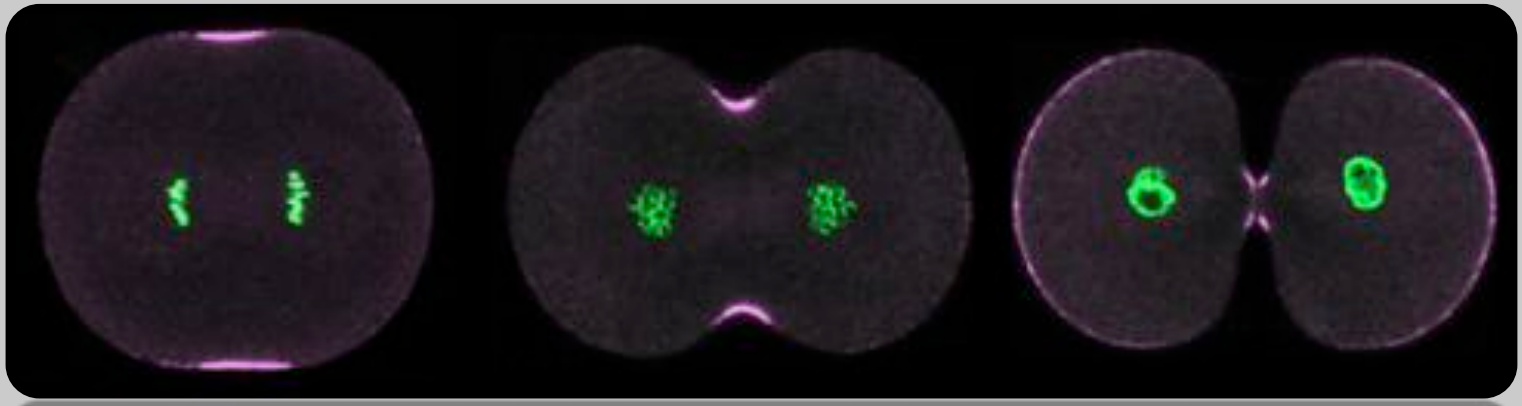
Modeling animal cell cytokinesis



Purple urchin zygotes

MyoII
DNA

(G. von Dassow)

Hervé Turlier
B. Audoly, J. Prost, J-F. Joanny

COMBINE – Institut Curie, Paris
Sept. 2013

institutCurie
Together, let's beat cancer.

UPMC
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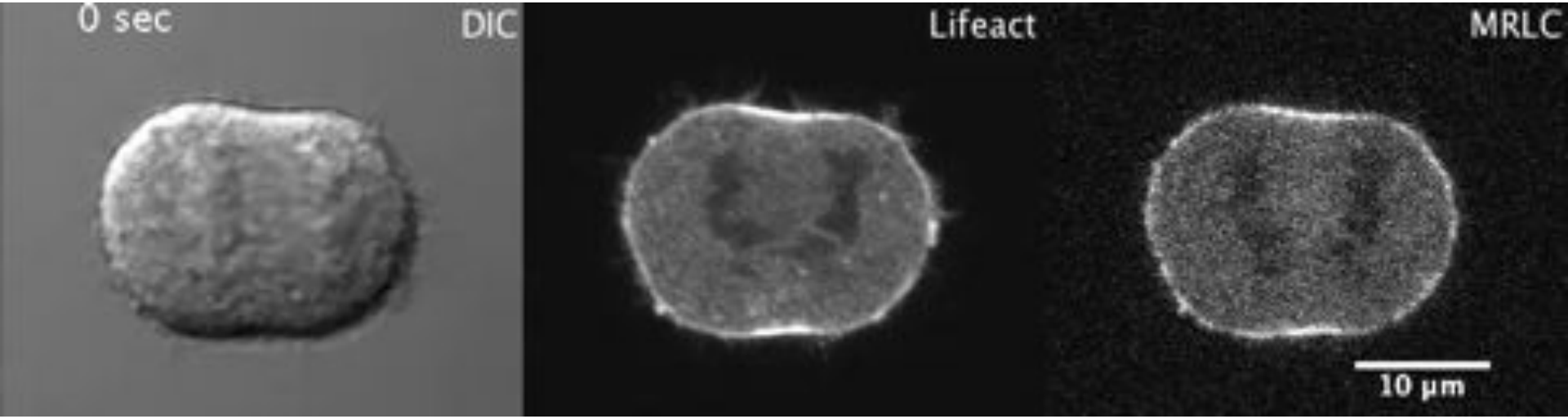
INTRODUCTION A complex biomechanical process

- Very biochemical complex process (involving more than **100 proteins**)
- The cytokinetic process is **very similar between animal cells**

Purely PHYSICAL/MECHANICAL DESCRIPTION?

- Drastic cell surface deformation: fully **non-linear geometry**
- Forces generation involves essentially the **cytoskeleton : cortex & MTs**
- **Cell shape** is mainly directed by **cortical elements**



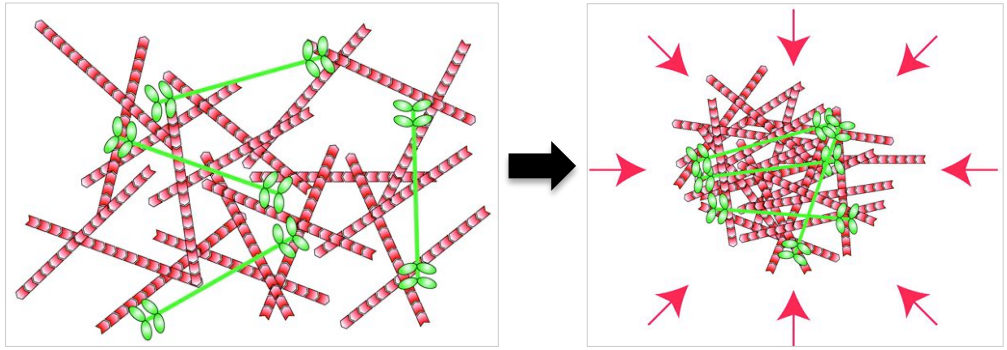
HeLa cells

Sedzinski et al. ***Nature*** *476* **2011**

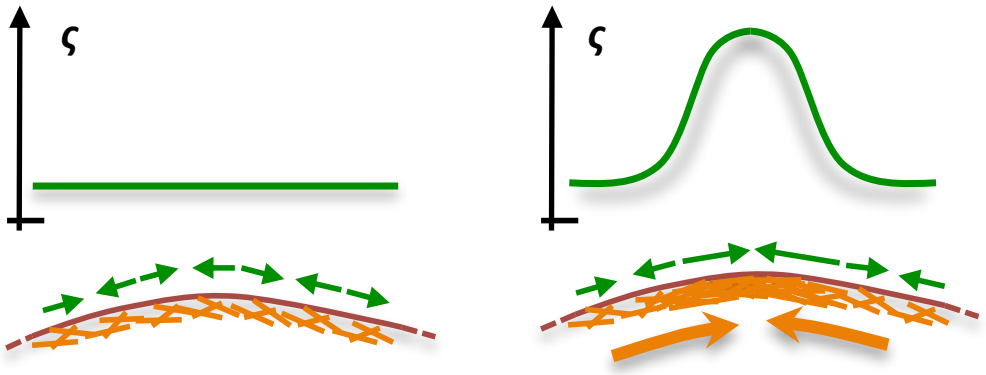
INTRODUCTION Cortical actomyosin gels

Actomyosin gels are active…

➥ **Myosin motors** create **contractile stress**

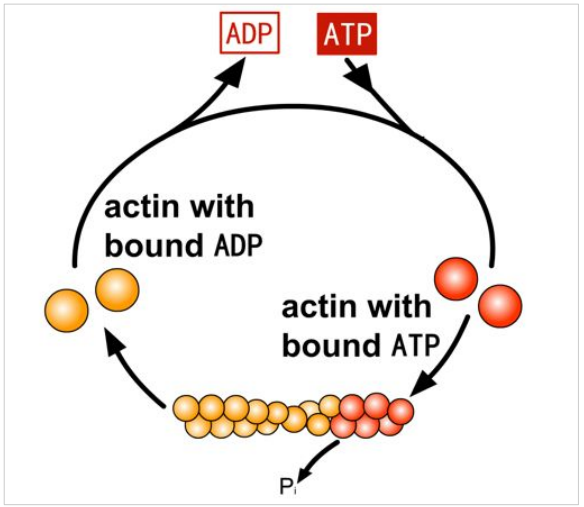


➥ **Gradients of contractility can generate flows**[2]

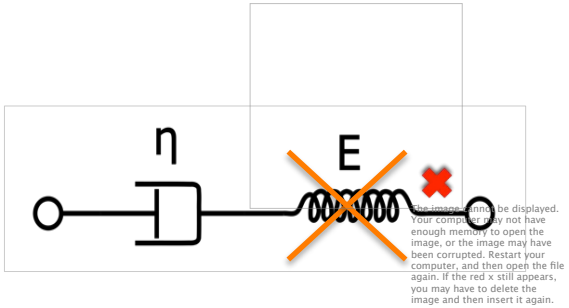


[2] G. Salbreux, J. Prost, JF. Joanny ***PRL*** *103* **2009**

…and under permanent turnover



➥ **Actomyosin is essentially viscous**



$\tau_{FRAP} \approx 30s \ll \Delta T \approx 5\text{-}30min$

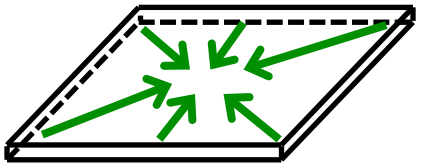
MODEL Visco-active membrane theory of the cortex

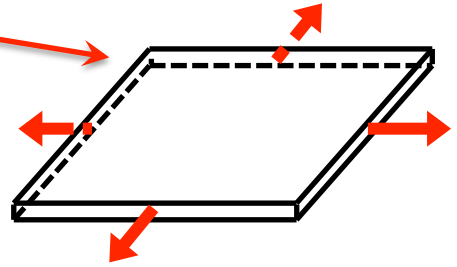
Contractile active term

$$N_s = \frac{e}{2}\zeta\Delta\mu + 2\,\eta\,e\,(2\,d_s + d_\varphi),$$

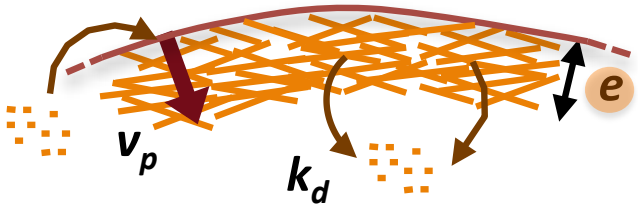
$$N_\varphi = \frac{e}{2}\zeta\Delta\mu + 2\,\eta\,e\,(d_s + 2\,d_\varphi).$$

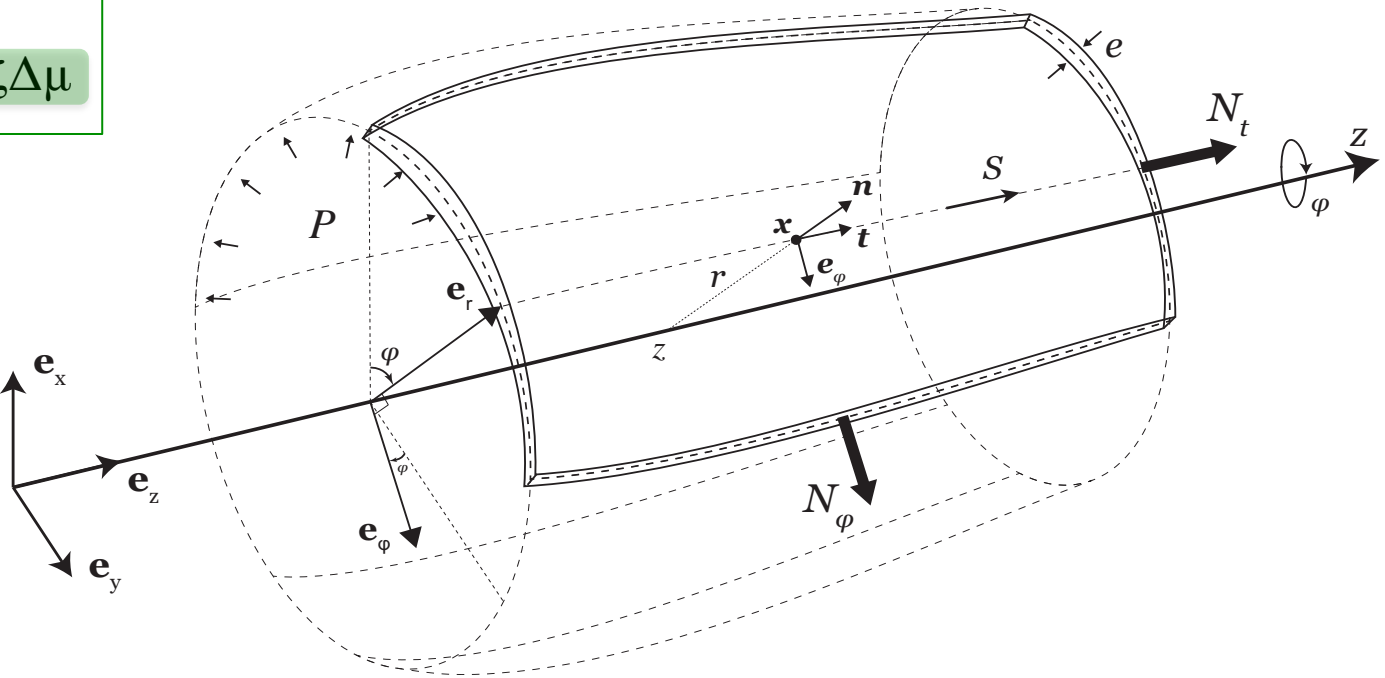
Viscous passive term





RhoA-GTP → ROCK → MLCP → $\zeta\Delta\mu$



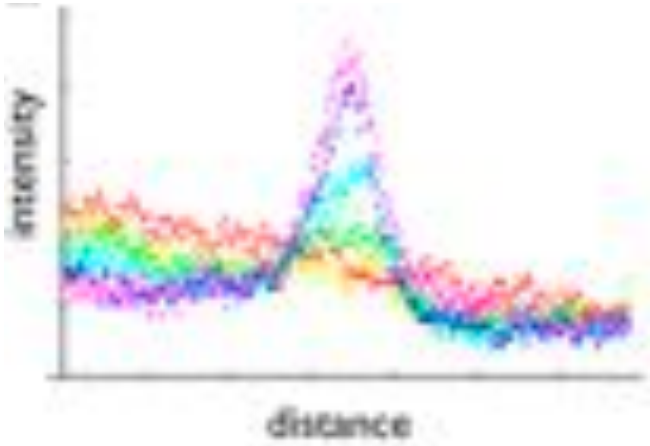


MODEL RhoA activity spatio-temporal regulation

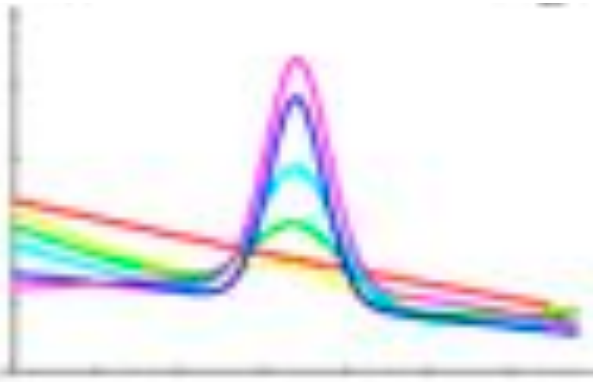
Active RhoA zone is Gaussian

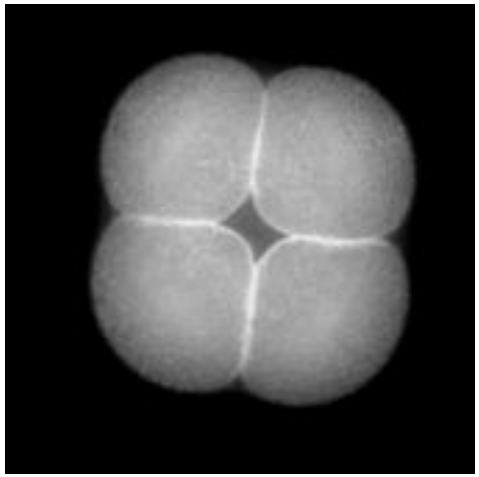
W Bement et al. **JCB**. *170(1)* **2005**

RhoA-GTP raw signal / 2min

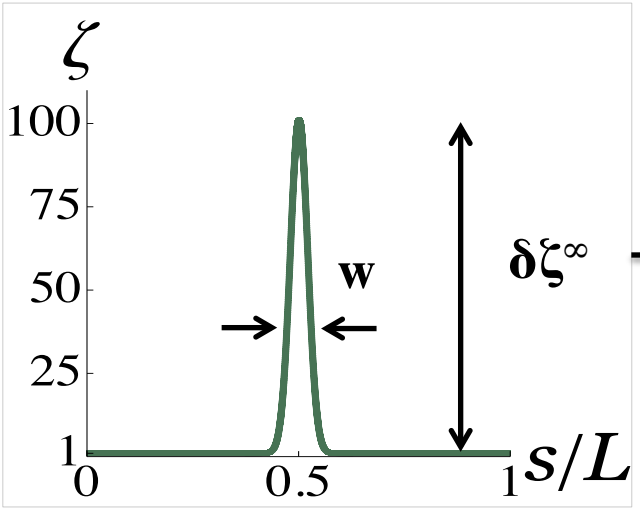


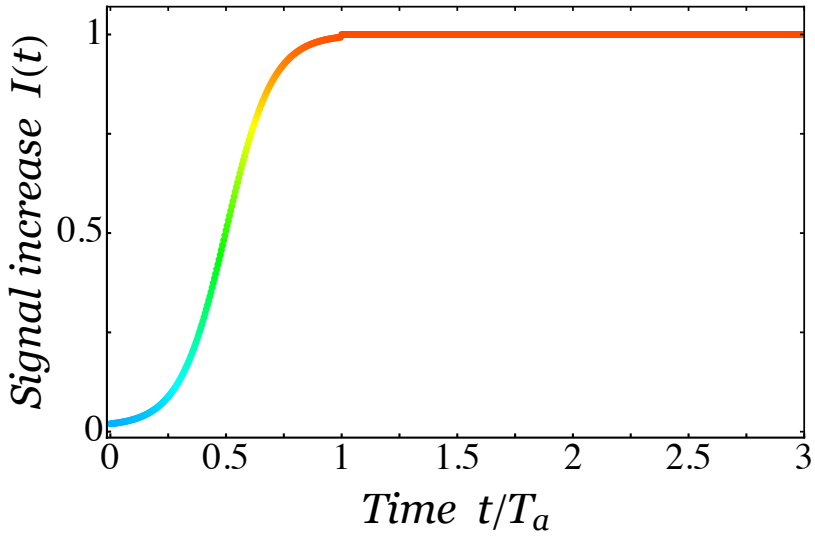
Gaussian fit of furrow signal



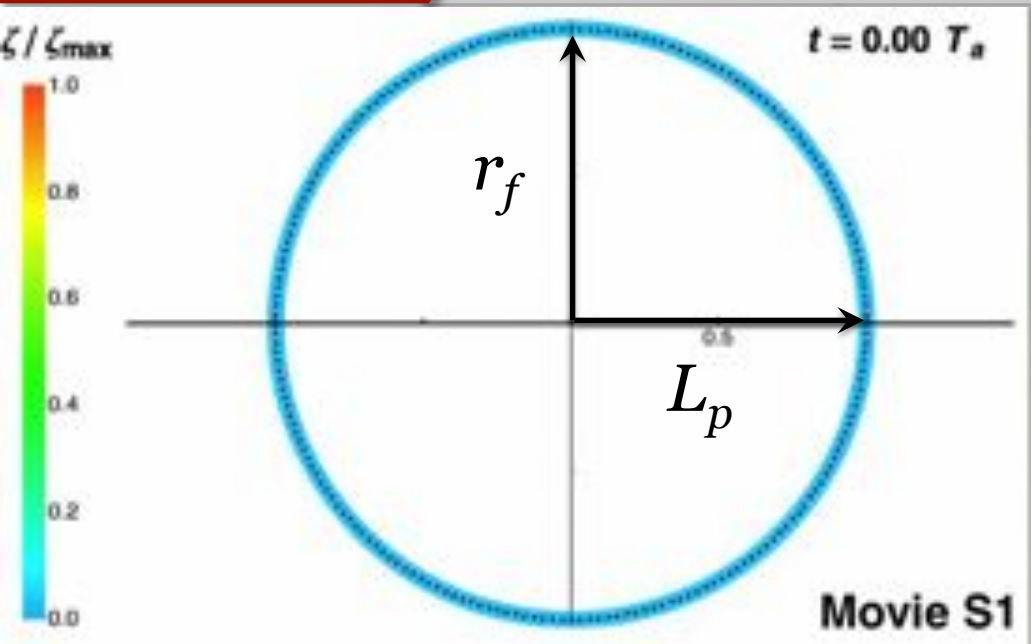


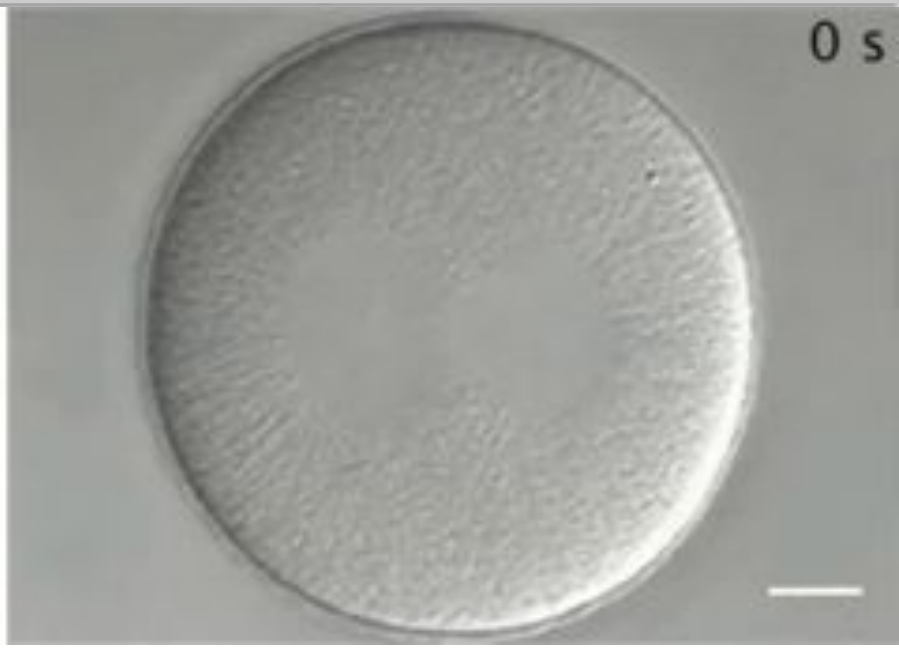
***Purple** urchin embryo*





RESULTS Cortex shape & thickness dynamics



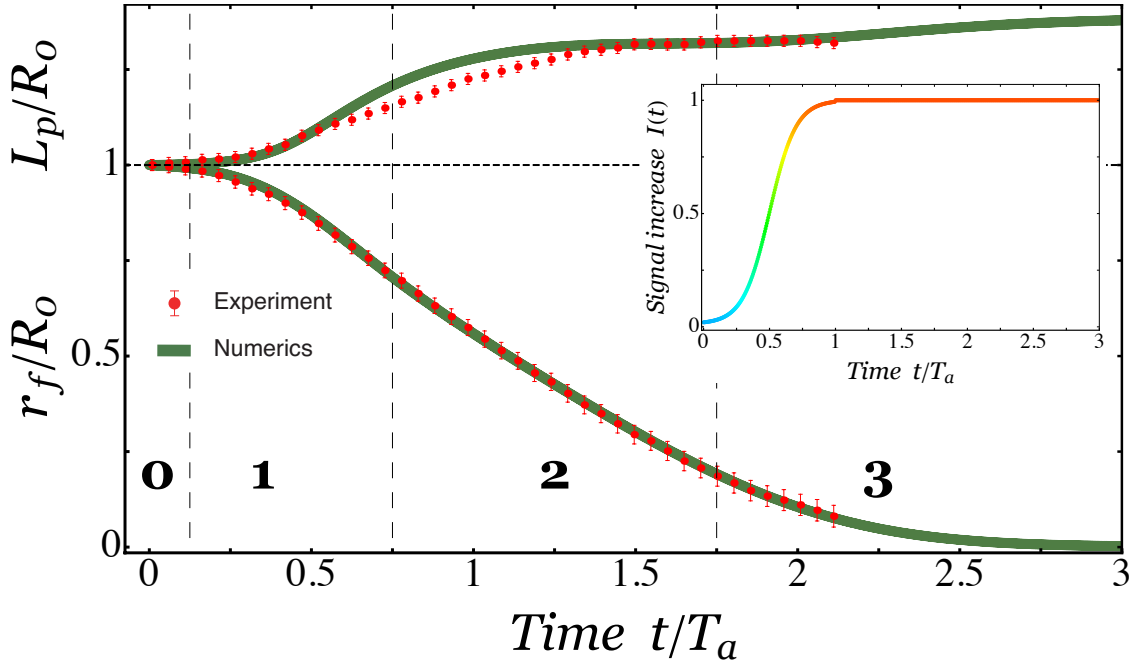


- Lagrangian geometric approach

- Variational solving method based on the principle of virtual works

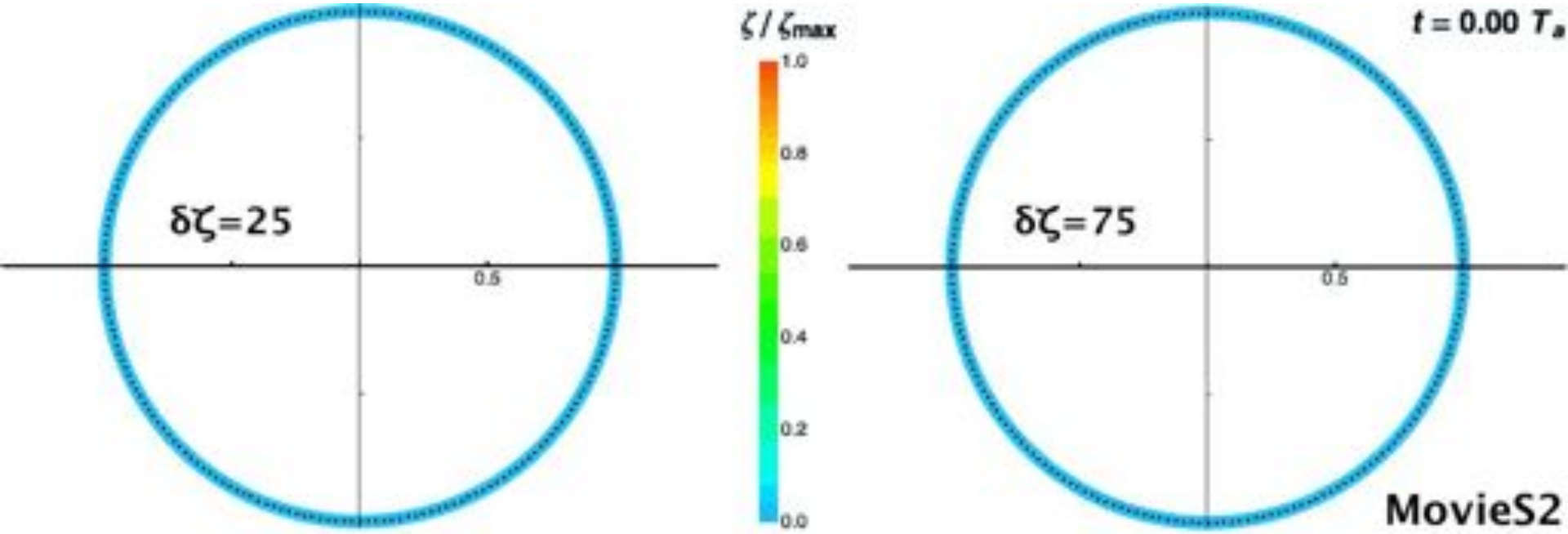
- Adaptation of *C++DVR code* originally developped for modeling viscous threads[1]

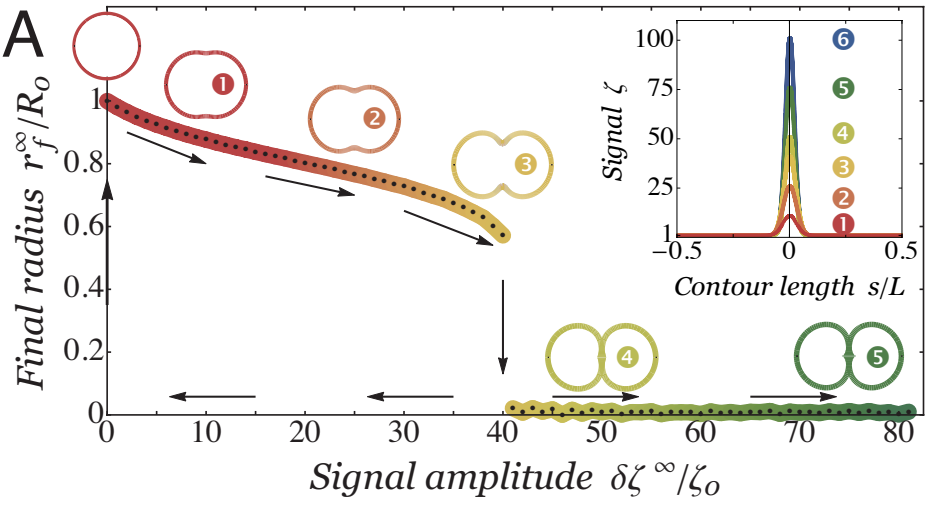
ref[1] B. Audoly, N. Clauvelin, P-T. Brun & al. ***arXiv:****1202.4971v2* **2012**

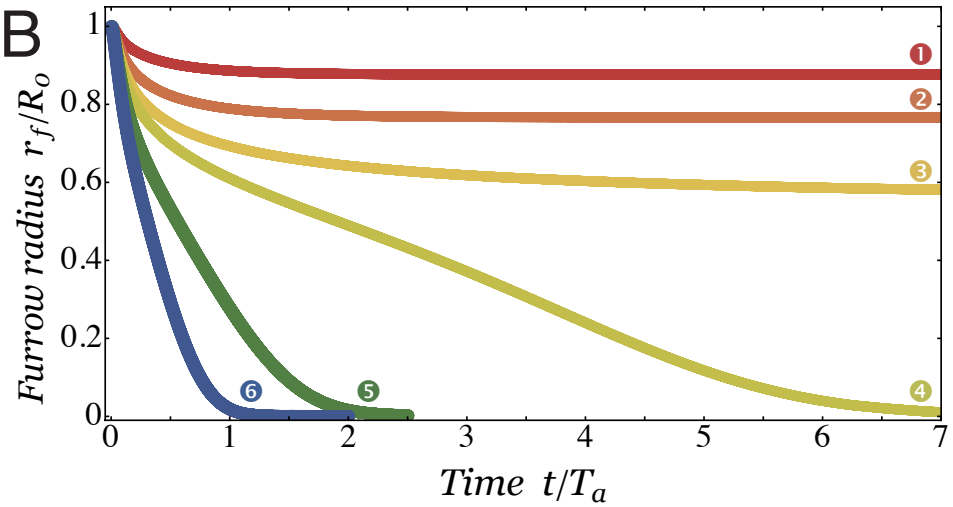


RESULTS

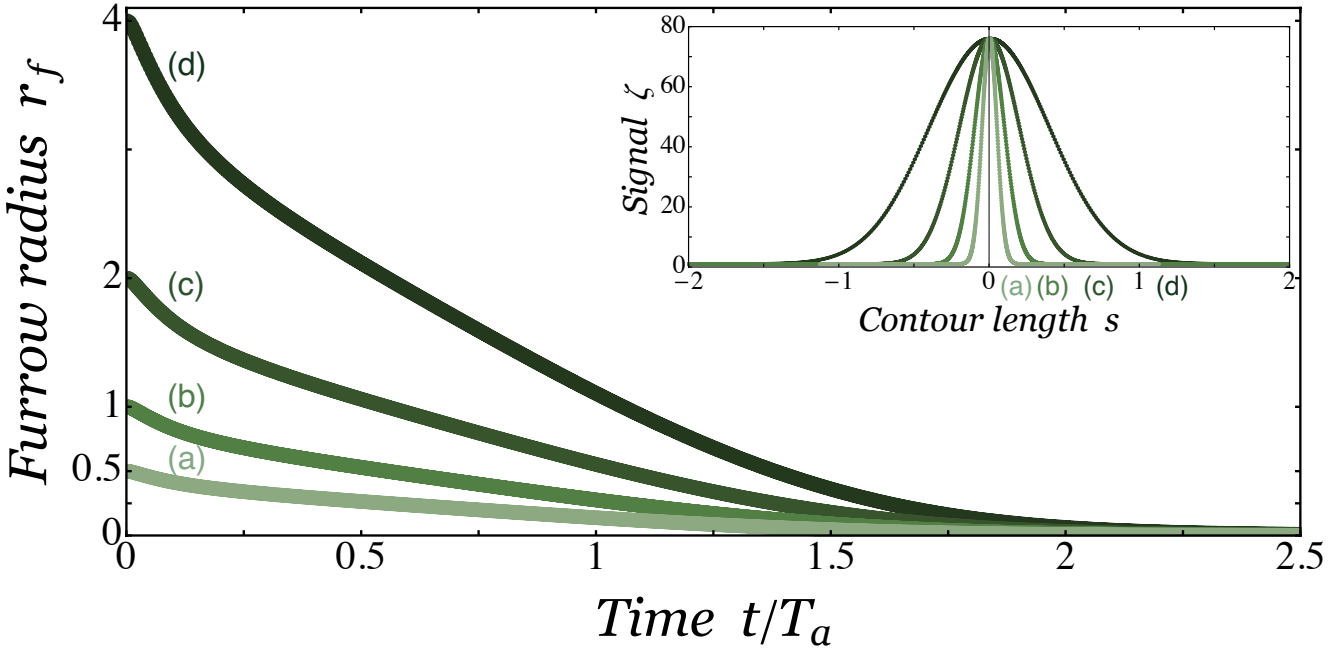
Bifurcation from failure to success of constriction



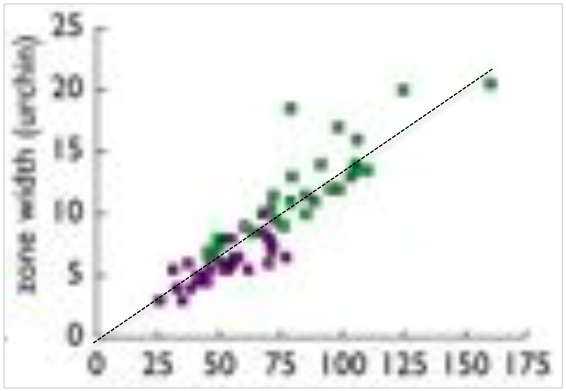




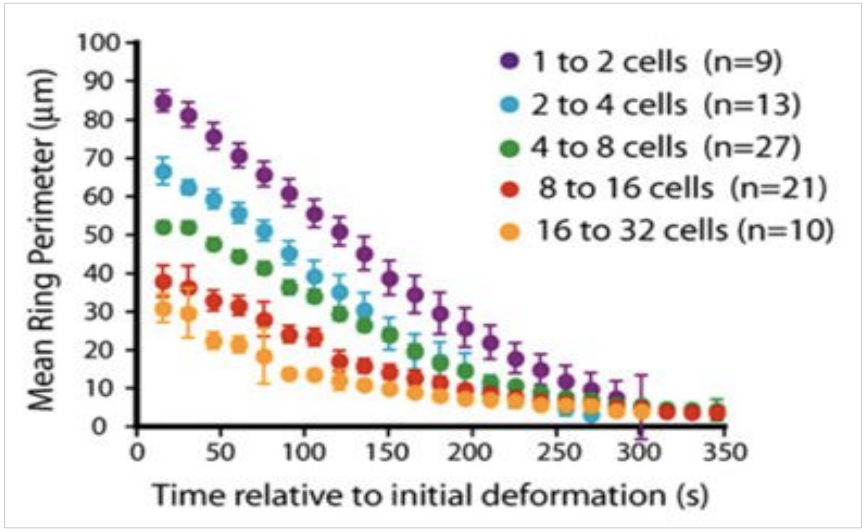
RESULTS Cytokinesis duration and cell size



$$w \propto R_0$$



W Bement et al. **JCB**. *170(1)* **2005**



➨ Cytokinesis duration is independant on cell size[1]

[1] A. Carvahlo ***Cell*** *137(5)* **2009**

CONCLUSION Let's mutualize our efforts !

To take home message

H Turlier, B Audoly, J Prost, J-F Joanny **Biophysical J**. *2013 (under review)*

- The key mechanism of constriction in cytokinesis is
  the competition between the furrow and the poles via volume conservation
- The **cytokinesis duration is independent of cell size**
- **Mechanics/physics can be very useful to biological modeling**
- **A promising and flexible numerical approach to study cell shape**
- **Integration of chemical pathways, stochasticity, cell-cell mechanical interactions …**

Acknowledgments

My advisors :

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Basile Audoly (IJLRDA) ***DVR-code***