Dynamical curvature instability controlled by inter-monolayer friction, causing tubule ejection in membranes

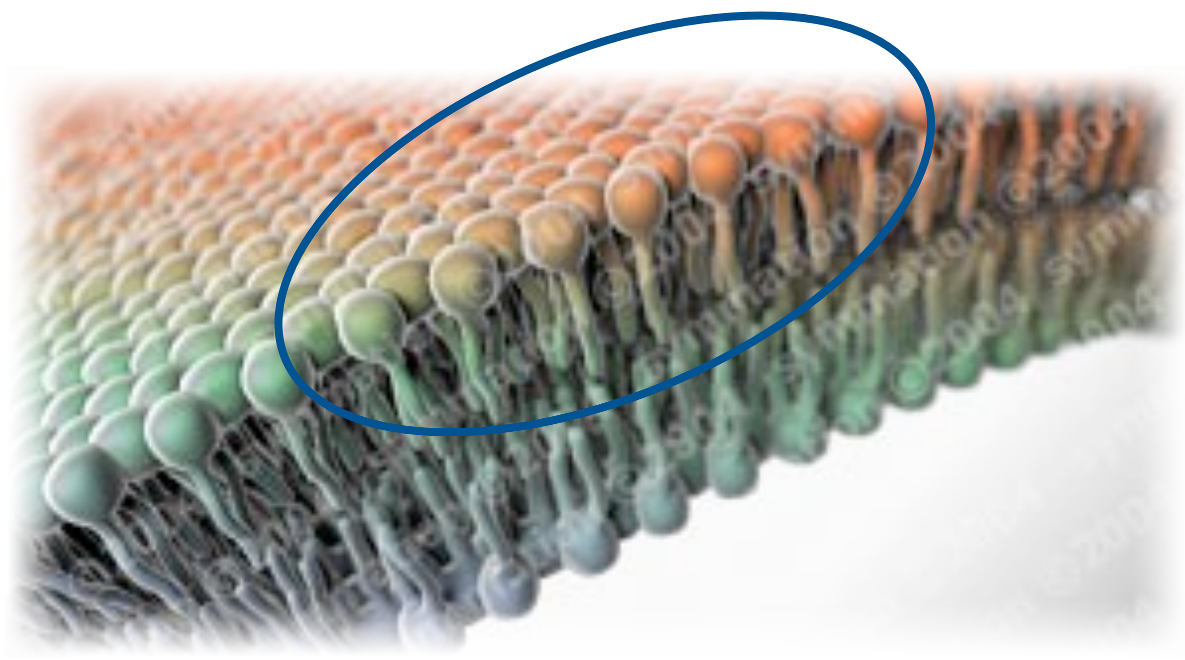
Jean-Baptiste Fournier

Laboratory « Matière et Systèmes Complexes » (MSC),
University Paris Diderot & CNRS,
France.

M. I. Angelova, A.-F. Bitbol, N. Khalifat, L. Peliti, N. Puff

Question :

Instantaneous local modification of the lipids
of one of the two monolayers:
what happens?



e.g., local pH variation.
M. I. Angelova, N. Puff et al.

Outline

1. Review of the elastic and dynamical models of membranes and monolayers.

2. Experiment by M. I. Angelova, N. Puff et al.

3. Theory of the curvature instability caused by a local modification of the lipids of one of the monolayers

4. Comparison with the pH-micropipette experiment of M. I. Angelova, N. Puff et al.

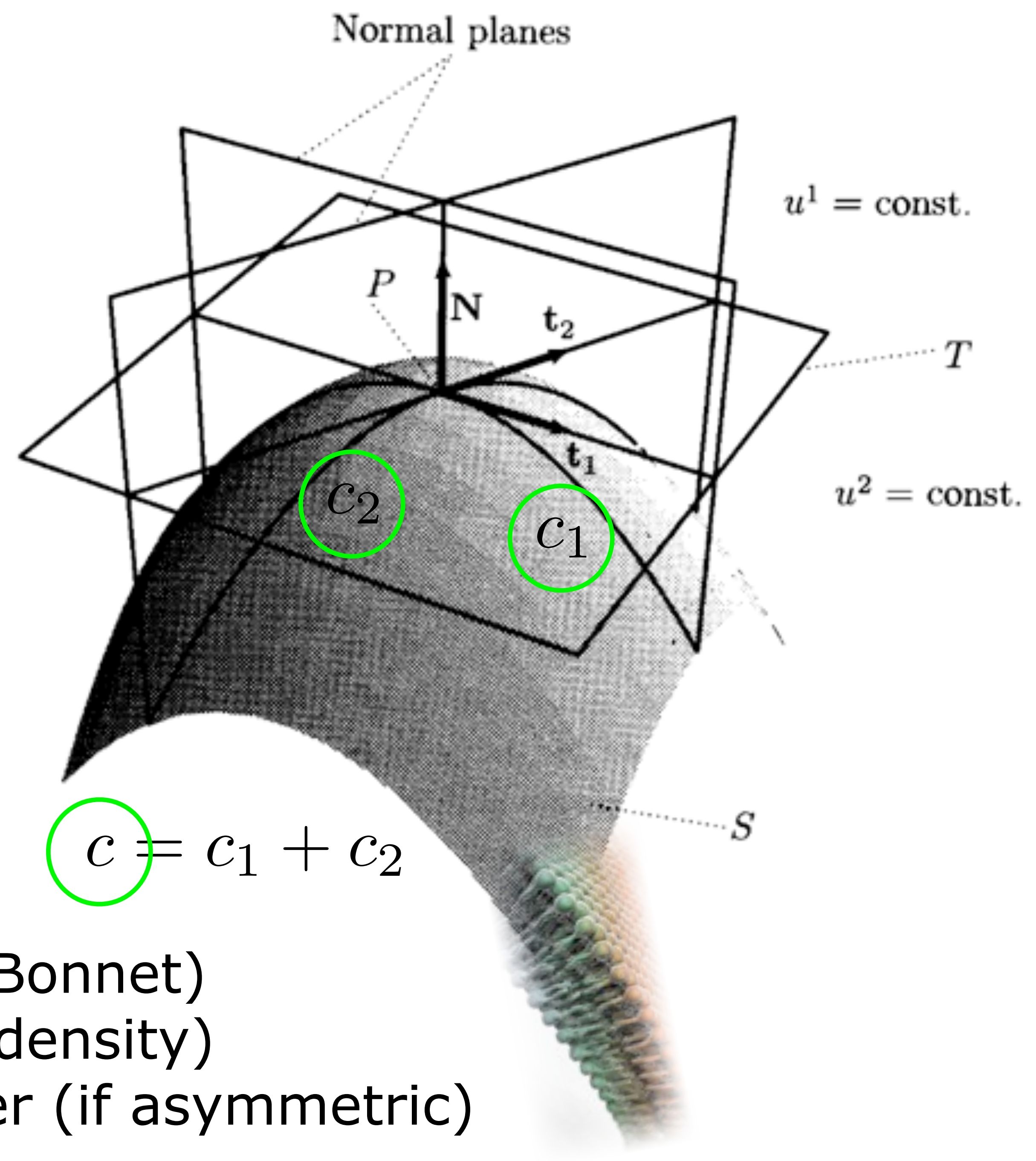
5. Non-linear development : tubule ejection

Helfrich model

P. Canham (1970), W. Helfrich (1973)

$$F = \int dA\, f$$

$$f = \sigma_0 + \frac{\kappa}{2} c^2 - \kappa c_0^b c$$



$$c = c_1 + c_2$$

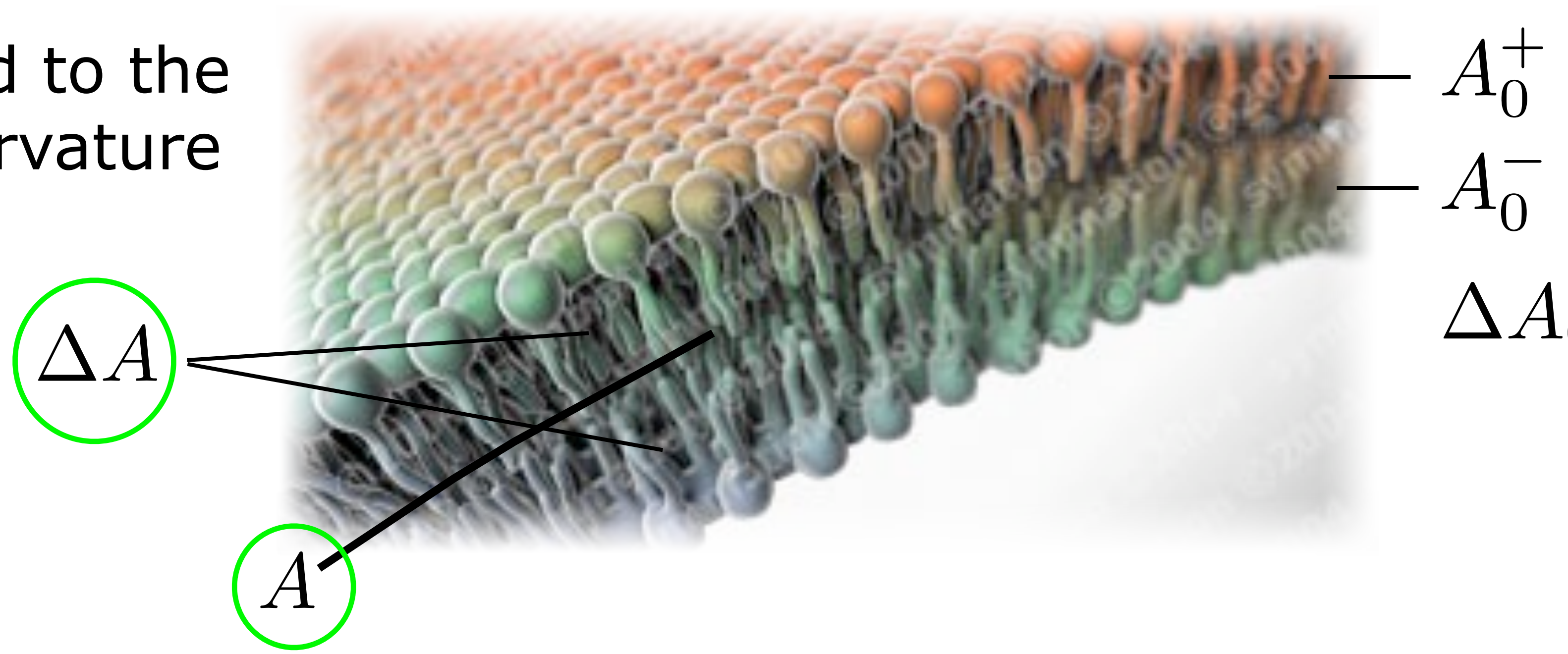
- ✤ Bilayer structure neglected
- ✤ Gaussian term $c_1 c_2$ discarded (Gauss Bonnet)
- ✤ σ_0 sets the area constraint (hides lipid density)
- ✤ c_0^b spontaneous curvature of the bilayer (if asymmetric)

Area Difference Elasticity (ADE) model

S. Svetina & B. Žekš (1989) –
U. Seifert, I. Miao, H.-G. Döbereiner & M. Wortis (1991)

- Lipid density is involved, but in a global manner
- ΔA related to the integrated curvature

Preferred (relaxed) area



$$\Delta A_0 = A_0^+ - A_0^-$$

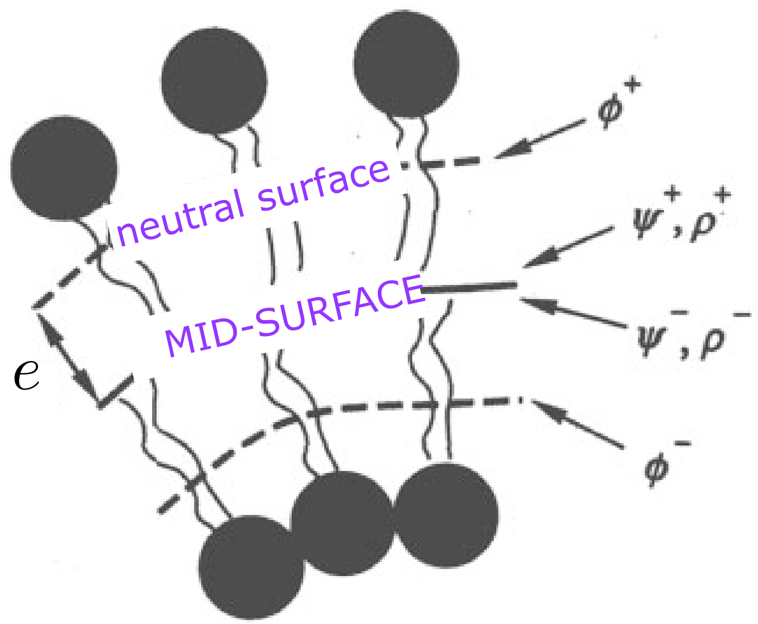
$$F = \int \left(\sigma_0 + \frac{\kappa}{2} c^2 - \kappa c_0^b c \right) dA + \boxed{\frac{k}{4A} \left(\Delta A - \Delta A_0 \right)^2}$$

Fixes $A = (A_0^+ + A_0^-)/2$

Cost to deviate from $\Delta A = \Delta A_0$

Bilayer curvature—density elasticity

U. Seifert & S. A. Langer (1993)



$$\rho = \frac{\text{density on midsurface}}{\text{equilibrium density}} - 1$$

$$F = \int dA \left\{ \frac{\kappa}{2} c^2 + \frac{k}{2} \left[\left(\rho^+ + ec\right)^2 + \left(\rho^- - ec\right)^2 \right] \right\}$$

✤ On the «neutral surface» density and curvature are independent variables (decoupled).
✤ Not if they are defined on the «mid-surface»

✤ Inter-monolayer friction and membrane bending : MID-SURFACE

E. Evans & Y. Yeung (1992)

Bilayer curvature—density elasticity

A.-F. Bitbol, L. Peliti & J.-B. Fournier (2010)

All quantities defined on the MID-SURFACE

$\rho_0 \neq \rho_{\mathrm{eq}}$: reference density

$$r = \frac{\rho - \rho_0}{\rho_0} = \mathcal{O}(\epsilon)\,,$$
$$H = (c_1 + c_2)\, e = \mathcal{O}(\epsilon)\,,$$
$$K = c_1 c_2\, e^2 = \mathcal{O}(\epsilon^2)\,,$$

$$f(r,H,K) = A_0 + A_1 H + A_2 (r+H)^2 + A_3 H^2 + A_4 K + \mathcal{O}(\epsilon^3)$$

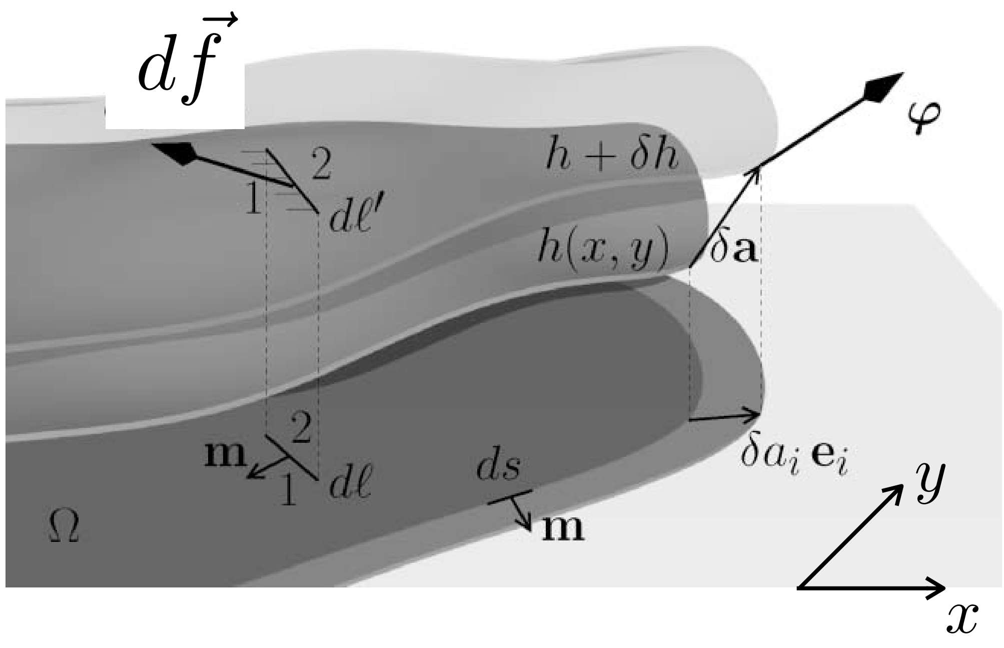
✤ No term $\propto r$: total number of lipids fixed
✤ Coupling term : rH -> sets e
✤ All terms (σ_0) depend on ρ_0

$$\boxed{f^\pm = \frac{\sigma_0}{2} + \frac{\kappa}{4} c^2 \pm \frac{\kappa c_0}{2} c + \frac{k}{2}\left(r^\pm \pm ec\right)^2}$$

NB. Minimizing with respect to the densities -> ADE

Monolayer stress tensor $d\vec{f} = \underline{\underline{\Sigma}} \cdot \vec{m}\, d\ell$

A.-F. Bitbol, L. Peliti & J.-B. Fournier (2010)



✤ Projected quantities (Monge)

$$h(x,y) \quad \bar{\rho}(x,y)$$

Two-component membrane

$$F = \int_\Omega d^2r\, \bar{f}\,(\bar{\rho}, \phi, h_i, h_{ij})$$

Ordinary isotropic fluid term = pressure (or tension)

$$\Sigma_{ij} = \boxed{\left(\bar{f} - \bar{\rho}\frac{\partial \bar{f}}{\partial \bar{\rho}}\right)\delta_{ij}} - \left(\frac{\partial \bar{f}}{\partial h_j} - \partial_k \frac{\partial \bar{f}}{\partial h_{kj}}\right) h_i - \frac{\partial \bar{f}}{\partial h_{kj}} h_{ki},$$

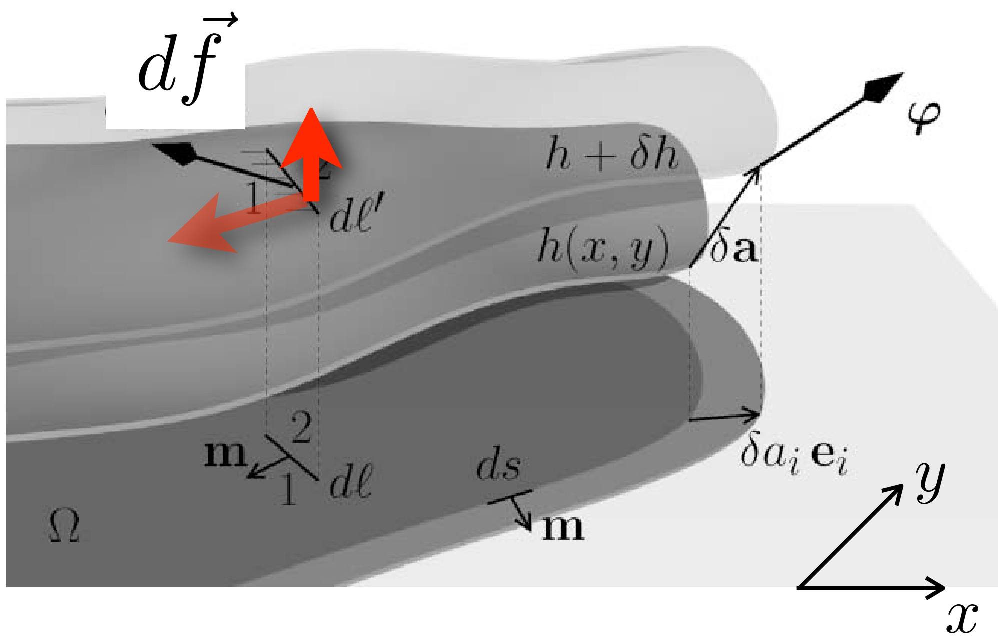
$$\Sigma_{zj} = \frac{\partial \bar{f}}{\partial h_j} - \partial_k \frac{\partial \bar{f}}{\partial h_{kj}},$$

Other terms due to the curved layer structure

$$i, j \in \{x, y\}$$

Monolayer stress tensor $d\vec{f} = \underline{\underline{\Sigma}} \cdot \vec{m}\, d\ell$

A.-F. Bitbol, L. Peliti & J.-B. Fournier (2010)



$$f^{\pm} = \frac{\sigma_0}{2} + \frac{\kappa}{4}c^2 \pm \frac{\kappa c_0}{2}c + \frac{k}{2}\left(r^{\pm} \pm ec\right)^2$$

$$r = \frac{\rho - \rho_0}{\rho_0}$$

$$c = \nabla^2 h + \mathcal{O}(\epsilon^2)$$

Stress tensor normal components

$$\Sigma^{+}_{zj} = \boxed{\frac{\sigma_0}{2}h_j - \frac{\kappa}{2}\partial_j \nabla^2 h} - ke\,\partial_j\left(r + e\nabla^2 h\right) + \mathcal{O}(\epsilon^2)$$

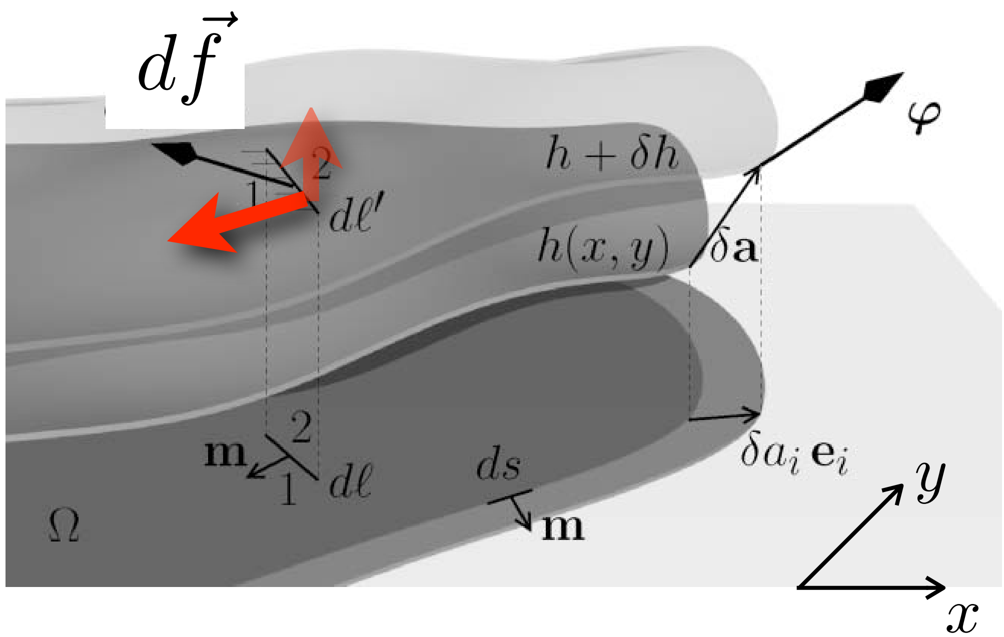
Force density

From Helfrich

$$p^{+}_{z} = \partial_j \Sigma^{+}_{zj} = \boxed{\frac{\sigma_0}{2}\nabla^2 h - \frac{\kappa}{2}\nabla^4 h} - ke\nabla^2\left(r + e\nabla^2 h\right) + \mathcal{O}(\epsilon^2)$$

Monolayer stress tensor $d\vec{f} = \underline{\underline{\Sigma}} \cdot \vec{m}\, d\ell$

A.-F. Bitbol, L. Peliti & J.-B. Fournier (2010)



$$f^{\pm} = \frac{\sigma_0}{2} + \frac{\kappa}{4}c^2 \pm \frac{\kappa c_0}{2}c + \frac{k}{2}\left(r^{\pm} \pm ec\right)^2$$

$$r = \frac{\rho - \rho_0}{\rho_0}$$

$$c = \nabla^2 h + \mathcal{O}(\epsilon^2)$$

Stress tensor tangential components

$$\Sigma_{ij}^{+} = \left[\frac{\sigma_0}{2} - k\left(r + e\nabla^2 h\right) - \frac{\kappa c_0}{2}\nabla^2 h\right]\delta_{ij} + \frac{\kappa c_0}{2}h_{ij} + \mathcal{O}(\epsilon^2)$$

tension of the flat membrane with r=0.

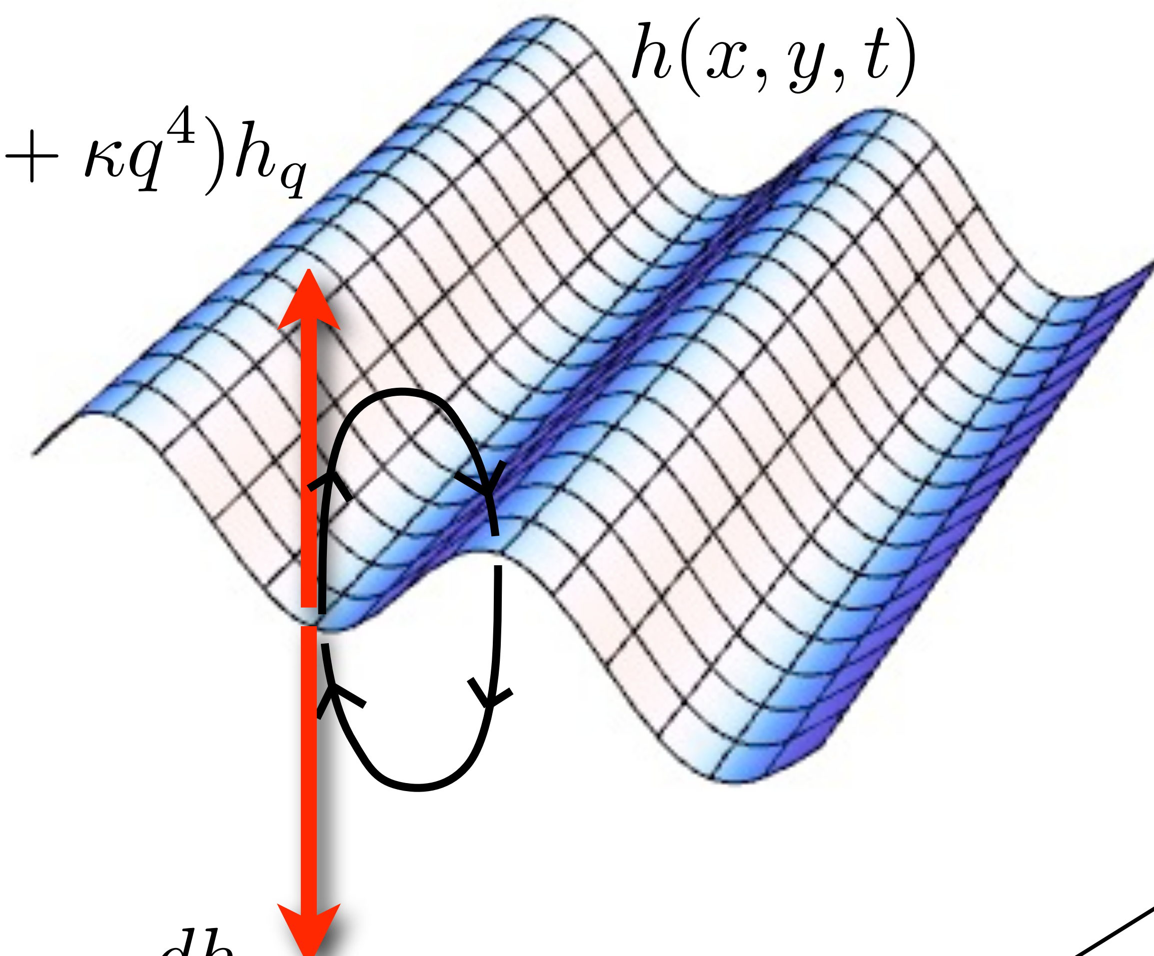
Force density

$$p_i^{+} = \partial_j \Sigma_{ij}^{+} = -k\,\partial_i\left(r + e\nabla^2 h\right) + \mathcal{O}(\epsilon^2)$$

Dynamics of structureless membranes

$$p_z^+ = \partial_j \Sigma_{zj}^+ = \boxed{\frac{\sigma_0}{2}\nabla^2 h - \frac{\kappa}{2}\nabla^4 h} \cancel{- ke\nabla^2\left(r + e\nabla^2 h\right)} + \mathcal{O}(\epsilon^2)$$

$$p_z(q) = -(\sigma_0 q^2 + \kappa q^4) h_q$$



$$T_{zz}(q) = -4\eta q \frac{dh_q}{dt}$$

✤ Relaxation time

$$\boxed{\tau_R = \frac{4\eta}{\sigma_0 q + \kappa q^3}}$$

✤ Valid if $\sigma_0 \approx 0$ at intermediate lengthscales (inter-monolayer friction).

$\sigma = 10^{-9}\,\mathrm{J/m^2} \rightarrow [10\,\mu\mathrm{m}, 3000\,\mu\mathrm{m}]$

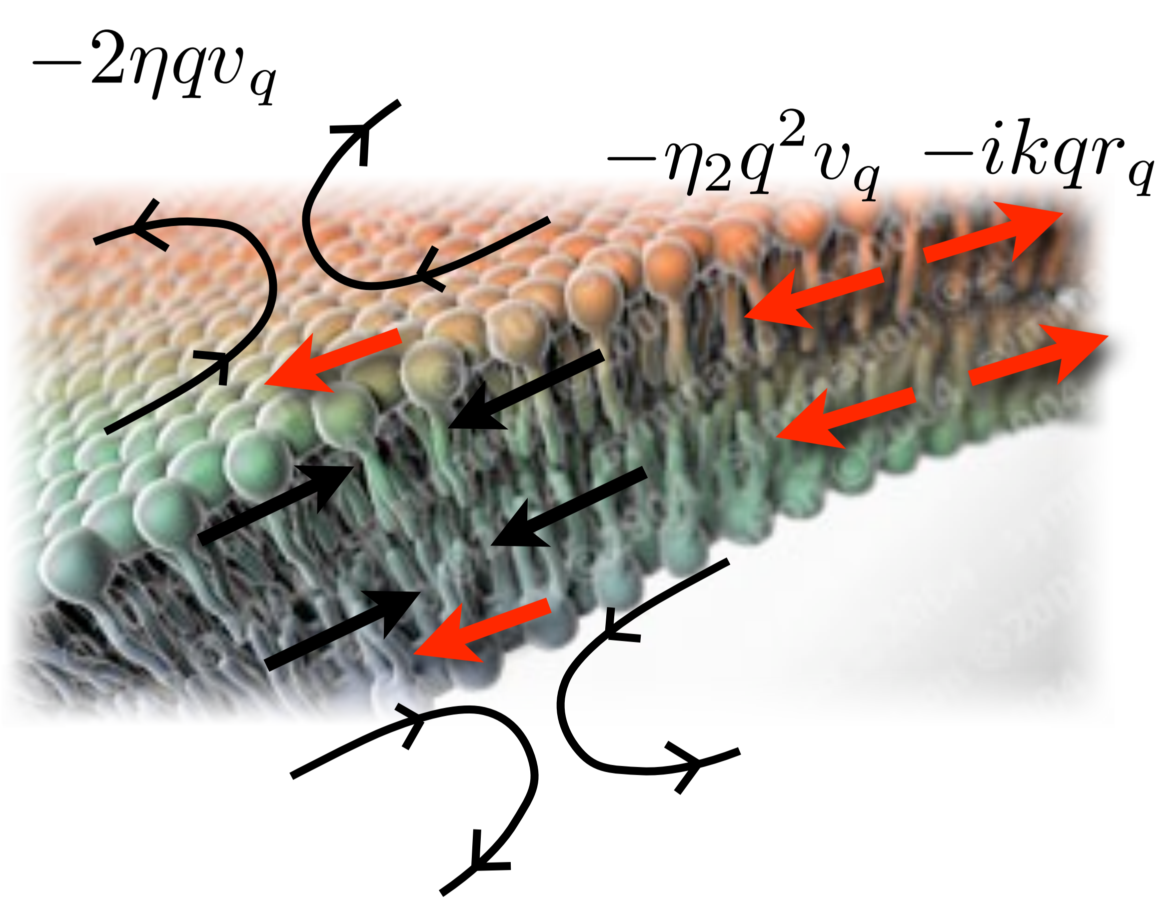
$\sigma = 10^{-8}\,\mathrm{J/m^2} \rightarrow [10\,\mu\mathrm{m}, 300\,\mu\mathrm{m}]$

$\sigma = 10^{-7}\,\mathrm{J/m^2} \rightarrow$ never valid

$\tau_R \simeq 10\,\mathrm{s}$ at $\lambda = 150\mu\mathrm{m}$

In-plane dynamics in a flat membrane (symmetric mode)

$$p_i^+ = \partial_j \Sigma_{ij}^+ = -k\,\partial_i \left(r + e\cancel{\nabla^2 h}\right) + \mathcal{O}(\epsilon^2)$$



$$\frac{dr_q}{dt} + iqv_q = 0$$

✤ Relaxation of a SYMMETRIC density modulation in a FLAT MEMBRANE

$$\boxed{\tau_R^s = \frac{\eta_2 + 2\eta/q}{k}}$$

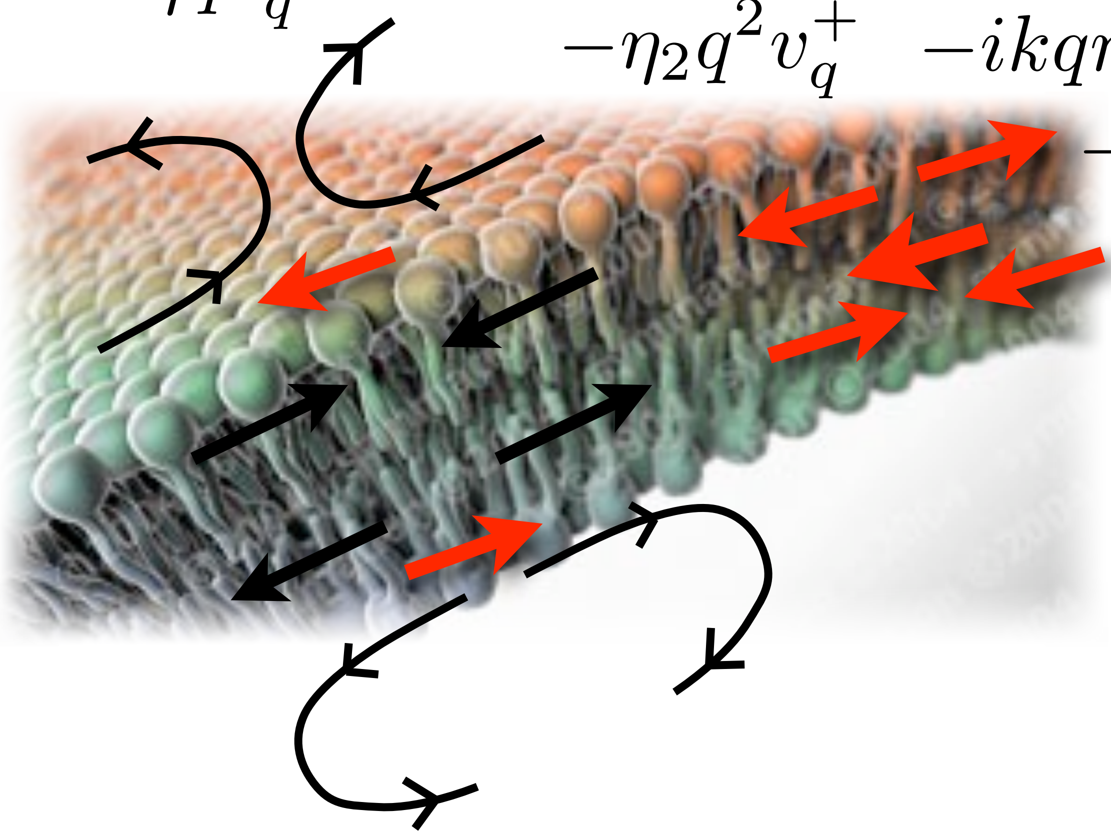
✤ Crossover in the μm range

$$\tau_R^s \approx 10\,\mathrm{ns}$$

In-plane dynamics in a flat membrane (anti-symmetric mode)

$$p_i^+ = \partial_j \Sigma_{ij}^+ = -k\,\partial_i(r^+ + \cancel{e\nabla^2 h}) + \mathcal{O}(\epsilon^2)$$

✤ Relaxation of an ANTI-SYMMETRIC density modulation in a FLAT MEMBRANE



$$\boxed{\tau_R^a = \frac{\cancel{\eta_2} + \cancel{2\eta/q} + 2b/q^2}{k}}$$

$$\tau_R^a \approx 10\,\mathrm{s} \text{ at } \lambda = 150\,\mu\mathrm{m}$$

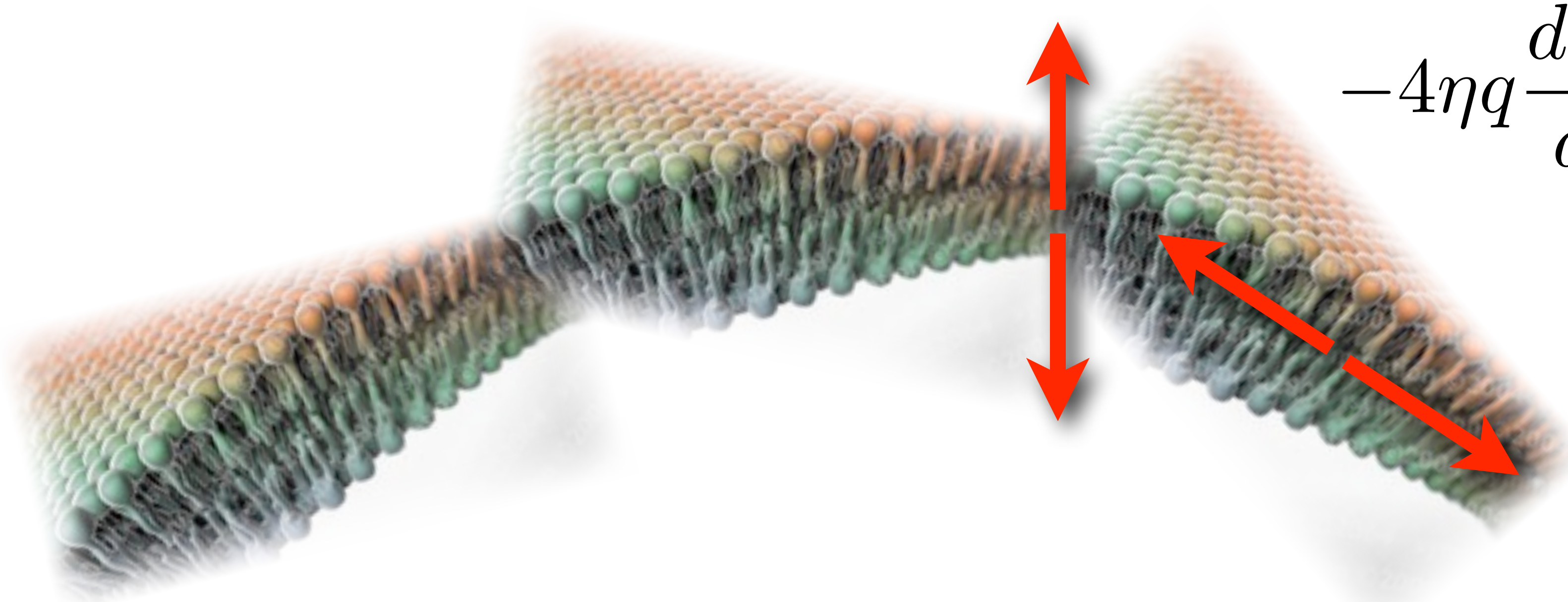
$$\frac{dr_q^\pm}{dt} + iqv_q^\pm = 0$$

Complete dynamics

U. Seifert & S. A. Langer (1993)

$$-(\sigma_0 q^2 + \kappa q^4) h_q + keq^2(r_q^+ - r_q^- - 2eq^2 h_q)$$

$$-4\eta q \frac{dh_q}{dt}$$

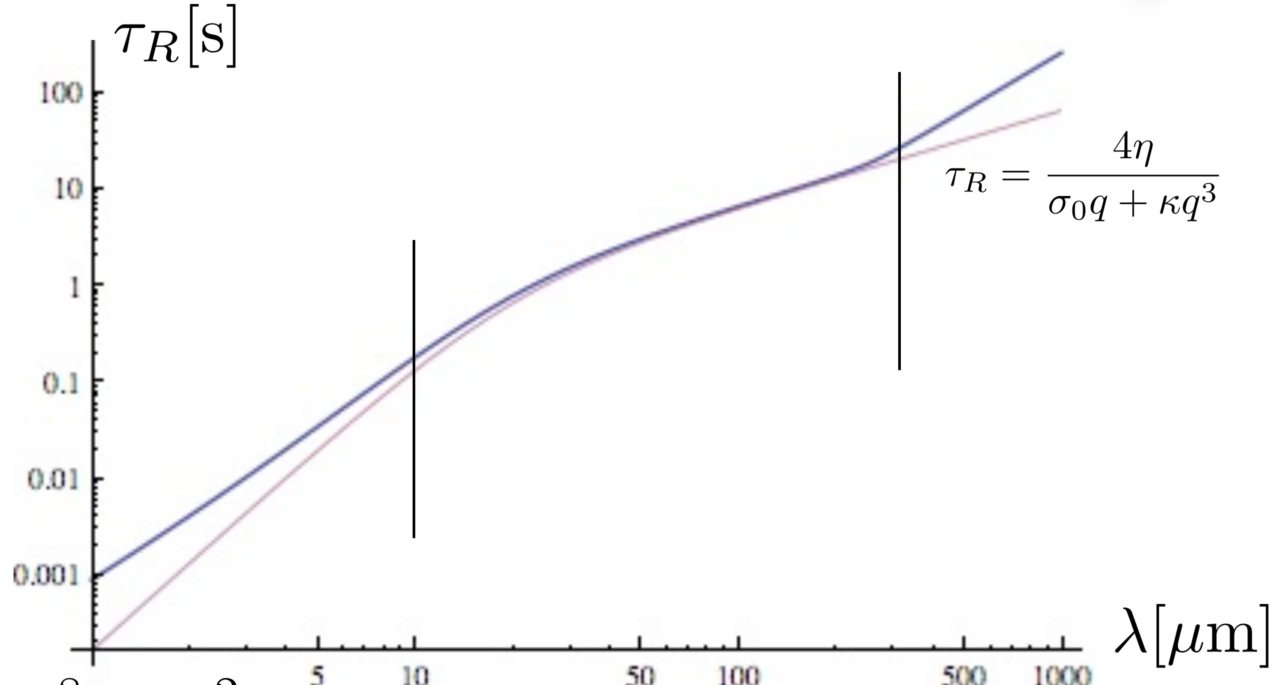


$$-ikq(r_q^\pm \mp eq^2 h_q)$$

$$-2\eta q v_q^\pm$$

$$-\eta_2 q^2 v_q^\pm$$

$$\mp b(v_q^+ - v_q^-)$$



$$\frac{dr_q^\pm}{dt} + iqv_q^\pm = 0$$

$\sigma \simeq 10^{-8}\ \mathrm{J/m^2}$

Outline

1. Review of the elastic and dynamical models of membranes and monolayers.

2. Experiment by M. I. Angelova, N. Puff et al.

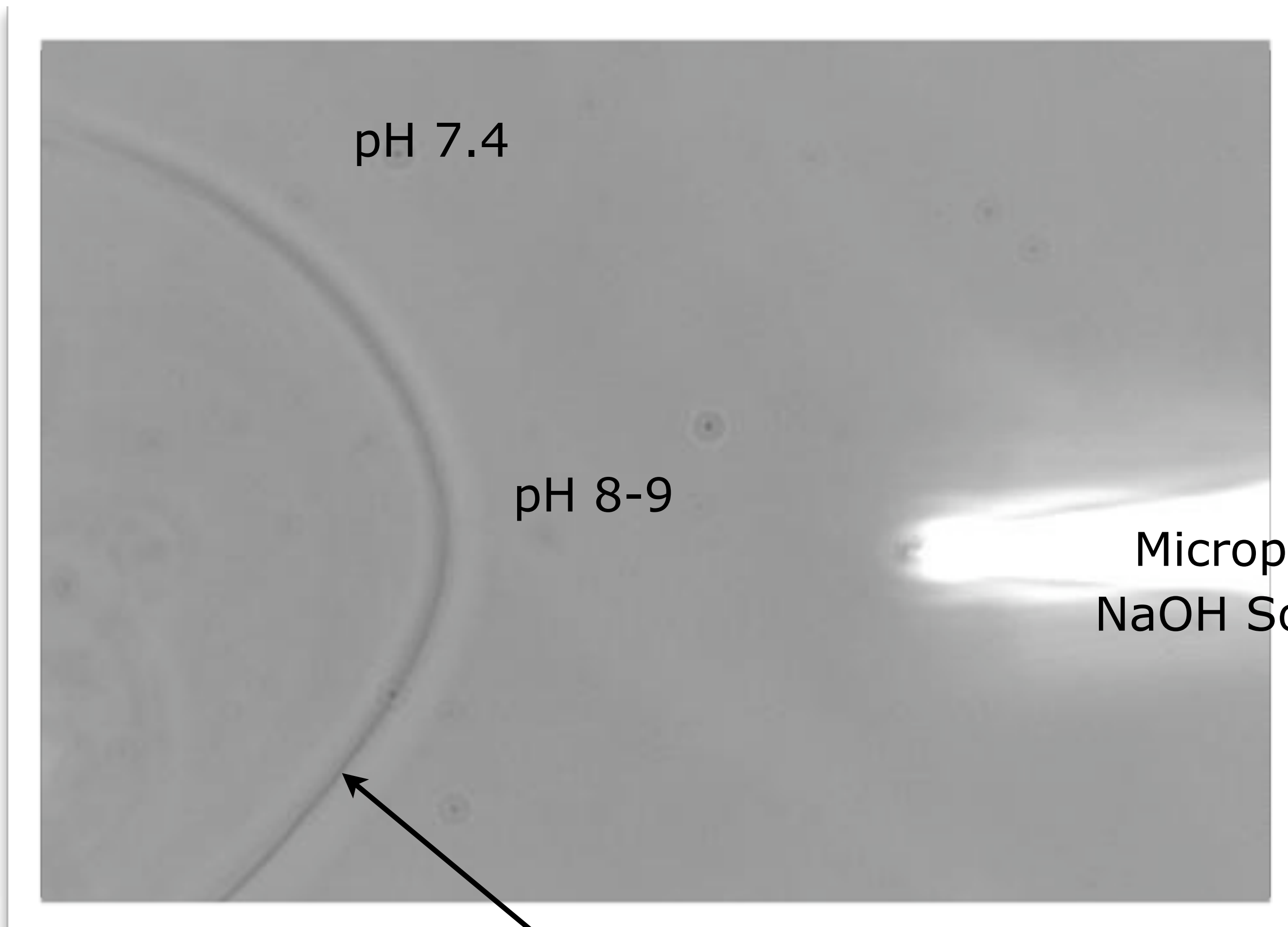
3. Theory of the curvature instability caused by a local modification of the lipids of one of the monolayers

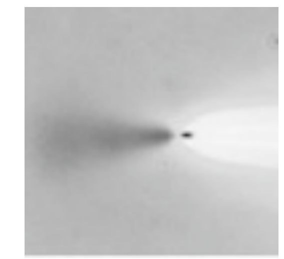
4. Comparison with the pH-micropipette experiment of M. I. Angelova, N. Puff et al.

5. Non-linear development : tubule ejection

Experimental setup

N. Khalifat, N. Puff, M. I. Angelova (2008)



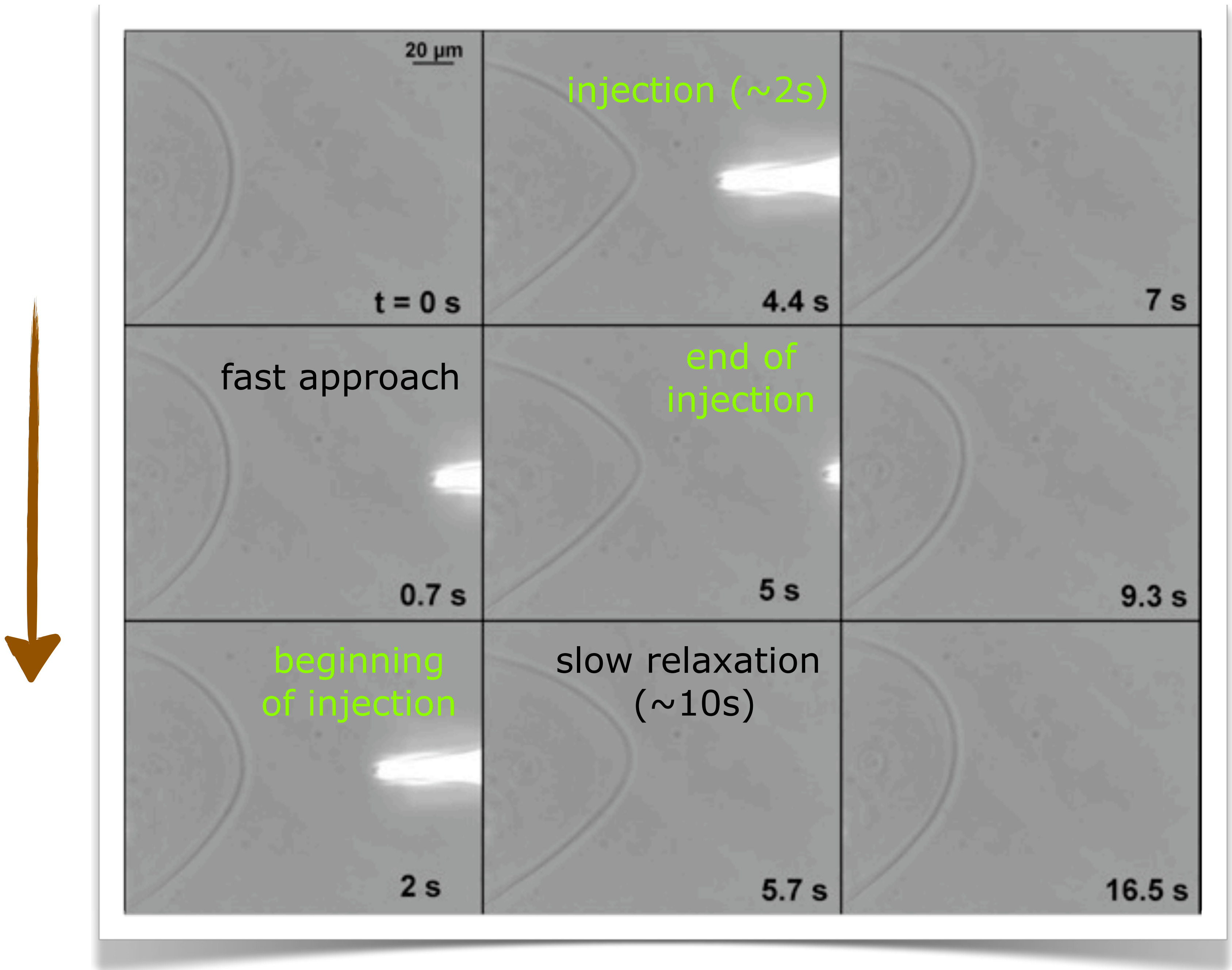


Giant vesicle (GUV)

Produced by electroformation,
mixture of EYPC/PS 90:10,
25°C, buffer at pH 7.4

Curvature instability

N. Khalifat, N. Puff, M. I. Angelova (2008)



Curvature instability

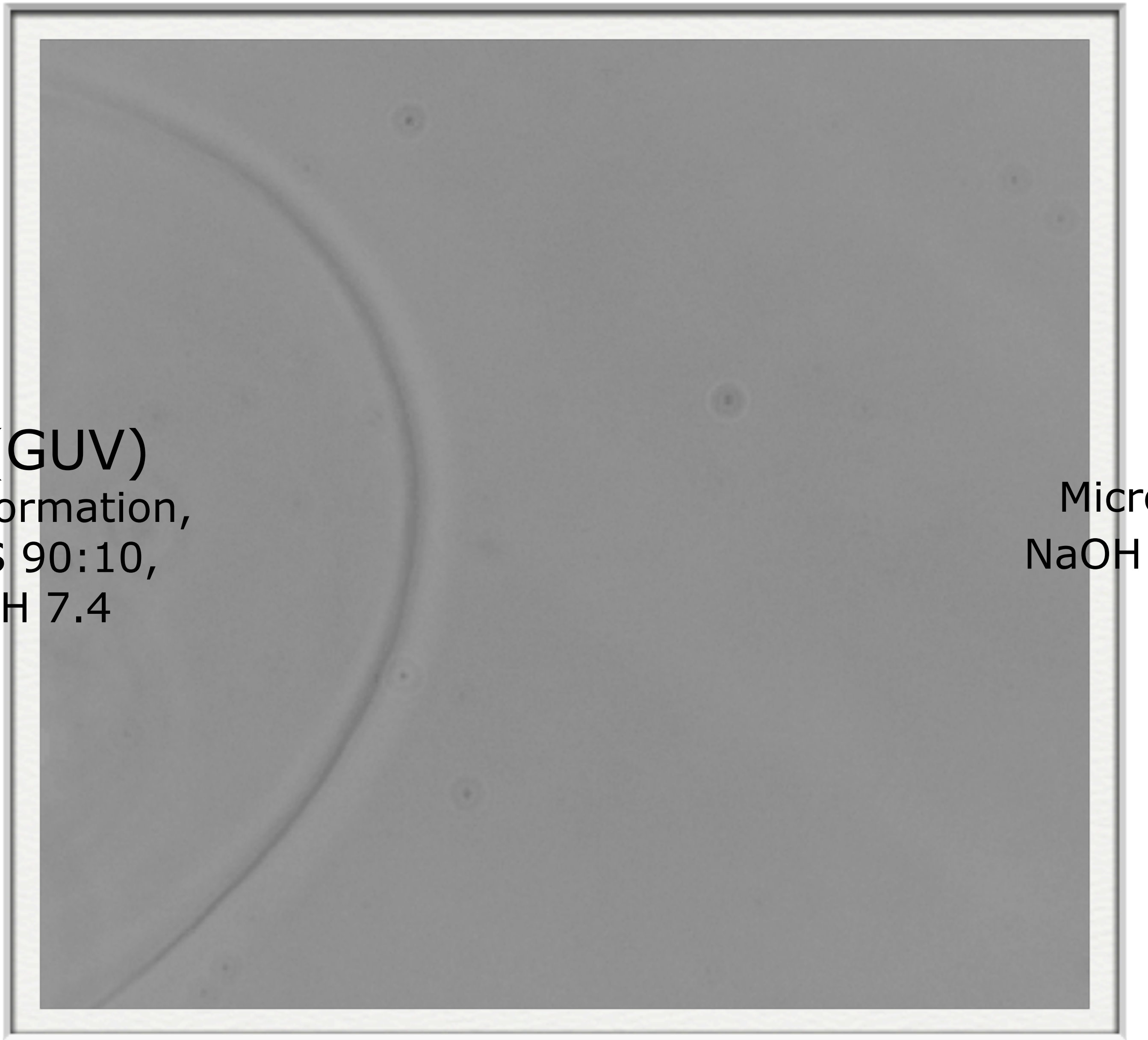
N. Khalifat, N. Puff, M. I. Angelova (2008)

Giant vesicle (GUV)
Produced by electroformation,
mixture of EYPC/PS 90:10,
25°C, buffer at pH 7.4

Micropipette ∅0.3 μm
NaOH Solution 1M pH 13

Curvature instability

N. Khalifat, N. Puff, M. I. Angelova (2008)



Giant vesicle (GUV)
Produced by electroformation,
mixture of EYPC/PS 90:10,
25°C, buffer at pH 7.4

Micropipette ⌀0.3 μm
NaOH Solution 1M pH 13

Outline

1. Review of the elastic and dynamical models of membranes and monolayers.

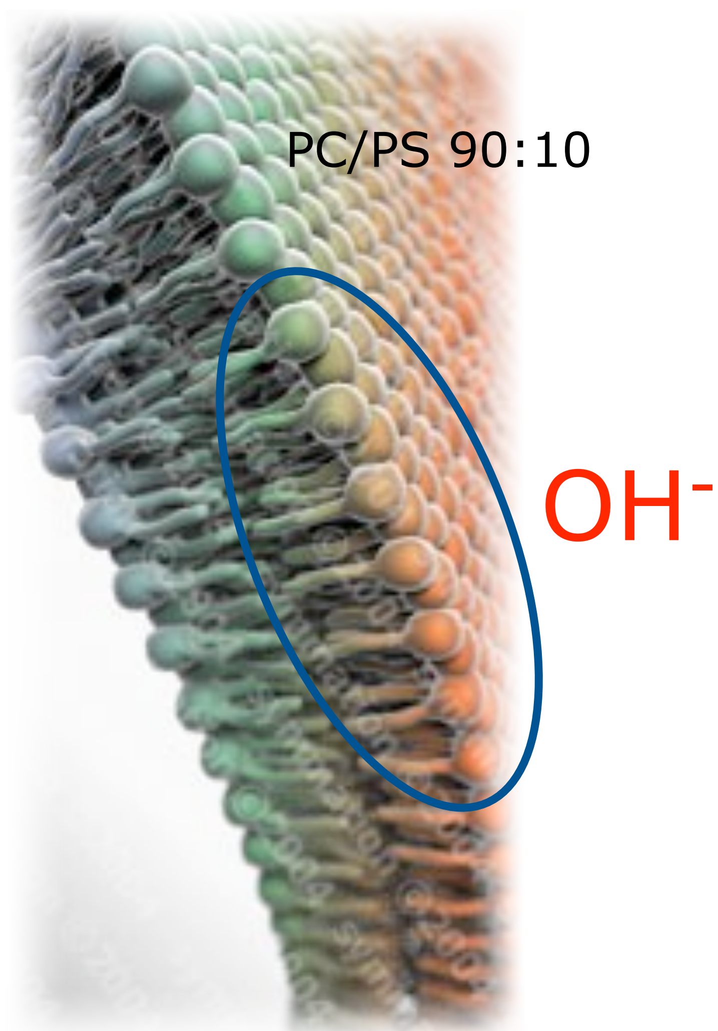
2. Experiment by M. I. Angelova, N. Puff et al.

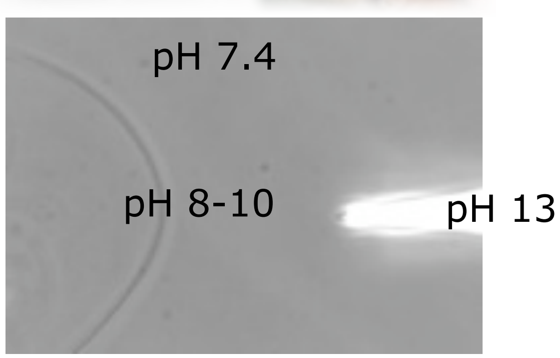
3. Theory of the curvature instability caused by a local modification of the lipids of one of the monolayers

4. Comparison with the pH-micropipette experiment of M. I. Angelova, N. Puff et al.

5. Non-linear development : tubule ejection

Local monolayer lipid modification?

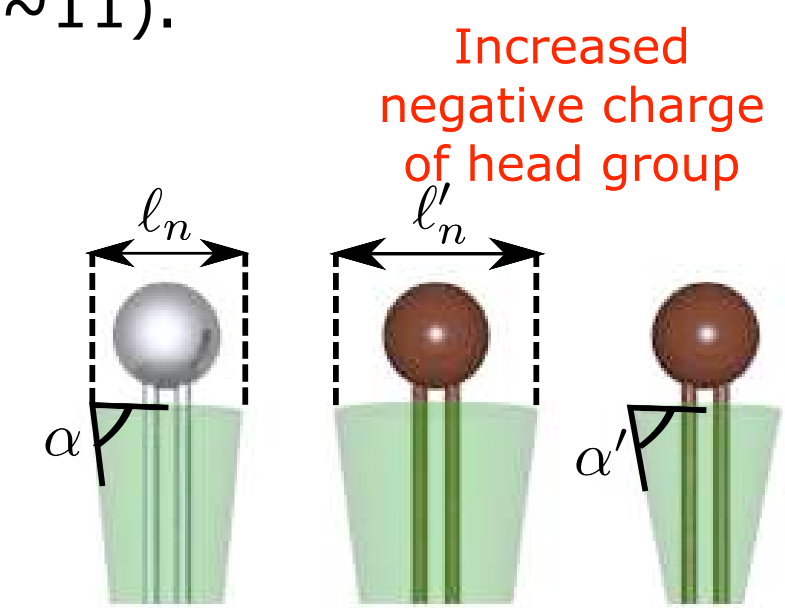




✤ <u>No molecular insertion. Only a local change of solvent environment.</u>

✤ Not hydrodynamic (buffer alone nothing)
✤ Specific of OH^- (NaCl not). Effect of pH?

✤ Amino NH_3^+ group of PS head deprotonates at high pH (pK_a~9.8). Positively charged trimethylammonium group of PC head associates with OH^- at high pH (pK_a^{eff}~11).

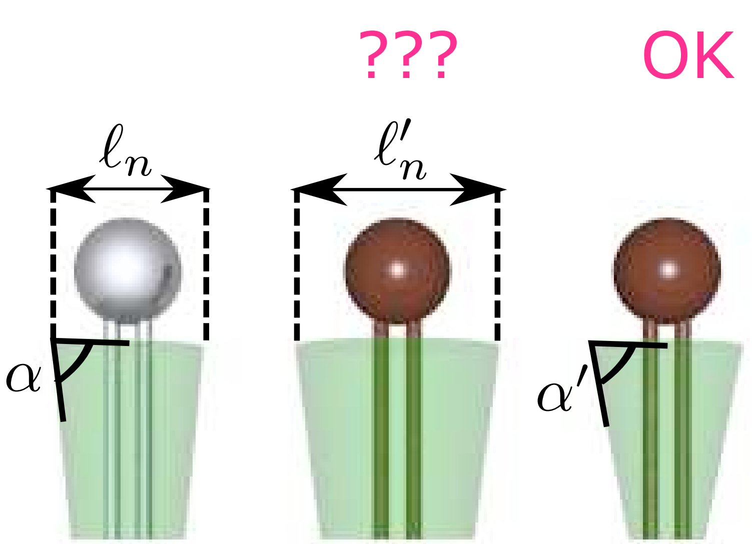


$\phi \ll 1$

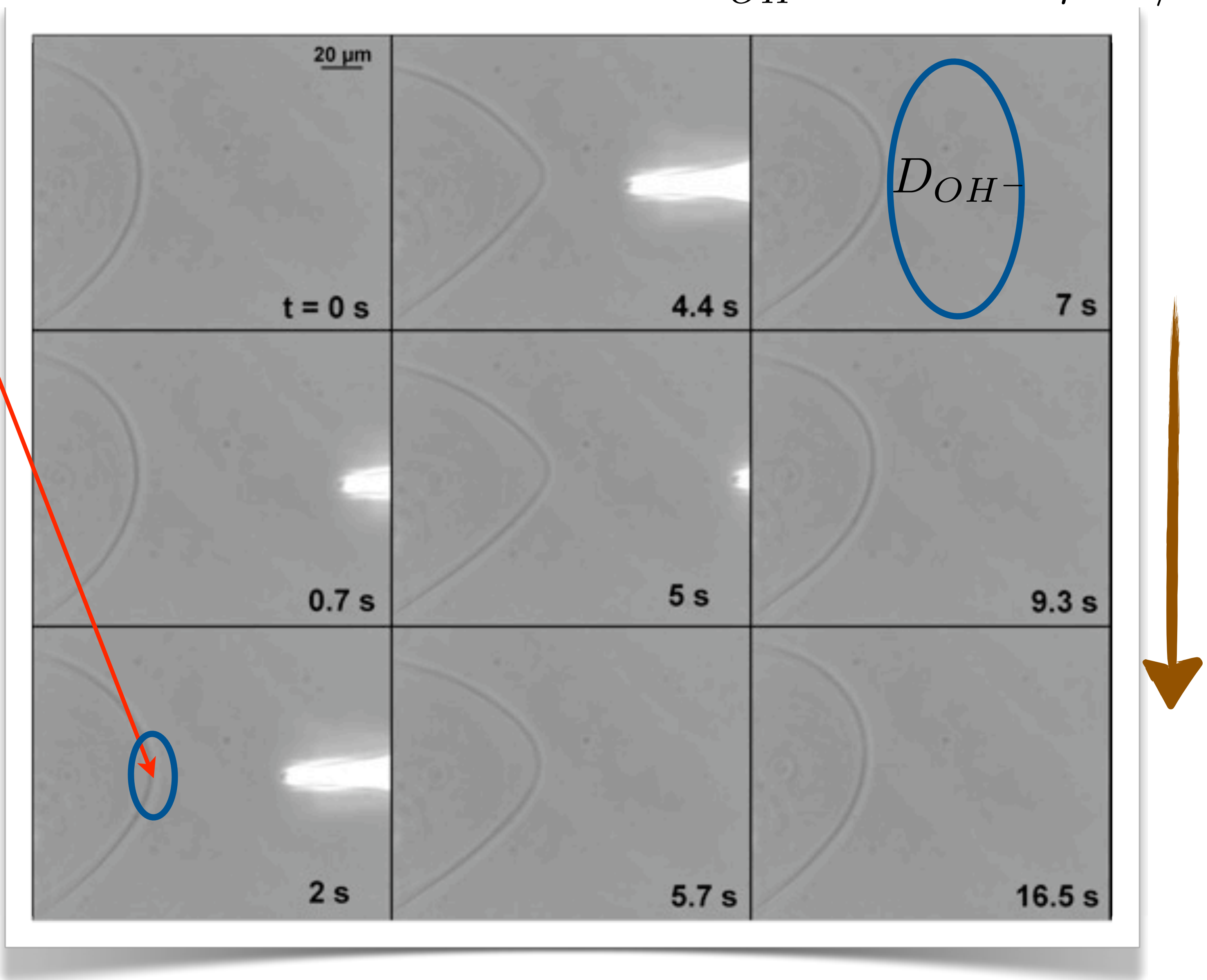
Local monolayer lipid modification

✤ A fraction $\phi \ll 1$ of the lipids of the outer monolayer are chemically modified.

✤ Depends on the local time-dependent pH.



$D_{OH^-} \sim 5 \times 10^3 \ \mu\mathrm{m}^2/\mathrm{s}$

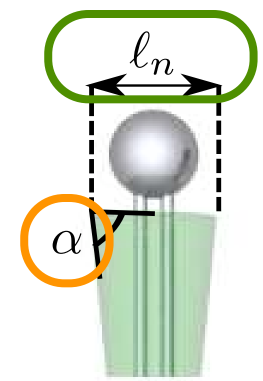


Bilayer curvature—density elasticity

A.-F. Bitbol, L. Peliti & J.-B. Fournier (2010)

ρ_0 : reference density, and $r^+ = (\rho^+ - \rho_0)/\rho_0$

$$f^\pm = \boxed{\frac{\sigma_0}{2}} + \frac{\kappa}{4}c^2 \pm \frac{\kappa c_0}{2}c + \frac{k}{2}\left(r^\pm \pm ec\right)^2$$



Determinant of the spontaneous curvature : c_0 (obvious)

How far is ρ_0 from the equilibrium density ? Let us miminizes the free energy <u>per unit mass</u> f^+/ρ^+ for the flat membrane (c=0) :

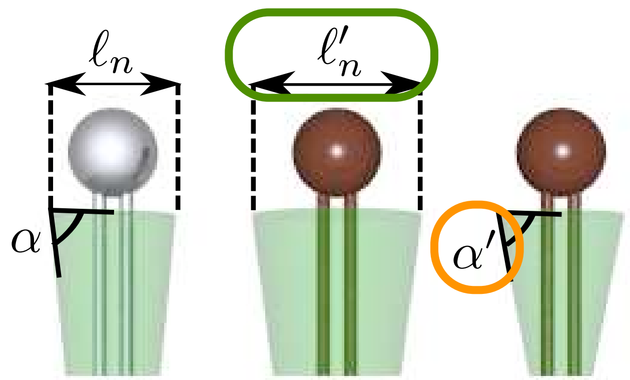
$$r^+_{\mathrm{eq}} = \frac{\boxed{\sigma_0/2}}{k}$$

Bilayer curvature—density elasticity

For a two-component monolayer

A.-F. Bitbol, L. Peliti & J.-B. Fournier (2010)

The monolayer includes a fraction $\phi \ll 1$ of other lipids



Change in spontaneous curvature

$$f^+ = \boxed{\frac{\sigma_0}{2} + \sigma_1 \phi + \frac{\sigma_2}{2}\phi^2 + \tilde{\sigma}\left(1 + r^+\right)\phi \ln \phi} + \frac{\kappa}{4}c^2 + \frac{\kappa}{2}\boxed{\left(c_0 + \tilde{c}_0 \phi\right)} c + \frac{k}{2}\left(r^+ + ec\right)^2 .$$

Change in equilibrium density

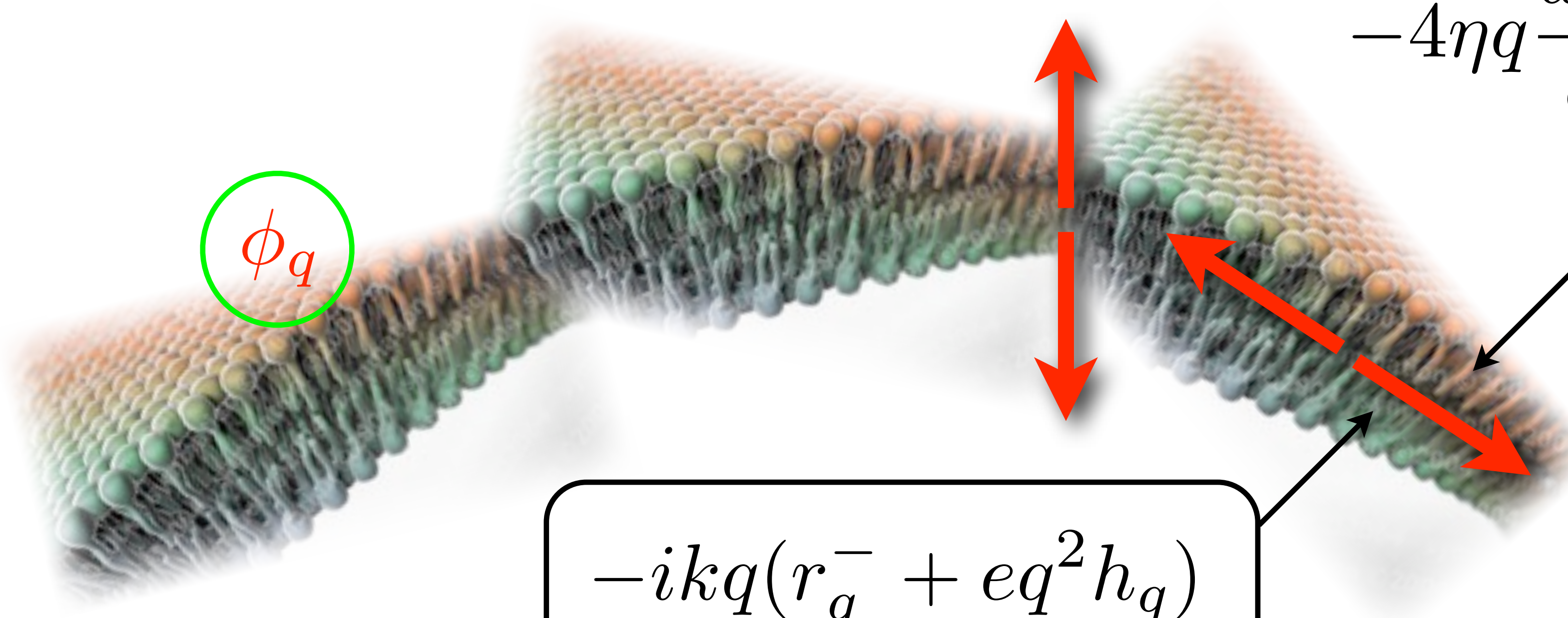
$$\delta r^+_{\mathrm{eq}} = r^+_{\mathrm{eq}}(\phi) - r^+_{\mathrm{eq}}(0) = \boxed{\frac{\sigma_1}{k}\phi}$$

(to $\mathcal{O}(\epsilon)$)

Complete dynamics with modified lipids

$$-(\sigma_0 q^2 + \kappa q^4)h_q + keq^2(r_q^+ - r_q^- - 2eq^2 h_q - \frac{\sigma_1}{k}\phi_q) + \frac{\kappa \bar{c}_0}{2} q^2 \phi_q$$

$$-4\eta q \frac{dh_q}{dt}$$



$$-ikq(r_q^+ - eq^2 h_q - \frac{\sigma_1}{k}\phi_q)$$
$$-2\eta q v_q^+$$
$$-\eta_2 q^2 v_q^+$$
$$-b(v_q^+ - v_q^-)$$

$$-ikq(r_q^- + eq^2 h_q)$$
$$-2\eta q v_q^-$$
$$-\eta_2 q^2 v_q^-$$
$$+b(v_q^+ - v_q^-)$$

$$\frac{dr_q^\pm}{dt} + iqv_q^\pm = 0$$

Complete dynamics with modified lipids

Exponential relaxations towards equilibrium state

$$\bar{r}_q(t) = r_q^- + r_q^+$$

$$\frac{\partial \bar{r}_q}{\partial t} = -\underbrace{\boxed{\frac{kq}{\eta_2 q + 2\eta}}}_{\gamma_0}\left(\bar{r}_q - \frac{\sigma_1}{k}\phi_q\right)$$

$$\hat{r}_q(t) = r_q^+ - r_q^-$$

$$\frac{\partial}{\partial t}\begin{pmatrix} q h_q \\ \hat{r}_q \end{pmatrix} = -\begin{pmatrix} \overbrace{\boxed{\frac{\sigma_0 q + \tilde{\kappa} q^3}{4\eta}}}^{\gamma_2} & -\frac{keq^2}{4\eta} \\ \cancel{-\frac{keq^3}{b}} & \underbrace{\boxed{\frac{kq^2}{2b}}}_{\gamma_1} \end{pmatrix}\begin{pmatrix} q h_q \\ \hat{r}_q \end{pmatrix} + \begin{pmatrix} \frac{\kappa \tilde{c}_0 q^2}{8\eta}\phi_q \\ \frac{\sigma_1 q^2}{2b}\phi_q \end{pmatrix}$$

$$\tau_0 \equiv \tau_R^s \simeq 10\,\mathrm{ns}$$

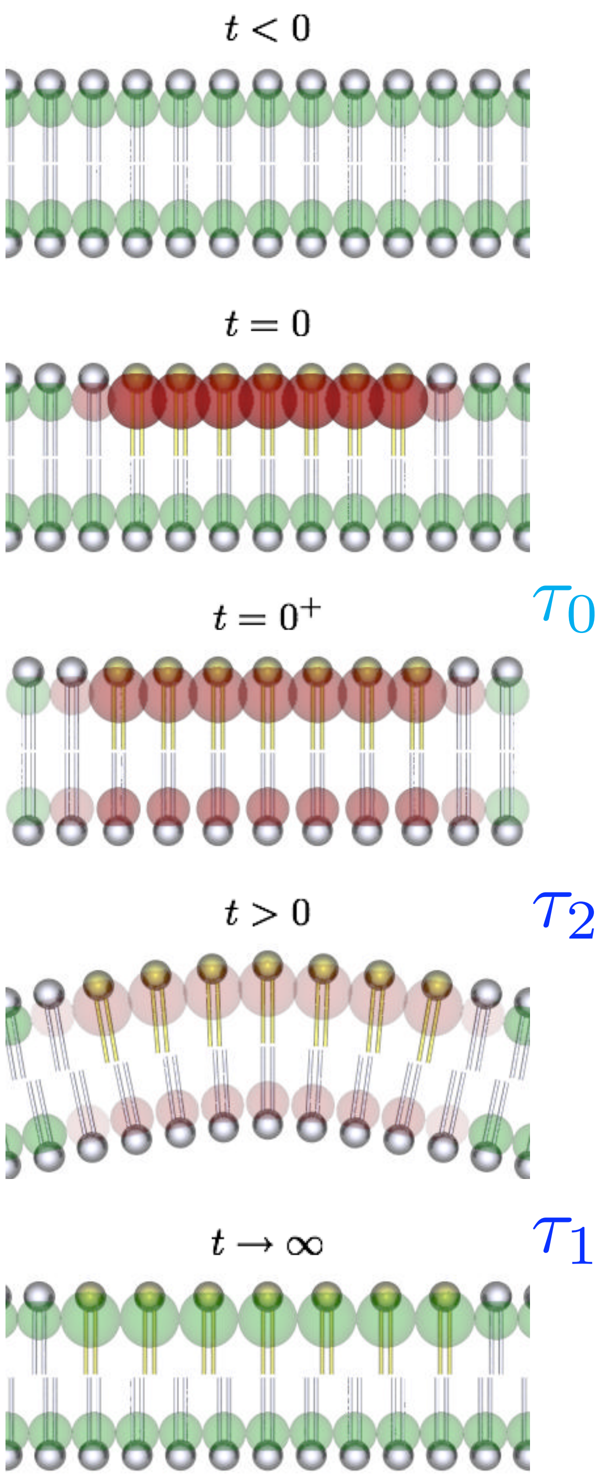
$$\gamma_0 \gg \gamma_2 > \gamma_1 \qquad \tau_2 \approx 0.1 - 0.5\,\mathrm{s} \quad \text{at } q_{\exp}, \sigma_{\exp}$$

$$\tau_1 \equiv \tau_R^a \approx 5\,\mathrm{s} \quad \text{at } q_{\exp}$$

$$\tilde{c}_0 = \bar{c}_0 - \frac{2\sigma_1 e}{\kappa}, \quad \tilde{\kappa} = \kappa + 2ke^2$$

Case #1 — *equilibrium density* only

$$\bar{c}_0 = 0 \text{ and } \sigma_1 \neq 0$$



Hypotheses:
(i) instantaneous modification,
(ii) permanent modification,
(iii) no diffusion

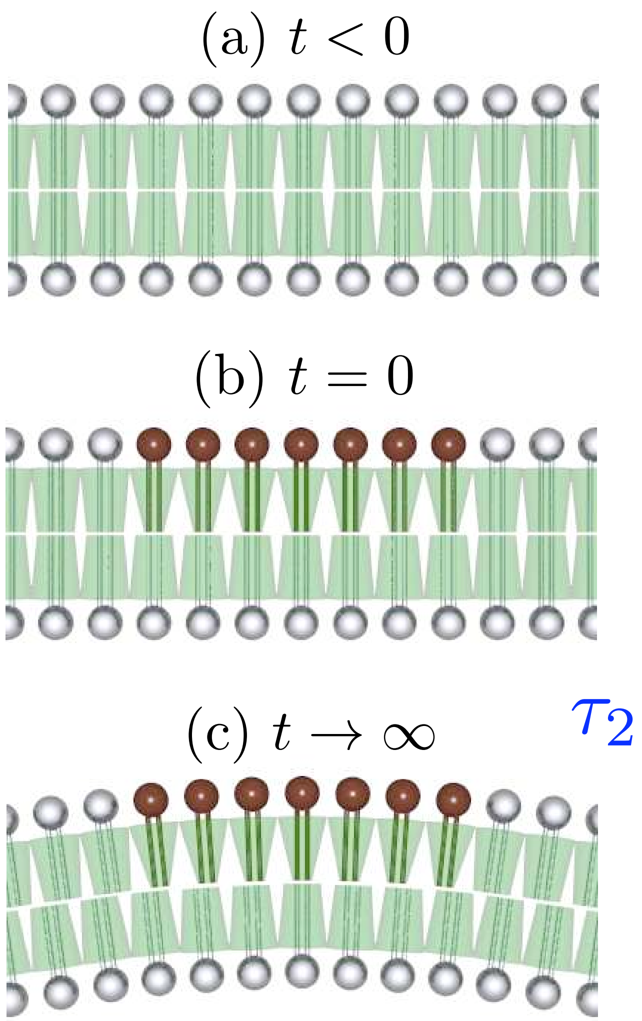
$$\frac{\partial \bar{r}_q}{\partial t} = -\underbrace{\boxed{\frac{kq}{\eta_2 q + 2\eta}}}_{\gamma_0}\left(\bar{r}_q - \frac{\sigma_1}{k}\phi_q\right)$$

$$\frac{\partial}{\partial t}\begin{pmatrix} q h_q \\ \hat{r}_q \end{pmatrix} = -\begin{pmatrix} \overset{\gamma_2}{\dfrac{\sigma_0 q + \tilde{\kappa} q^3}{4\eta}} & -\dfrac{keq^2}{4\eta} \\ \cancel{-\dfrac{keq^3}{b}} & \underbrace{\boxed{\dfrac{kq^2}{2b}}}_{\gamma_1} \end{pmatrix}\begin{pmatrix} q h_q \\ \hat{r}_q \end{pmatrix} + \begin{pmatrix} \dfrac{\kappa \tilde{c}_0 q^2}{8\eta}\phi_q \\ \dfrac{\sigma_1 q^2}{2b}\phi_q \end{pmatrix}$$

Case #2 — *spontaneous curvature* only

$$\bar{c}_0 \neq 0 \text{ and } \sigma_1 = 0$$

Hypotheses: idem
(i) instantaneous modification,
(ii) permanent modification,
(iii) no diffusion



$$\frac{\partial}{\partial t}\begin{pmatrix} q h_q \\ \hat{r}_q \end{pmatrix} = -\begin{pmatrix} \overset{\gamma_2}{\boxed{\dfrac{\sigma_0 q + \tilde{\kappa} q^3}{4\eta}}} & -\dfrac{keq^2}{4\eta} \\ \cancel{-\dfrac{keq^3}{b}} & \underset{\gamma_1}{\boxed{\dfrac{kq^2}{2b}}} \end{pmatrix}\begin{pmatrix} q h_q \\ \hat{r}_q \end{pmatrix} + \begin{pmatrix} \dfrac{\kappa \tilde{c}_0 q^2}{8\eta}\phi_q \\ \dfrac{\sigma_1 q^2}{2b}\phi_q \end{pmatrix}$$

τ_1 essentially not involved

Outline

1. Review of the elastic and dynamical models of membranes and monolayers.

2. Experiment by M. I. Angelova, N. Puff et al.

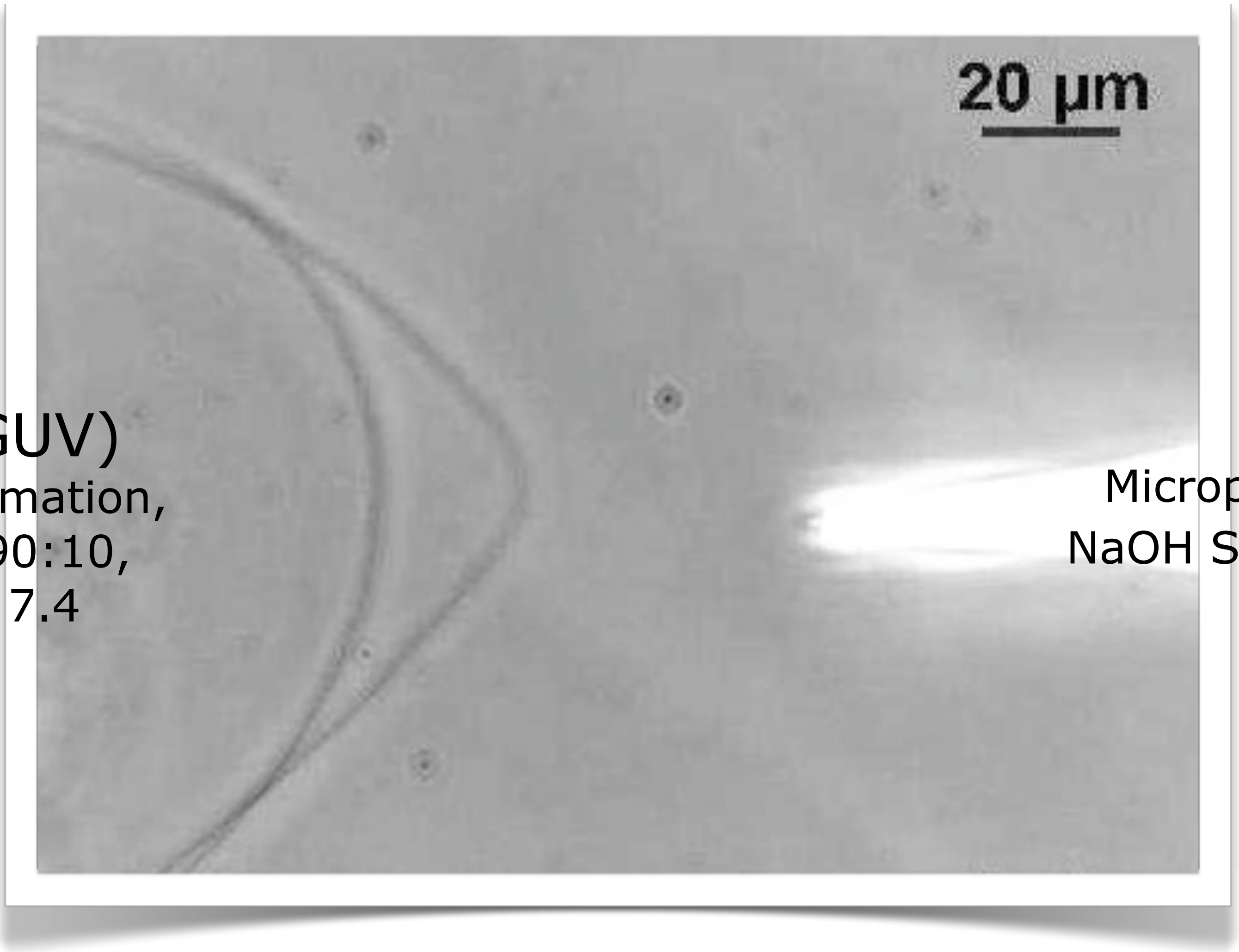
3. Theory of the curvature instability caused by a local modification of the lipids of one of the monolayers

→ 4. Comparison with the pH-micropipette experiment of M. I. Angelova, N. Puff et al.

5. Non-linear development : tubule ejection

Local dynamical shape instability

N. Khalifat, N. Puff, M. I. Angelova (2008)



Giant vesicle (GUV)
Produced by electroformation, mixture of EYPC/PS 90:10, 25°C, buffer at pH 7.4

Micropipette ⌀0.3 µm
NaOH Solution 1M pH 13

Adequacy? Case #1 or #2, or both?

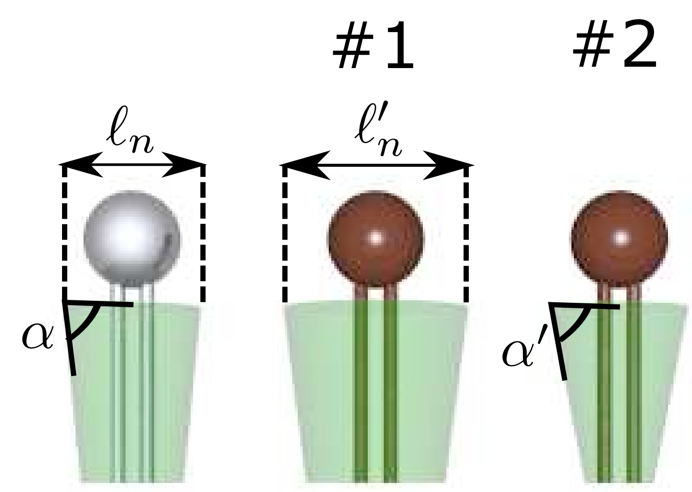
✤ Instantaneous modification? Idealized. But OK for the relaxation stage.

✤ Permanent modification? Strong approximation. Difficult to quantify, depends on time-dependent OH^- concentration field and local pH vs. pK_a.

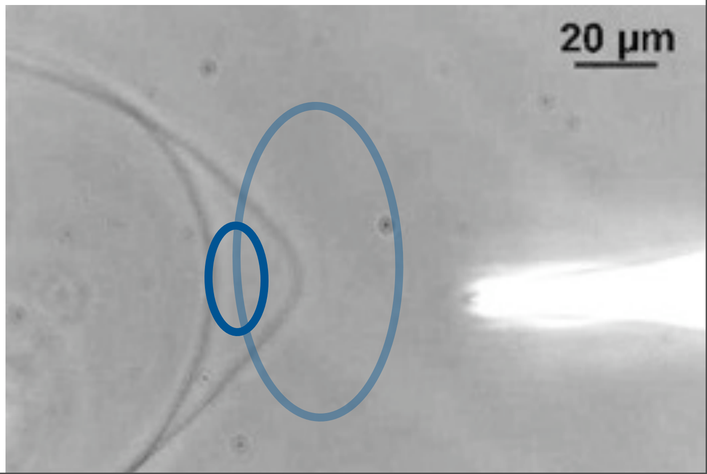
✤ Case #2 alone? Possible, but then the diffusion of OH^- would be responsible for the relaxation towards the flat state.

✤ Case #1 alone? Possible! Indeed even if the lipid modification is permanent there is a relaxation toward the flat state.

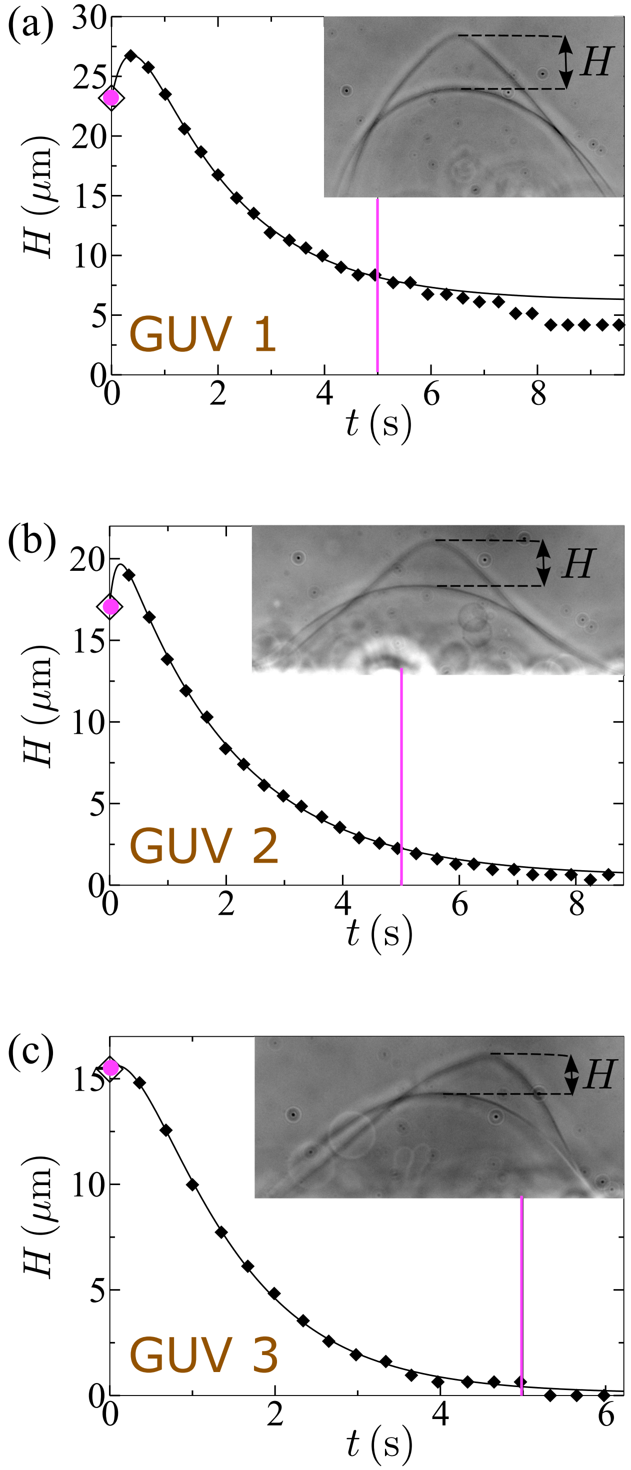
✤ Probably both #1 and #2 involved. Increasing the effective size of the polar head both increases the equilibrium density (#1) and the conical shape (#2).



D_{OH^-} : $\simeq 150\,\mu\text{m}$ in $5\,\text{s}$



Fits of the experimental data



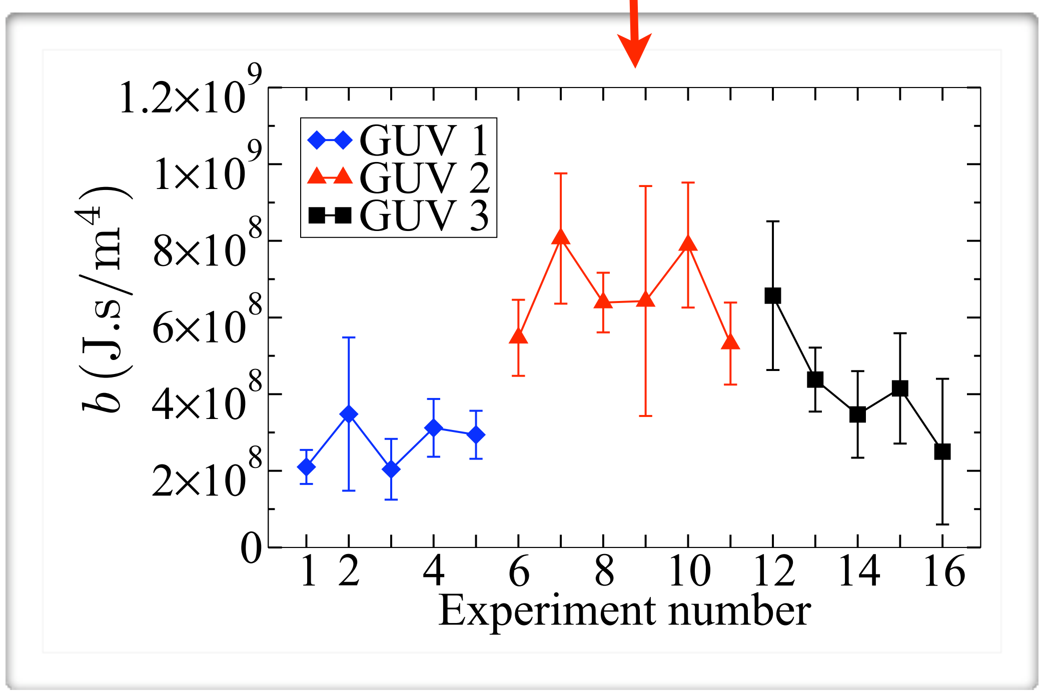
Fits of the relaxation with one-mode (q) theory:

$$H(t) = (H_0 - C - B)\, e^{-\gamma_1 t} + B\, e^{-\gamma_2 t} + C$$

with initial condition $H(0) = H_0$

Doubtful signification because of late OH^- diffusion

$$\gamma_1 \approx \frac{kq^2}{2b} \text{ and } \gamma_2 \approx \frac{\sigma_0 q}{4\eta}$$



$$\sigma_0 \approx 1 - 8 \times 10^{-7}\ \mathrm{J/m^2}$$

Fitted amount of dilation (if all): a few %.

Partial conclusions

✤ Good agreement between theory and experiment.

✤ Direct means of measuring intermonolayer friction coefficient b.

✤ In principle allows to discriminate between modification of equilibrium density $\delta\rho_{\mathrm{eq}}$ and modification of intrinsic curvature δc_0 (alas not here because of OH^- diffusion).

✤ Further (theoretical) work: (i) Evolution of the width of the instability by multimode Fourier analysis. (ii) Effect of the diffusion of modified lipids (if permanent modification).

Outline

1. Review of the elastic and dynamical models of membranes and monolayers.

2. Experiment by M. I. Angelova, N. Puff et al.

3. Theory of the curvature instability caused by a local modification of the lipids of one of the monolayers

4. Comparison with the pH-micropipette experiment of M. I. Angelova, N. Puff et al.

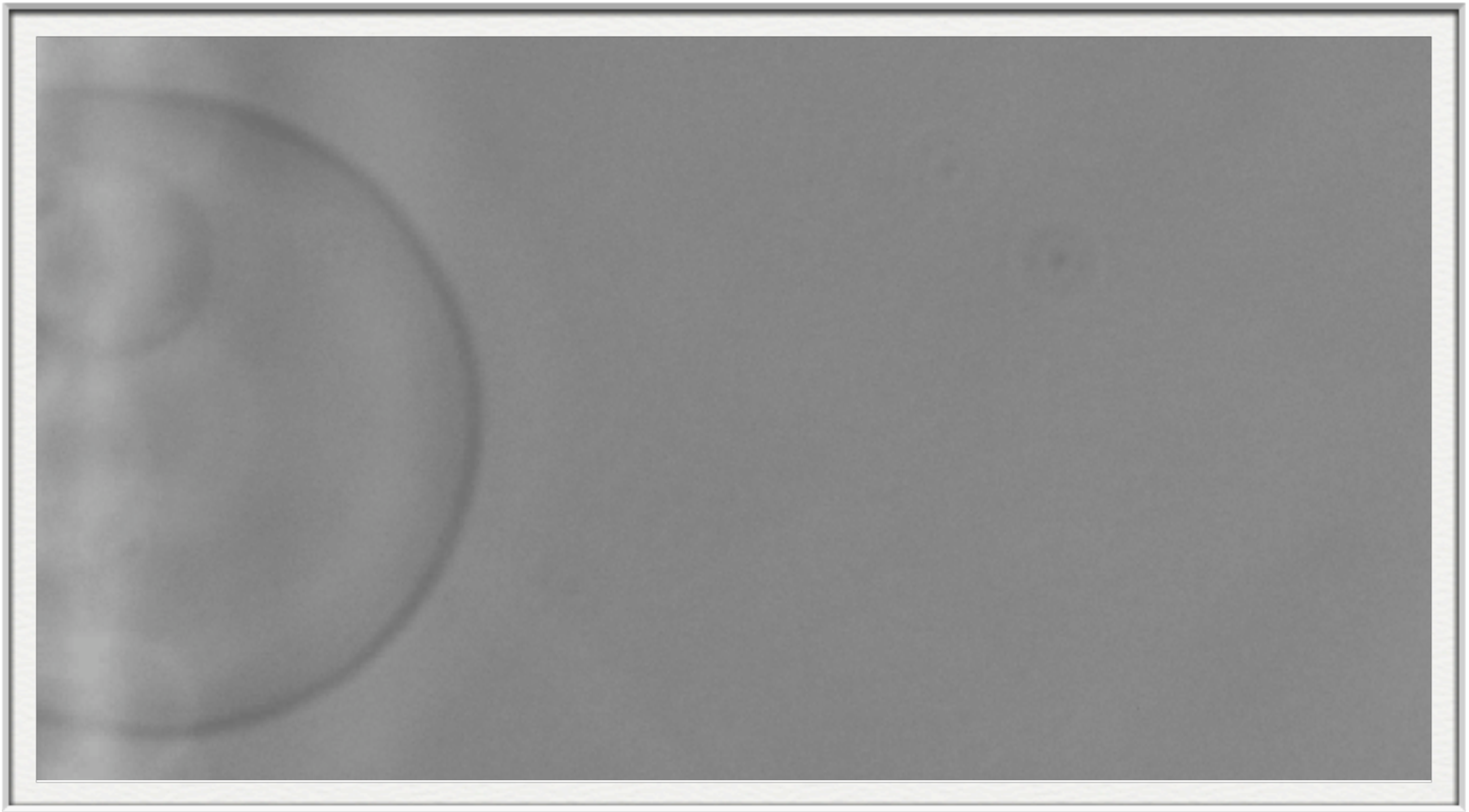
→ 5. Non-linear development : tubule ejection

Ejection of a tubule aiming at the pipette

Giant vesicle (GUV)
Produced by electroformation,
mixture of EYPC/PS 90:10,
25°C, buffer at pH 7.4

Micropipette ∅0.3 μm
NaOH Solution 1M pH 13

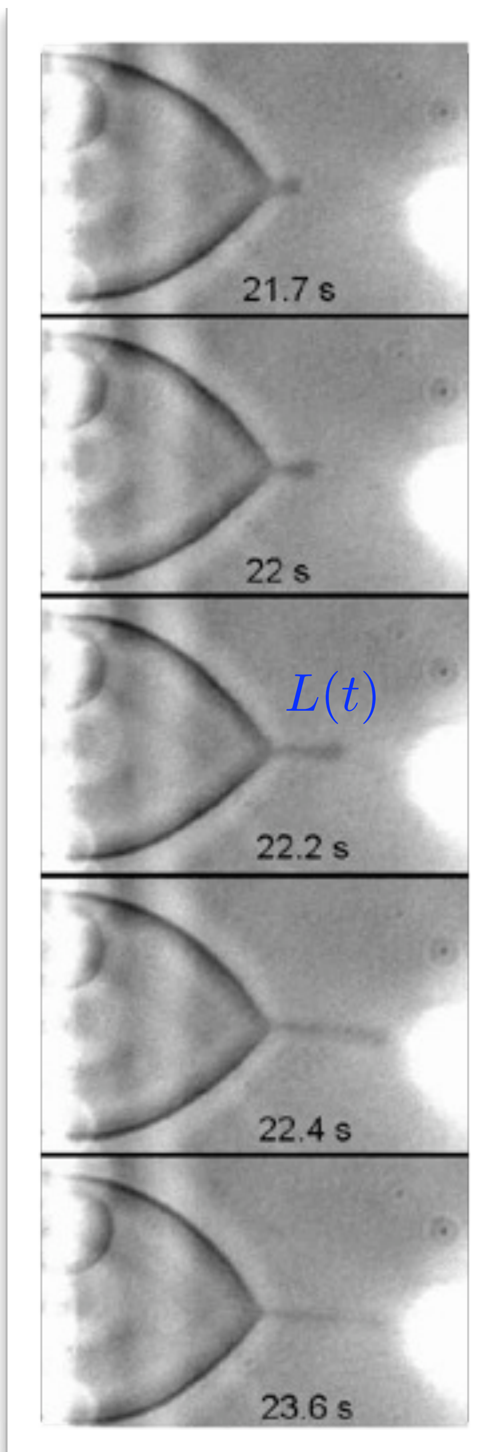
Ejection of a tubule aiming at the pipette



Giant vesicle (GUV)
Produced by electroformation,
mixture of EYPC/PS 90:10,
25°C, buffer at pH 7.4

Micropipette ∅0.3 μm
NaOH Solution 1M pH 13

Gradient of in-plane force: 'Marangoni-like' effect?



✤ Integrated normal force enough to draw tubule $f > 2\pi\sqrt{2\kappa\sigma_0}$

✤ 'Marangoni-like' effect:

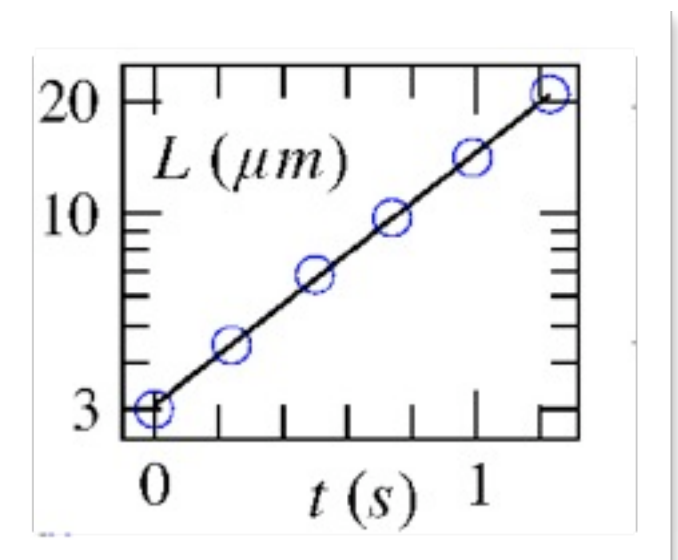
$$p_i^+ = \partial_j \Sigma_{ij}^+ = -k\,\partial_i \left(r^+ + ec - \frac{\sigma_1}{k}\phi \right)$$

$$\nabla \cdot \Sigma \sim \sigma_1 \nabla \phi$$

✤ Basic dynamical model:

E. Evans and A. Yeung (1994)

$$2\pi r L \times \sigma_1 \nabla\phi = \lambda \frac{dL}{dt}$$



$$L(t) \propto \exp(\gamma t)$$

Conclusions

✤ Direct means of measuring intermonolayer friction coefficient b .

✤ Local, dynamical instability allows to discriminate between modification of equilibrium density $\delta\rho_{\rm eq}$ and modification of intrinsic curvature δc_0 .

DIFFERENT FROM a global modification of the environment: for a vesicle with fixed volume, the equilibrium shape, within the ADE model, is fully determined by the value of quantity:

$$\overline{\Delta a_0} = \Delta a_0 + \frac{2}{\alpha} c_0^b$$

combining the preferred area difference and bilayer spontaneous curvature.

Many thanks to collaborators:

<u>Experimental</u>

N. Khalifat (PhD), N. Puff, M. I. Angelova

<u>Theoretical</u>

A.-F. Bitbol (PhD), L. Peliti

[J.-B. Fournier, N. Khalifat, N. Puff and M. I. Angelova,
Phys. Rev. Lett. <u>102</u>, 0181102 (2009)]