Vesicle micro-hydrodynamics

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Outline

Vesicles in equilibrium

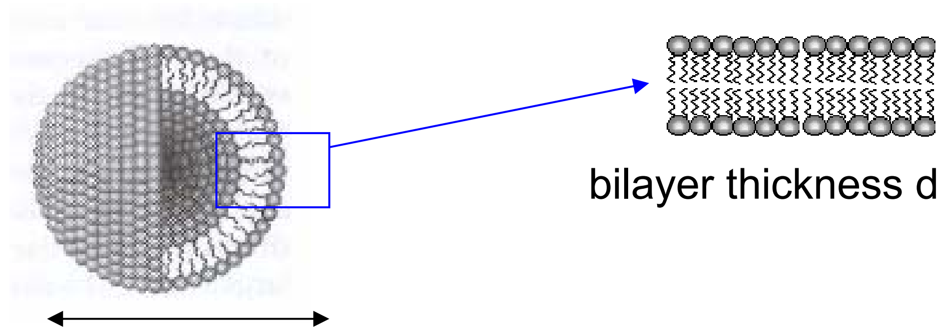
Vesicles in flow: *deformation does matter!*
Motivation: cell hydrodynamics

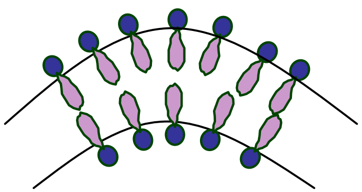
Examples:
deformation in unbounded flow
migration in wall-bounded flow
“parachutes” in microchannels
(rheology of suspensions)

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

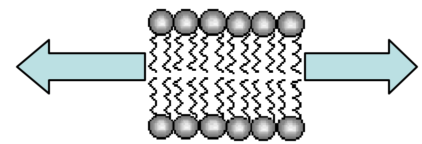
Vesicle adhesion

Vesicles: equilibrium





$\kappa \approx 10\kappa_B T$



bending

stretching

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

free energy
(Helfrich)

area
conservation

volume
conservation

κ bending modulus

H mean curvature=$1/R_1+1/R_2$

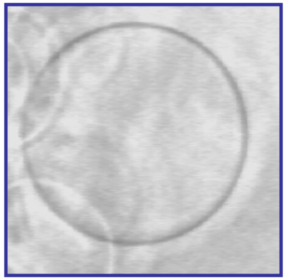
σ surface tension

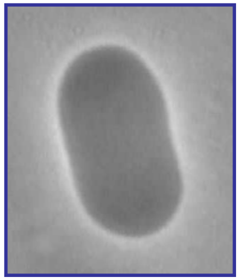
A area

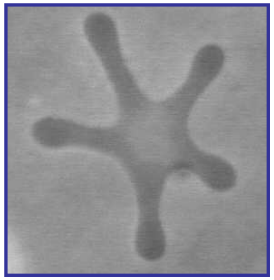
V volume

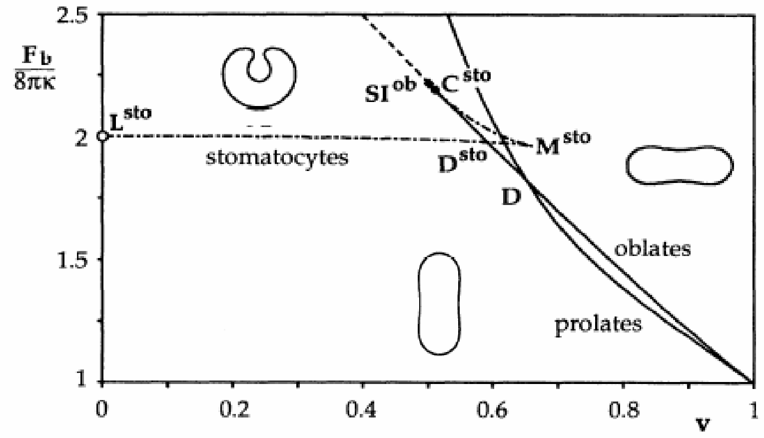
Δp pressure jump across the membrane

Vesicles: equilibrium shapes









Reduced volume
('excess' area)

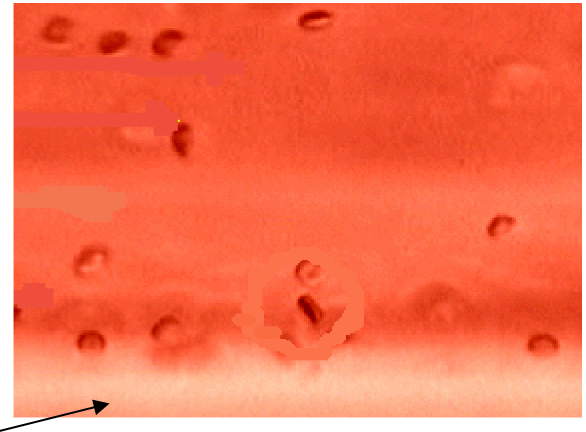
$$v = \frac{V}{\frac{4\pi}{3}\left(\frac{A}{4\pi}\right)^{3/2}}$$

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

Motivation: cell hydrodynamics

Fahraeus effect

decrease in blood apparent viscosity



layer depleted of red blood cells near the wall

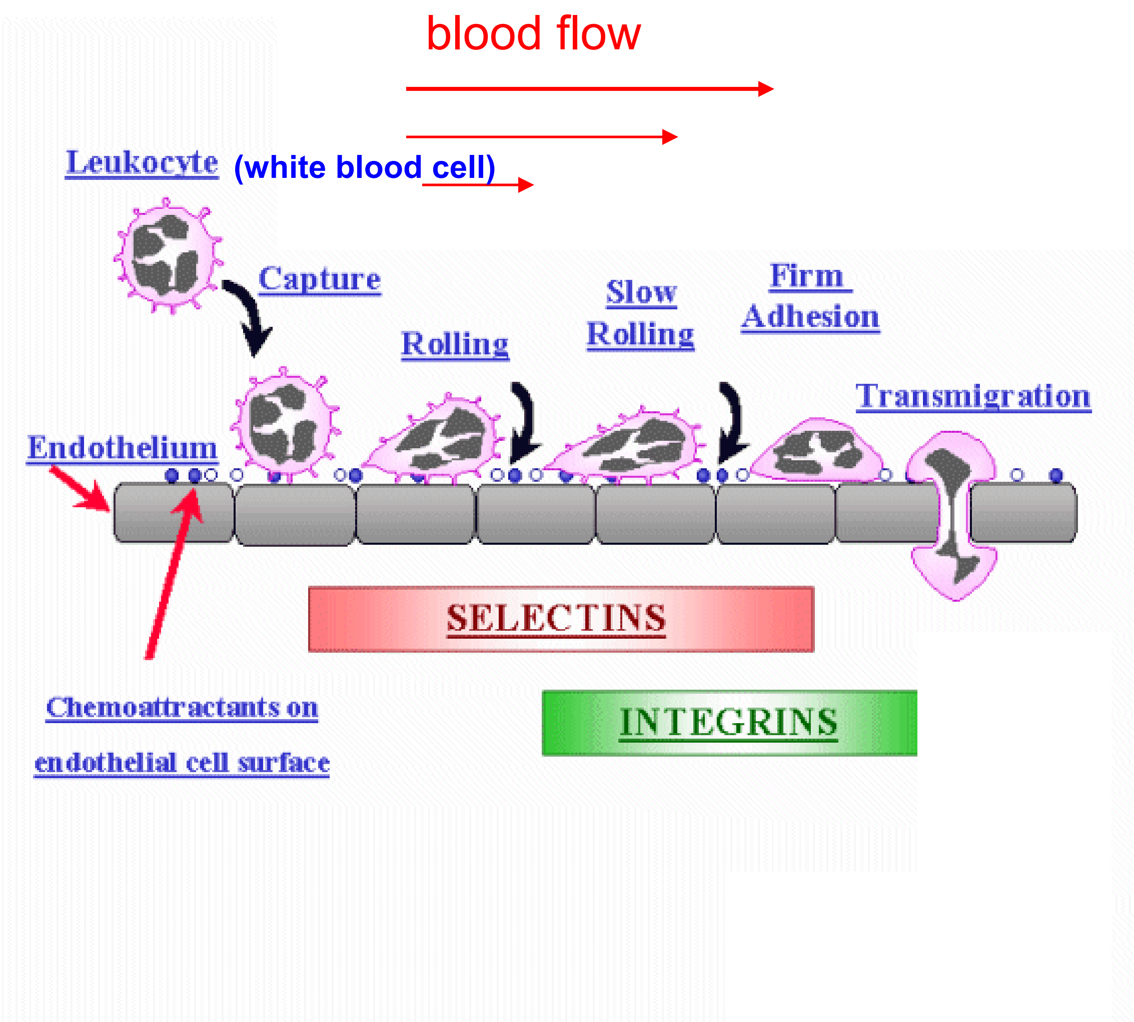
(A. Viallat, Grenoble)

Cell traffic between blood stream and tissues

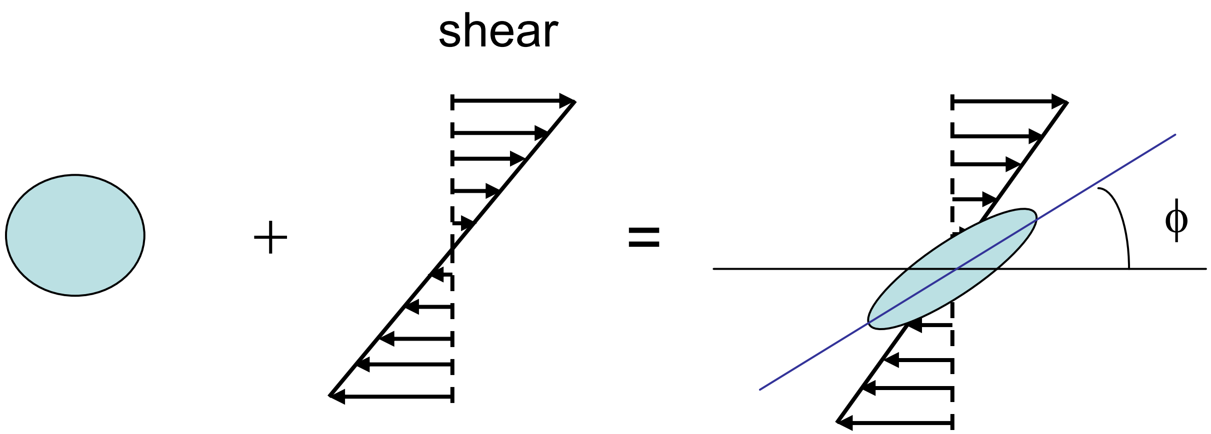
- inflammatory response
- tumor metastasis
- formation of atherosclerotic plaques

Motivation: cell hydrodynamics

inflammatory response (healing an injury)



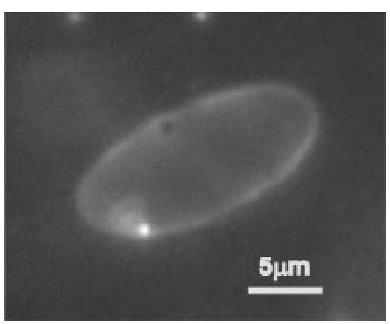
Vesicle dynamics in flow: unbounded shear 1



The shape is not given a priori !

low shear rates: *tank-treading*

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



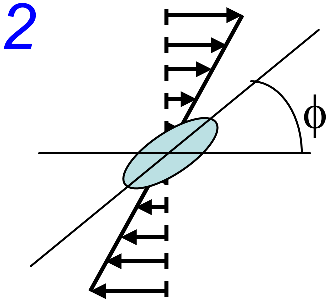
Kantsler and Steinberg, PRL **95** (2005)

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

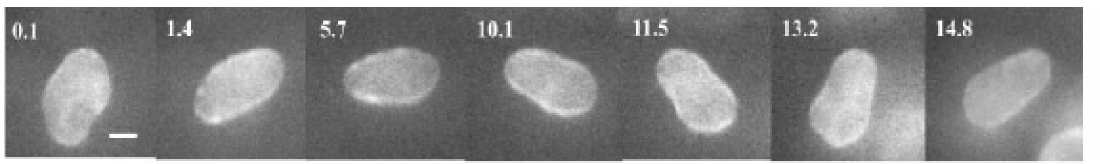
$$\Delta = A - 4\pi a^2$$

Seifert, Eur. Phys. J. B **8** (1999)
Misbah, PRL **96** (2006)

Vesicle dynamics in flow: unbounded shear 2



high shear rate: *tumbling*



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

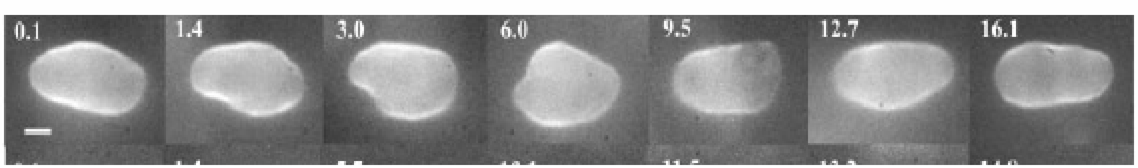
theory (Misbah) a=0.5

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

transition to tumbling?

"breathing" vesicle?

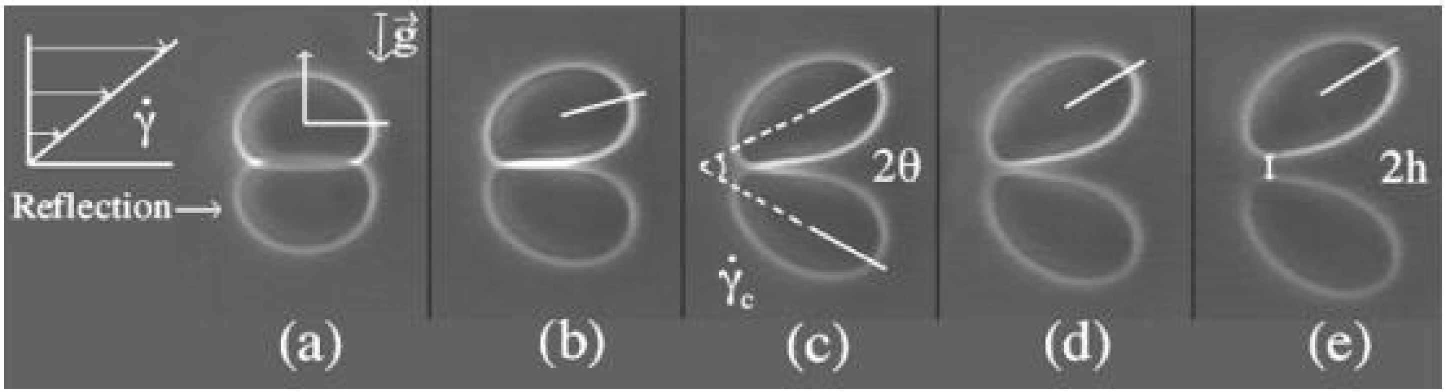
high shear rate, high viscosity contrast λ



Vesicle dynamics in flow: near a wall

vesicle detachment ? ↔ cell adhesion

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



side view microscope

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

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

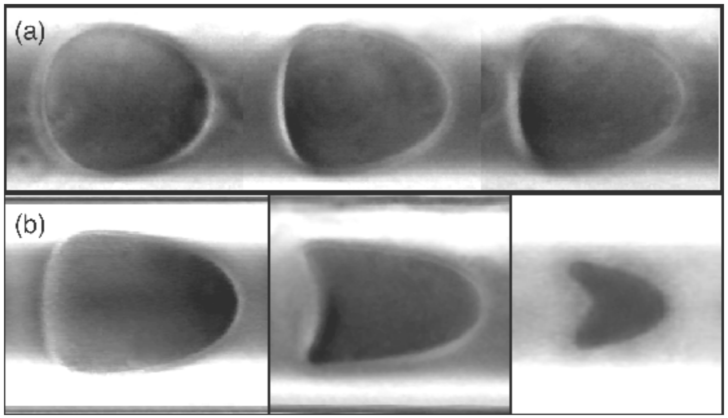
lift force?

$$F_L\left(\dot{\gamma}, v, h, \kappa\ldots\right)$$

Vesicle dynamics in flow: microchannel

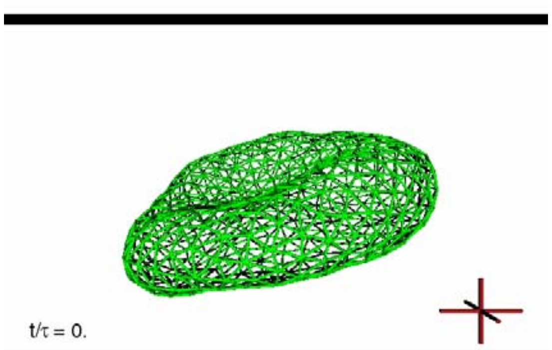
vesicle “parachutes” ? ↔ RBC in capillaries

flow



Vitkova et al. Europhys. Lett. (2004)

discocyte – parachute transformation:



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

shapes?
shape transitions?

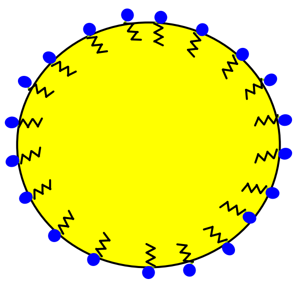
Deformable "objects" in flow

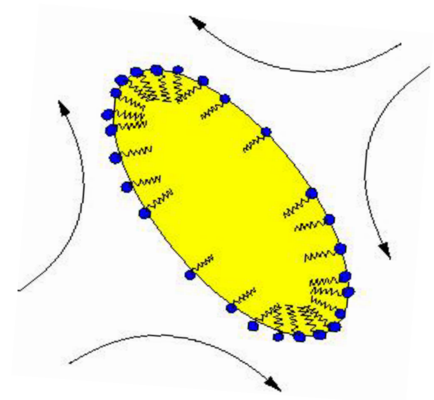
$\boxed{\text{a free-surface boundary problem}}$

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

Flow:
Drop deforms
$\rightarrow$ nonuniform curvature
capillary stresses
Surfactant is redistributed
$\rightarrow$ gradients in surface tension $\nabla_s \sigma$
Marangoni stresses

Laplace's equation

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

area changes (compressible interface)

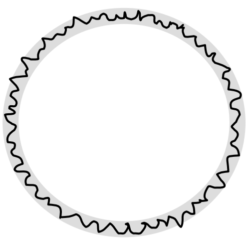
Vesicles – what's new?

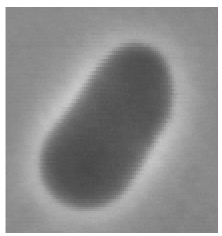
Vesicle dynamics in flow

Equilibrium:

shape need not to be spherical

vesicle is "rough" → fluctuations

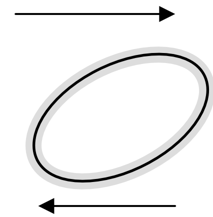




Laplace's equation

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

Flow:

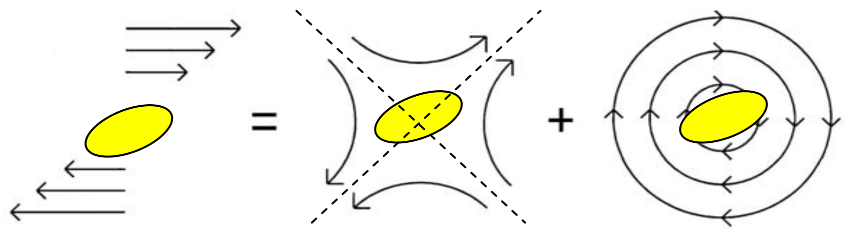


shape deforms
→ nonuniform curvature
capillary stresses
bending stresses

area is conserved
incompressible interface

→ gradients in effective tension
Marangoni stresses

vesicle dynamics: time scales



shear extension rotation

"distorting" $t_{\mathrm{d}} = \hat{\lambda}\dot{\gamma}^{-1}$ convection by the extensional component of the flow

"restoring"

$$t_{\mathrm{cap}} = \frac{\hat{\lambda}\eta a}{\sigma}$$ capillary relaxation

$$t_{\mathrm{ben}} = \frac{\hat{\lambda}\eta a^3}{\kappa}$$ bending relaxation

$$t_{\mathrm{mar}} = \frac{\hat{\lambda}\eta a}{\Delta\sigma}$$ relaxation driven by interfacial tension gradients

$$t_{\mathrm{rot}} = \dot{\gamma}^{-1}$$ rotation
(gets to be important at high λ)

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

λ viscosity ratio

Dimensionless parameters

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

Capillary number

relaxation / *distortion*

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

Bending parameter

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

Marangoni parameter

$$\frac{t_{\text{rot}}}{t_{\text{d}}} = \widehat{\lambda}^{-1}$$

rotation parameter

interplay of different time scales $\Rightarrow$ complex dynamics

Dimensionless parameters

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

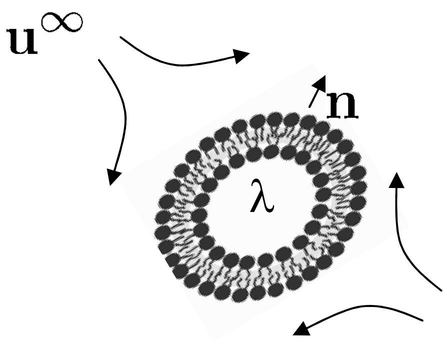
Capillary number =flow strength

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

bending number

‘elastic vesicle’ regime (area not conserved)

Problem formulation: governing equations



Stokes flow $Re = \dfrac{\rho a u^\infty}{\eta} \ll 1$

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

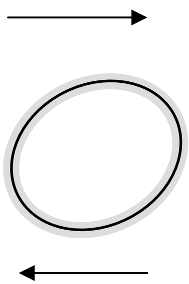
viscosity ratio
$\lambda = \eta_{in}/\eta_{out}$

Boundary conditions:

continuity of velocity across the membrane $\mathbf{u_{in}} = \mathbf{u_{out}} \equiv \mathbf{u_s}$

shape evolution $\dfrac{\partial r_s}{\partial t} = \mathbf{u_s} \cdot \mathbf{n}$

Problem formulation: *stress boundary condition* & more



hydrodynamics stress balanced by *interfacial stresses*

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

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

capillary *bending* *Marangoni*

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incompressible surface:

area conservation

$$\frac{\mathrm{d}A}{\mathrm{d}t} = 0 \longrightarrow \nabla_s \cdot \mathbf{u} = 0$$

$$\sigma(A)$$

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

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

$\mathbf{u}^{\infty}$ flow at infinity

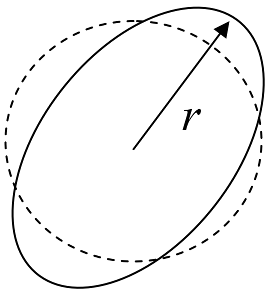
(integration along the particle surface)

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:

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

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

Problem solution

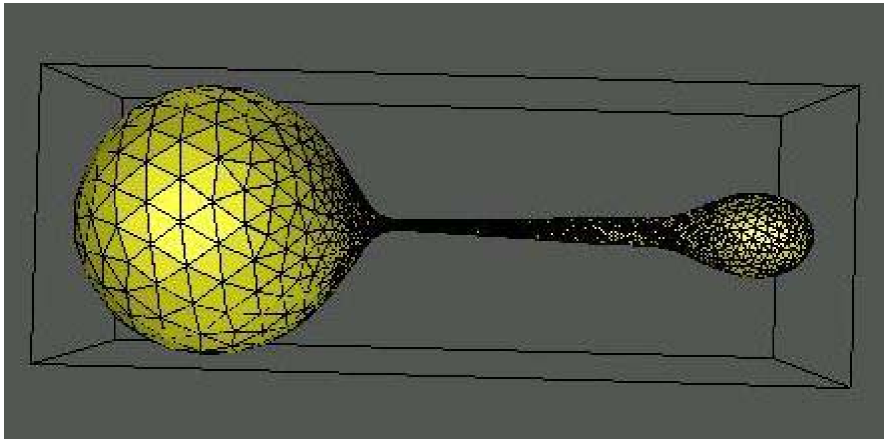
Large distortions: Numerical simulations

boundary integral method

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

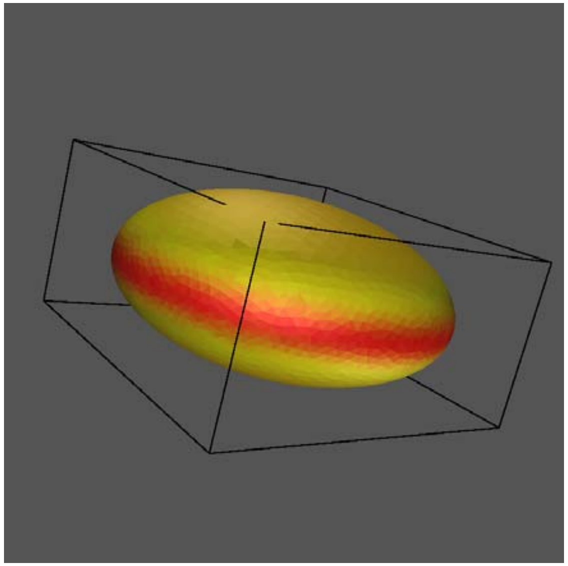
viscosity ratio λ=1

adaptive remeshing



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

bending stresses



ellipsoid

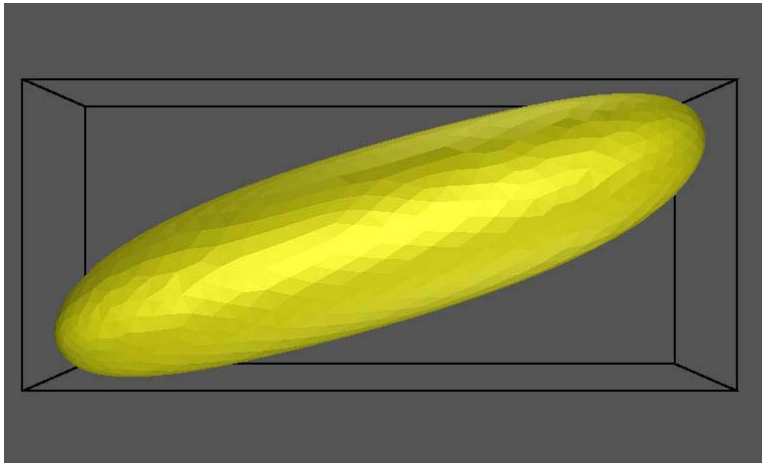
red color signifies the magnitude of the bending stresses

Bending effects on deformation

Be=0 (no bending)

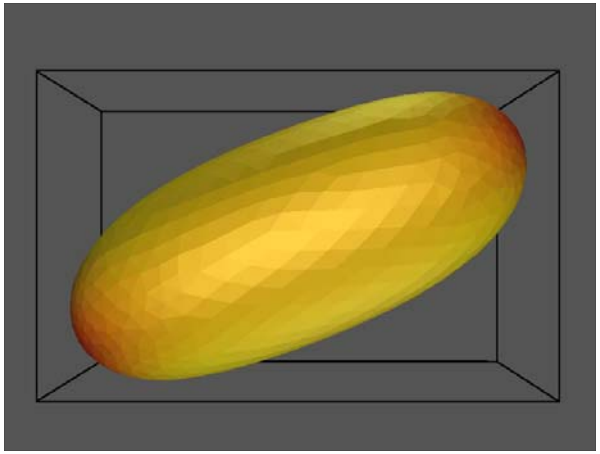
strong flow Ca=0.5

endtime=10

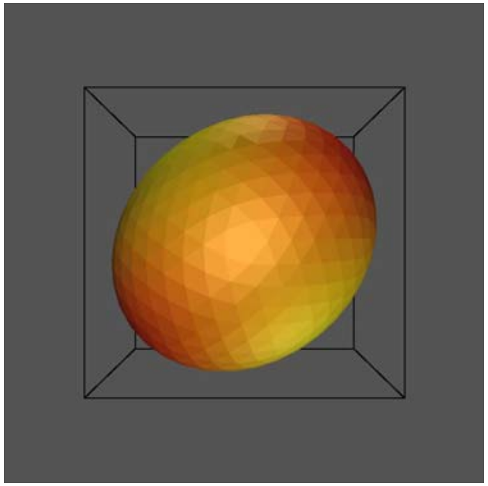


same drop!

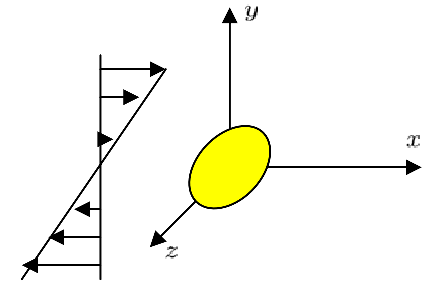
Be=0.1



Be=10



Bending effects on deformation

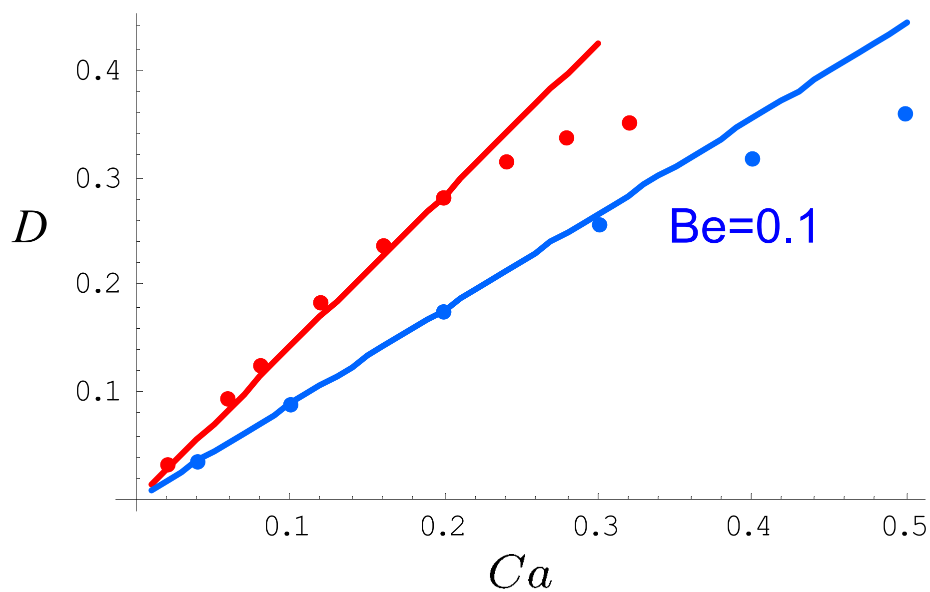


$$r(\theta,\phi) = 1 + \sum f_{lm} Y_{lm}(\theta,\phi)$$

Deformation parameter (ellipsoid)

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

No bending stiffness



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

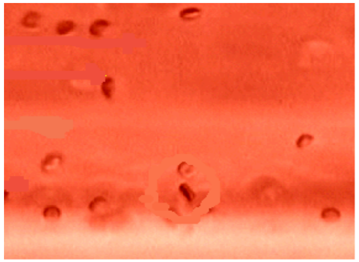
$$Be = \frac{\kappa}{\sigma a^2}$$ bending / tension

symbols: BIM simulations

lines: small deformation theory $O\left(Ca^2\right)$

Effects of the wall: particle migration

Why do red blood cells go away from the wall?



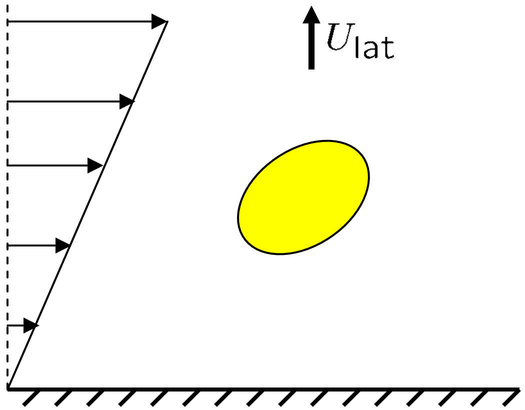
spherical neutrally-buoyant particle does not drift !

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

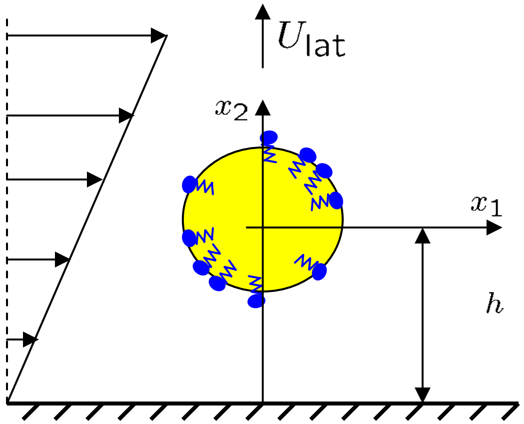
$\mathbf{u}$, $\mathbf{U}_{\text{lat}}$ $\xrightarrow{\text{reversing the flow}}$ $-\mathbf{u}$, $-\mathbf{U}_{\text{lat}}$

Particle migration away from a wall in shear flows

deformed drop



surfactant-covered, spherical drop



far-away from the wall

nonlinear effect

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

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

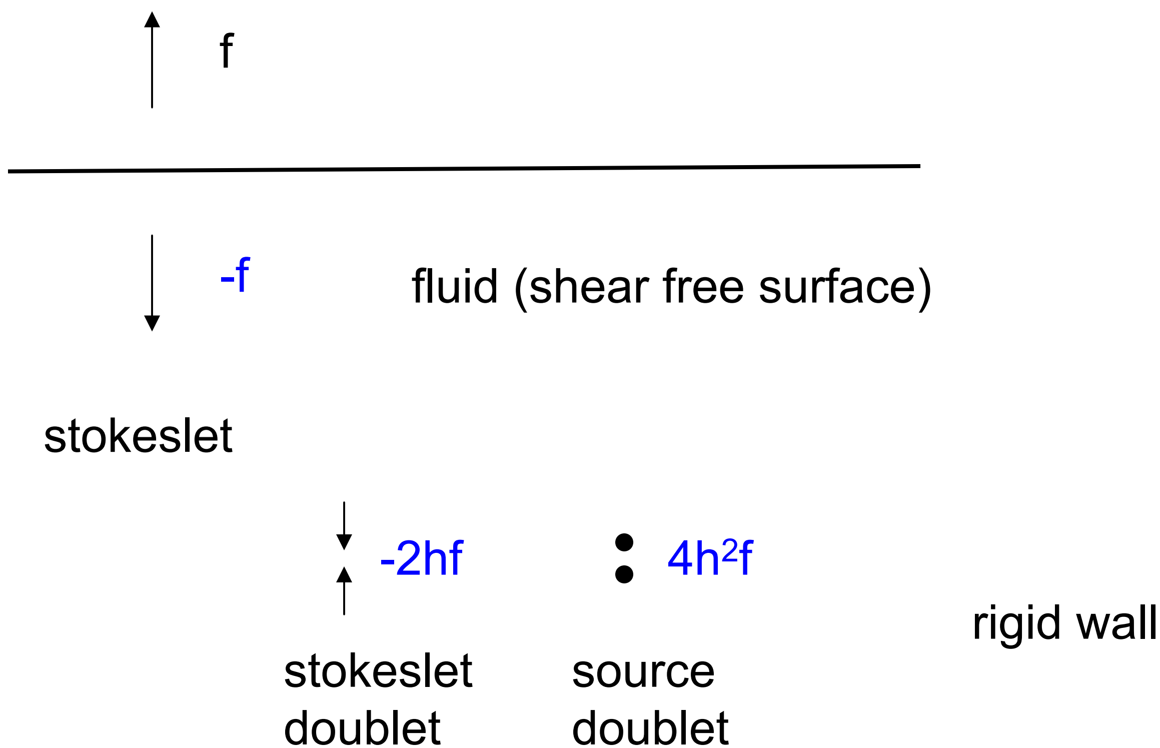
Problem solution

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

image system



Vesicle detachment

flow

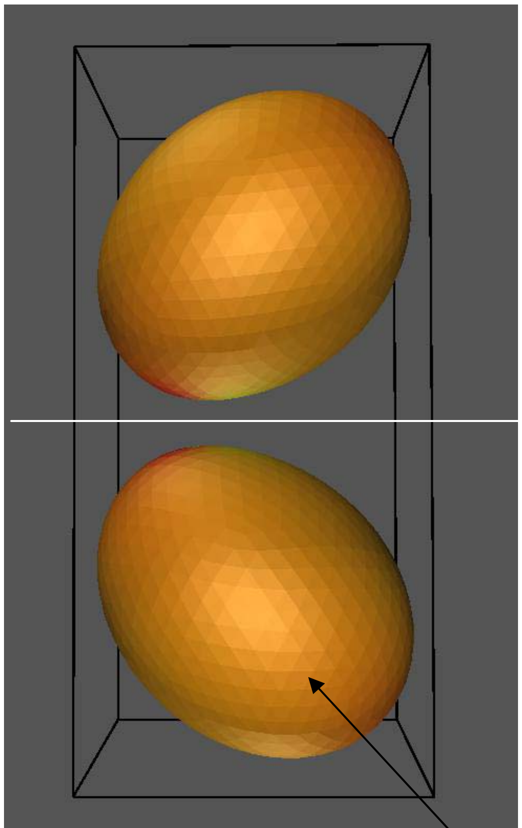
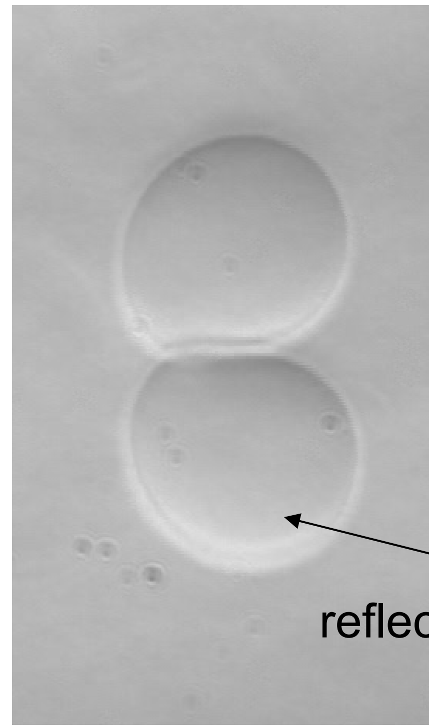


image drop

BIM simulation (shear free surface)

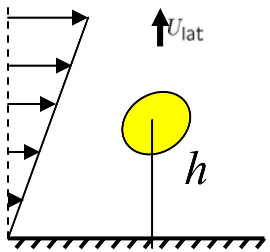


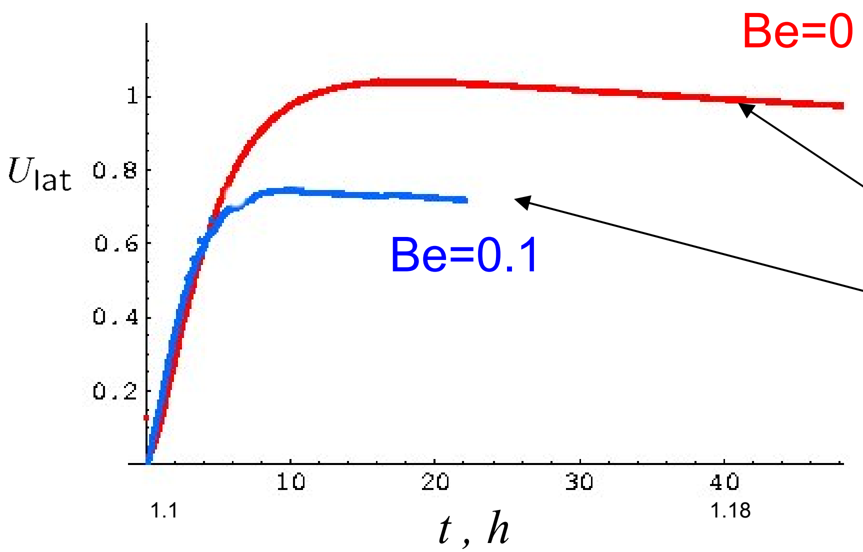
reflection

experiment:
side view microscope
vesicle on a glass substrate

Vesicle migration velocity

BIM simulations: preliminary results
$Ca = 0.06$





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

Bending stiffness decreases migration velocity

time?

Vesicle adhesion

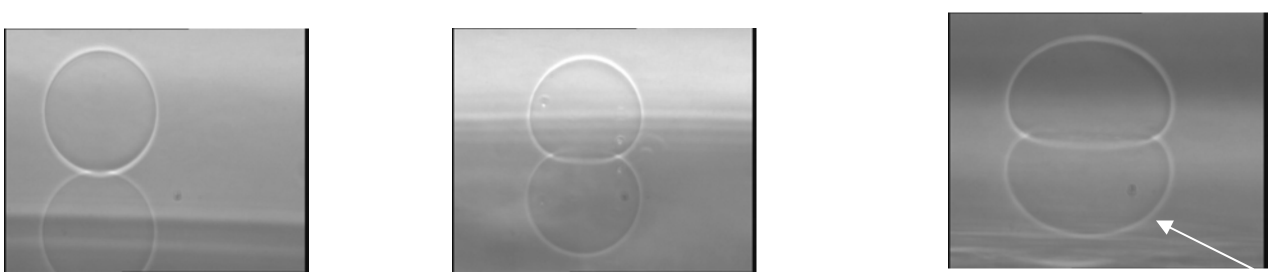
A non-destructive method to obtain *adhesion strength* and *bending rigidity*.

idea: compare vesicle shapes for different reduced volumes

Gruhn and Lipowsky PRE **71** (2005)

Materials: DOPC, DOPC+DOPG, DOPC+cholesterol

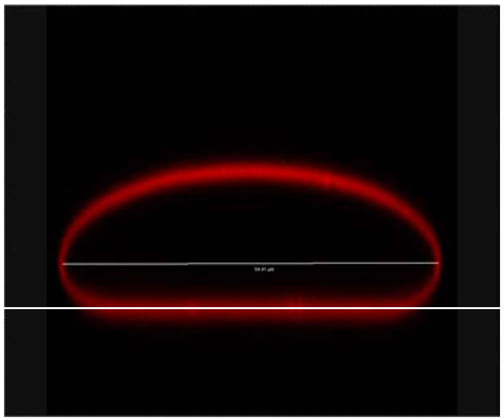
Experiment 1:
Side-view observation with the phase-contrast microscope



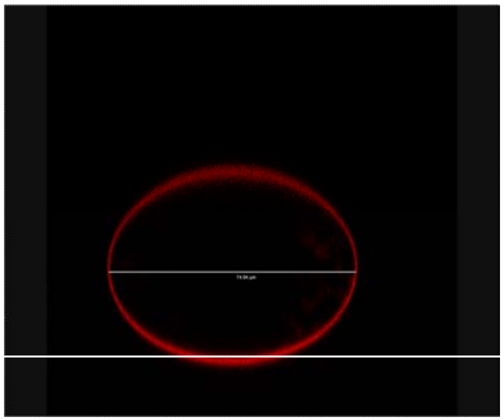
Vesicle adhesion

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⇔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
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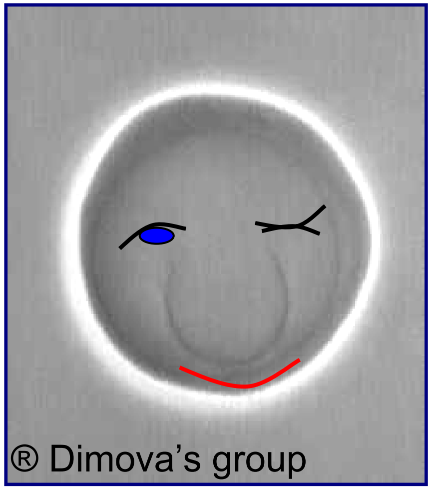
Said Aranda Espinoza, Natalya Bezlyepkina

Prof. Thomas Powers (Brown)

Prof. Michael Loewenberg and Prof. Jerzy Blawzdziewicz (Yale)
Prof. Vittorio Crisitini (UC Irvine)

Dr. Manouk Abkarian (Montpellier)

Thank you!



http://www.mpikg-golm.mpg.de/th/people/dimova/