

Vesicle micro-hydrodynamics

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Outline

Vesicles in equilibrium

Vesicles in flow: *deformation does matter!*

Motivation: cell hydrodynamics

Examples:

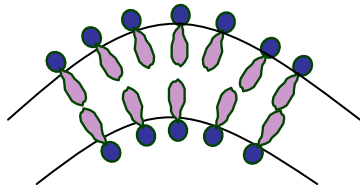
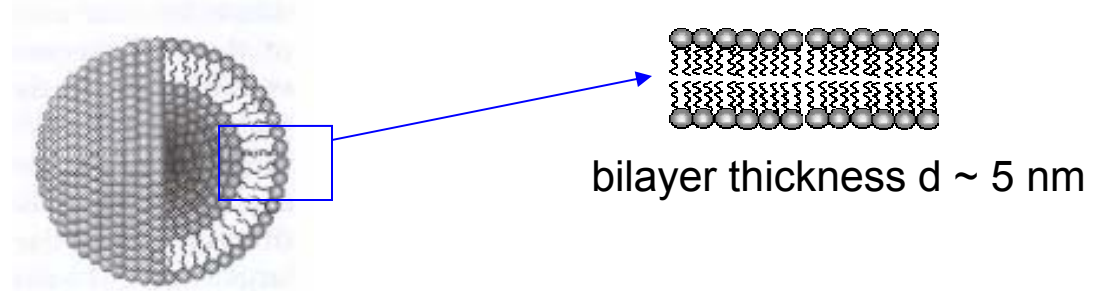
- deformation in unbounded flow
- migration in wall-bounded flow
- “parachutes” in microchannels
(rheology of suspensions)

Theory:

- simulations: boundary integral method
- analytical: small deformation expansion

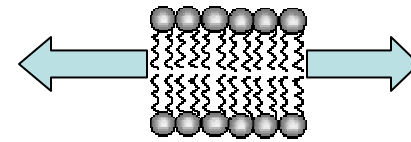
Vesicle adhesion

Vesicles: equilibrium



$$\kappa \approx 10\kappa_B T$$

bending



stretching

$$F = \kappa \int 2H^2 dA + \sigma A + \Delta p V$$

free energy
(Helfrich)

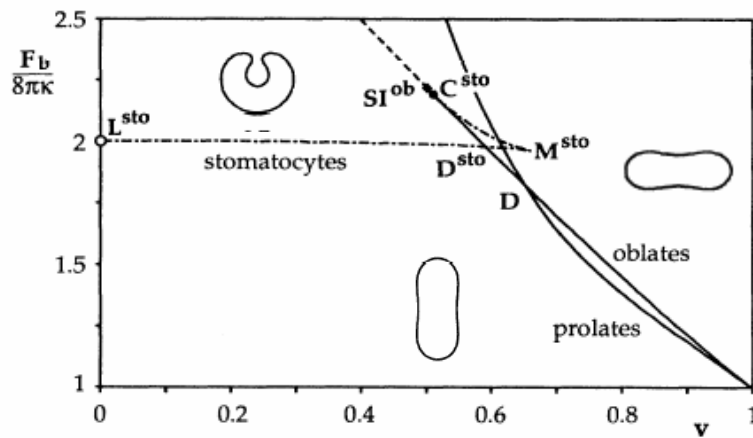
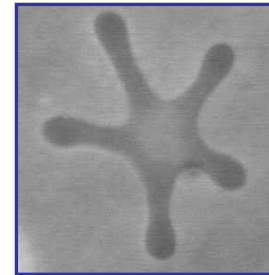
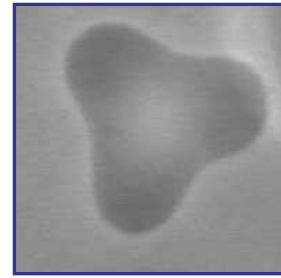
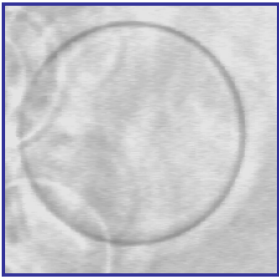
area
conservation

volume
conservation

κ bending modulus
 H mean curvature = $1/R_1 + 1/R_2$
 σ surface tension

A area
 V volume
 Δp pressure jump across the membrane

Vesicles: equilibrium shapes



Reduced volume
(‘excess’ area)

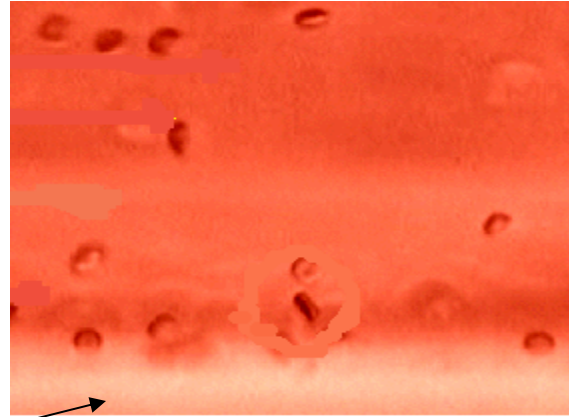
$$v = \frac{V}{\frac{4\pi}{3} \left(\frac{A}{4\pi}\right)^{3/2}}$$

Seifert, *Adv.Phys.* **46** (1997)

Motivation: cell hydrodynamics

Fahraeus effect

decrease in blood apparent viscosity



layer depleted of red blood cells near the wall

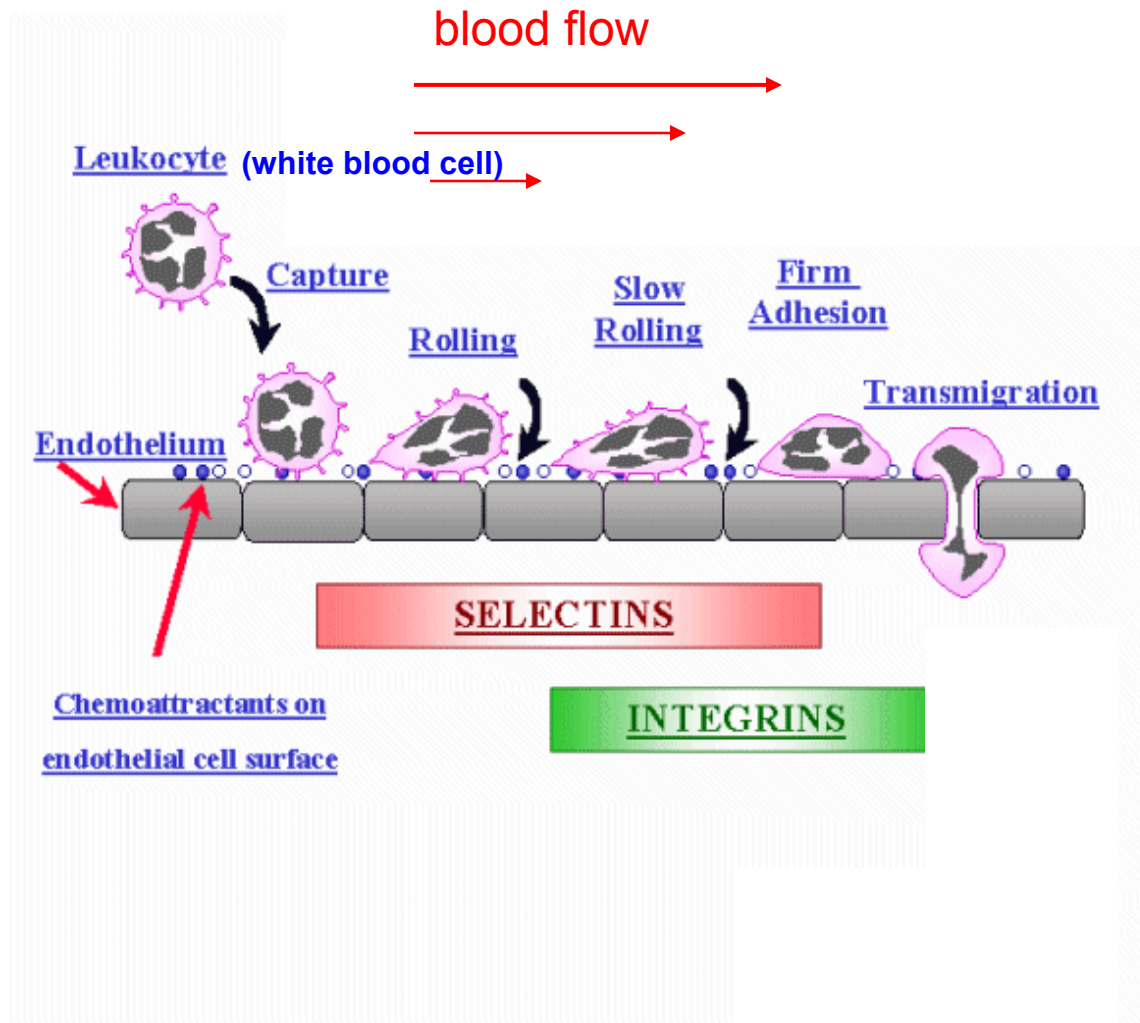
(A. Viallat, Grenoble)

Cell traffic between blood stream and tissues

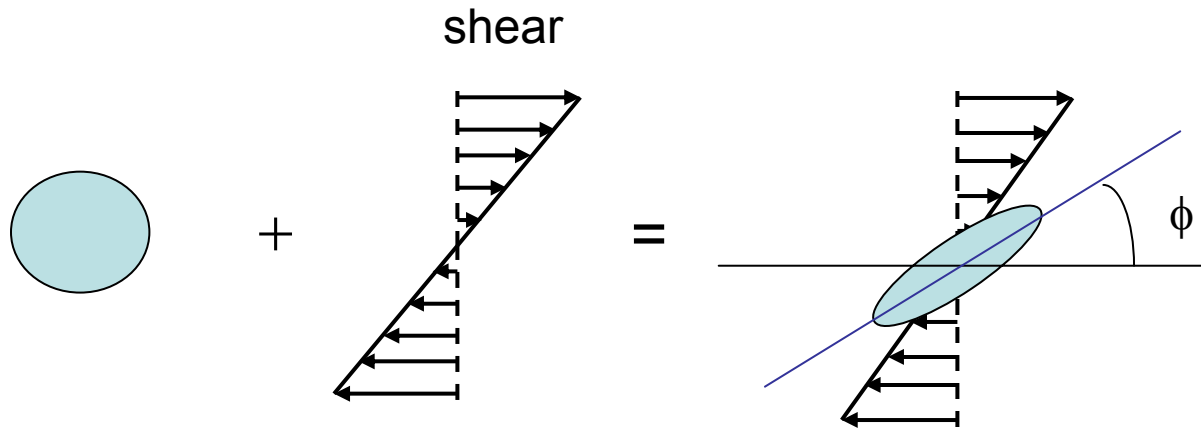
- inflammatory response
- tumor metastasis
- formation of atherosclerotic plaques

Motivation: cell hydrodynamics

inflammatory response (healing an injury)

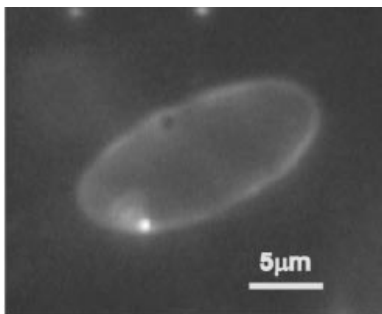


Vesicle dynamics in flow: unbounded shear 1



The shape is not given a priori !

low shear rates: *tank-treading*



Kantsler and Steinberg, PRL **95** (2005)

vesicle deformation?
 orientation?
 stationary shapes?
 flow-induced shape transitions?

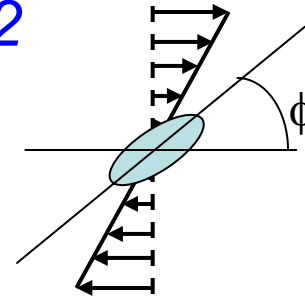
$$\phi - \frac{\pi}{4} \sim \sqrt{\Delta}$$

$$\Delta = A - 4\pi a^2$$

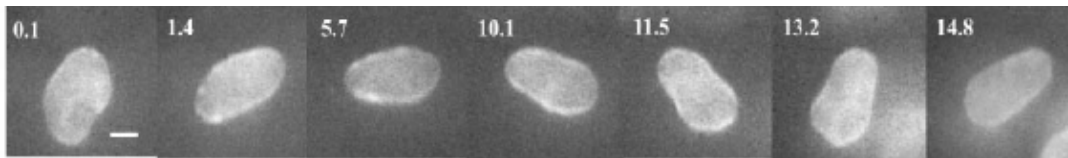
Seifert, Eur. Phys. J. B **8** (1999)

Misbah, PRL **96** (2006)

Vesicle dynamics in flow: unbounded shear 2



high shear rate: *tumbling*



$$\phi \sim (\lambda - \lambda_c)^a$$

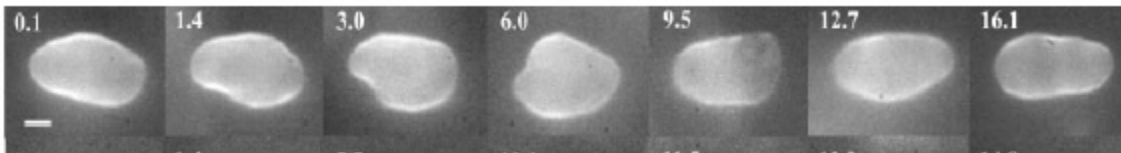
theory (Misbah) $a=0.5$

Kantsler and Steinberg, PRL **96** (2006)

transition to tumbling?

high shear rate, high viscosity contrast λ

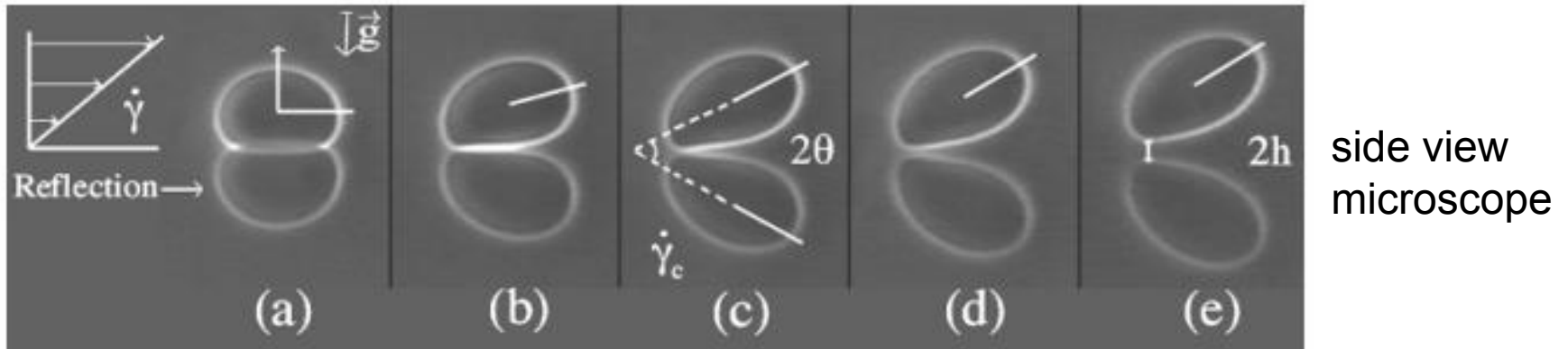
“breathing” vesicle?



Vesicle dynamics in flow: near a wall

vesicle detachment ? \leftrightarrow cell adhesion

Abkarian et al. PRL **88** (2002), Biophys. J. **89** (2005)



$$F_L \sim \dot{\gamma}^2$$

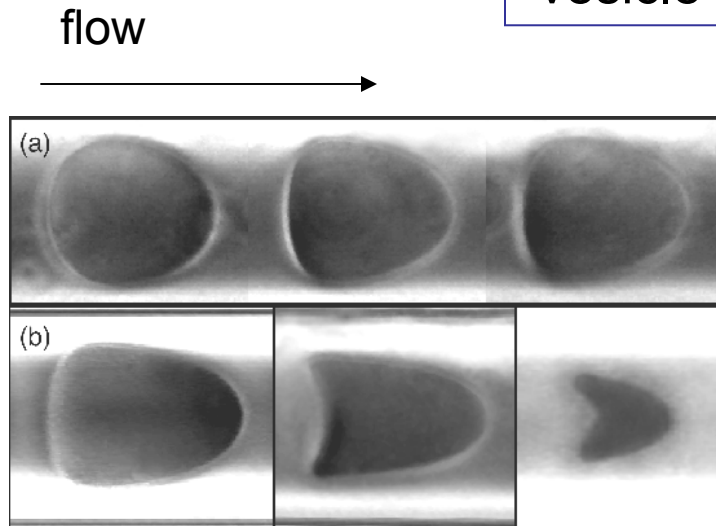
$$F_L \sim \dot{\gamma}$$

lift force?

$$F_L (\dot{\gamma}, v, h, \kappa \dots)$$

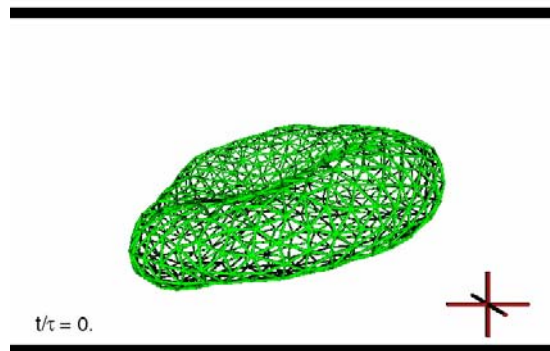
Vesicle dynamics in flow: microchannel

vesicle “parachutes” ? \leftrightarrow RBC in capillaries



Vitkova et al. Europhys. Lett. (2004)

discocyte – parachute transformation:



shapes?
shape transitions?

Noguchi and Gompper, PNAS 102(40) (2005)
(see supplemental info)

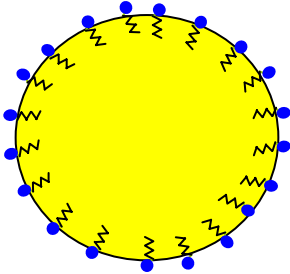
Deformable “objects” in flow

a free-surface boundary problem

Drops: compressible interface, surface tension rules

Vesicles: incompressible interface, bending stresses rule

Drop dynamics in flow

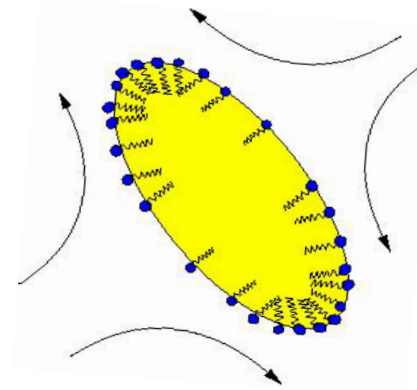


Equilibrium:

Drop shape is spherical
Surfactant distribution is uniform

Laplace's equation

$$p_{in} - p_{out} = 2\sigma H$$



Flow:

Drop deforms
→ nonuniform curvature
capillary stresses

Surfactant is redistributed
→ gradients in surface tension $\nabla_s \sigma$
Marangoni stresses

area changes (*compressible interface*)

Vesicles – what's new?

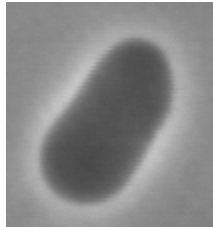
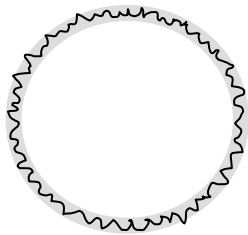
Vesicle dynamics in flow

Equilibrium:

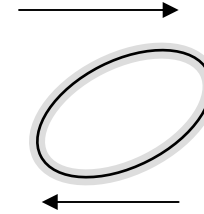
shape need **not** to be spherical



vesicle is “rough” → **fluctuations**



Flow:



shape deforms
→ nonuniform curvature
capillary stresses

bending stresses

area is conserved

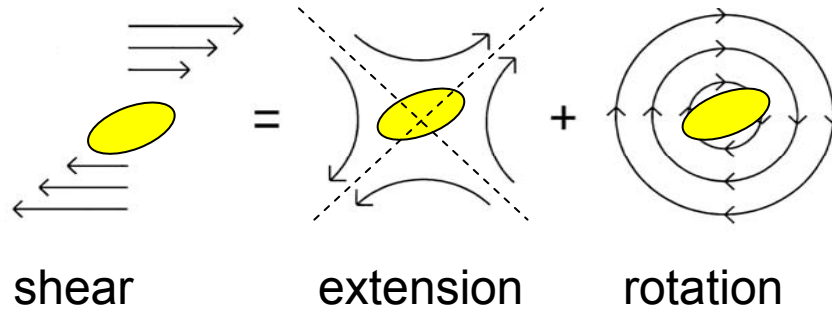
incompressible interface

→ gradients in effective tension
Marangoni stresses

Laplace's equation

$$p_{in} - p_{out} = 2\sigma H - \kappa \left[4H^3 - 4HK + 2\nabla_s^2 H \right]$$

vesicle dynamics: time scales



“distorting”

$$t_d = \hat{\lambda} \dot{\gamma}^{-1}$$

convection by the extensional component of the flow

“restoring”

$$t_{\text{cap}} = \frac{\hat{\lambda} \eta a}{\sigma}$$

capillary relaxation

$$t_{\text{ben}} = \frac{\hat{\lambda} \eta a^3}{\kappa}$$

bending relaxation

$$t_{\text{mar}} = \frac{\hat{\lambda} \eta a}{\Delta \sigma}$$

relaxation driven by interfacial tension gradients

$$t_{\text{rot}} = \dot{\gamma}^{-1}$$

rotation

(gets to be important at high λ)

$$\hat{\lambda} = \lambda + 1$$

λ viscosity ratio

Dimensionless parameters

$$\frac{t_{\text{cap}}}{t_d} = Ca$$

Capillary number

relaxation
distortion

$$\frac{t_{\text{ben}}}{t_d} = Ca_{\kappa}$$

Bending parameter

$$\frac{t_{\text{mar}}}{t_d} = Ma$$

Marangoni parameter

$$\frac{t_{\text{rot}}}{t_d} = \hat{\lambda}^{-1}$$

rotation parameter

interplay of different time scales \Rightarrow complex dynamics

Dimensionless parameters

$$\frac{t_{\text{cap}}}{t_{\text{d}}} = Ca$$

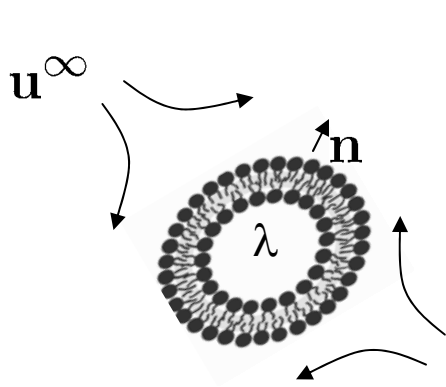
Capillary number = flow strength

$$Be = \frac{t_{\text{cap}}}{t_{\text{ben}}} = \frac{\kappa}{\sigma a^2}$$

bending number

'elastic vesicle' regime (area not conserved)

Problem formulation: governing equations



Stokes flow

$$Re = \frac{\rho a u^\infty}{\eta} \ll 1$$

$$\eta_i \nabla^2 \mathbf{u}_i - \nabla p_i = 0 \quad i=in, out$$

viscosity ratio

$$\lambda = \eta_{in}/\eta_{out}$$

Boundary conditions:

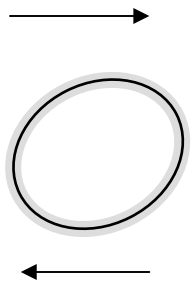
continuity of velocity across the membrane

$$\mathbf{u}_{in} = \mathbf{u}_{out} \equiv \mathbf{u}_s$$

shape evolution

$$\frac{\partial r_s}{\partial t} = \mathbf{u}_s \cdot \mathbf{n}$$

Problem formulation: stress boundary condition & more



hydrodynamics stress balanced by *interfacial stresses*

$$\mathbf{t}[\mathbf{u}_{\text{out}}] - \mathbf{t}[\mathbf{u}_{\text{in}}]$$

$$= \boxed{2\sigma H \mathbf{n}} - \boxed{\kappa (4H^3 - 4HK + 2\nabla_s^2 H) \mathbf{n}} - \boxed{-\nabla_s \sigma}$$

capillary

bending

Marangoni

incompressible surface:

area conservation

$$\frac{dA}{dt} = 0 \quad \longrightarrow \quad \nabla_s \cdot \mathbf{u} = 0$$

$\sigma(A)$

compressible surface:

lipid conservation $\frac{\partial \Gamma}{\partial t} = \nabla_s \cdot (\Gamma \mathbf{u})$

$\sigma(\Gamma)$

Problem solution: general

unbounded flow, single particle

$$\nabla^2 \mathbf{u} - \nabla p = -\mathbf{f} \delta(\mathbf{r})$$

Green's function
(Oseen tensor)

point force solution
(stokeslet)

$$\mathbf{u}(\mathbf{r}) = \mathbf{G}(\mathbf{r}) \cdot \mathbf{f}$$

$$G_{ij} = \frac{\delta_{ij}}{r} + \frac{x_i x_j}{r^3}$$

stokes equation is linear

$$\mathbf{u}(\mathbf{r}) = \mathbf{u}^\infty + \int \mathbf{G}(\mathbf{r}, \mathbf{r}') \cdot \mathbf{t}(\mathbf{r}') d\mathbf{r}'$$

\mathbf{u}^∞ flow at infinity

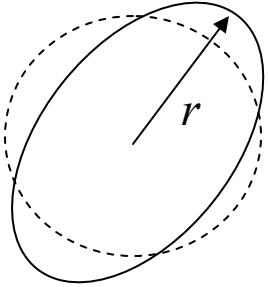
(integration along the particle surface)

integral representation for the velocity

Problem solution

Small deformations: Analytical solutions

perturbation expansions for small deviation from spherical shape
(*quasi-spherical vesicle*)



$$r(\theta, \phi) = 1 + \sum f_{lm} Y_{lm}(\theta, \phi)$$

θ, ϕ spherical coordinates

strong bending/strong tension/weak flow:

$$\varepsilon \equiv Ca \ll 1 \quad Be = \frac{\kappa}{\sigma a^2} \sim 1$$

$$f_{lm} = \varepsilon f_{lm}^{(1)} + \varepsilon^2 f_{lm}^{(2)} + \dots$$

Problem solution

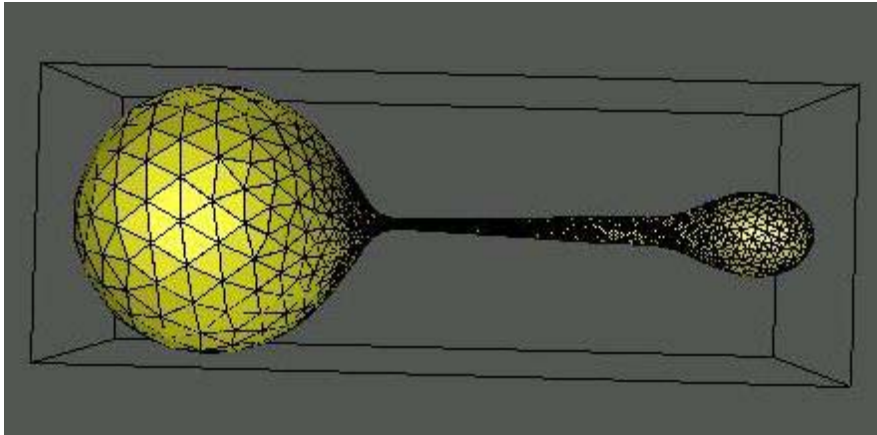
Large distortions: Numerical simulations

boundary integral method

$$\mathbf{u}(\mathbf{r}) = \mathbf{u}^\infty + \int \mathbf{G}(\mathbf{r}, \mathbf{r}') \cdot \mathbf{t}(\mathbf{r}') d\mathbf{r}'$$

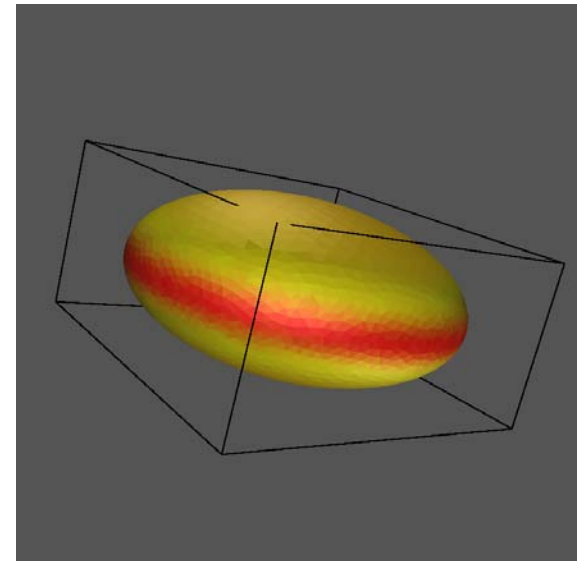
viscosity ratio $\lambda=1$

adaptive remeshing



Cristini et al. *Phys. Fluids* **10** (1998)

bending stresses

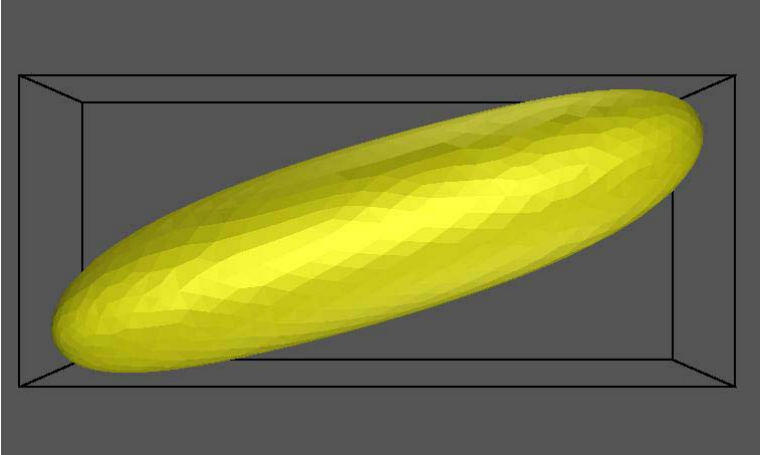


ellipsoid

red color signifies the magnitude²¹
of the bending stresses

Bending effects on deformation

Be=0 (no bending)

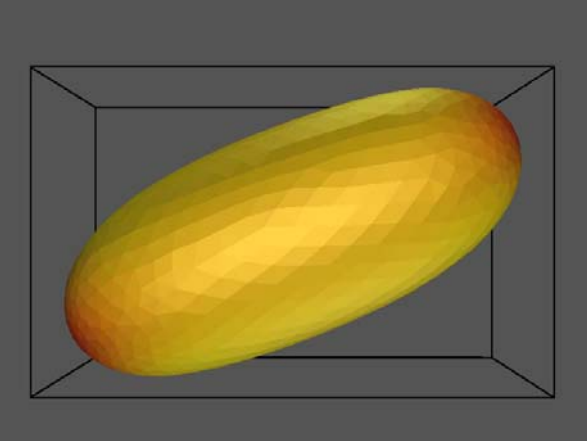


strong flow Ca=0.5

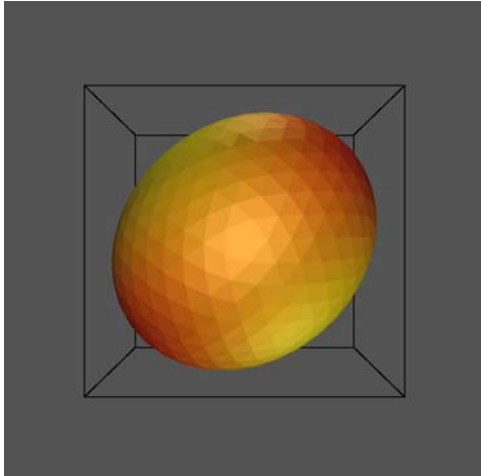
endtime=10

same drop!

Be=0.1



Be=10

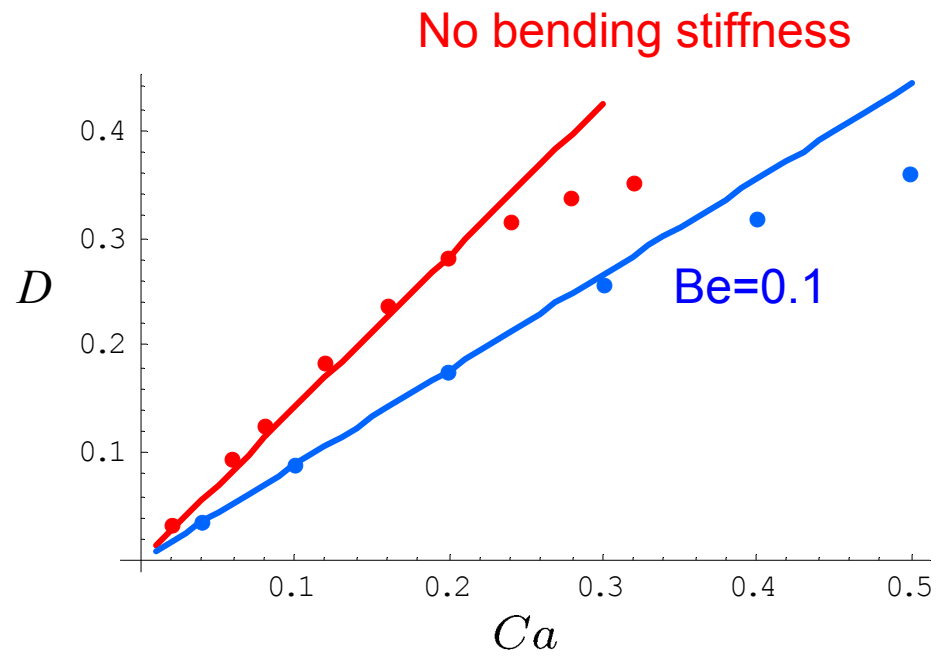
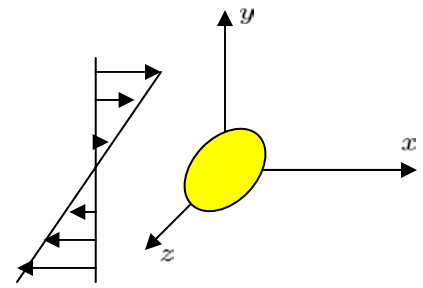


Bending effects on deformation

$$r(\theta, \phi) = 1 + \sum f_{lm} Y_{lm}(\theta, \phi)$$

Deformation parameter (ellipsoid)

$$D = f_{22} - f_{2-2}$$



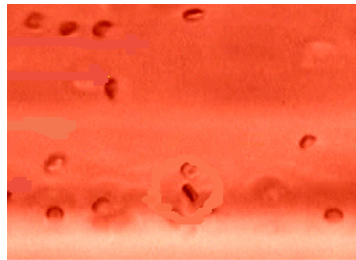
$$Ca = \frac{\eta \dot{\gamma} a}{\sigma} = \text{flow strength}$$

$$Be = \frac{\kappa}{\sigma a^2} \quad \begin{array}{l} \text{bending} \\ \text{-----} \\ \text{tension} \end{array}$$

symbols: BIM simulations
 lines: small deformation theory $O(Ca^2)$

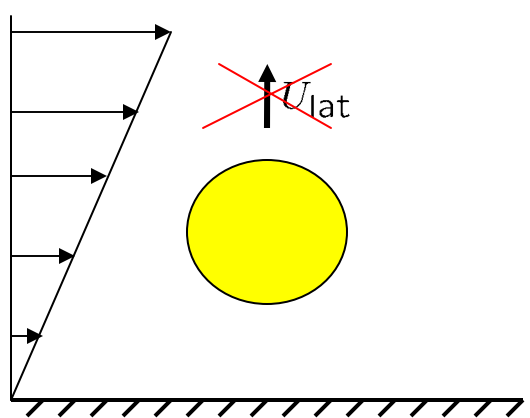
Effects of the wall: particle migration

Why do red blood cells go away from the wall?



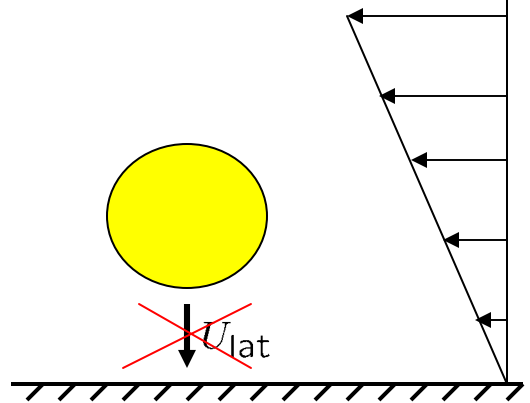
spherical neutrally-buoyant particle does not drift !

Stokes flow equations $\eta \nabla^2 \mathbf{u} = \nabla p \longrightarrow$ linear



\mathbf{u} , U_{lat}

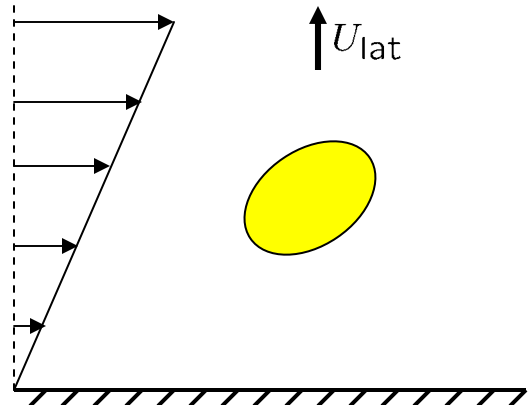
reversing the flow \longrightarrow



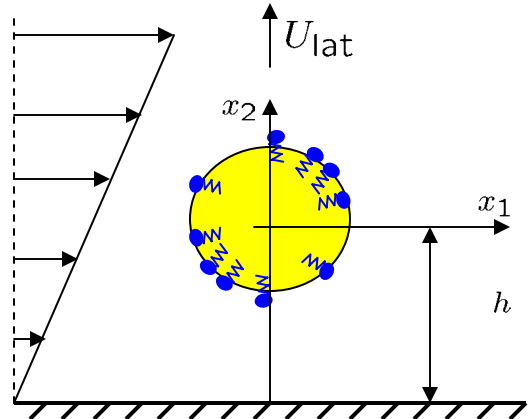
$-\mathbf{u} , -U_{lat}$

Particle migration away from a wall in shear flows

deformed drop



surfactant-covered, spherical drop



far-away from the wall

$$U_{lat} \sim \frac{Ca^2}{h^2}$$

nonlinear effect

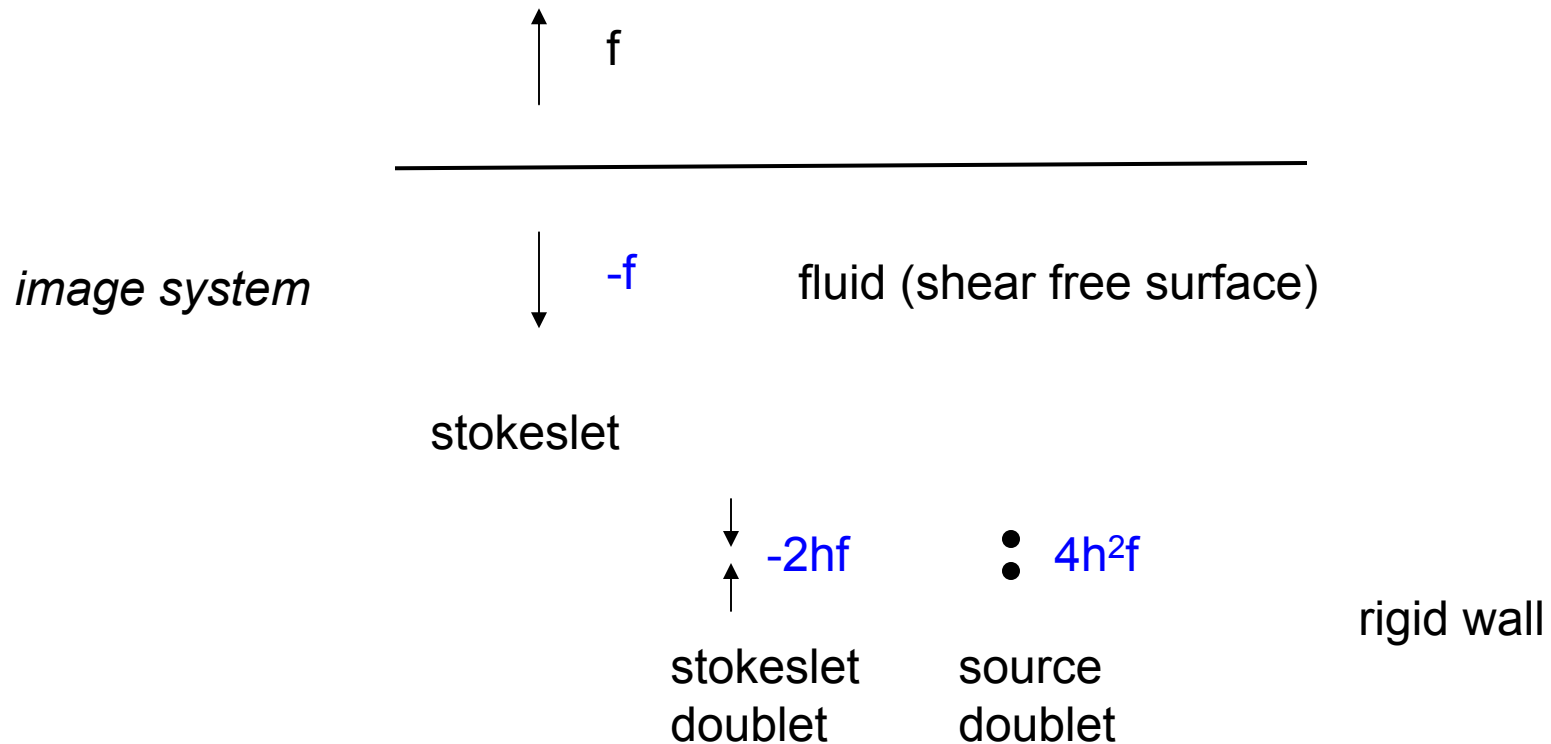
close to the wall – lubrication type analysis, numerical simulations....

Problem solution

wall-bounded flow

$$\mathbf{u}(\mathbf{r}) = \mathbf{u}^\infty + \int \mathbf{G}(\mathbf{r}, \mathbf{r}') \cdot \mathbf{t}(\mathbf{r}') d\mathbf{r}'$$

singularities formalism



Vesicle detachment

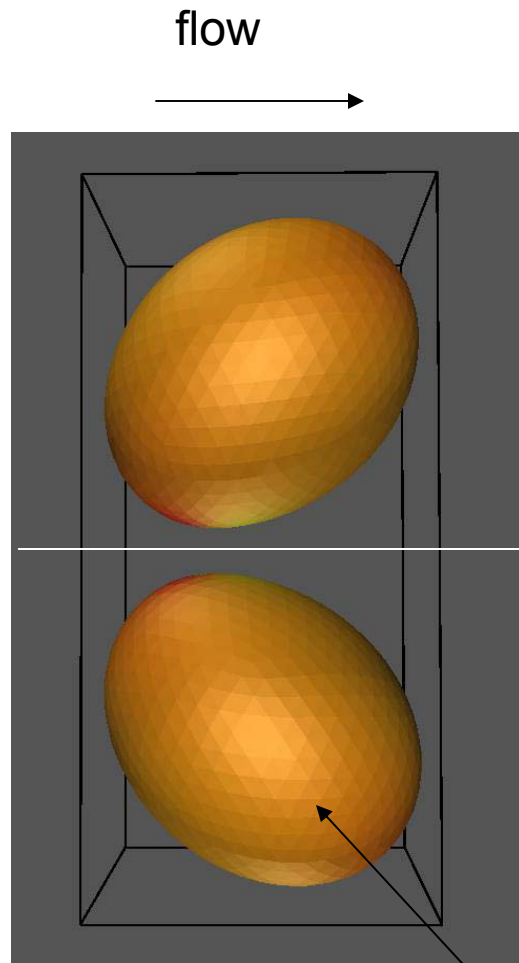
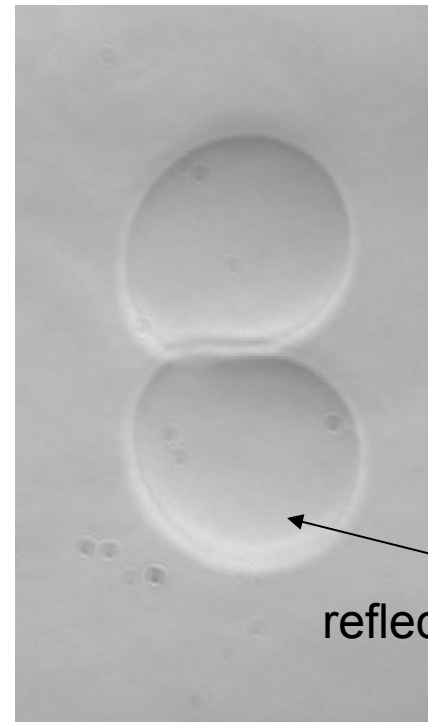


image drop

BIM simulation (shear free surface)



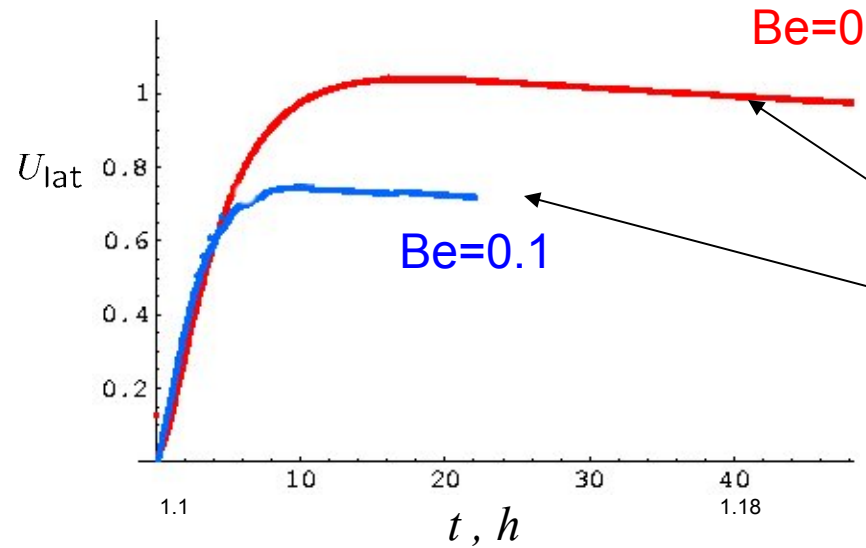
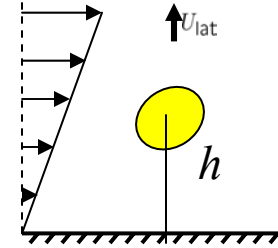
reflection

experiment:
side view microscope
vesicle on a glass substrate

Vesicle migration velocity

BIM simulations: preliminary results

$$Ca = 0.06$$



$$U_{lat} \sim \frac{1}{h^2} \frac{Ca^2}{1 + 6Be}$$

Bending stiffness decreases migration velocity

time?



Vesicle adhesion

A non-destructive method to obtain *adhesion strength* and *bending rigidity*.

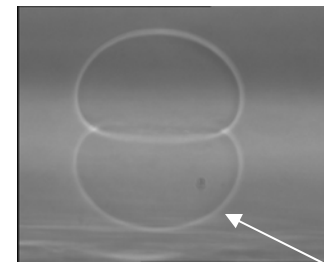
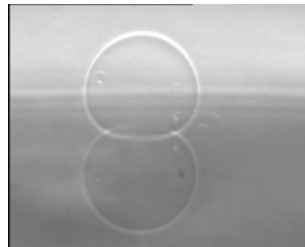
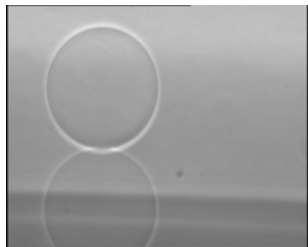
idea: compare vesicle shapes for different reduced volumes

Gruhn and Lipowsky PRE 71 (2005)

Materials: DOPC, DOPC+DOPG, DOPC+cholesterol

Experiment 1:

Side-view observation with the phase-contrast microscope

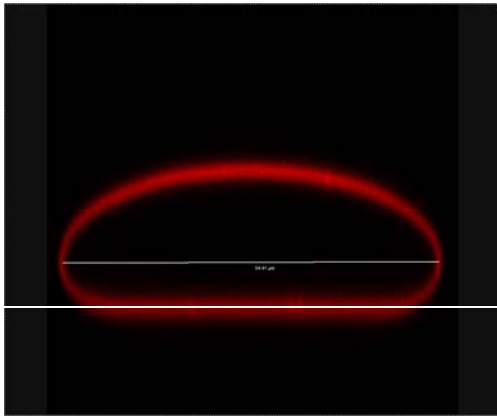


reflection

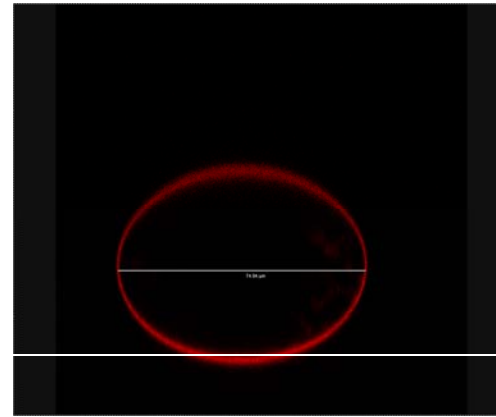
Vesicle adhesion

Experiment 2: side-view observation with the confocal microscope

DOPC:DOPG 9:1



DOPC:Cholesterol 8:2



D=70 microns

← substrate
(approximately)

increase in bending rigidity \Leftrightarrow less deformation

Data for DOPC:DOPG on a glass substrate

$$\kappa \sim 10 kT$$

$$W \sim 5kT \mu m^{-2}$$

(weakly adhering)

Summary

vesicle = deformable “drop” with bending stiffness

BIM simulations and small deformation analytical theory quantify:

- * deformation in unbounded flow
- * migration in wall-bounded flow

Future work

include membrane incompressibility

study: flow-induced shape transformations

budding

lift of adherent vesicles

near-contact motion ...

Acknowledgements

Theory group at MPIKG: <http://www.mpikg-golm.mpg.de/theorie/index.html>
Prof. Reinhard Lipowsky, Dr. Rumiana Dimova, Dr. Ruben Gracia,
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Thank you!

