INHOMOGENEOUS LIPID MEMBRANE:ELASTICITY AND FLUIDITY

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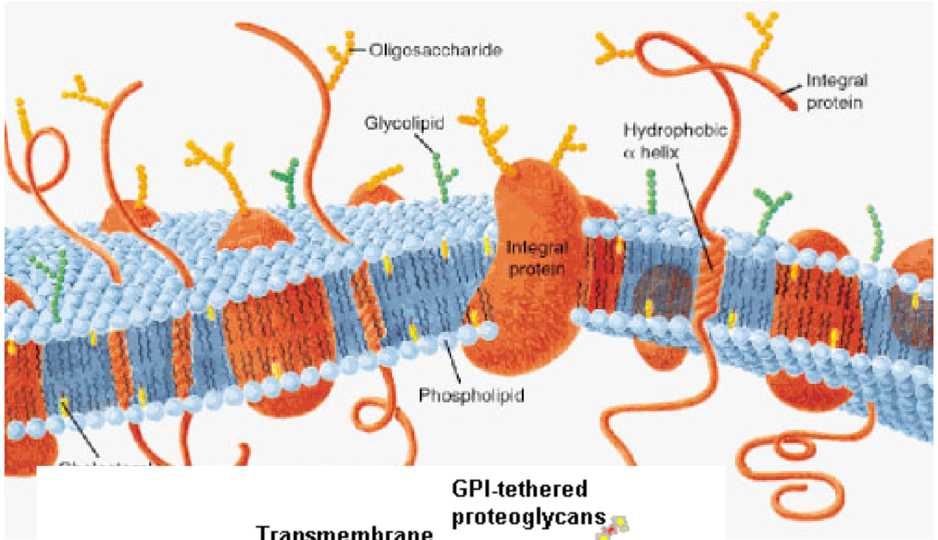
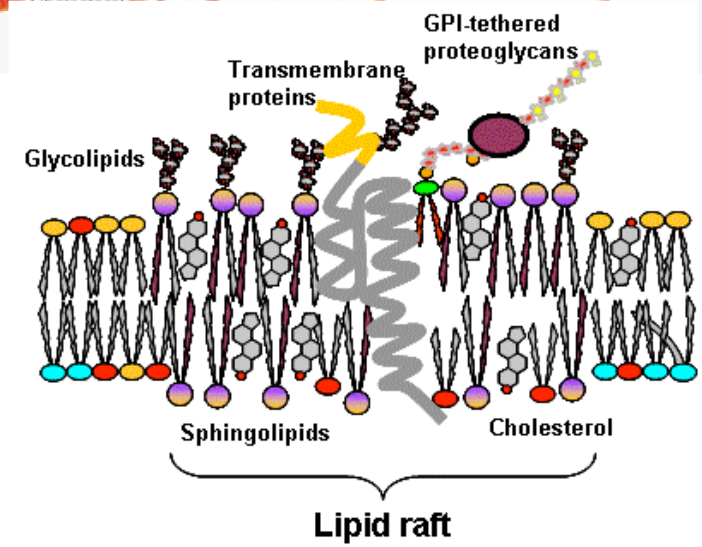
& MIGLENA ANGELOVA

INHOMOGENEOUS VESICLE AS MODEL SYSTEM FOR PLASMIC MEMBRANE

- Cell membrane:bilayer of lipids
  More than one hundred: sphingolipids,phospholipids,chole sterol
- Proteins: integral,peripheral
- Sugar
- Possible existence of rafts
  Growing elastic membrane. Branching (3D network structure).



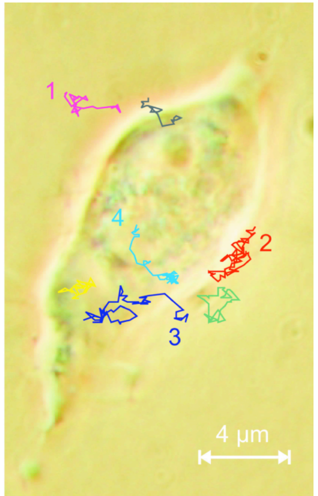


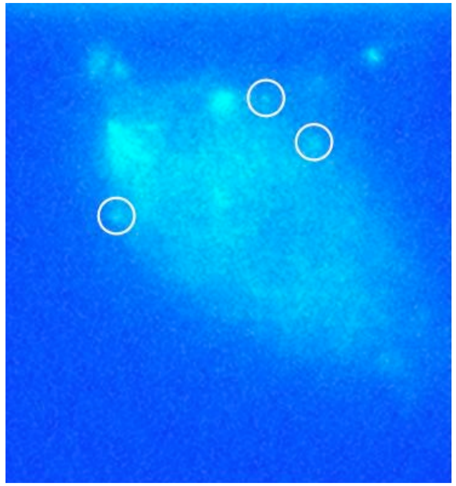
Raft or liquid-ordered domain:sphingo-lipids+cholesterol.
In cells:10 nanometers. Observe the thickness variation!

Elastic properties of the plasma membrane

- Undulations: cell motility

- Endocytose or exocytose
  Very important in virology.
  (Pr C. Brauche,Munich)

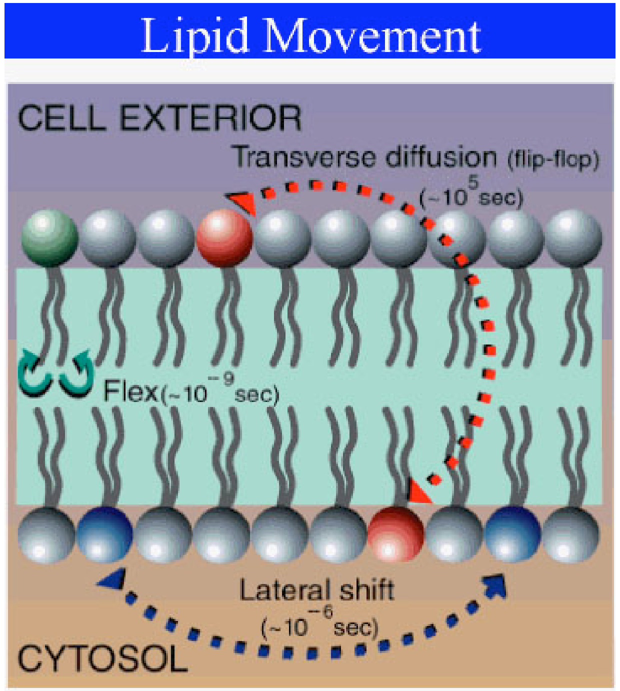




- Fusion:

Fluidity of the plasmic membrane

- Lipid fluidity
  - Lateral dislacement:1 micron/s
  - Flip-flop:10^5 seconds (in discussion)



Fluidity of proteins by cell fusion

Experience of D. Frye and M. Edidin,J. Cell Sci (1970)

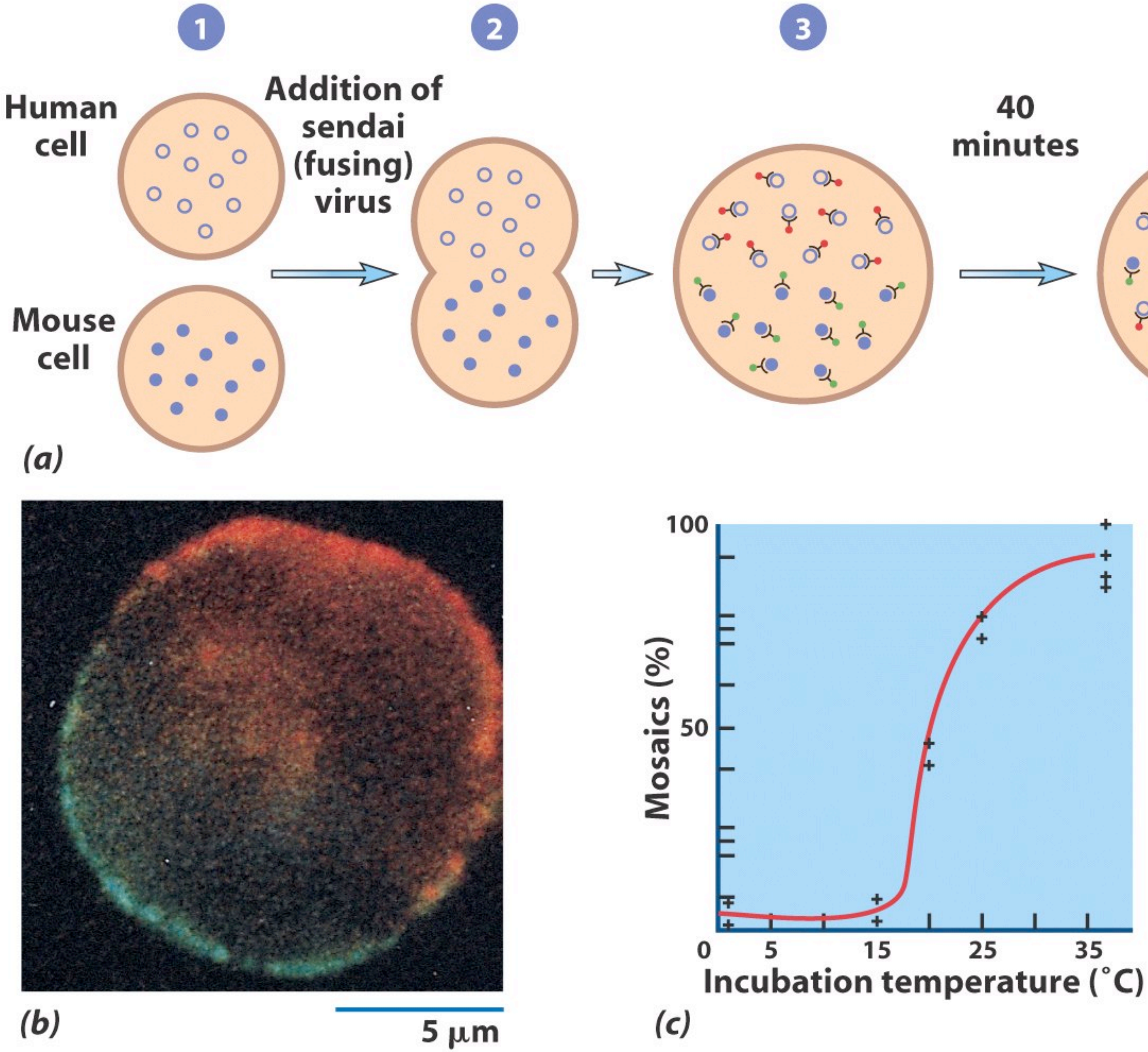
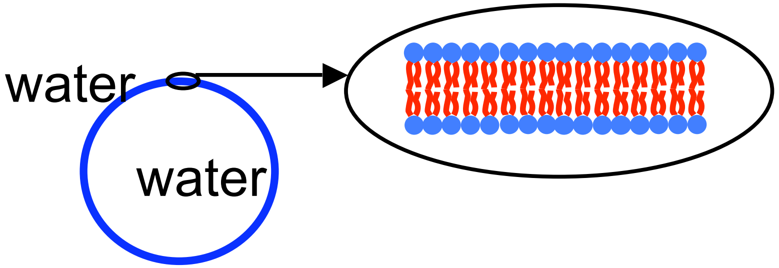
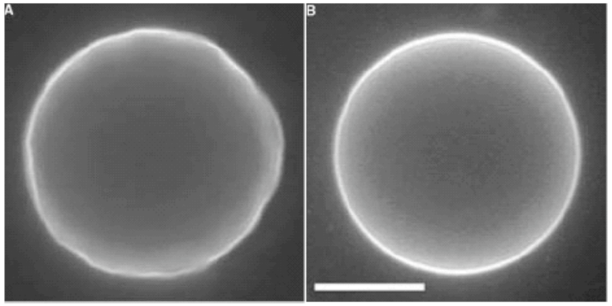


Figure 4-25 Cell and Molecular Biology, 4/e (© 2005 John Wiley & Sons)

Model system: vesicle

- Vesicles: a bag of lipids in water
- Different physical properties: more or less stretched: E. Karatekin et al ,biophys.(2003)





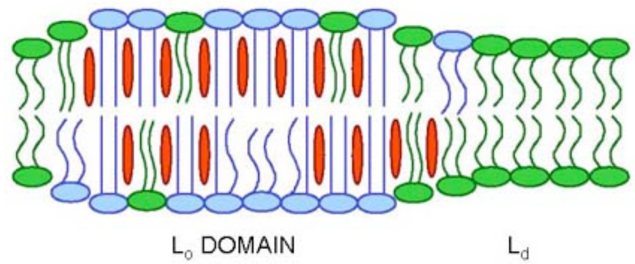
- Basic modeling
  Fluid in the plane (Saffman and Delbruck model ,P.N.A.S. 1975)
  Elastic for deformations out of the plane but with pressure and tension

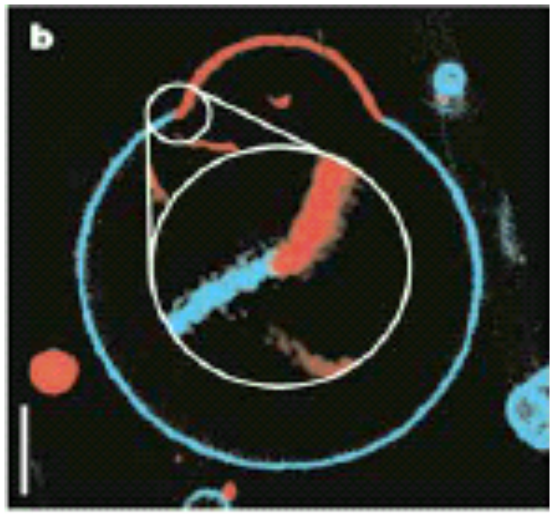
Ref:Canham -Helfrich model

Inhomogeneous vesicles

- With ternary mixtures: lo and ld domains.

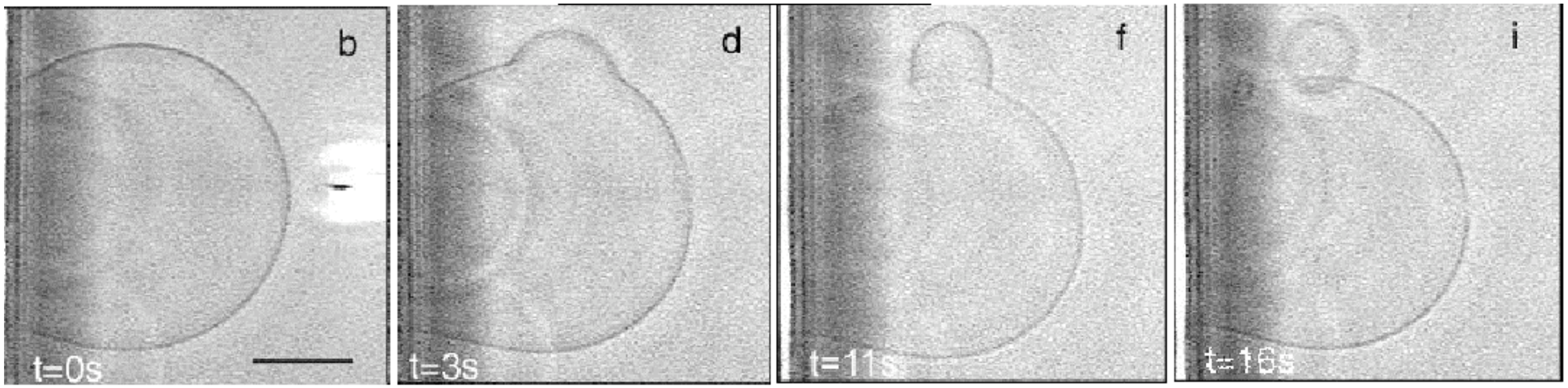
- Same physical properties but (lo) more “viscous” or more “resistant” to elastic deformations and also to detergents.





T. Baumgart, S.T. Hess, W.W. Webb, Nature, **425**, pp 821-824 (2003), bar = 5 μ m

Absorption of PLA2: budding of the raft phase



(1) Initial state: vesicle including a raft, stable (about 8 hours)

(2) After protein injection, the system becomes instable.

(3) Under appropriate experimental conditions, the raft can be ejected

G. Staneva, M. Angelova, K. Koumanov, Chemistry and Physics of Lipids, 129, 53, 2004

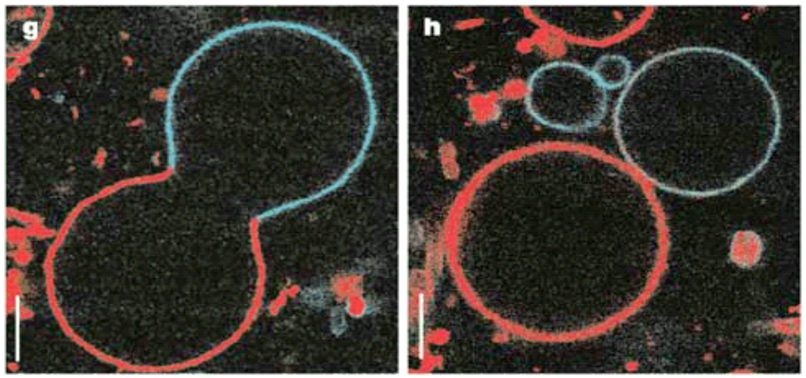
Budding events:detergent and osmotic chocs

Detergents

- Specific ejection of domains
- Small domains are ejected first.
- Possible shape instability.

Osmotic shocks

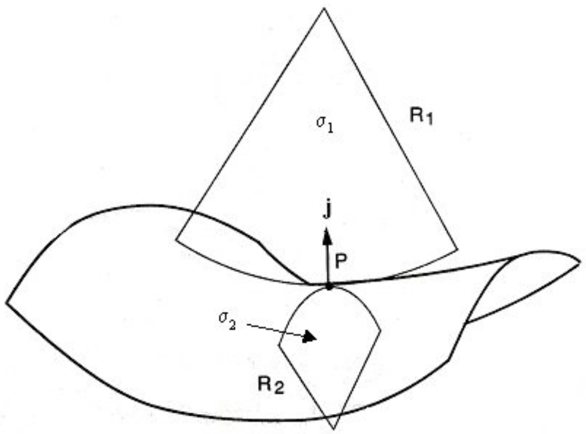
- Fast fission:T. Baumgart,S.T. Hess and W.W. Webb , Nature 03.
- T<0.5 s. domain in red: liquid-disordered
  domain in blue : liquid-ordered



bar = 5 μ m

Bilayer description

- Membrane elasticity (Canham-Helfrich model). Only bending energy ,no stretching!!!!
- Two bending rigidities: κ and κ_G



$$H = -\frac{1}{2}\left(\frac{1}{R_1} + \frac{1}{R_2}\right) \quad \text{et} \quad K = \frac{1}{R_1}\frac{1}{R_2}$$

Bending energy:

$$\frac{\kappa}{2}\int_S (\mathrm{H} - \mathrm{H}_0)^2 dS + \kappa_G \int_S \mathrm{K} dS$$

H0: the spontaneous curvature. Important for plasmic membrane and tubes.

Physical description of a two-phase vesicle

Membrane with two domains

Same description for the two domains in liquid state

$$F_b^i = \frac{\kappa_i}{2}\int_{\mathcal{S}} (\mathsf{H} - \mathsf{H}_0)^2 dS + \kappa_{G_i}\int_{\mathcal{S}} \mathsf{K} dS + \Sigma_i \int_{\mathcal{S}} dS$$

Sharp interface =⟩ line tension σ

$$F_{ves} = \sum_{i=1,2} F_b^i - P\int_{\mathcal{V}} dV + \sigma \int_{\mathcal{C}} dl$$

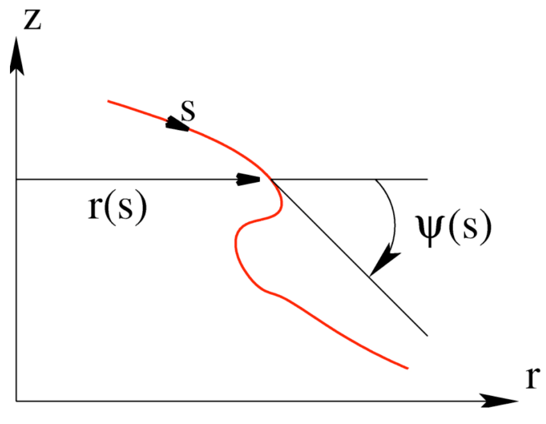
Parameterization

- ➥ Axisymmetric vesicle
- ➥ Parameter: arc-length s

=⟩ Shape given by r(s) and ψ (s)

➥ Geometric relation $\dot{r} = \cos\psi$

=⟩ Local Lagrange multiplier



Euler-Lagrange equations

$$\frac{\kappa}{P}\left(\ddot{\psi}-\frac{\sin\psi\cos\psi}{r^2}+\dot{\psi}\frac{\cos\psi}{r}\right)=-\frac{r}{2}\cos\psi+\frac{\gamma(s)}{P}\frac{\sin\psi}{r}$$

<<1

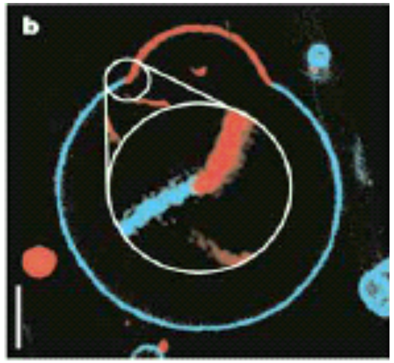
<<1

$$\frac{1}{P}\dot{\gamma}(s)=\frac{\kappa}{2P}\left(\dot{\psi}^2-\frac{\sin^2\psi}{r^2}\right)+\frac{\Sigma}{P}-r\sin\psi$$

$$\dot{r}=\cos\psi$$

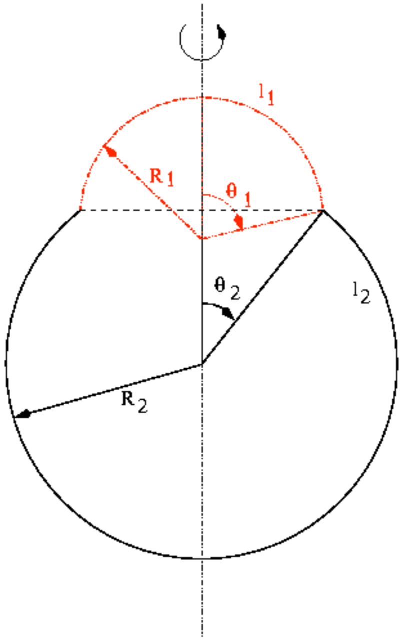
Case κ = 0, balance of pressure P and tension Σ

Two spherical caps



Stretched vesicle

- κ = 0,Euler-Lagrange=> two-spherical caps
- Boundary-conditions: 1) Surface constraints



$$2\pi R_1^2(1-\cos\theta_1) = S_1 = Cte$$

$$2\pi R_2^2(1+\cos\theta_2) = S_2 = Cte$$

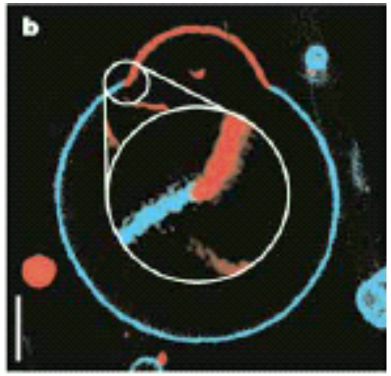
- 2) Interface continuity:

$$R_1 \sin\theta_1 = R_2 \sin\theta_2$$

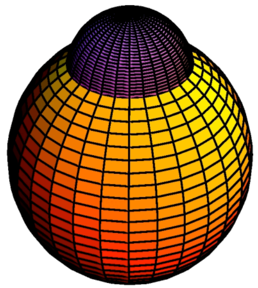
-3) Force equilibrium:

$$\frac{1}{2}R_1^2\cos\theta_1\sin\theta_1 = \frac{1}{2}R_2^2\cos\theta_2\sin\theta_2 - \frac{\sigma}{P}$$

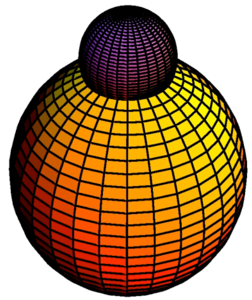
Stretched vesicles (κ=0)



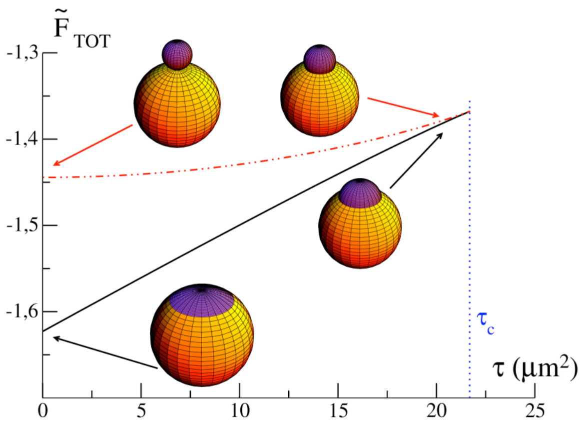
$$\tau = 20.5\mu m^2$$



Stable



Instable



=> Capillary bifurcation

(as a soap film between rings)

Taking into account bending elasticity

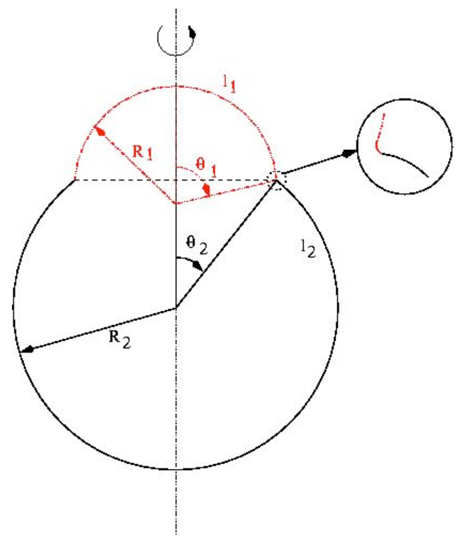
- Consequences of this model
  - The order parameter "τc" depends on "f", the surface fraction
  - Small domains are ejected first,contrary to alternative theory: balance of elasticity and line tension

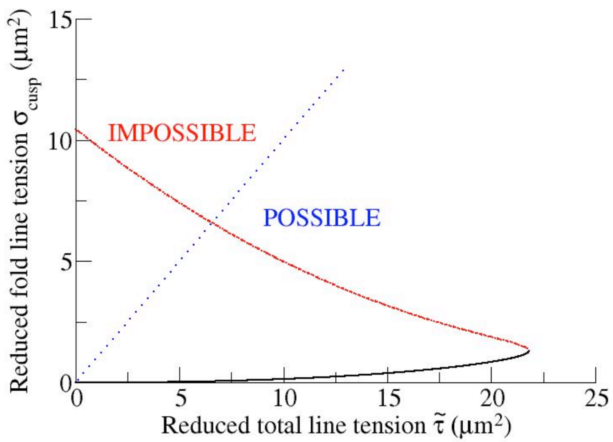
- Elasticity via a boundary layer analysis

$$l_e = \sqrt{\frac{\kappa_i}{PR_i}} \simeq 0.5\mu m$$

  - Elastic length:
    Effective line tension
  - Effective order parameter:

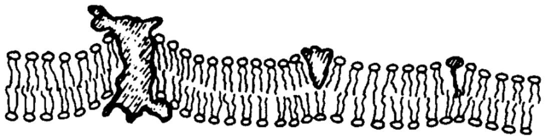
➥ Same bifurcation with $\tau = \dfrac{\sigma + \sigma_{el}}{P}$





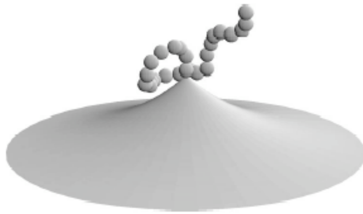
Protein inclusion

- 1. Addition of proteins
- 2. Model:
    - Coupling between concentration and curvature



S. Leibler, J. Physique, **47**, 507-516, 1986

conical defects



T. Bickel *et al.*, PRE, **62** (1), 1124-1127, 2000

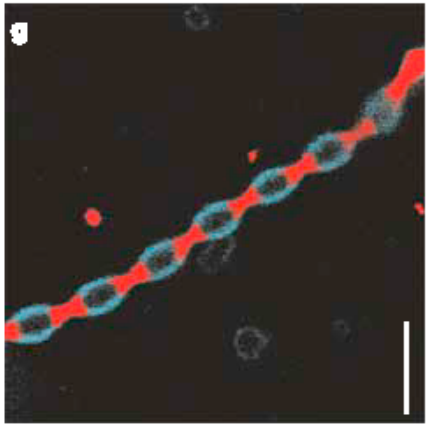
entropic pressure

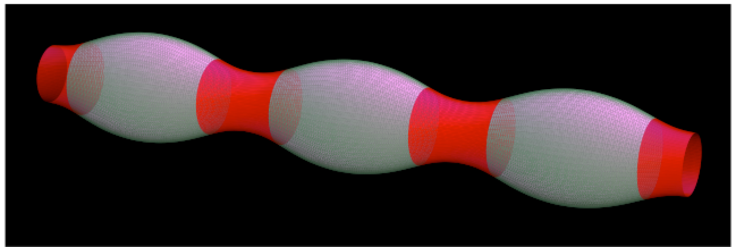
- 3. Adsorption of proteins via a Landau model

$$F^{i}_{mol} = \int_{S_i} \left\{ \Lambda_i H \phi + \left[\frac{\alpha_i}{2} (\phi - \phi_{eq})^2 - \mu_i \phi + \frac{\beta_i}{2} (\nabla \phi)^2 \right] \right\} dS$$

Tubes of membrane

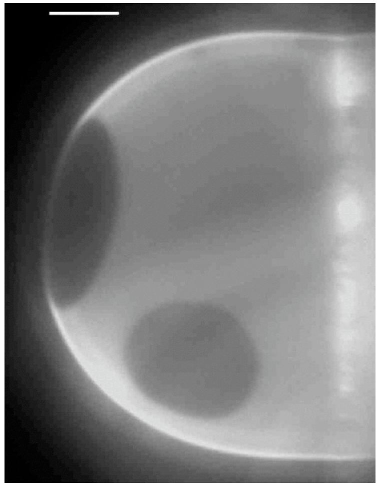
- Exists in the cell:trasport of proteins
- Extraction from   vesicles by laser or molecular motors-> a force is necessary
- One can play with temperature (Cornell group)
- Ab-initio simulations of Felix Campelo and Jean-Marc Allain (Europhys. let.07)
- No adjustable parameters:agreement for the wavelength





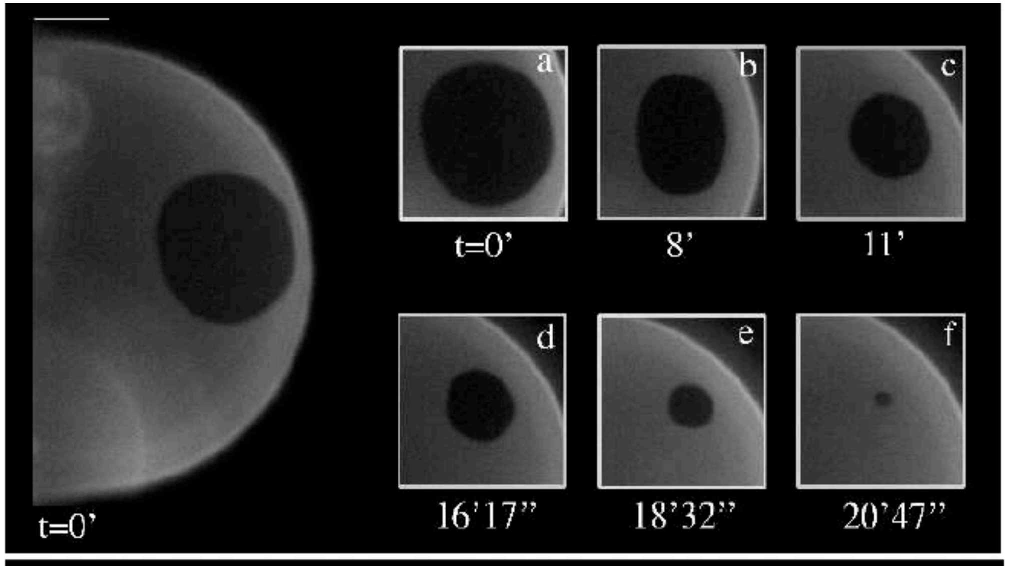
Complete Euler-Lagrange equations. Minimization for the wavelength selection.

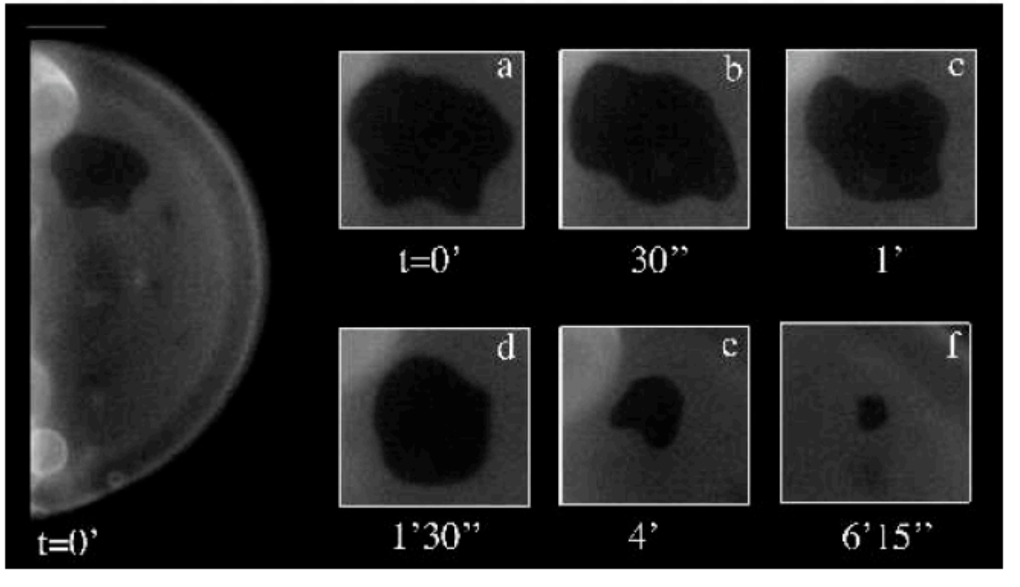
TEST OF MEMBRANE FLUIDITY: suction



- Cell membrane: inhomogeneous medium. « rafts »
- Rafts: domains enriched in cholesterol.
- Rafts: domain assumed more viscous that the lipidic membrane.
- Idea: make an instability of suction induced by lipo-proteins HDL
- Hydrodynamic instability or out-of-equilibrium instability.

SUCTION BY HDL



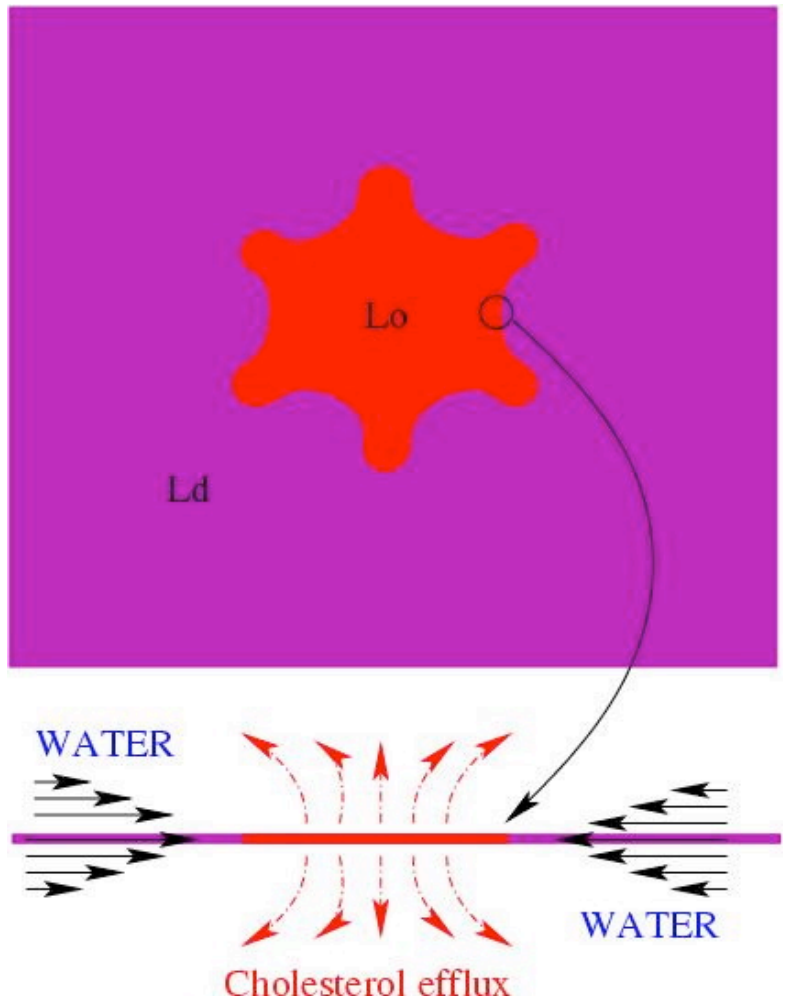


MODEL OF SAFFMAN-DELBRUCK

- We neglect the thickness of the bilayer h=5nm compared to the size of the raft R=5 μm
- Can we neglect water ?
- With 3 phases:dual integral equations (P.Saffman,H.Stone,A. Bernoff) or Green's Functions (D.Lubensky and R. Goldstein)

$$N = (\mu_w / \mu_l)(R / h)$$

- We restrict to two phases: two-dimensional Stokes flow with a suction process.
- Analogy with the Saffman-Taylor viscous fingering instability



STOKES INSTABILITY OF SUCTION

- Linear stability

$$R = R_0(t)[1 + \varepsilon_n \Omega_n \cos(n\theta)]$$

$$\Omega_n = \frac{2Q}{R^2{}_0} - \frac{n}{2}\frac{\sigma}{(\mu_o + \mu_d)R_0}$$

Selection: variationnal calculus

$$\Xi = \gamma \oint \kappa(\vec{V}_l.\vec{n})dl + \sum_l \Big[\Lambda_l \iint (div\vec{V}_l + q_l)dS$$

$$+ \sum_{ij} \iint \{-p_l\delta_{ij} + \mu_l(2e_{ij} - e_{ii}\delta_{ij})\}e_{ij}dS \Big]$$

With e_{ij} the viscous stress tensor and Λ, the Lagrange parameters in each phase.

$$n_s = \frac{8}{3}\eta^2(\mu_{lo} + \mu_{ld})\frac{Q}{\sigma R_0}$$

CONCLUSIONS

1) J.-M. Allain et M. Ben Amar,

« Bi-phasic vesicle: Instability induced by adsorption of proteins », Physica A 337,531-545 (2004)

2)J.M. Allain, C. Storm,A. Roux,M. Ben Amar and J.F. Joanny, ’’Fission of a multiphase membrane", P.R.L. 93 (15),158104-1,158104-4 (2004)

3)J.M. Allain and M. Ben Amar,

« Budding and fission of a multi-phase vesicle »,E.P.J.E.20,409-420 (2006)

4) J.B. Fournier and M. Ben Amar

« Creases and effective contact-angle betwenn membrane domains with high spontaneous curvature », E.P.J.E. 21 11-17 (2006)

5)F. Campelo,Jean-Marc Allain and M. Ben Amar

« Periodic lipidic membrane tubes », Europhysics letters 77,38007 (2007)