



FONDATION
PIERRE-GILLES
DE GENNES

POUR LA RECHERCHE



Cortex dynamics in cell division

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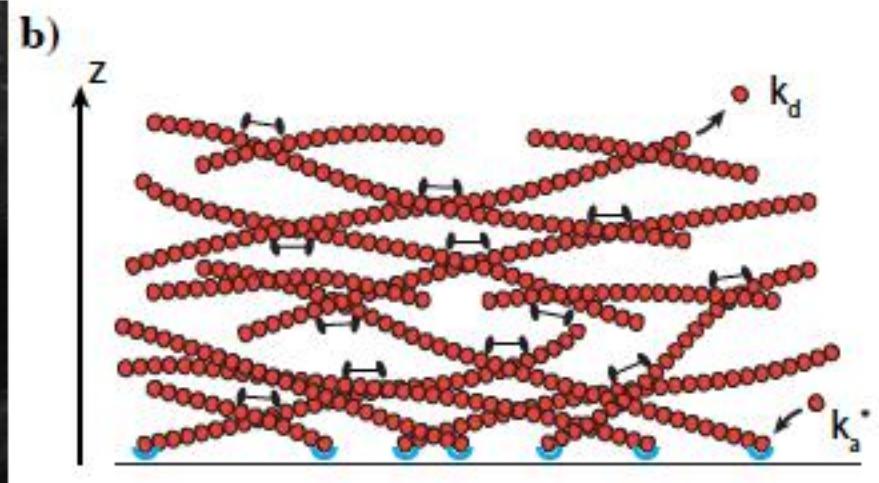
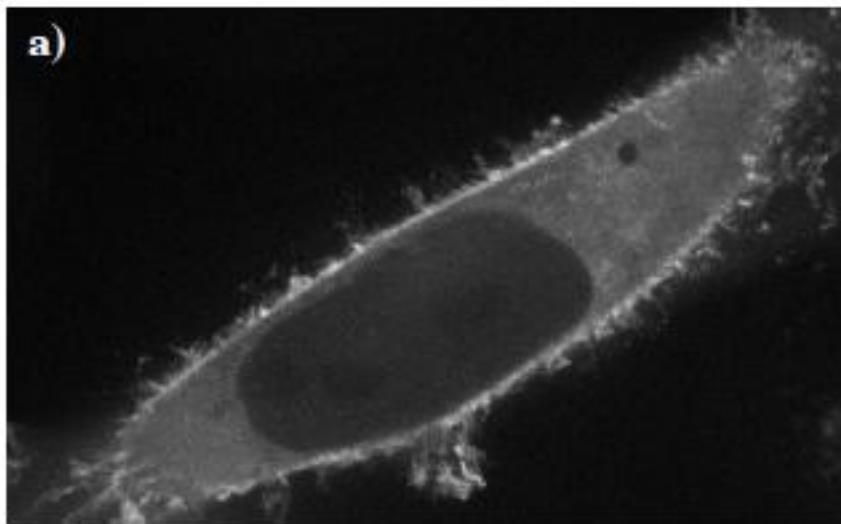
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Outline

- Physics of cortex
- Cytokinesis
- Active tissue



$$\frac{\nabla r}{\nabla t} + \operatorname{Div}(\tilde{J}_r) = - k_d r$$

Steady state : $\frac{\nabla r}{\nabla t} = 0$

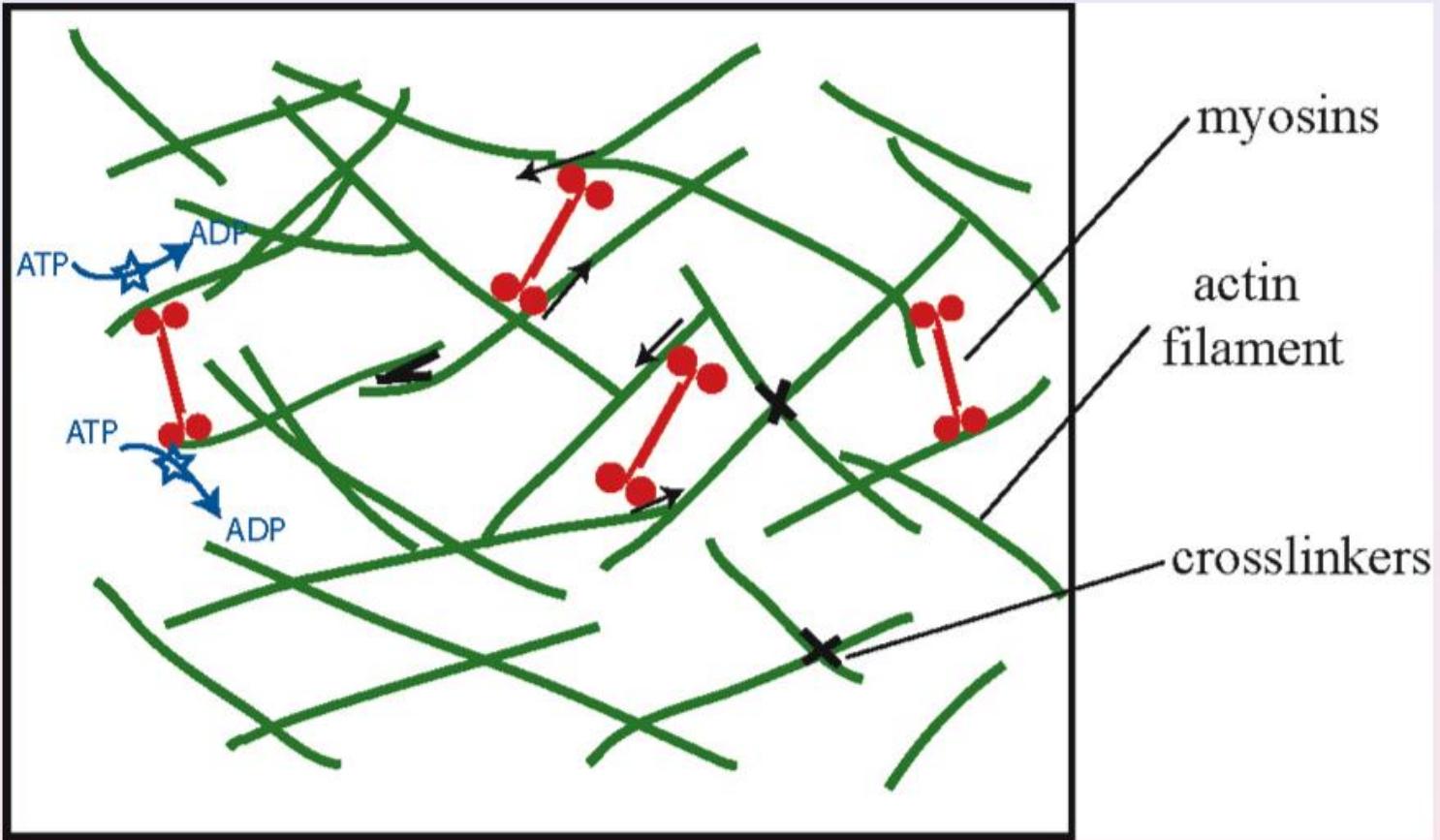
Homogeneous layer :

$$\frac{d(r v_z)}{dz} = - k r$$

Take for granted : $v_z = v_p$

Then :

$$r = r_0 \exp(-z/l) \quad \text{with : } l = v_p / k_d$$



Many microscopic mechanisms

Two component description
(Homogeneous myosin distribution)

A. Callan Jones, F. Jülicher

$$v \neq v_p$$

$$\tilde{J} = r(\tilde{v} - \tilde{v}_B) = -\lfloor \nabla \tilde{m} + \lfloor' \nabla \cdot \tilde{\zeta}^g + \lfloor'' \nabla Dm$$

$$\tilde{\zeta}^g = 2h^g (\nabla \tilde{v})_d + Z(r) Dm; \quad t = \frac{h^g}{Z Dm} (= T_a)$$

$$\frac{r}{\lfloor'} (v_z - v_{z,B}) = -\nabla_z m^{eff} + h^g \frac{d^2 v_z}{dz^2} \quad m^{eff} = ar + br^2 + gr^3 + dr^4 + \dots$$

band / or g < 0

Permeation versus gel viscosity

$$\frac{r}{L'} (\nu_z - \nu_{z,B}) = - \nabla_z m^{eff} + h^g \frac{d^2 \nu_z}{dz^2} \quad \nu_{z,B} \equiv 0 \quad \frac{r}{L'} \square \frac{h_s}{\chi^2}$$

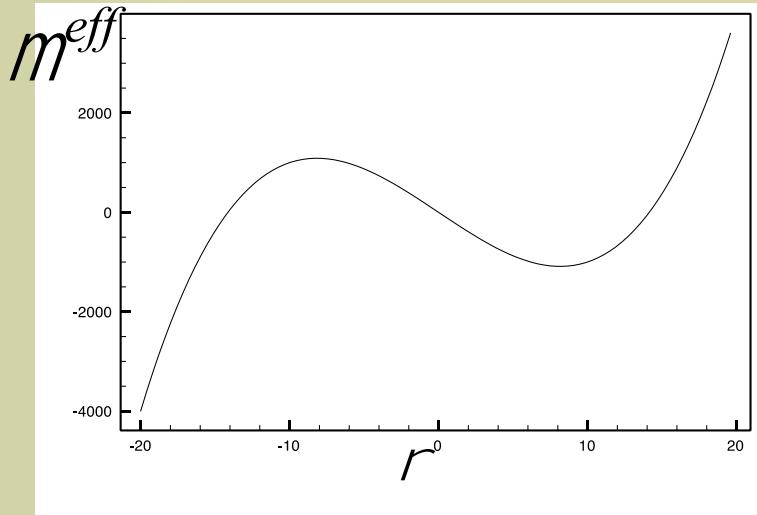
$$l = \sqrt{\frac{h^g}{h^s}} \chi \quad \chi \square 10 \text{ nm} \quad h^g \square 10^5 \text{ Ps} \quad h^s \square 10^{-3} \text{ Ps} \quad l \square 100 \text{ mm}$$

$$m + h^g \frac{d\nu_z}{dz} \square const$$

+ Conservation equation : $\frac{d(r\nu_z)}{dz} = - k_d r$

+ boundary condition : $r(z=0)\nu(z=0) = r_0 \nu_p$

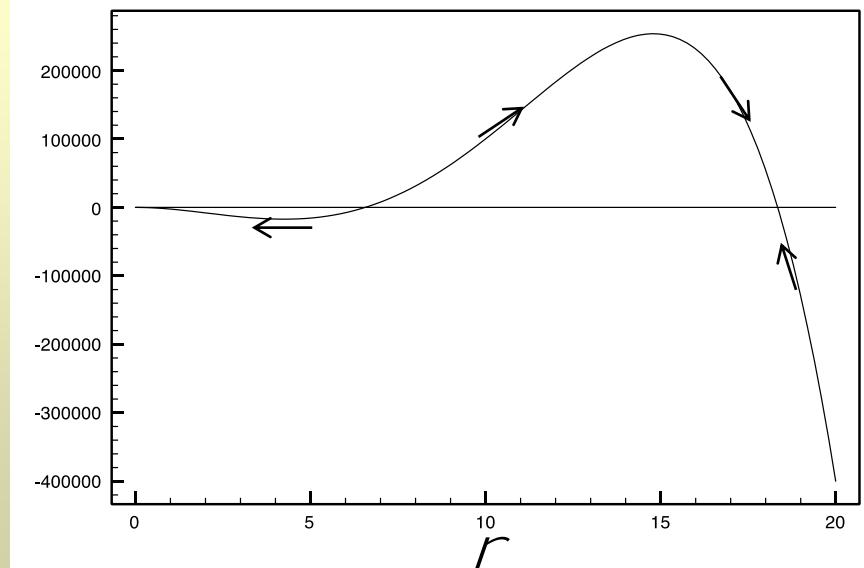
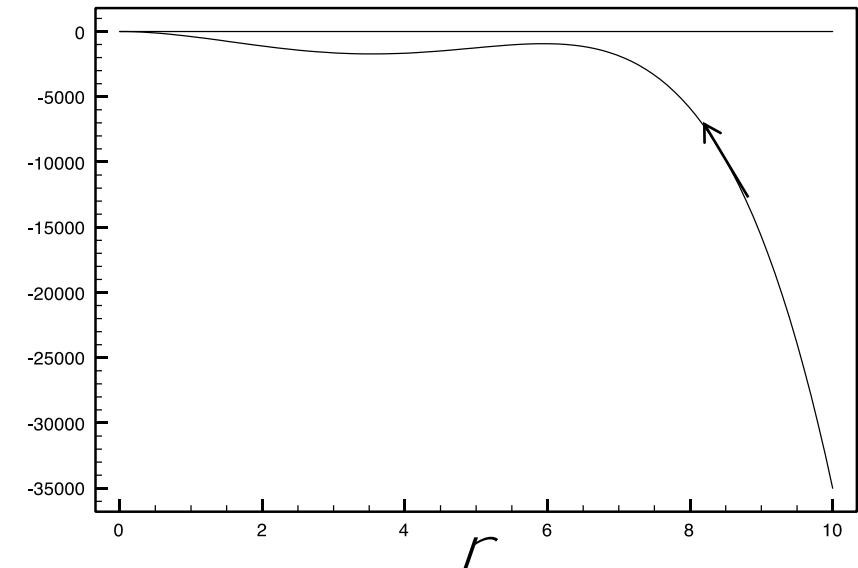
Condensation/wetting transition:



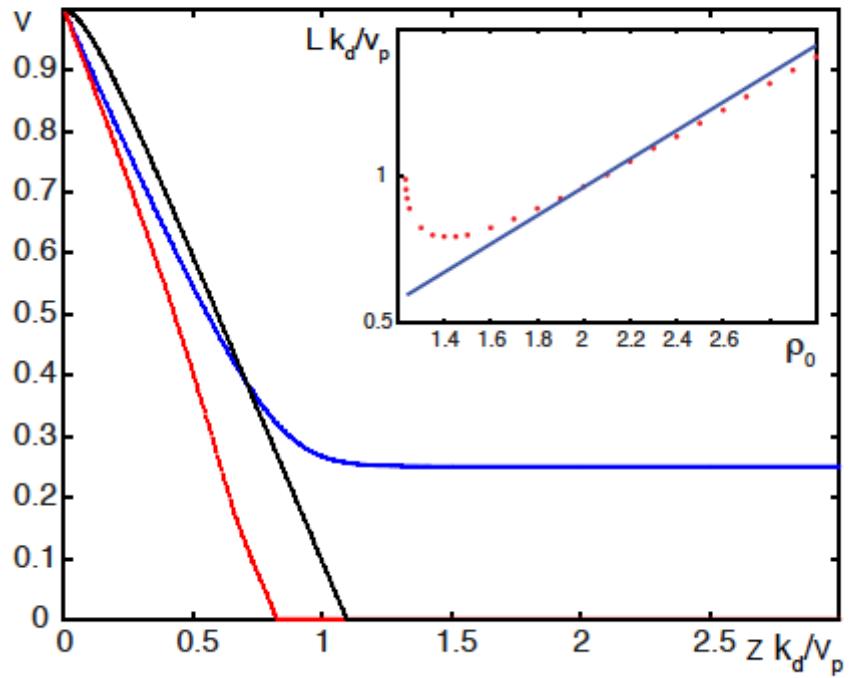
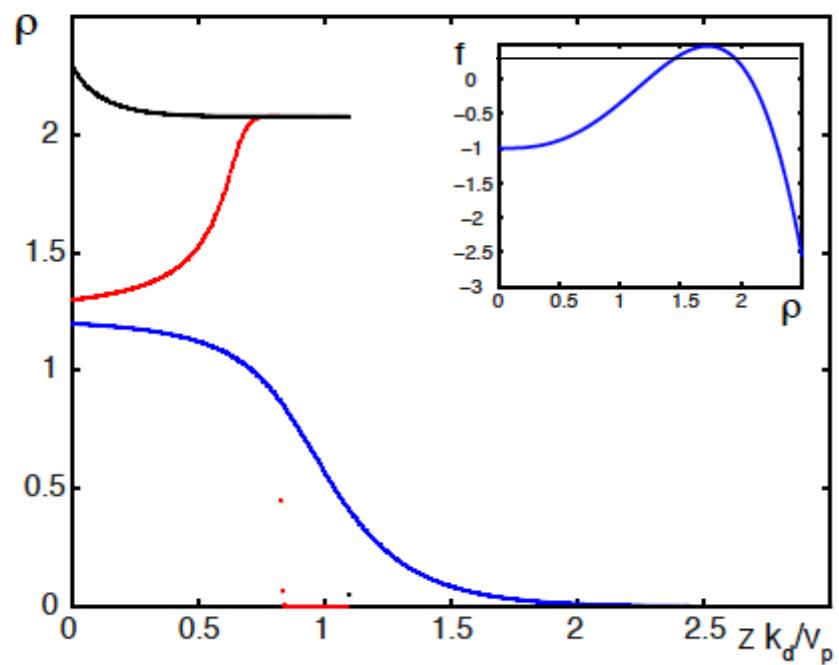
$$\frac{d\rho}{dz} = \frac{1}{\rho_0 \eta v_p} \rho^2 f(\rho) \exp \left\{ \int_{\rho_0}^{\rho} \frac{k_d \eta}{\rho' f(\rho')} d\rho' \right\}$$

$$v = \frac{\rho_0}{\rho} v_p \exp \left\{ - \int_{\rho_0}^{\rho} \frac{k_d \eta}{\rho' f(\rho')} d\rho' \right\}$$

$$r^2 f(r) = - r^2 (k_d h + m^{eff}(r))$$



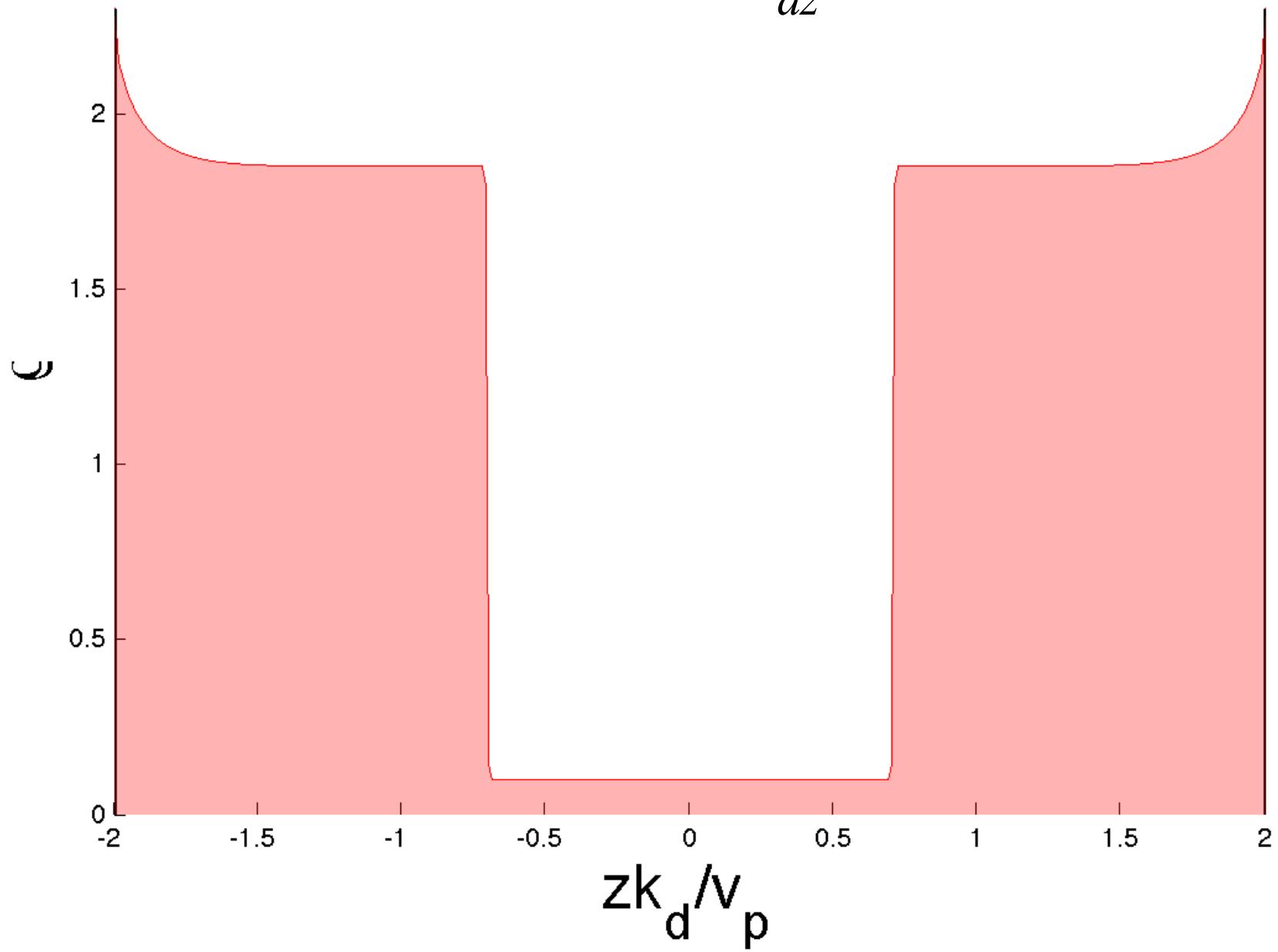
$$e = v_p / \bar{k}_d(r)$$

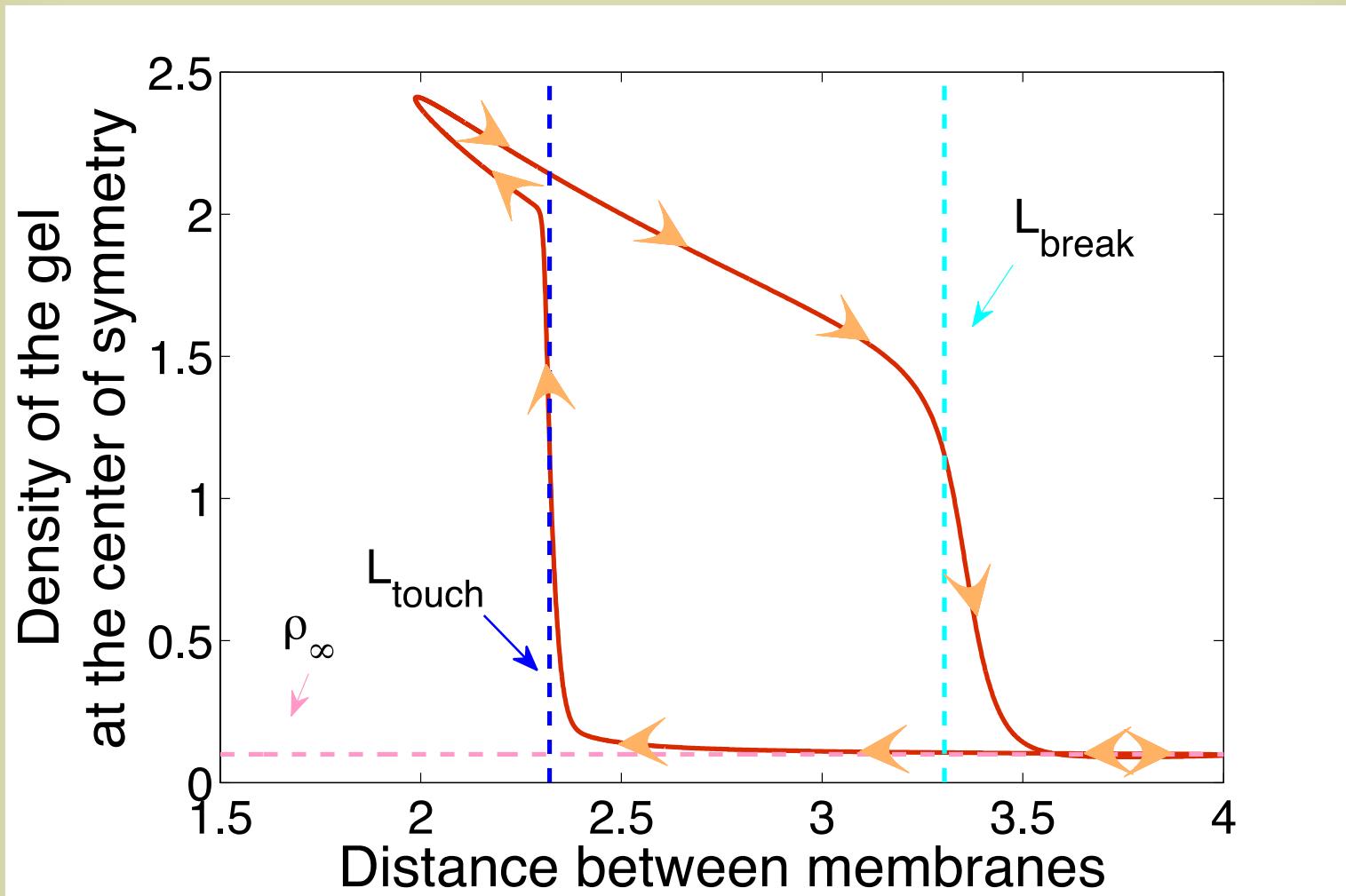


Active wetting transition

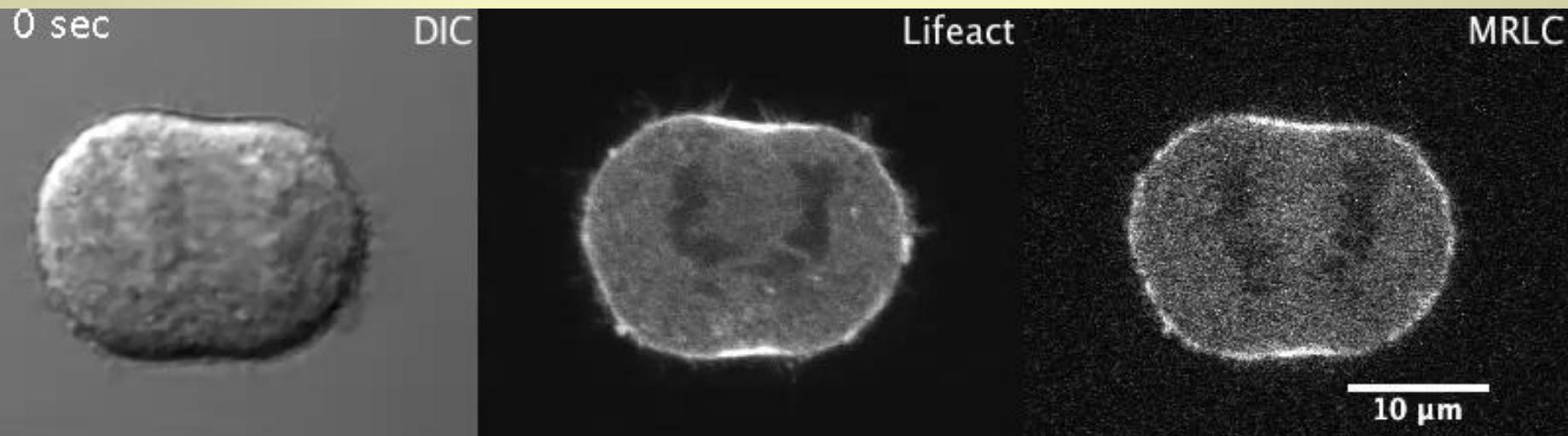
Symmetric case + bulk polymerization

+ Conservation equation : $\frac{d(rv_z)}{dz} = -k_d(r - r_{\pm})$





Cytokinesis



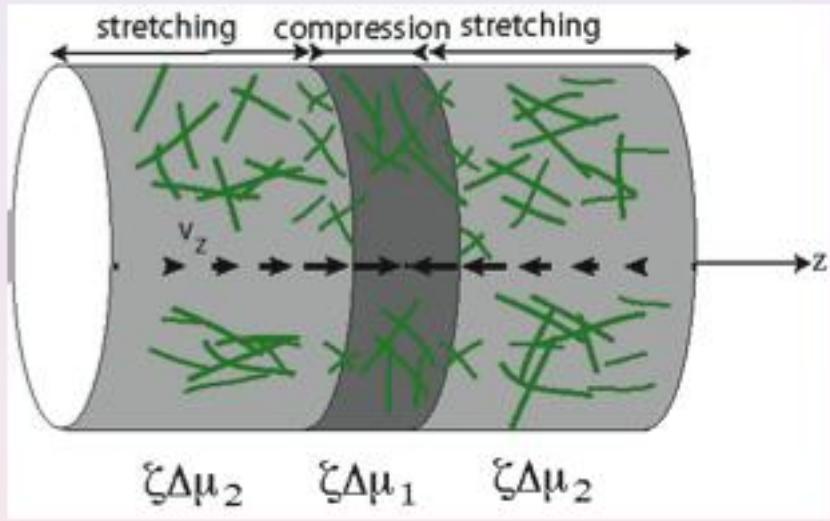
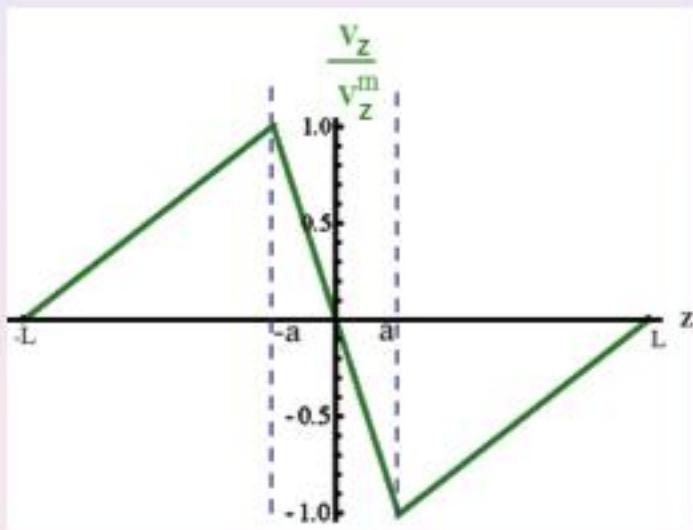
L929 Cell, myosin GFP, J. Sedzinski, E. Paluch

Challenges

- Orientation pattern and flow
- Cell division failure
- Constriction dynamics (non monotonous)
- Constriction time independent of initial size
- Constriction speed decreases when turn over increases

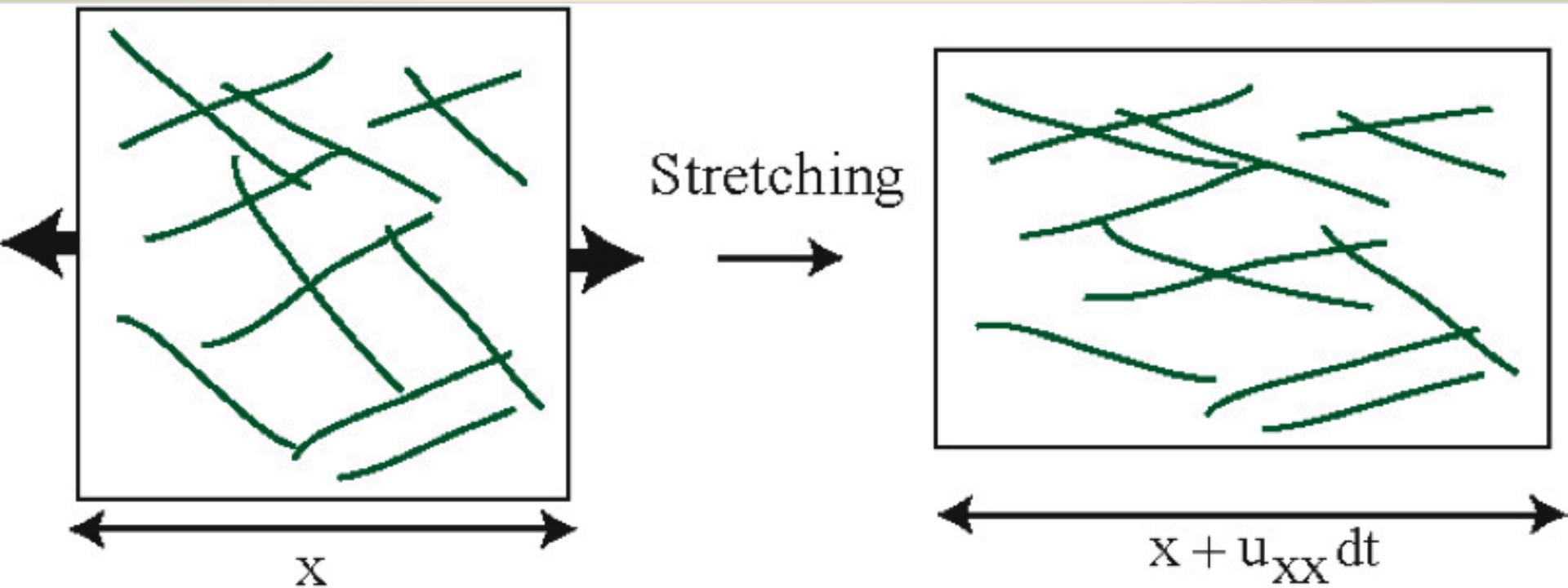
Facts: Myosin and Actin densities constant
Width of extra contractility scales with size

Results

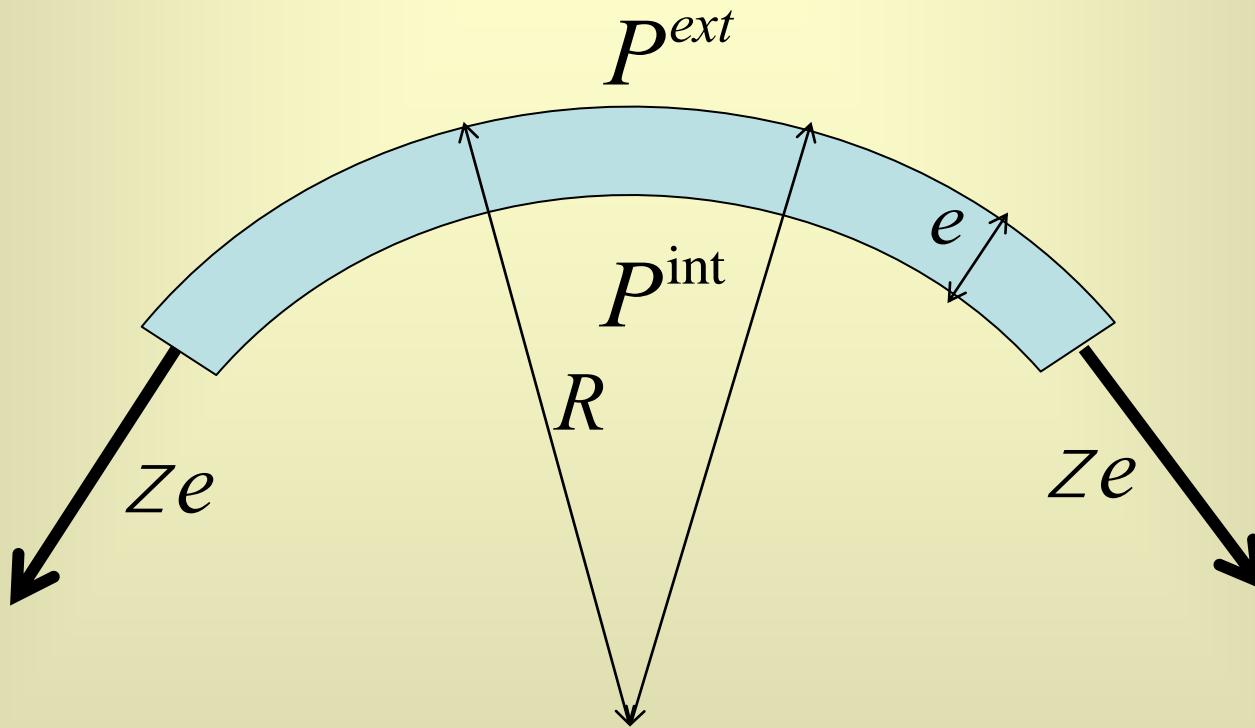


$$\text{Maximal speed } v_m = \frac{(\zeta\Delta\mu_1 - \zeta\Delta\mu_2)a}{8\eta + \beta_1^2\beta_2}$$

Actin : $a = 0$



Contractility provides 2d tension



Laplace's Law

$$P^{int} - P^{ext} = \frac{2g^{eff}}{R} = \frac{2ZDme}{R}$$

Contractility generates flow

Simple balance:

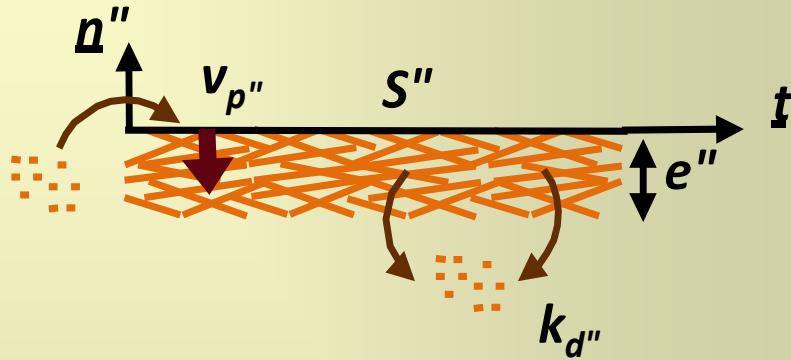
Gel conservation law

$$\frac{\partial e}{\partial t} + \vec{\nabla}_{\wedge} \cdot (e \vec{v}_{\wedge}) = -\bar{k}_d e + v_p$$



Stationary thickness :

$$e_0 = \frac{v_p}{\bar{k}_d}$$

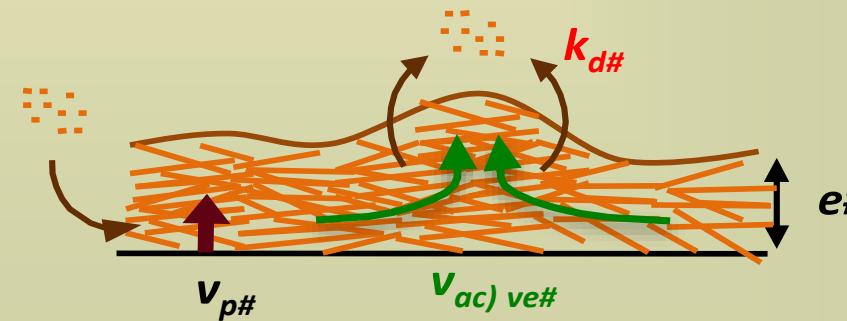


Intrinsic instability in active viscous thin layers :

$$\text{Flow time : } t = \frac{h}{z D m}$$

unstable if : $t k_d < 1$

Cortex renewal time : k_d^{-1}



Hervé Turlier, Basile Audoly

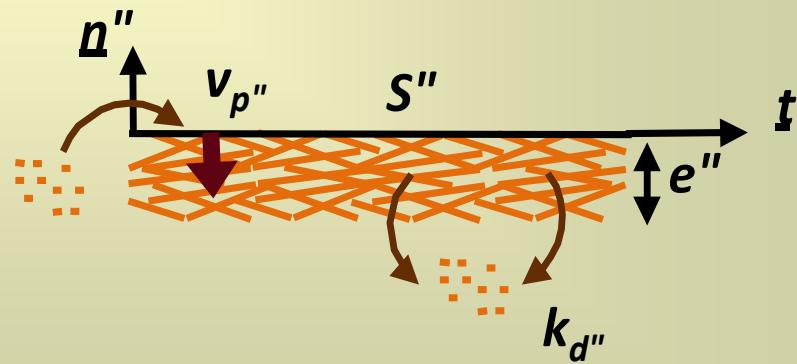
2d curvilinear contractile fluid

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

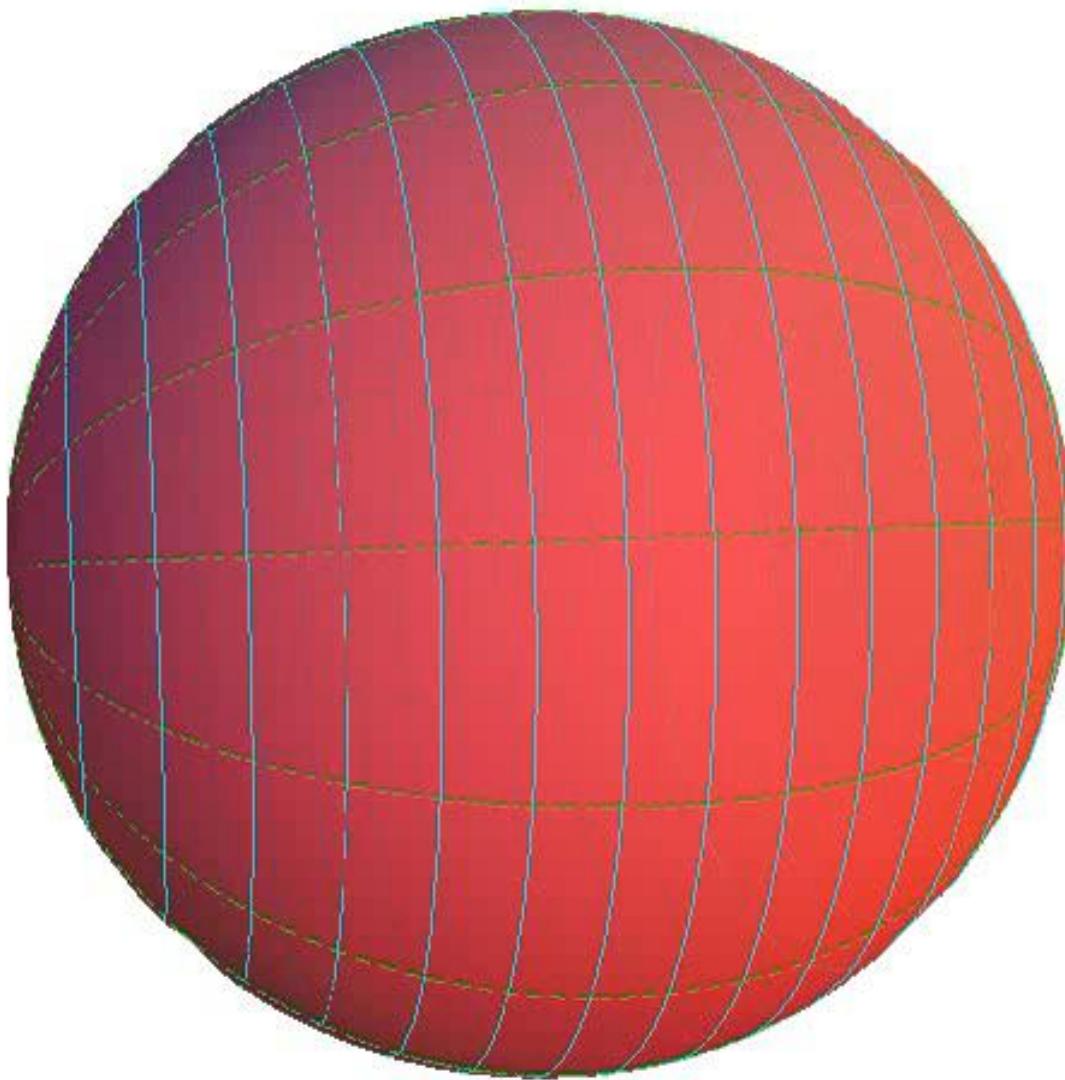
Laplace's Law

Gel conservation :

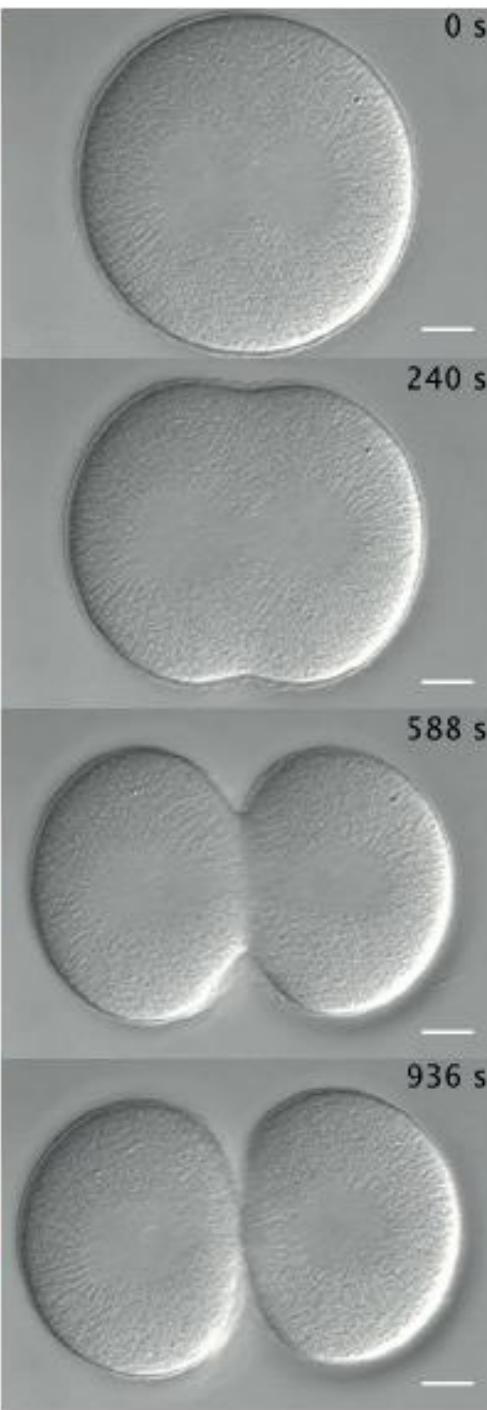
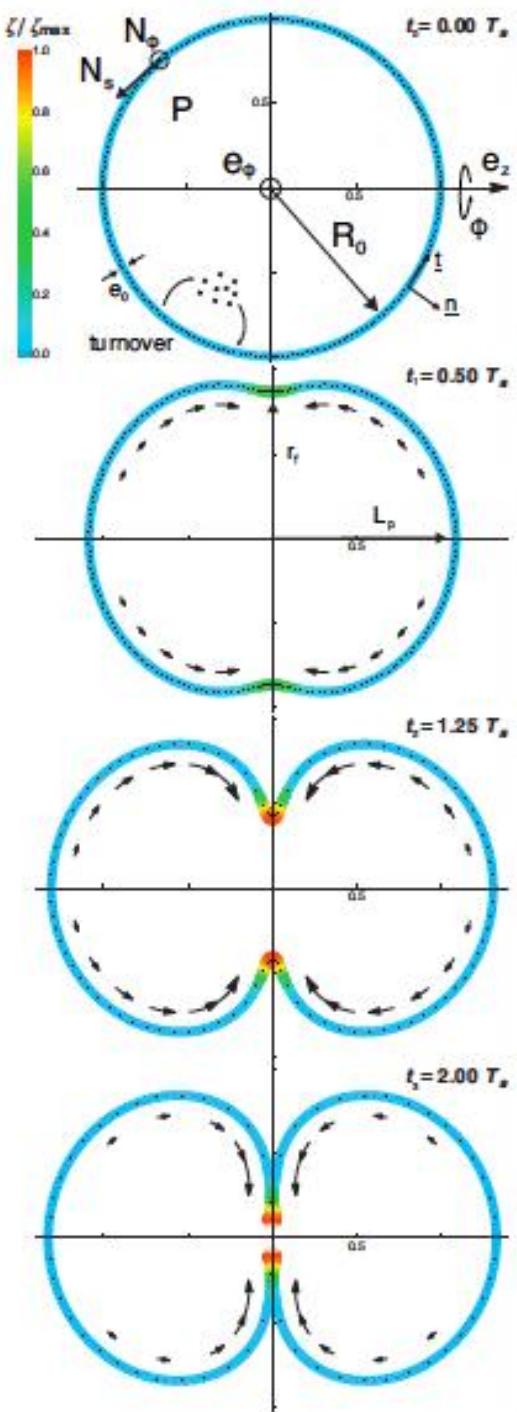
$$\frac{d(a e)}{dt} = -k_d a e + v_p a.$$



0.00 Ta

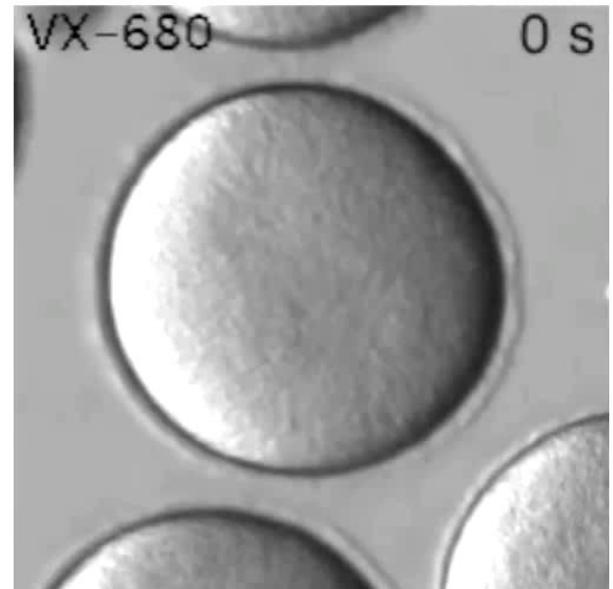
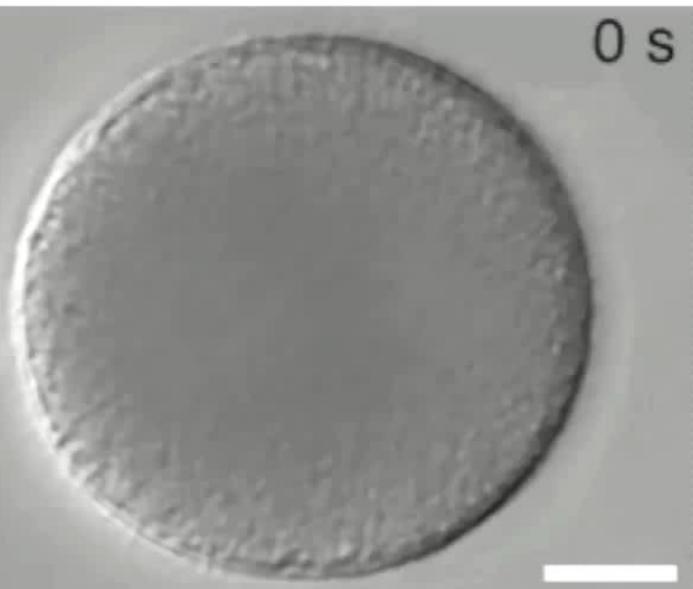
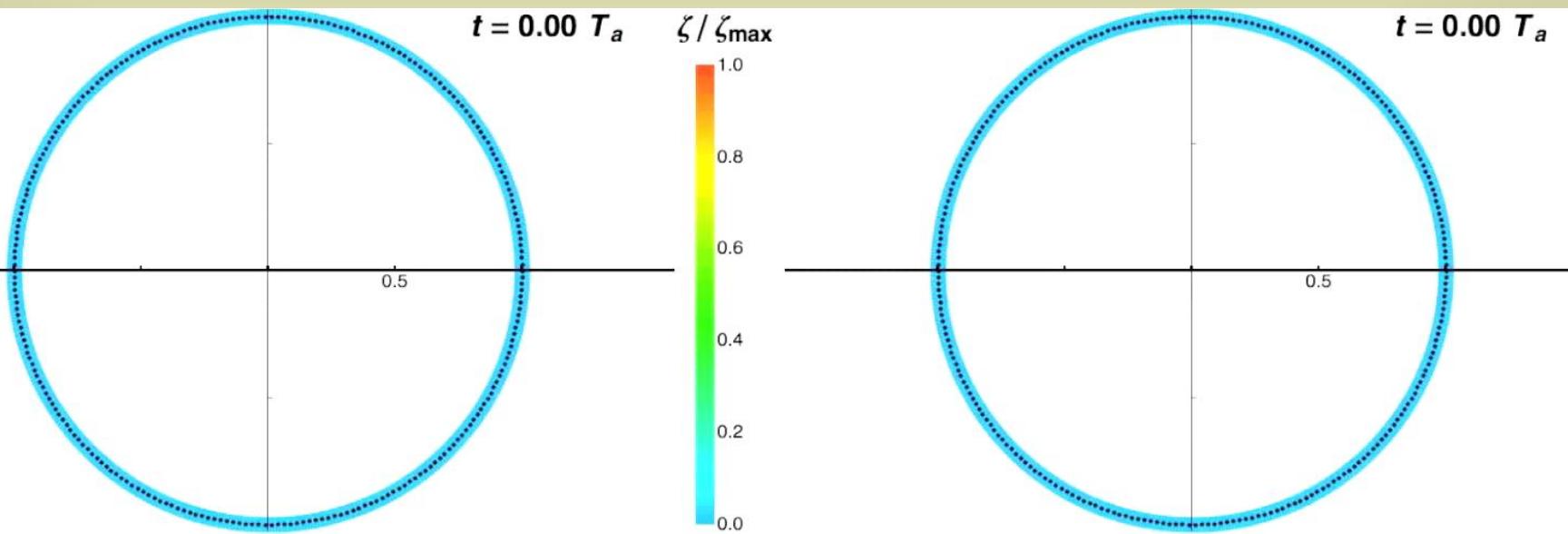


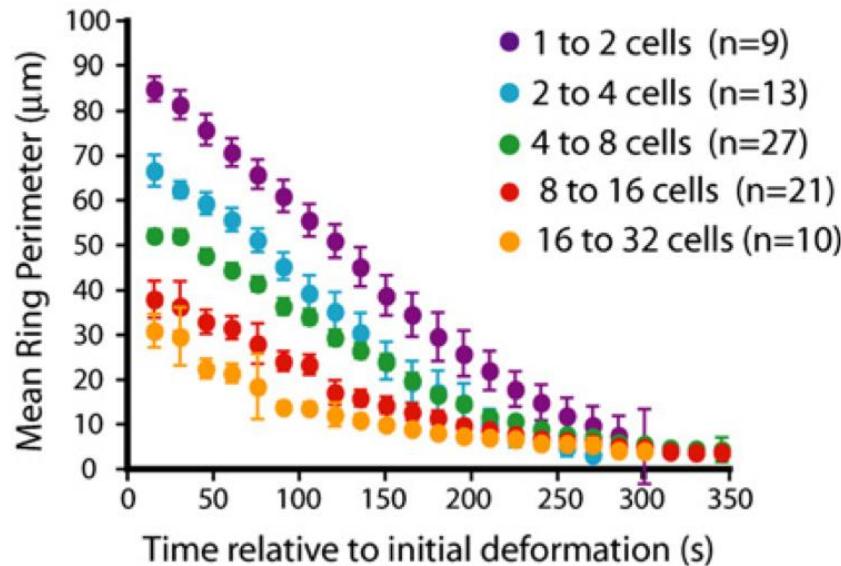
MovieS4



Sand-dollar zygote
G Von Dassow

Cell division success/failure





Carvalho A, Desai A, Oegema K (2009) Structural memory in the contractile ring makes the duration of cytokinesis independent of cell size. *Cell* 137(5):926–937.

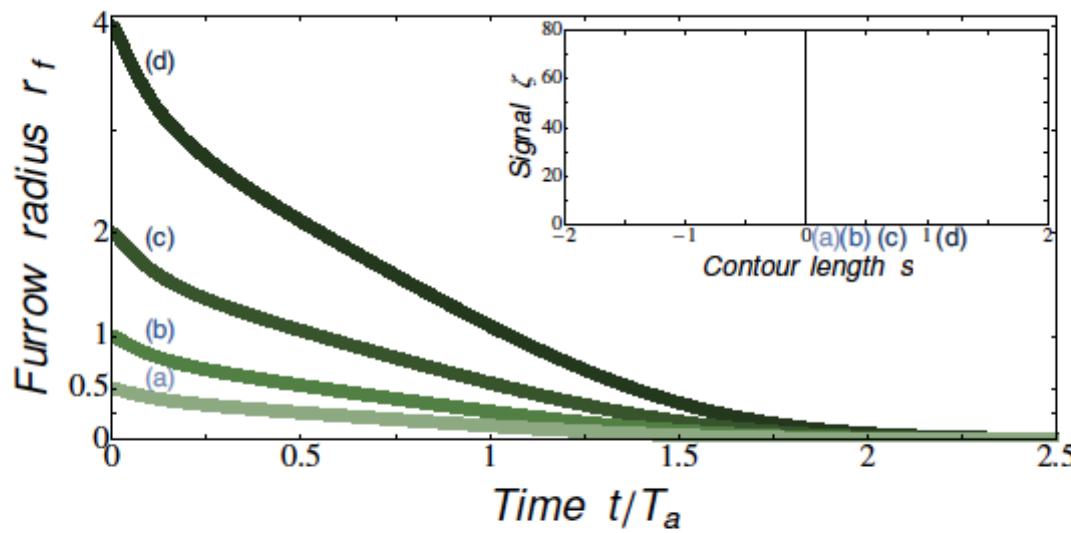
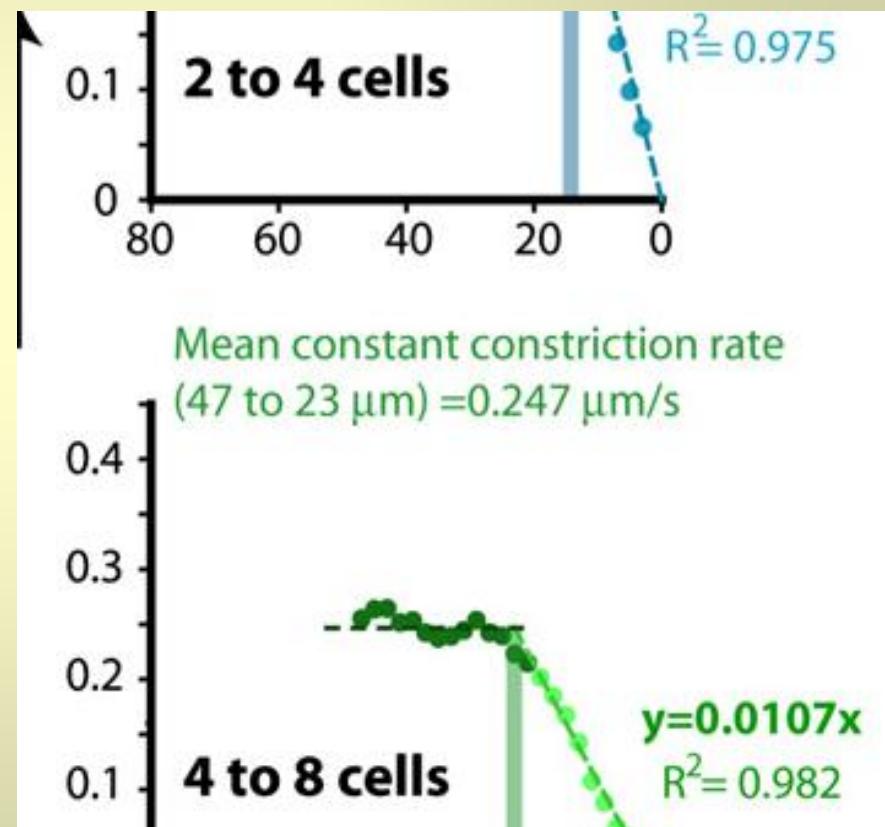
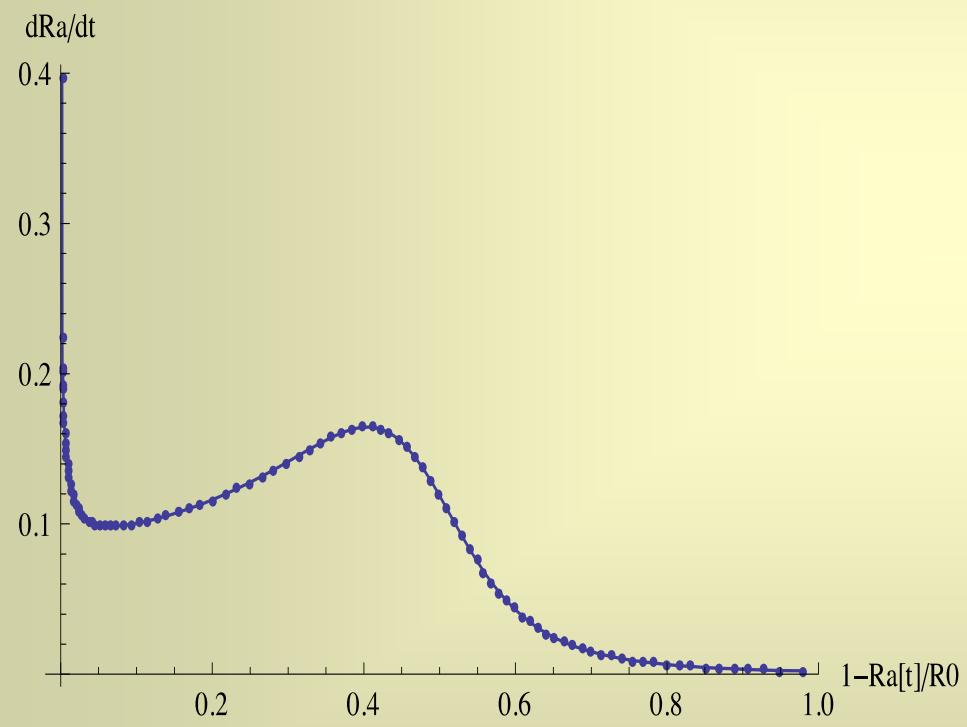
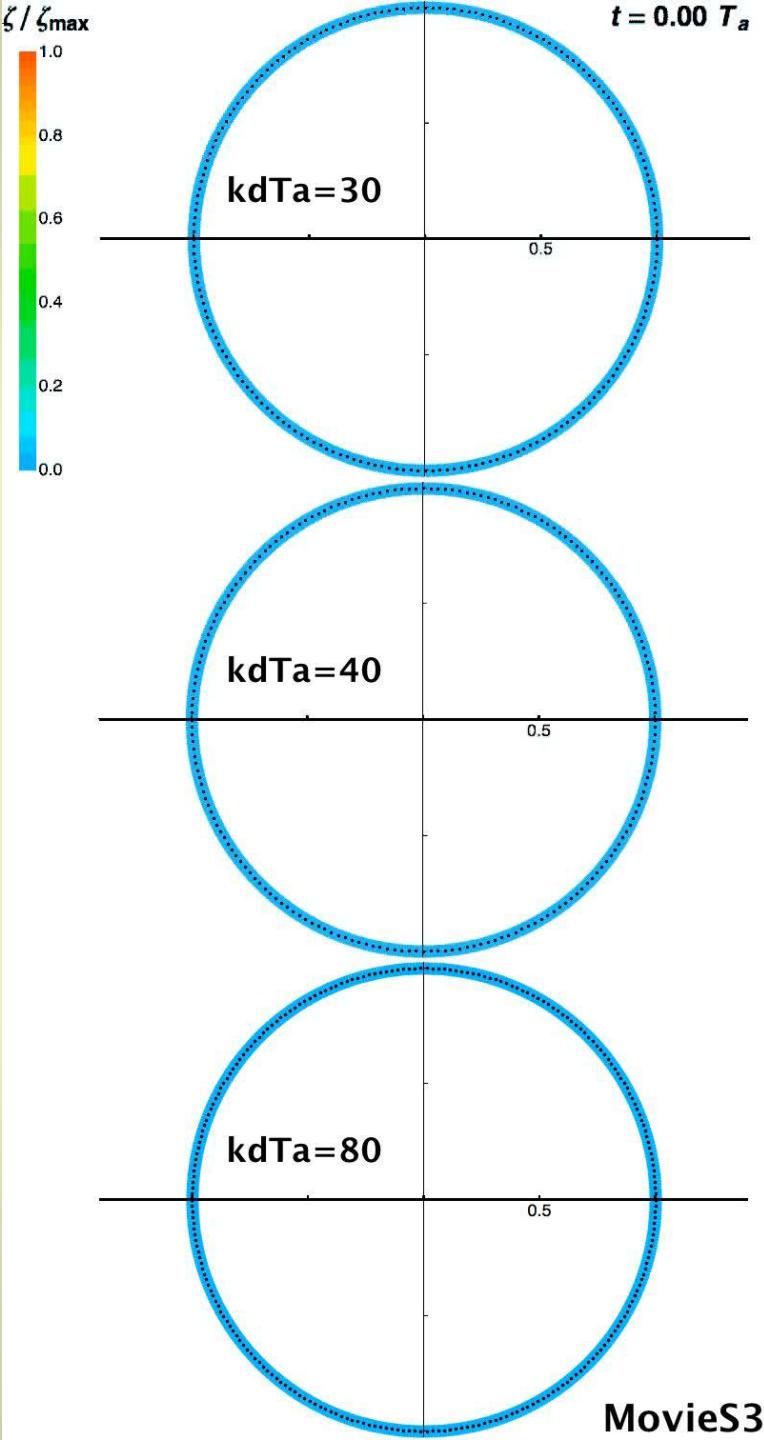


Fig. 5. Cytokinesis duration is independent of initial cell size: Furrow radius r_f as a function of time t/T_a for four initial cell radii $R_0 = 0.5, 1, 2$ and 4 . (Inset) Corresponding activity signals of width proportional to R_0 , plotted as a function of the contour length s .

Non monotonic constriction rate



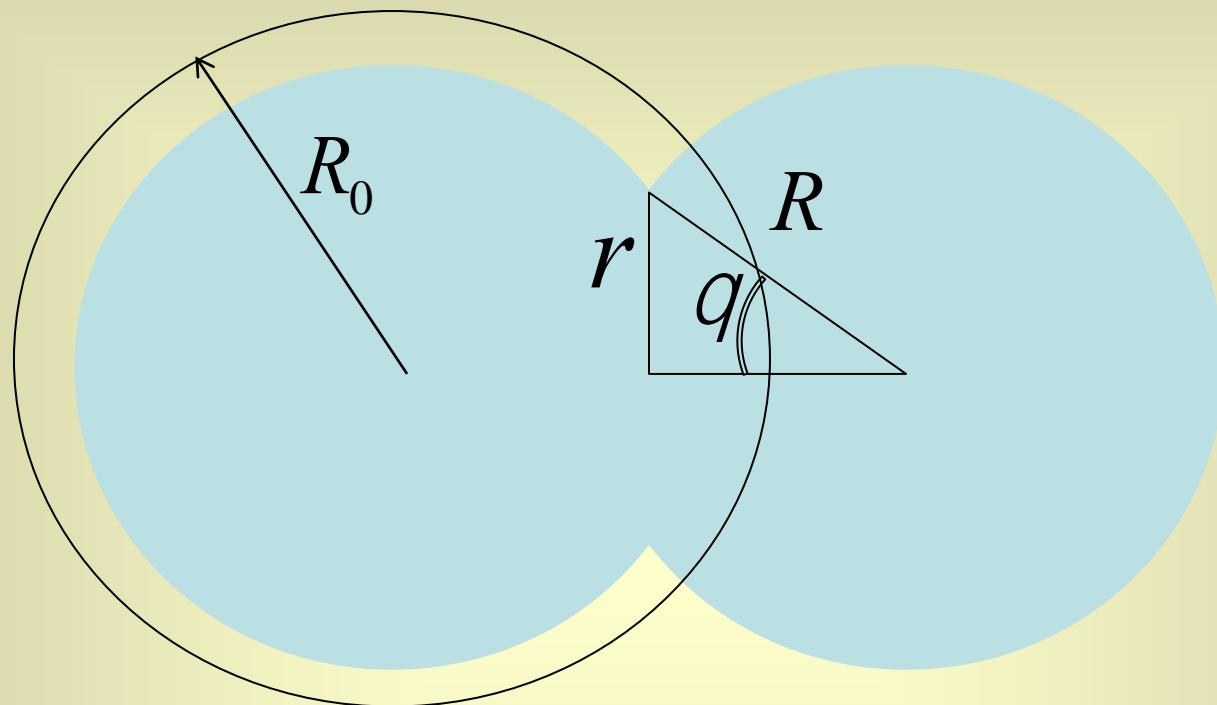
Changing turnover



MovieS3

$$g_a = \int_{-\infty}^{+\infty} (Z Dm e - Z^\infty Dm e^\infty) ds$$

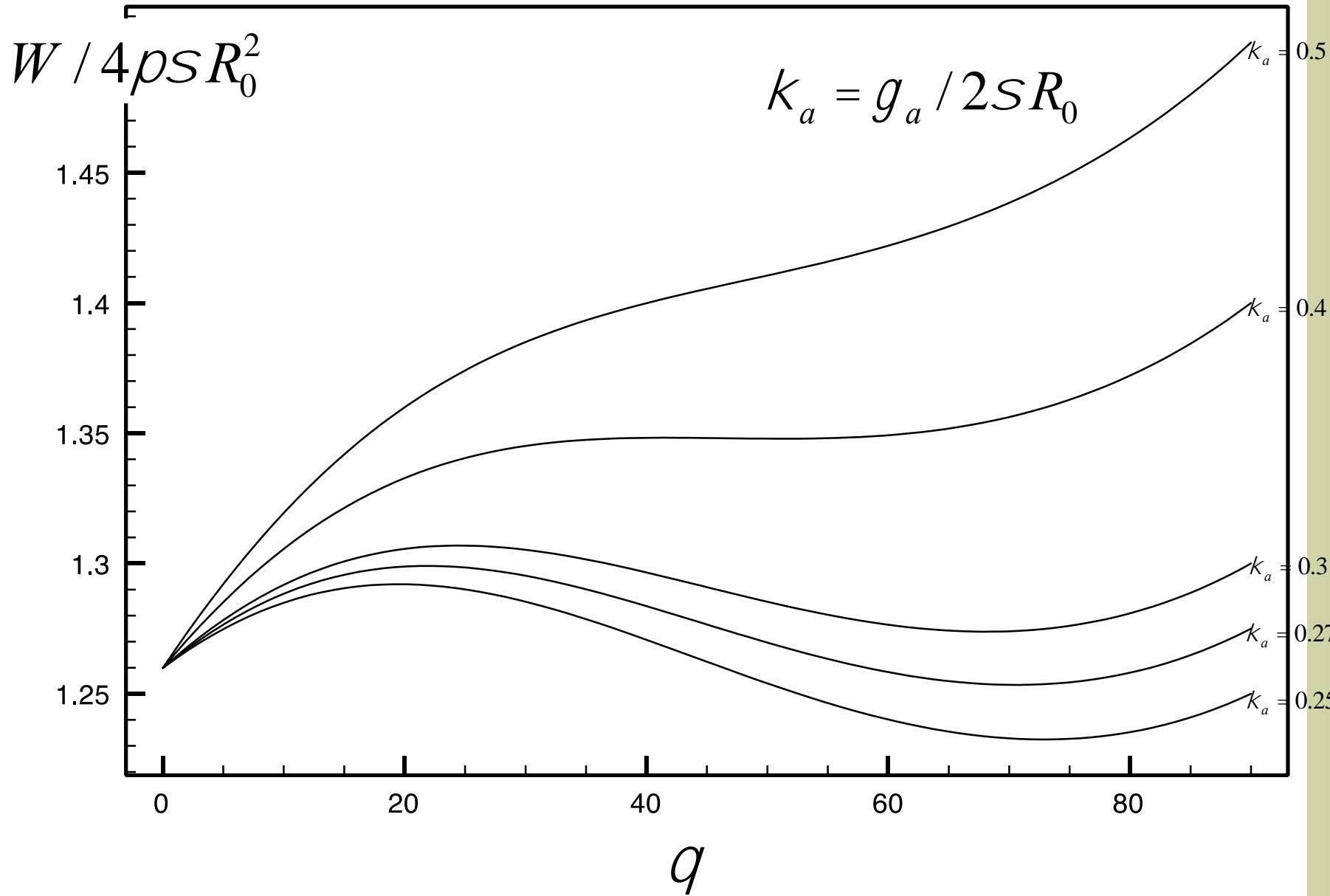
$$W = 2\rho g_a r + 2S A_R$$



$$\frac{W}{4\rho S R_0^2} = \frac{1 + \cos q}{(1 + \frac{3}{2} \cos q - \frac{1}{2} \cos^3 q)^{2/3}} + k_a \frac{\sin q}{(1 + \frac{3}{2} \cos q - \frac{1}{2} \cos^3 q)^{1/3}}$$

Marsland D, J Cell and comp Physiology 1950
Yoneda M and Dan K, J Exp Bio 1972

$$k_a = g_a / 2S R_0$$



Why division time independent of initial size?

Dissipation due to cortex "viscosity":

$$h \left(\frac{1}{R} \frac{dr}{dt} \right)^2 2A_r e$$

Work done upon contraction per unit time:

$$\frac{\partial W}{\partial r} \frac{dr}{dt}$$

Area: $2A_r = \frac{4\rho R_0^2 (1 + \cos q)}{\left(1 + \frac{3}{2} \cos q - \frac{1}{2} \cos^3 q\right)^{2/3}}$

$$k_a = g_a / 2S R_0$$

$$\frac{d \sin q}{d(t/t)} = g(k_a, q)$$

$$q = h(k_a, t/t)$$

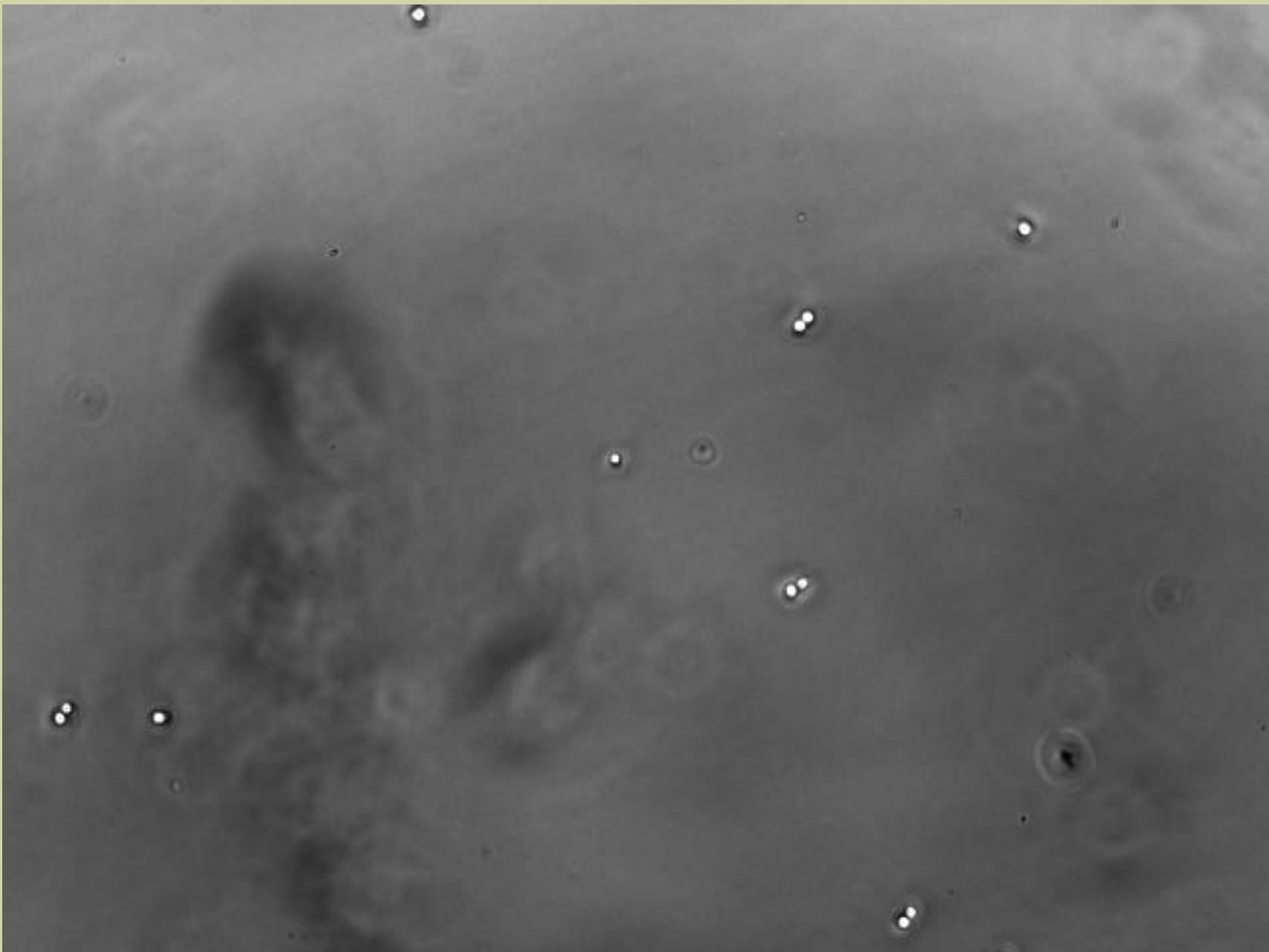
$$t_a = \frac{h}{ZDm} = t_M \frac{E}{ZDm}$$

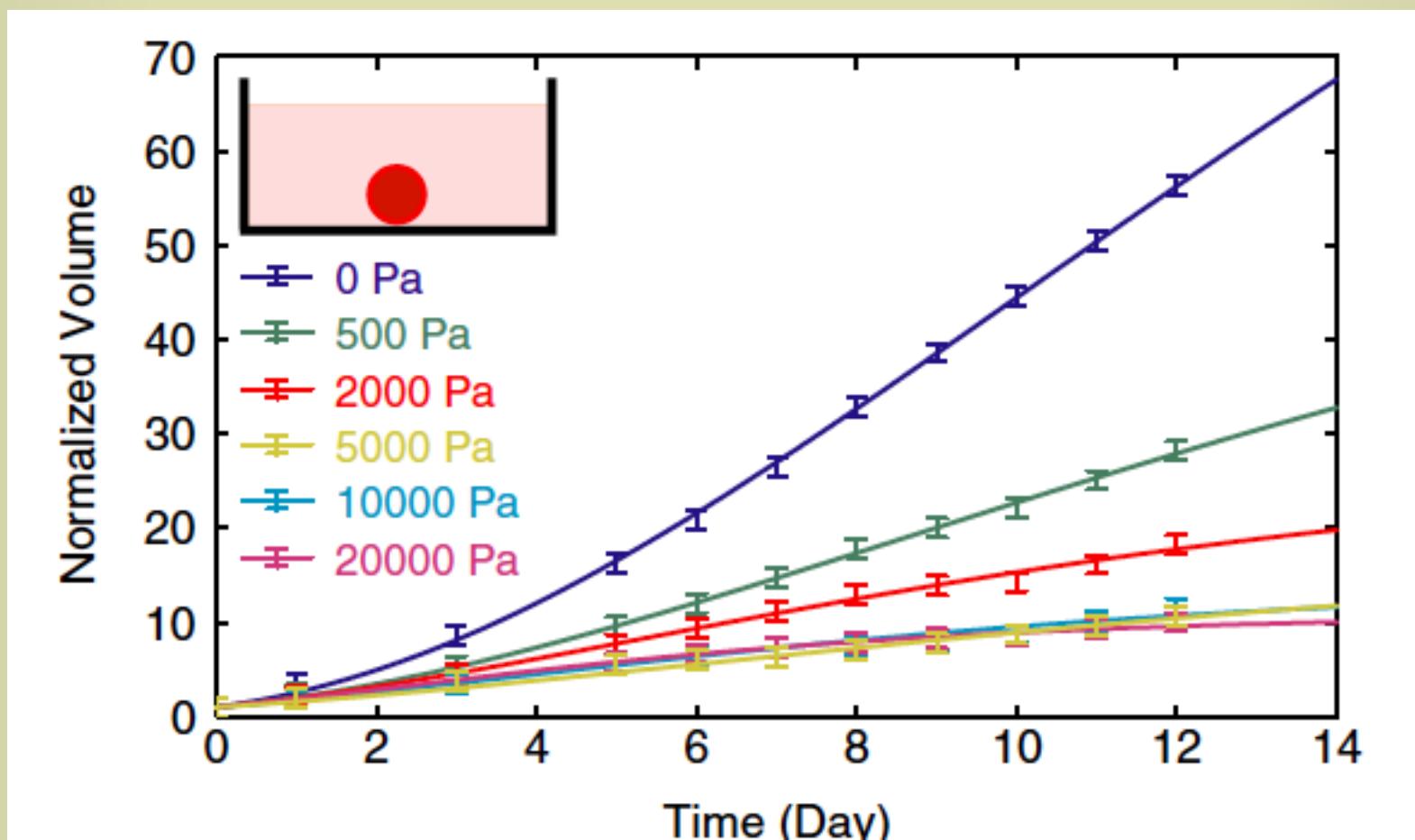
Explains:

- Discontinuous character of the transition
- Constriction time independence if furrow width scales like initial radius
- Correct order of magnitude
- Effect of furrow width at constant extra contractility
- Non monotonic constriction rate
- Slowing down upon increasing turnover

Are Tissues Active?

Colon Carcinoma





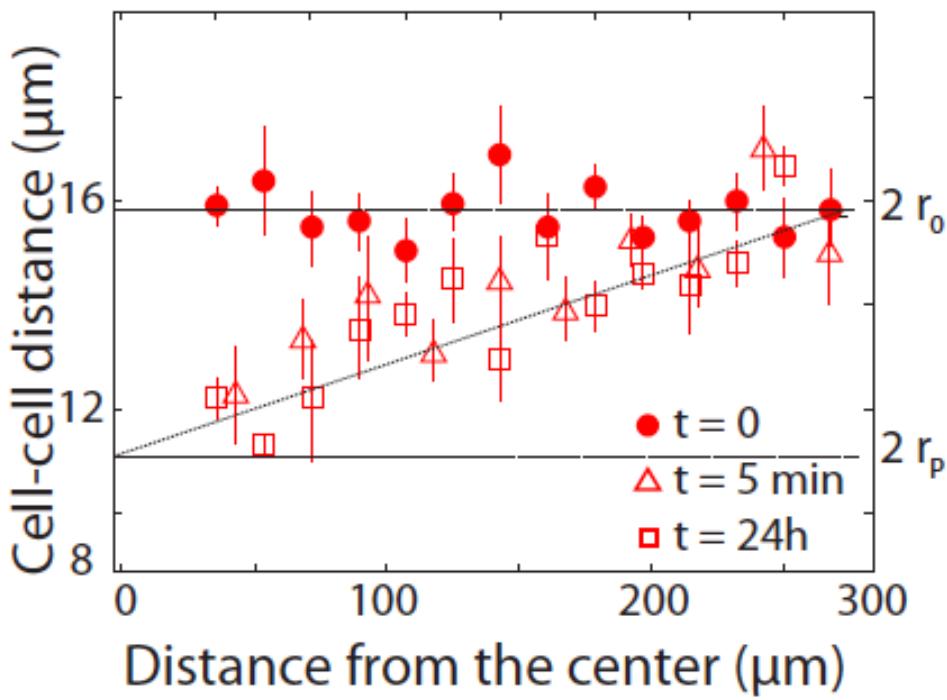


FIG. 3. Cell-cell distance as a function of the distance from the center for different time points: day 0 (\bullet), 5 minutes (\triangle) and day 1 (\square). The error bar obtention is described in the Supplementary Information.

What do we learn?

- Response time < 5 min

$$t_{resp} = t_M \left(\frac{R}{l}\right)^2 \quad \rightarrow \quad l = R \sqrt{\frac{t_M}{t_{resp}}} \quad \rightarrow \quad l \geq 2\text{cm}$$

- Deformation stable for one day

OK with : $t \square 2$ days

- Deformation maximum in the center

Requires anisotropy:

$$S_{ij} = \text{usual terms} + V(P)n_i n_j \quad \text{like cortex : active matter}$$

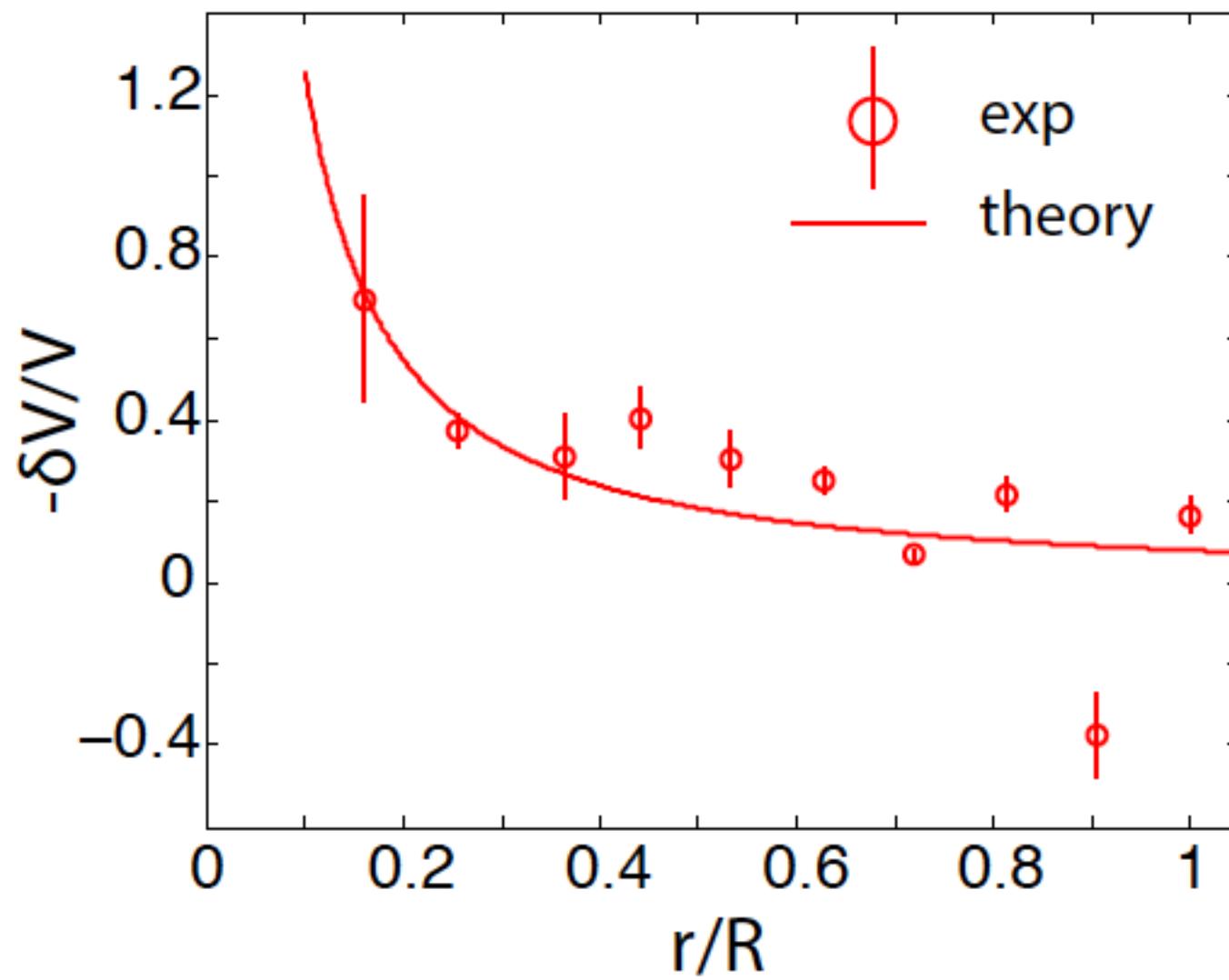
$$\left(1+\tau_t\frac{D}{Dt}\right)(\tilde{\sigma}_{\alpha\beta}~-~\zeta\Delta\mu q_{\alpha\beta})=2\eta \tilde{v}_{\alpha\beta}$$

$$k_d-k_a\simeq \bar{\eta}^{-1}(P_h-P+\nu\tilde{\sigma}_{\alpha\beta}q_{\alpha\beta})$$

$$\zeta\Delta\mu=\zeta_0\Delta\mu+\zeta_1\Delta\mu(P-P_h)$$

$$-\frac{dV}{V}=\frac{\delta n}{n}=\frac{\Delta P(3+\beta_e)}{K(3+\beta_e)(1-\frac{2}{3}\zeta_1\Delta\mu)+\frac{4}{3}(\beta_eG)}\left(\frac{r}{R_0}\right)^{\beta_e}$$

$$b_e = \frac{2 Z_1 Dm}{1 - \frac{2}{3} Z_1 Dm + \frac{4 G}{3 K}}$$



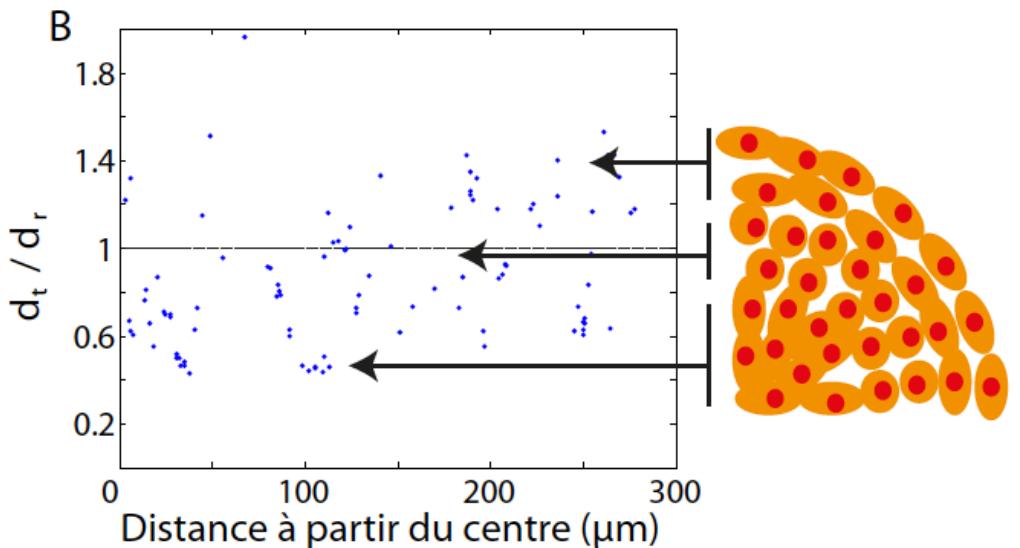
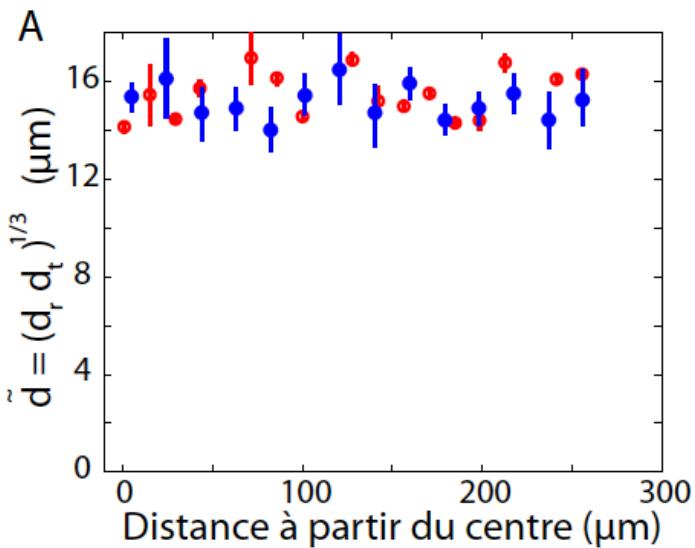


FIGURE 2.11 – Étude de l'anisotropie pouvant exister dans les sphéroïdes de HT29 sans contrainte mécanique. A : le diamètre \tilde{d} de la cellule (○ rouge) et le diamètre d (● bleu), B : le rapport entre d_r et d_t . Un schéma de sphéroïde est ajouté : les cellules sont étirées au centre, et allongées au bord.