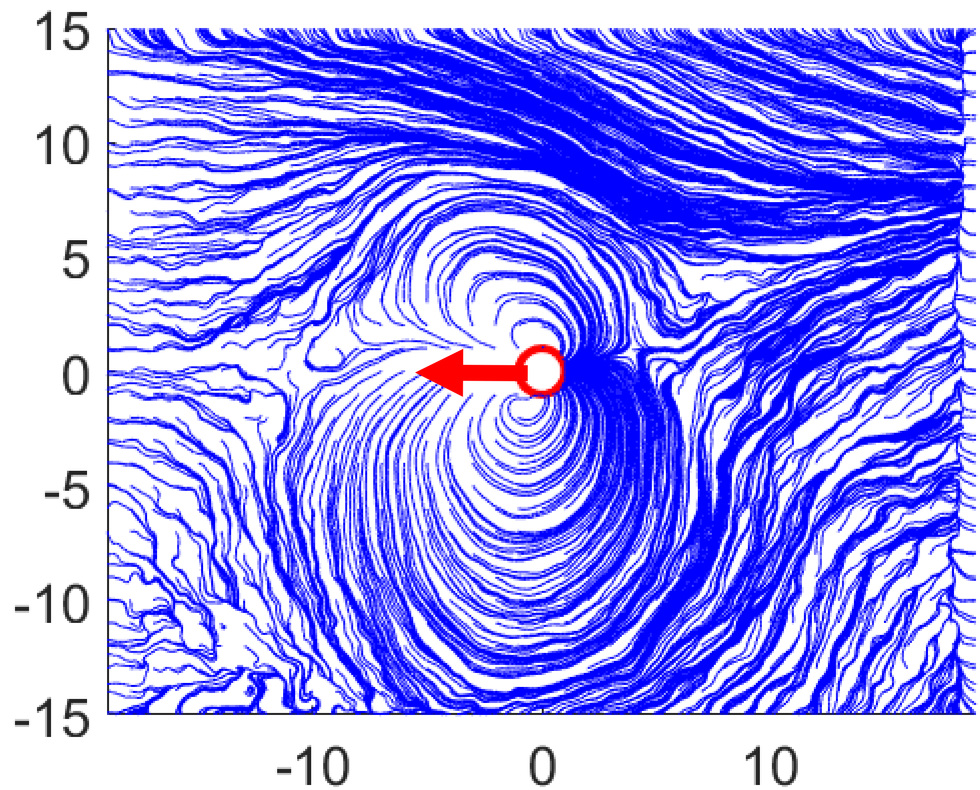
Velocity field mean over a whole run (> 100 s)

Mean streamlines for passive colloids



Theoretical Newtonian fluid
No slip and infinite fluid

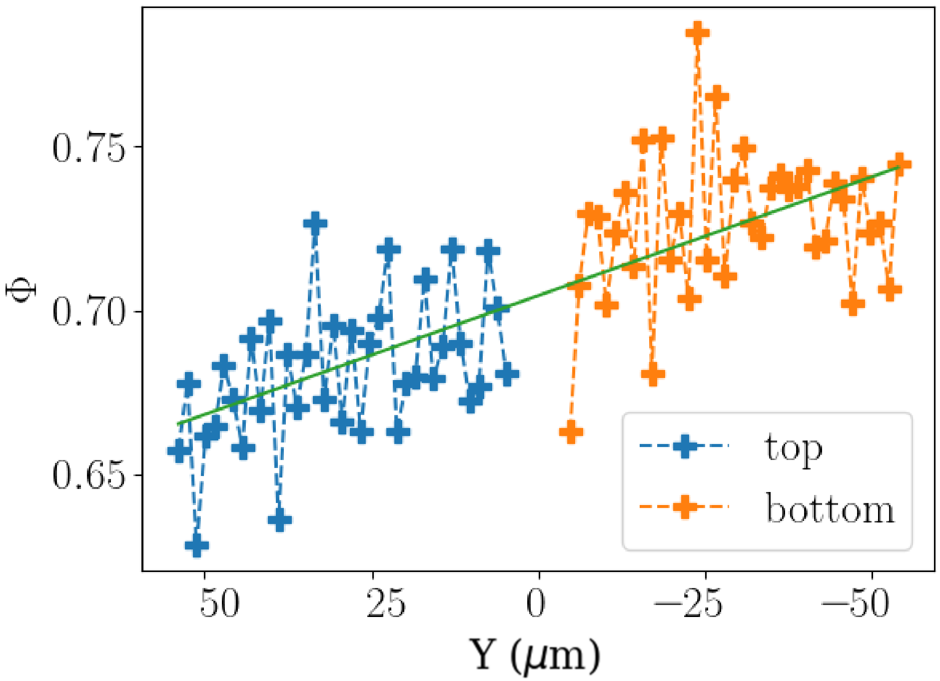
≠

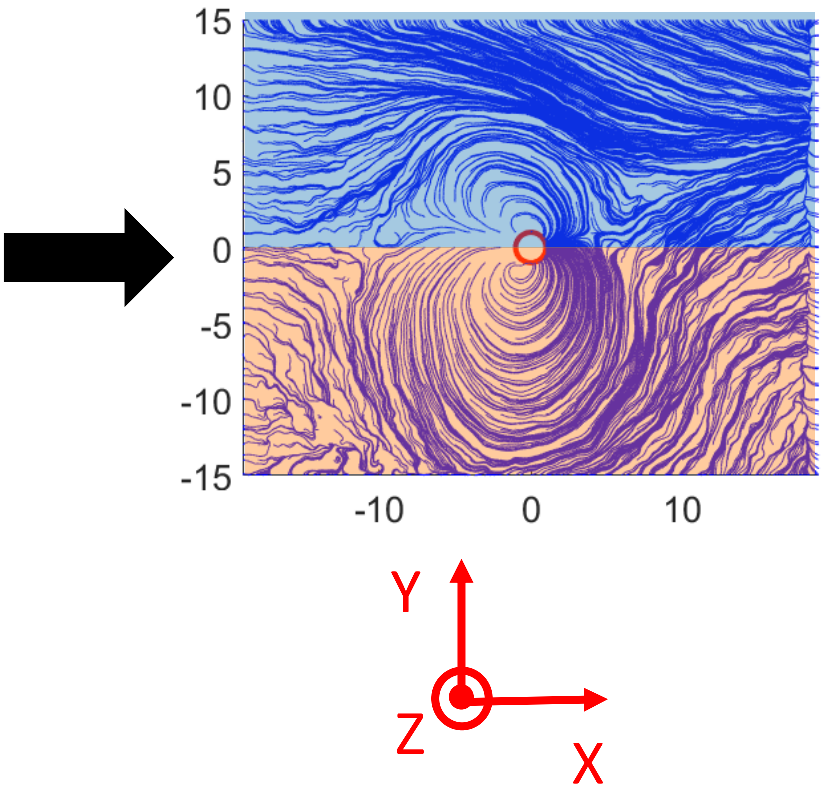


Experimental passive colloids

- **Non Newtonian? Boundary conditions?**
- **Asymmetries?**

Asymmetry top/bottom

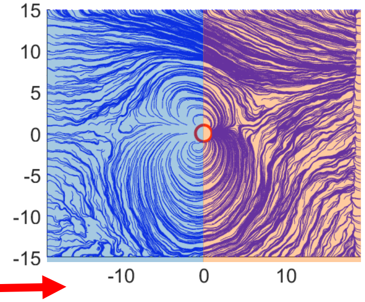


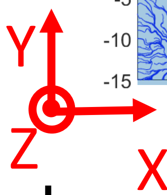


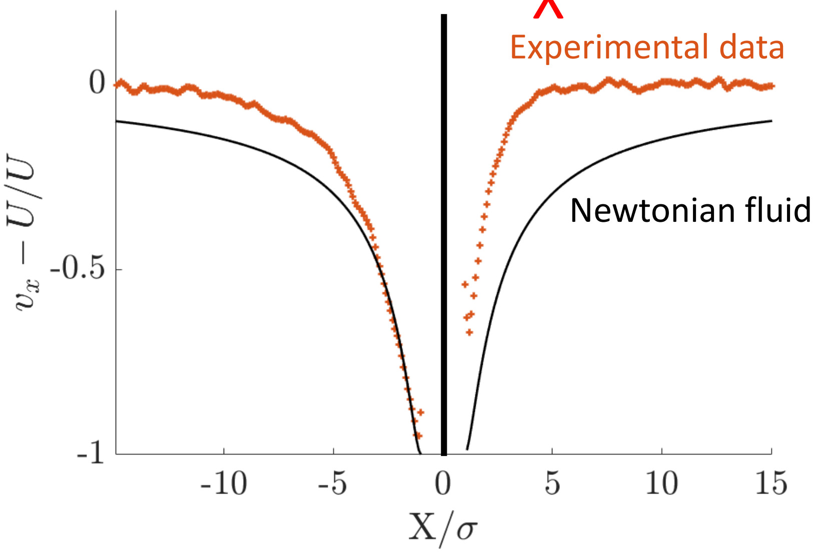
Imposed by the sediment

Front/back asymmetry in velocity

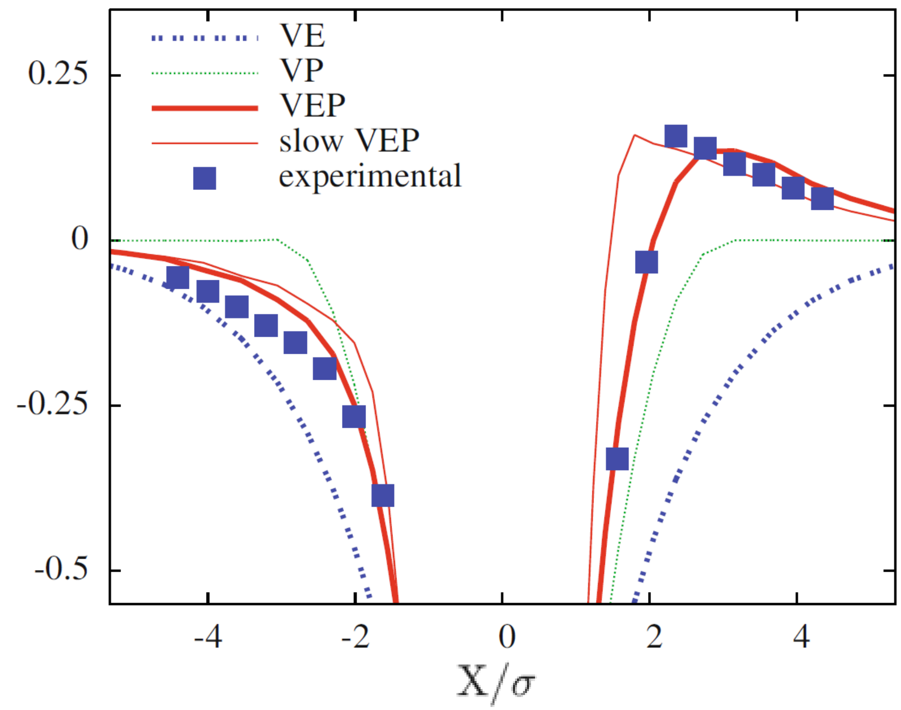
Experimental data
Passive colloids







Experimental data foam

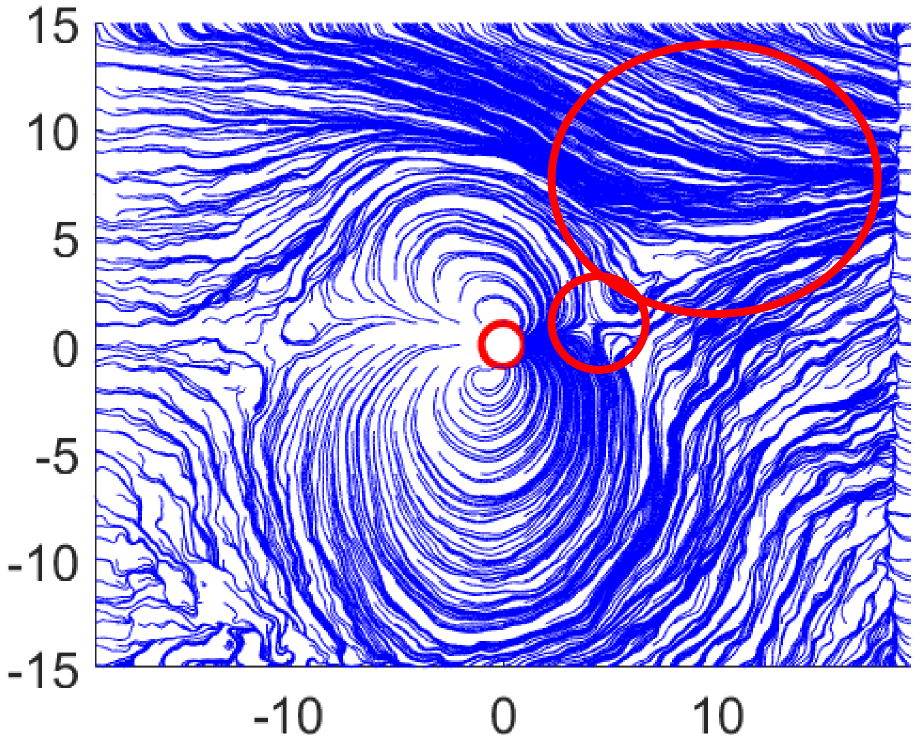


I. Cheddadi *et al.* Eur. Phys. J. E 2011

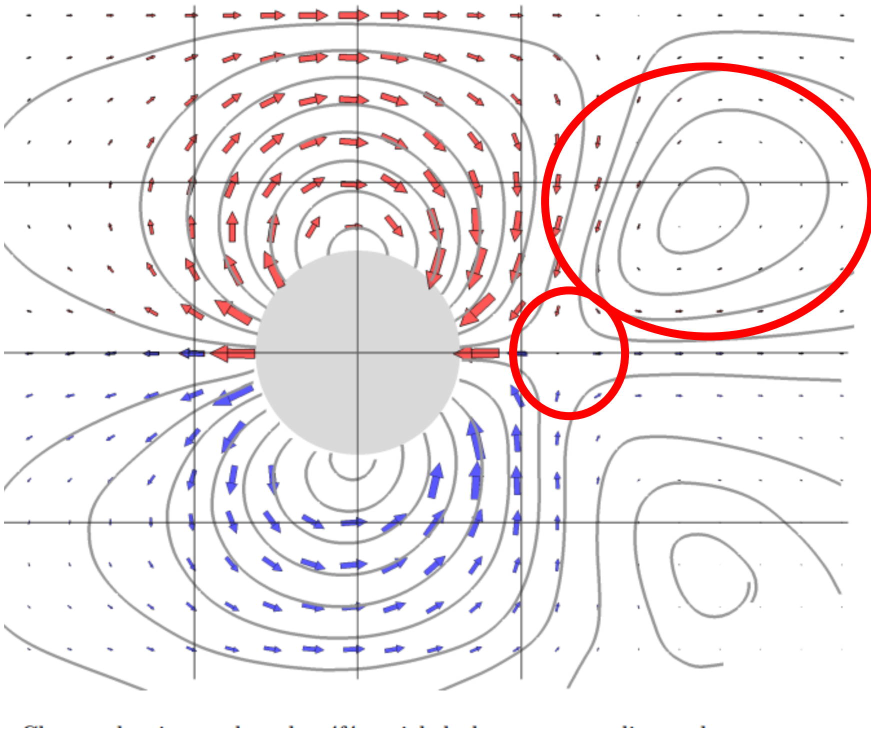
Asymmetry in the velocity profile:
characteristic of a visco-elasto-plastic fluid

Comparison to foams

Streamline of the colloids



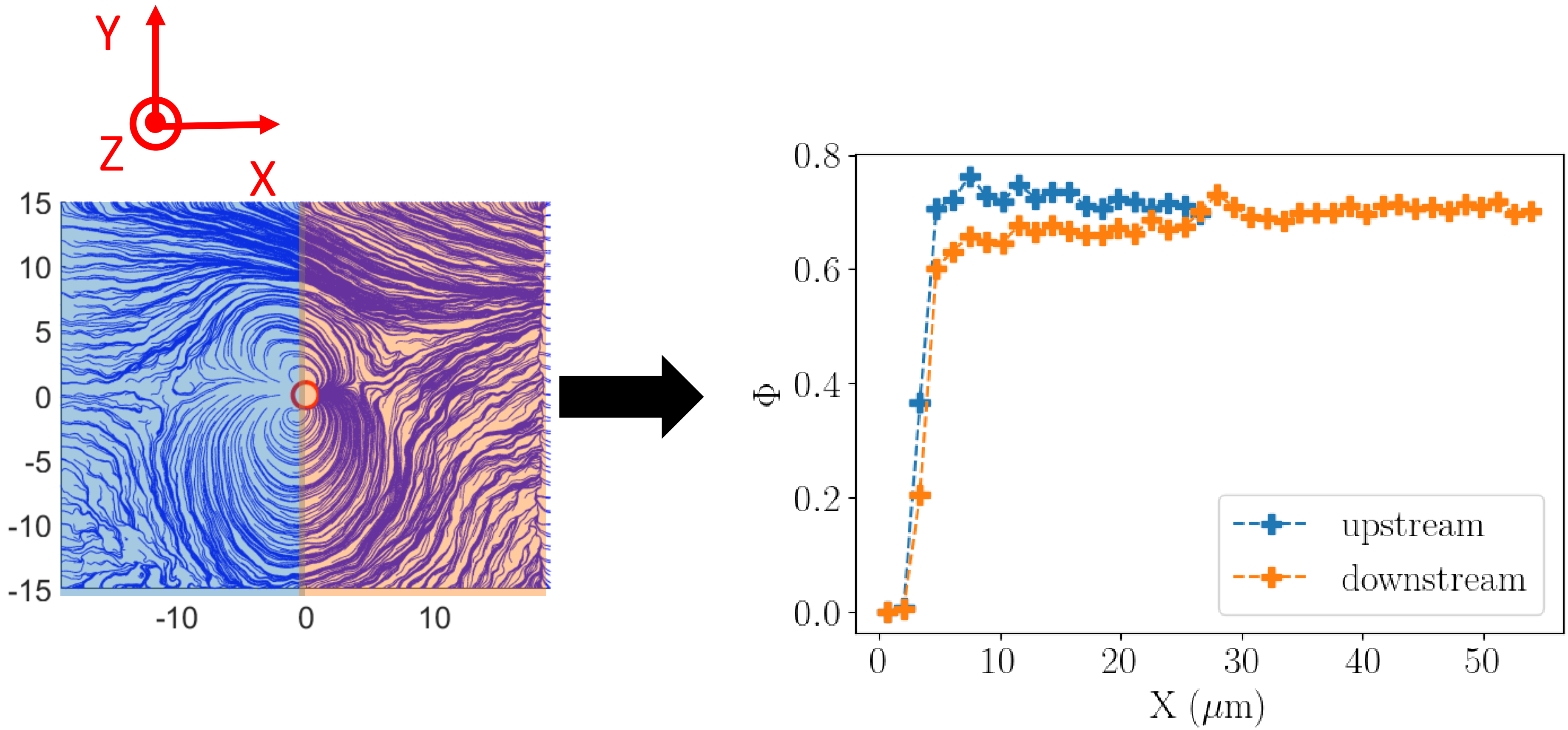
Streamline in foam (up model prediction/down data)



I. Cheddadi PhD 2010

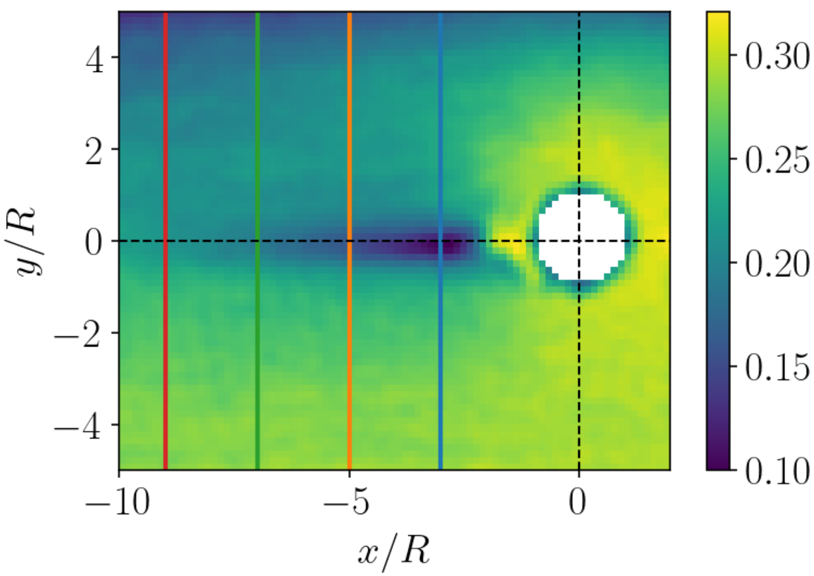
Also observed with carbopol (D. Fraggedakis *et al.* Soft Matter 2016)

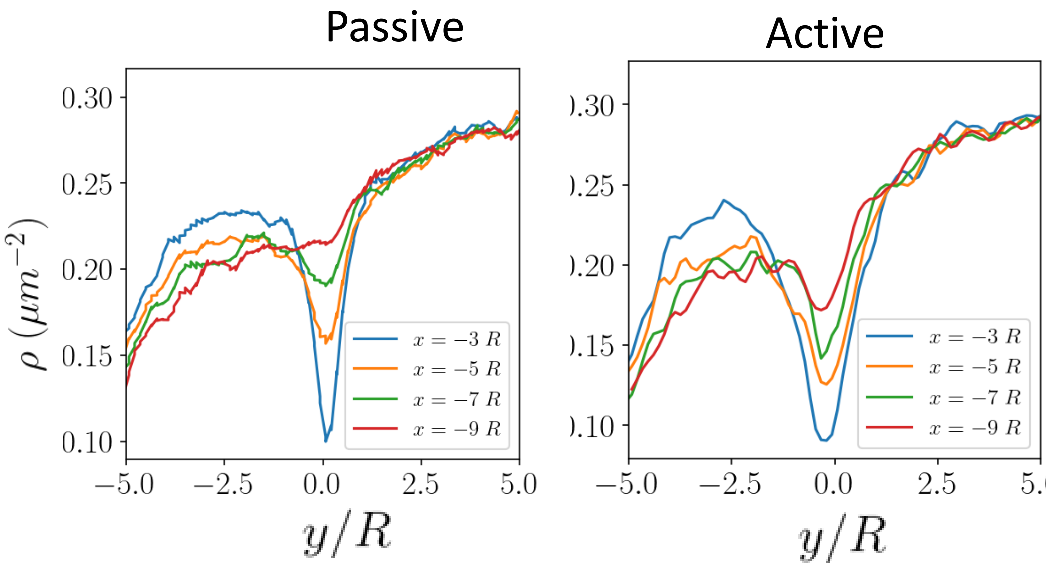
Front/back asymmetry in density



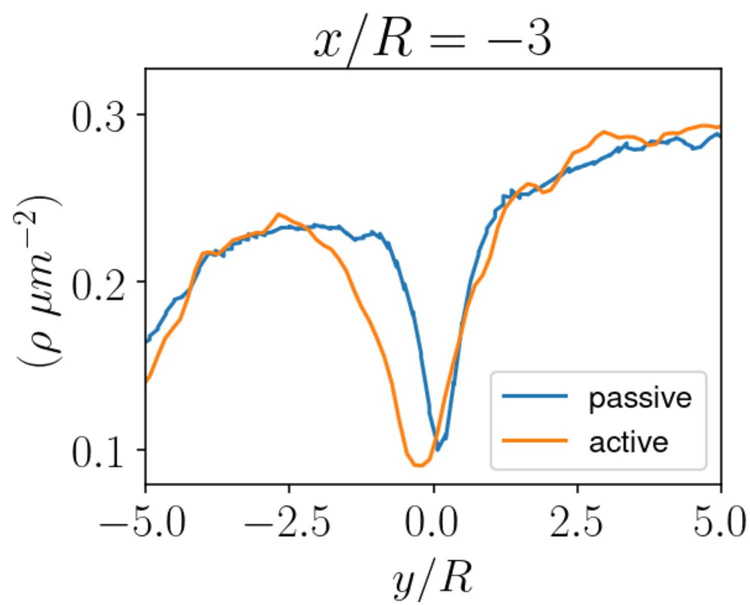
Compressible flow of the colloids

Healing behind the obstacle





$R = 9.5 \mu m$



Healing slower in the active case

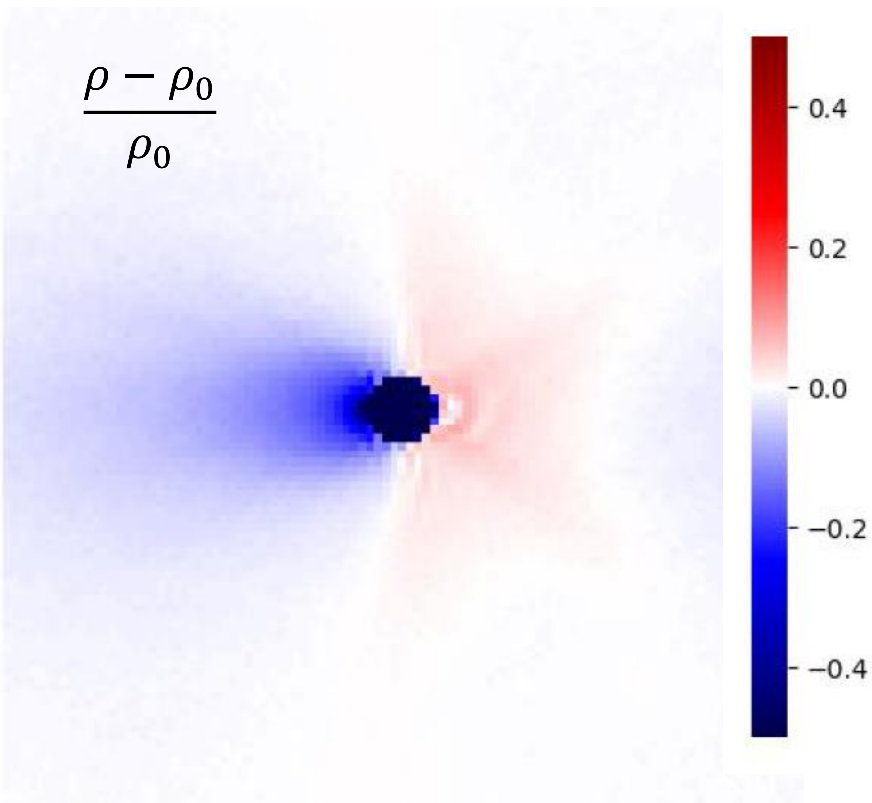
Is it due to persistency?

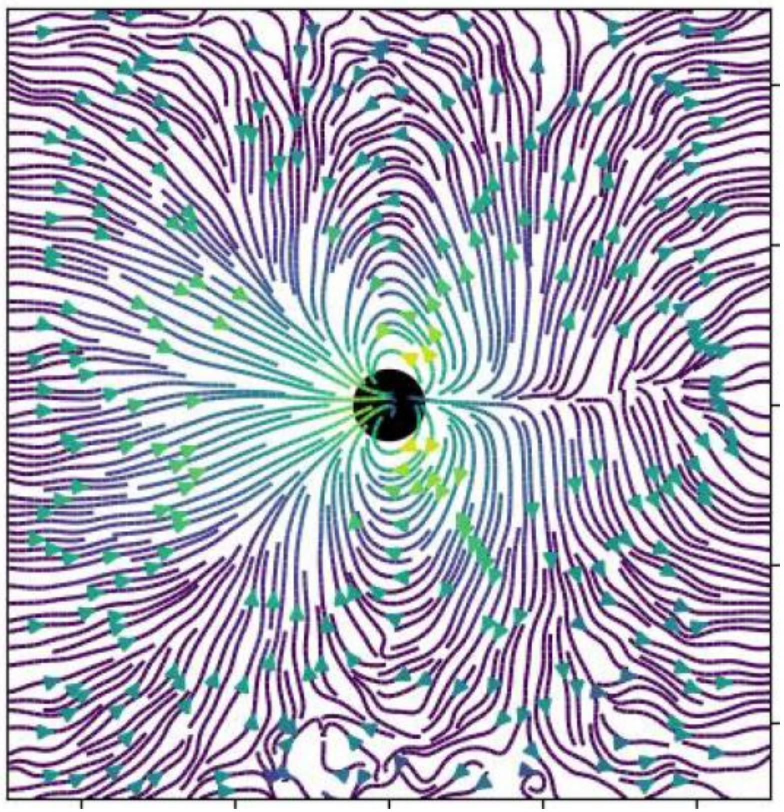
Particle Based Models

$$\dot{\mathbf{r}}_i = v_0\mathbf{u}(\theta_i) + \mu \sum_{jVi} \mathbf{F}_{ji} + \sqrt{2D_t}\boldsymbol{\eta}_i + f_g\mathbf{e}_y + \mathbf{f}_s(\mathbf{R}(t))$$

$$\dot{\theta} = \sqrt{2D_r}\xi$$

$$V(r) = \begin{cases} 4\varepsilon\left[\left(\frac{a}{r}\right)^{12} - \left(\frac{a}{r}\right)^{6}\right] & \text{if} \quad r < r_0 \\ 0 & \text{if} \quad r \geq r_0 \end{cases}$$

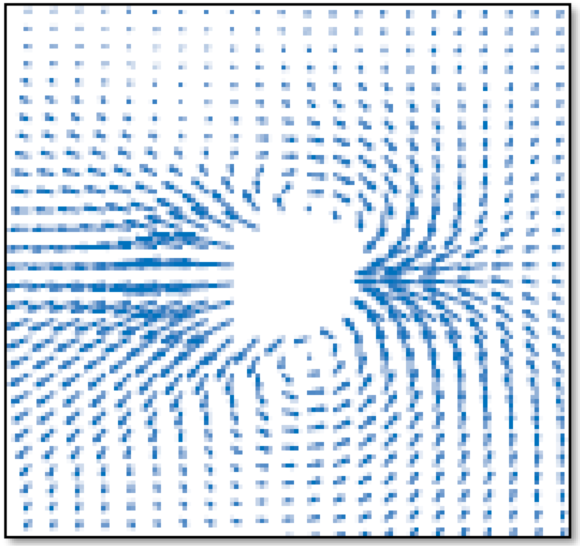




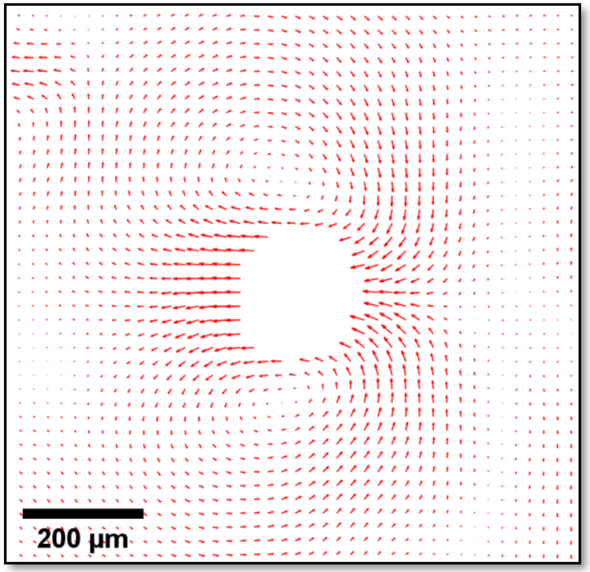
Simulation G Spera, F. Graner

Conclusion and Perspectives:

- Experiments leads to very rich and discriminative outputs



Passive colloids



Cells – S. Tlili PhD 2015

- **Qualitatively similar, quantitatively?**
- **Role of activity?**

A clear need of thorough comparisons with simulations. Which ones?

Biophysics Team : https://tinyurl.com/BiophysicsULyon

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