Mesoscale Modeling of Blood Flow: From Single Cells to Blood Rheology

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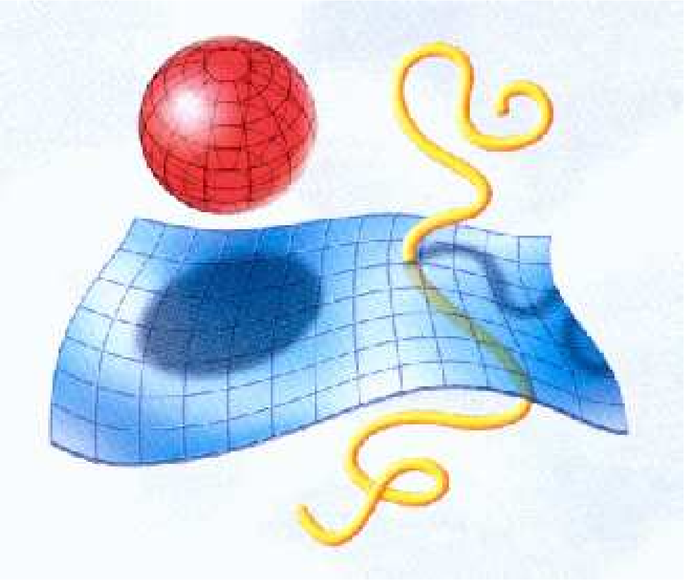
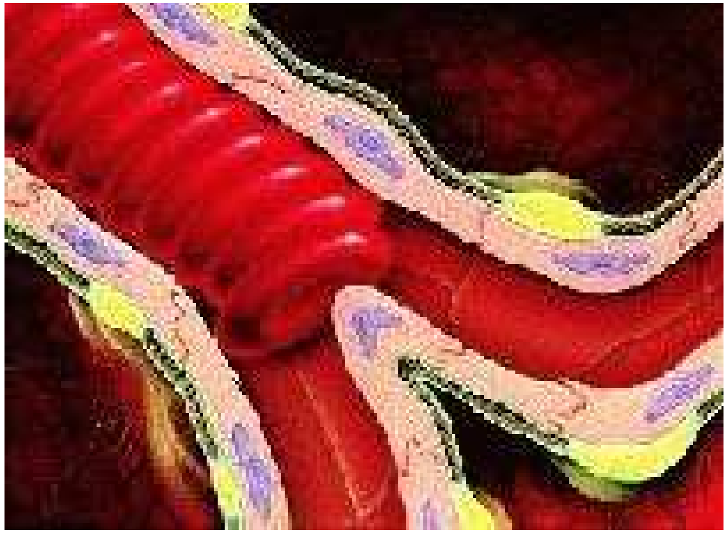
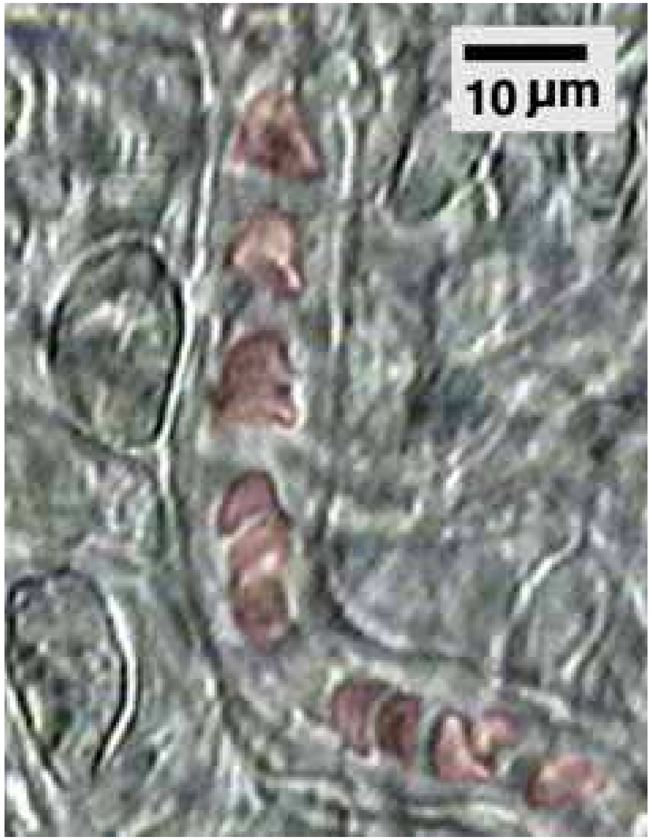
Forschungszentrum Jülich, Germany



Blood Hydrodynamics

- Red blood cells in microvessels:



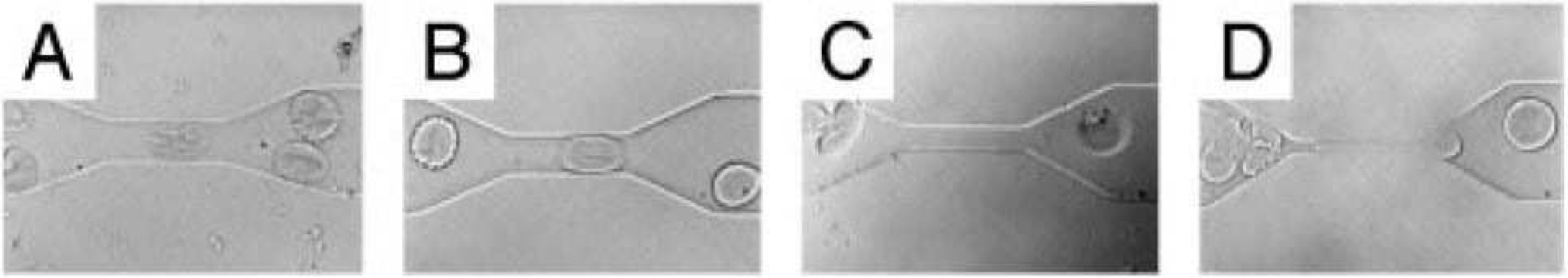


  - Flow behavior depends on cell elasticity.
  - Diseases such as diabetes reduce deformability of red blood cells!

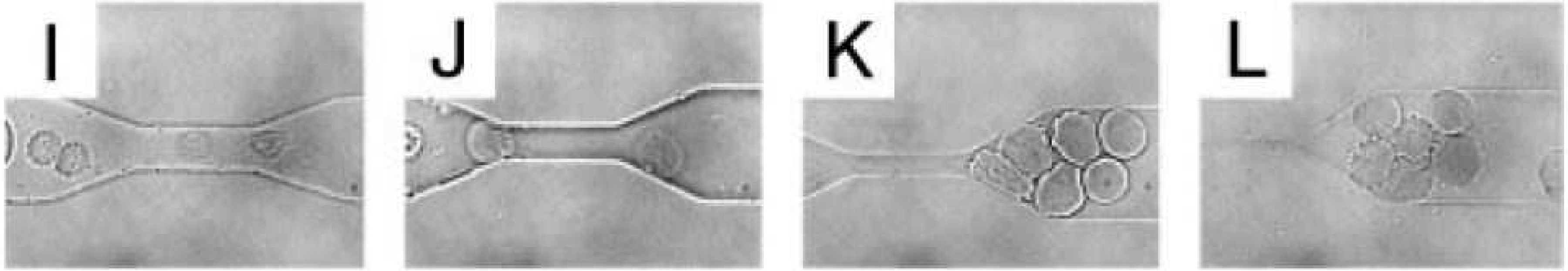
Soft Matter Hydrodynamics

Example: Flow behavior of malaria-infected red blood cells in microchannels

Just after infection:



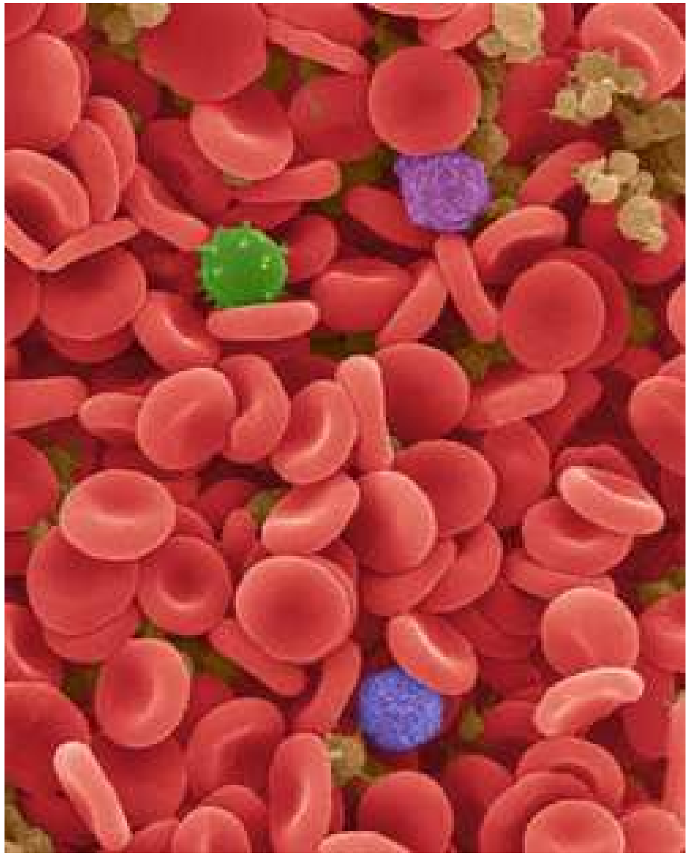
Late stage:



Diameter: 8 μm 6 μm 4 μm 2 μm

J.P. Shelby et al., Proc. Natl. Acad. Sci. **100** (2003)

Some Facts about Blood



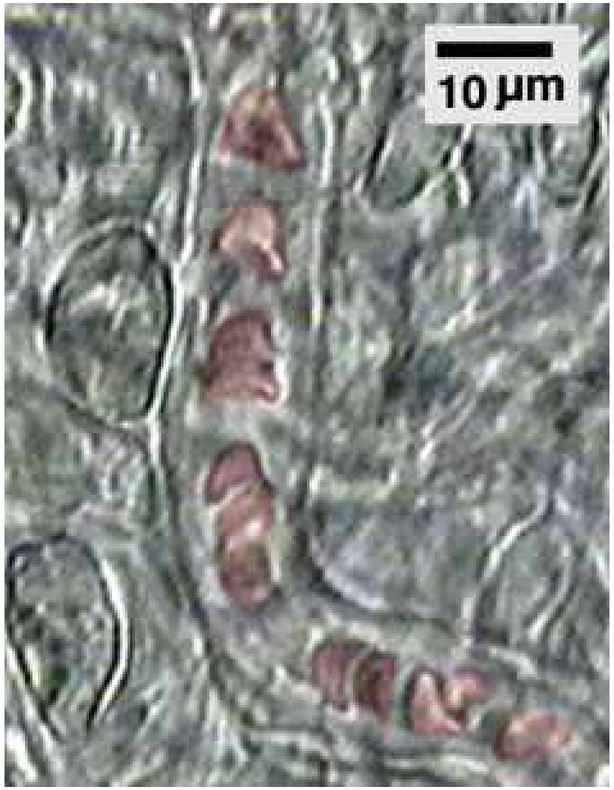
One micro-liter of blood contains

- liquid called blood plasma, 55% by volume
- blood cells suspended within the plasma, 45% by volume
  - 5 million red blood cells (RBCs)
  - 5,000 white blood cells (leucocytes)
  - 250,000 platelets (thrombocytes)

Red blood cells contain hemoglobin, iron-containing protein which facilitates transportation of oxygen by reversible binding.

Red Blood Cells

- RBCs are produced in the red bone marrow
- at rate of 2 million per second
- production stimulated by hormone erythropoietin (EPO)
- lifetime in human vascular system about 120 days
- heart pumps volume of about 5 liters/min
- RBCs travel through the human body about 180,000 times
- corresponds to traveled distance of 180 km!



Mesoscale Flow Simulations

Complex fluids: length- and time-scale gap between

- atomistic scale of solvent
- mesoscopic scale of dispersed particles (colloids, polymers, membranes)

⟶ **Mesoscale Simulation Techniques**

Basic idea:

- drastically simplify dynamics on molecular scale
- respect conservation laws for mass, momentum, energy

Examples:

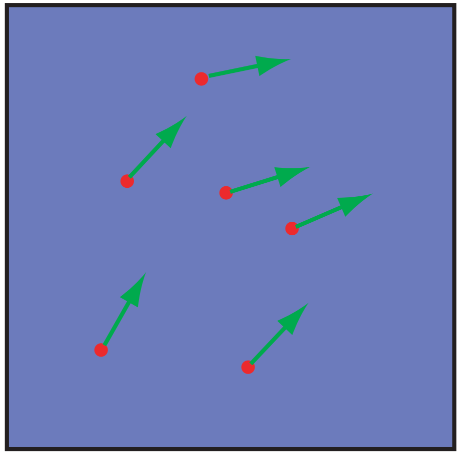
- Lattice Boltzmann Method (LBM)
- Dissipative Particle Dynamics (DPD)
- Multi-Particle-Collision Dynamics (MPC)

Alternative approach: Hydrodynamic interactions via Oseen tensor

Multi-Particle Collision Dynamics (MPC)

Flow dynamics: Two step process

Streaming



- ballistic motion

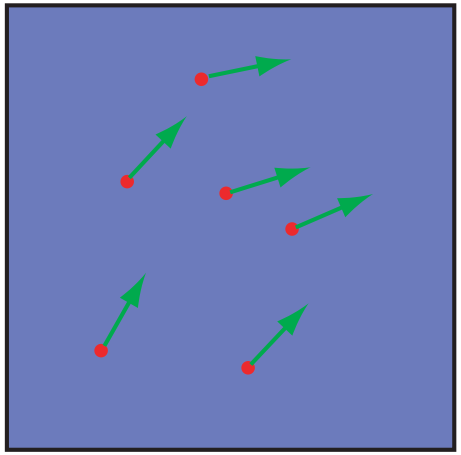
$$\mathbf{r}_i(t+h) = \mathbf{r}_i(t) + \mathbf{v}_i(t)h$$

A. Malevanets and R. Kapral, J. Chem. Phys. **110** (1999)

Multi-Particle Collision Dynamics (MPC)

Flow dynamics: Two step process

Streaming

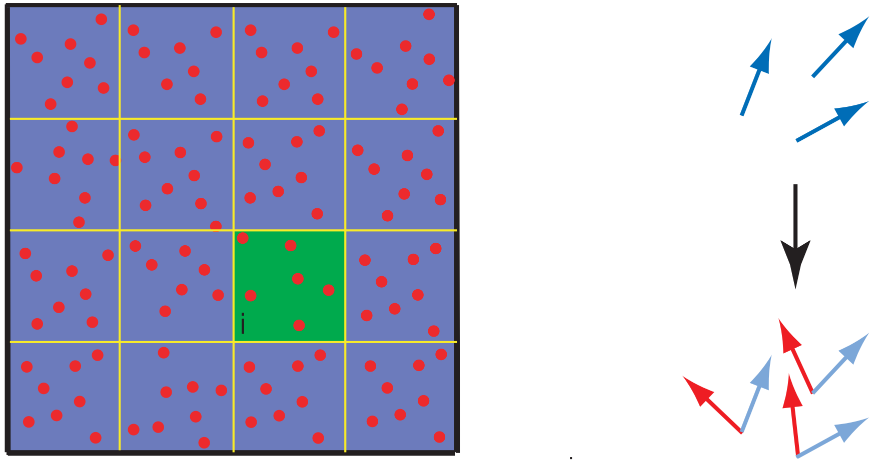


- ballistic motion

$$\mathbf{r}_i(t+h) = \mathbf{r}_i(t) + \mathbf{v}_i(t)h$$

A. Malevanets and R. Kapral, J. Chem. Phys. **110** (1999)

Collision



- mean velocity per cell

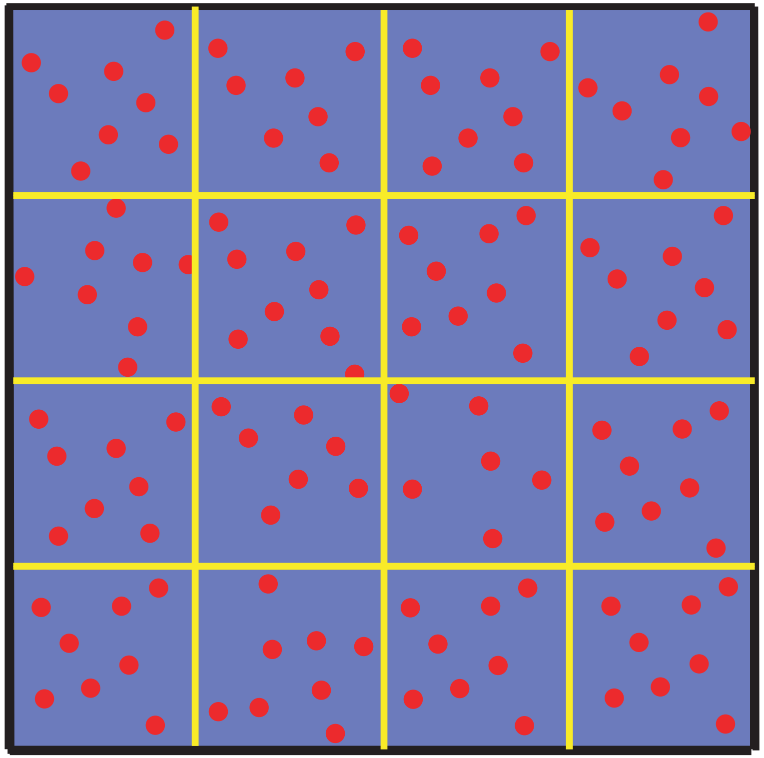
$$\bar{\mathbf{v}}_i(t) = \frac{1}{n_i} \sum_{j \in C_i}^{n_i} \mathbf{v}_j(t)$$

- rotation of relative velocity by angle α

$$\mathbf{v}_i' = \bar{\mathbf{v}}_i + \mathbf{D}(\alpha)(\mathbf{v}_i - \bar{\mathbf{v}}_i)$$

Mesoscale Flow Simulations: MPC

- Lattice of collision cells: breakdown of Galilean invariance
- Restore Galilean invariance exactly: random shifts of cell lattice



T. Ihle and D.M. Kroll, Phys. Rev. E **63** (2001)

Mesoscale Flow Simulations: MPC

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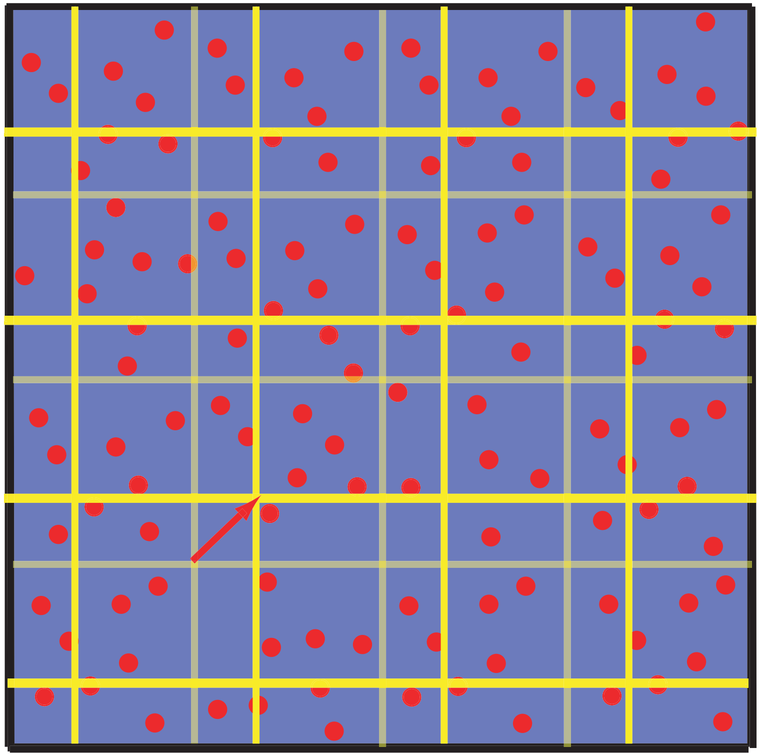
- Restore Galilean invariance exactly: random shifts of cell lattice



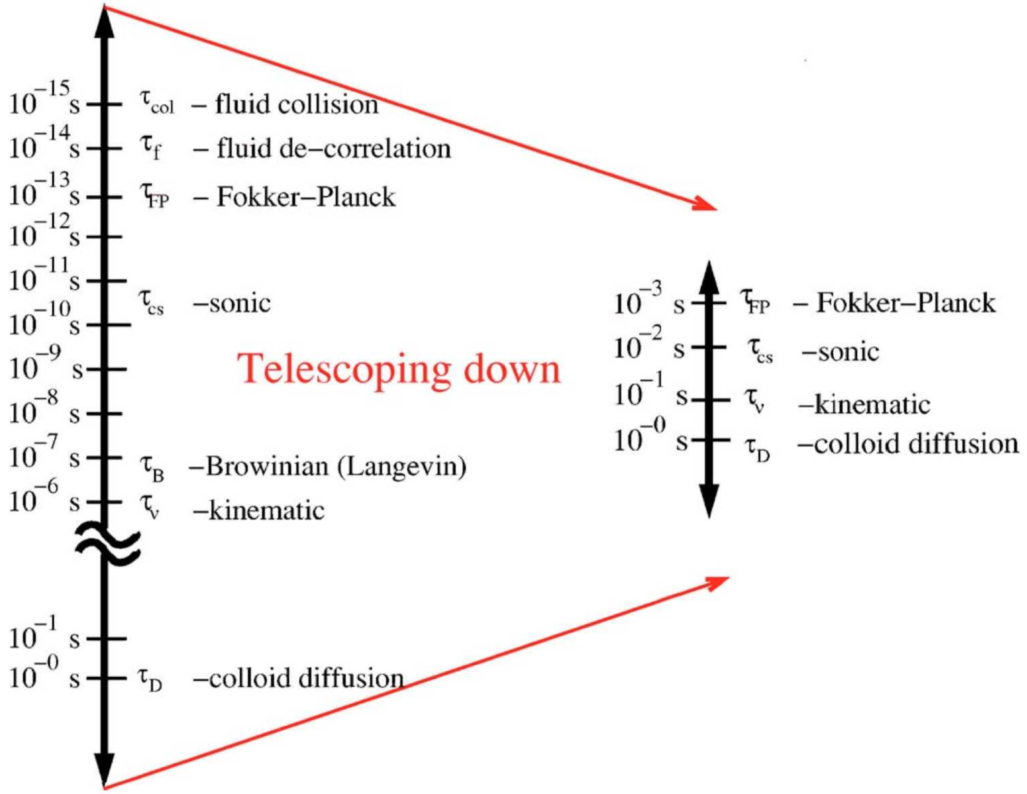
T. Ihle and D.M. Kroll, Phys. Rev. E **63** (2001)

Complex Fluid Dynamics: Time Scales

Hierarchy of time scales:

(for colloidal particle of diameter σ)

- molecular time scales
- sonic time: $\tau_{cs} = \sigma / c_s$
- kinematic time: $\tau_\nu = \sigma^2 / \nu$
  (momentum diffusion)
- colloid diffusion time: $\tau_D = \sigma^2 / D_T$



With flow:

- Mach number: $Ma = v_f / c_s$
- Reynolds number: $Re = v_f L / \nu$

J.T. Padding and A.A. Louis, Phys. Rev. E **74**, 031402 (2006)

Low-Reynolds-Number Hydrodynamics

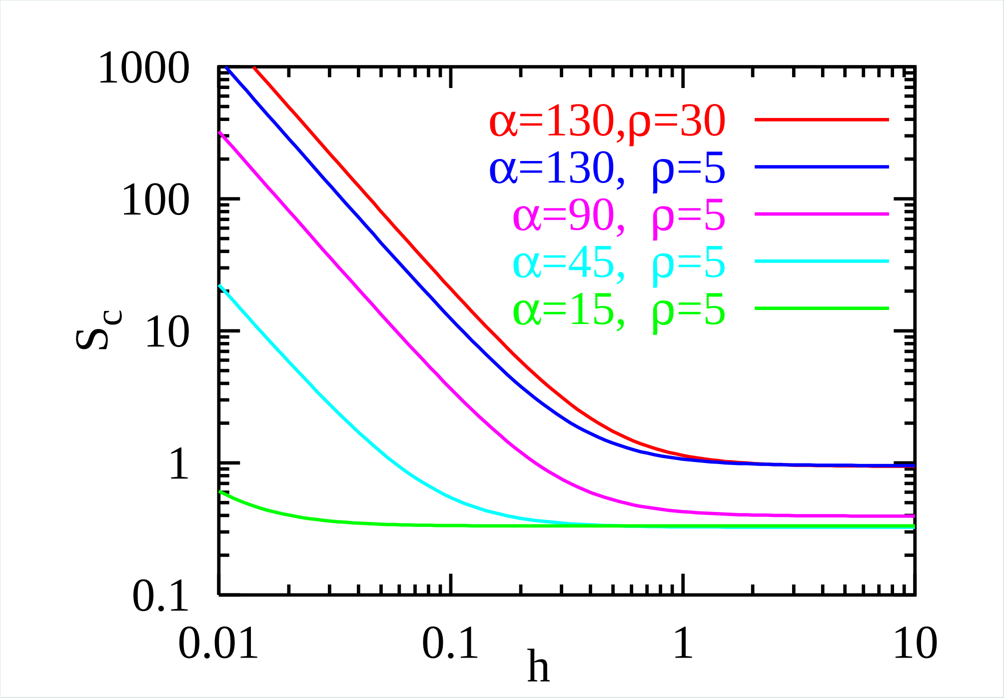
- Reynolds number $Re = v_{\max} L/\nu \sim$ inertia forces / friction forces

  For soft matter systems with characteristic length scales of μm:

  $Re \simeq 10^{-3}$

- Schmidt number $Sc = \nu/D \sim$ momentum transp. / mass transp.

  Gases: $Sc \simeq 1$, liquids: $Sc \simeq 10^3$



M. Ripoll, K. Mussawisade, R.G. Winkler and G. Gompper, Europhys. Lett. **68** (2004)

Other MPC Methods

What about angular-momentum conservation?

Previous MPC methods do not conserve local angular momentum!

However: MPC-AT can easily be modified to do so

$$\mathbf{v}_i^{\mathrm{new}} = \mathbf{v}_{\mathrm{c}}^{\mathrm{G}} + \mathbf{v}_i^{\mathrm{ran}} - \sum_{j \in \mathrm{cell}} \mathbf{v}_j^{\mathrm{ran}} / N_{\mathrm{c}} + m \boldsymbol{\Pi}^{-1} \sum_{j \in \mathrm{cell}} \left\{ \mathbf{r}_{j,\mathrm{c}} \times \left(\mathbf{v}_j - \mathbf{v}_j^{\mathrm{ran}} \right) \right\} \times \mathbf{r}_{i,\mathrm{c}}$$

with moment-of-inertia tensor $\boldsymbol{\Pi}$ in each cell.

Is local angular-momentum conservation relevant?

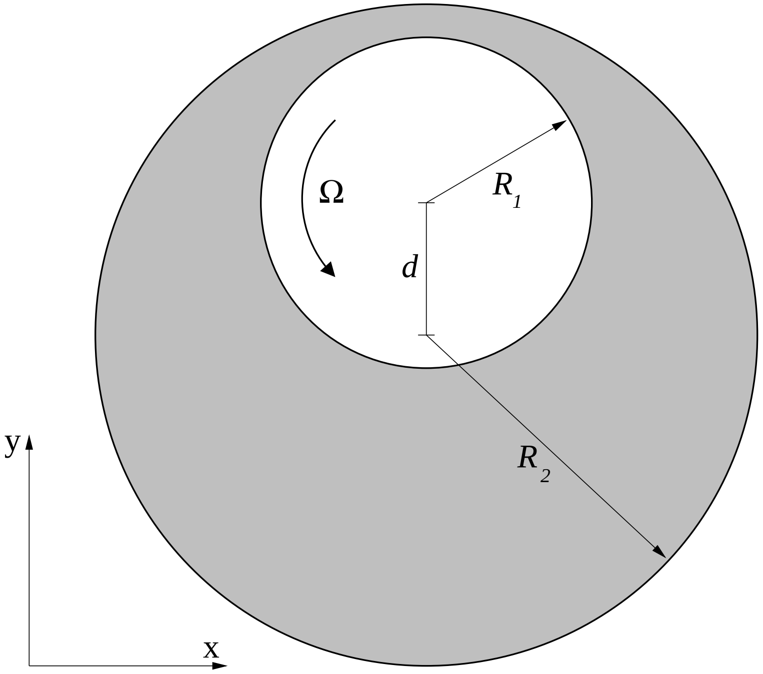
H. Noguchi, N. Kikuchi, and G. Gompper, Europhys. Lett. **78** (2007)

I. Götze, H. Noguchi, and G. Gompper, Phys. Rev. E **76** (2007)

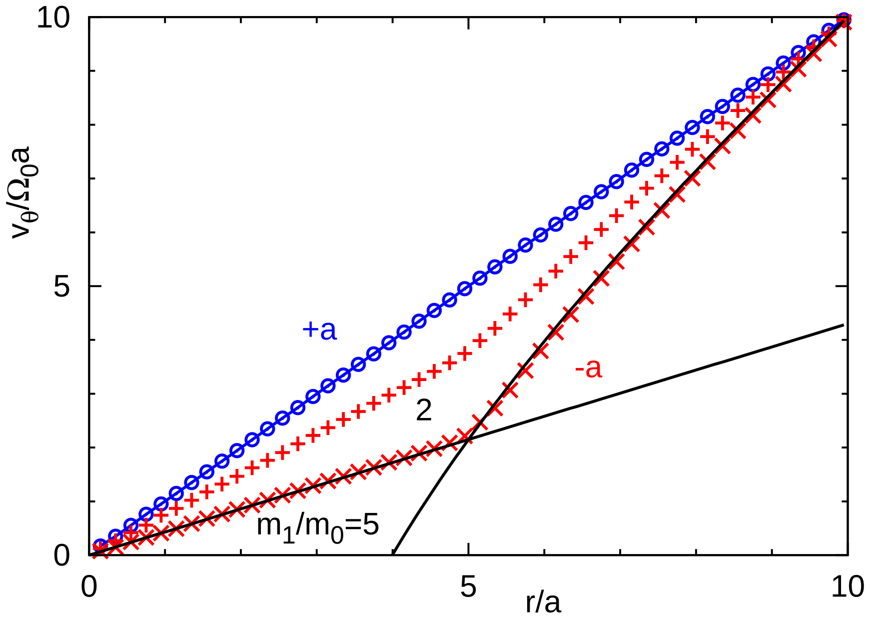
Other MPC Methods

Importance of angular-momentum conservation:

Rotating fluid drop with different viscosity in circular Couette flow



Angular velocity profile



I. Götze, H. Noguchi, and G. Gompper, Phys. Rev. E **76** (2007)

Particle-Based Mesoscale Hydrodynamics (MPC & DPD)

Advantages:

- Unconditionally stable
- Galilean invariance
- Boundary conditions easily implemented
    - Curved wall
    - Deformable boundaries
    - Slip / no-slip walls
- Thermal fluctuations naturally included
- High Schmidt numbers

MPC Reviews:

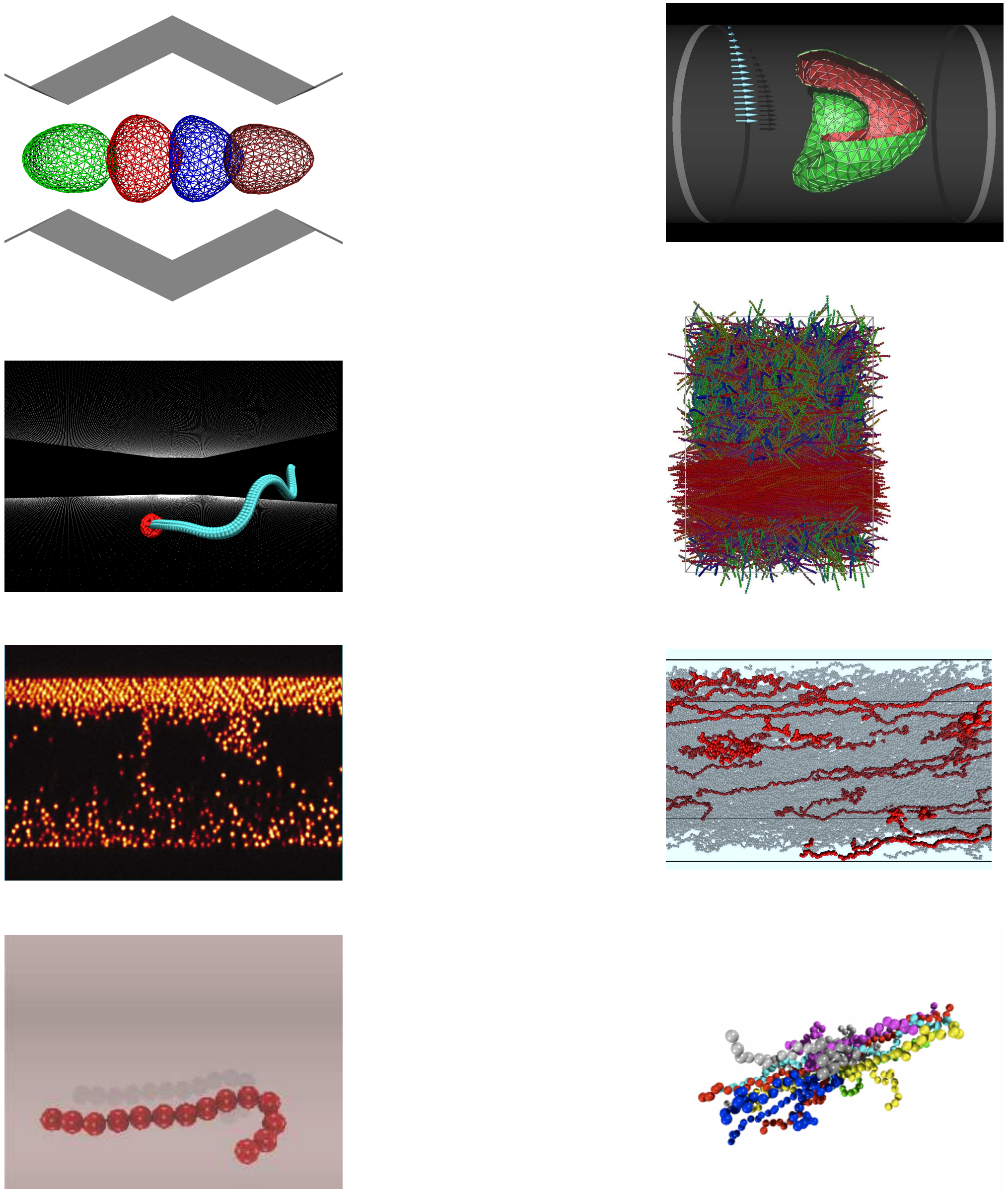
R. Kapral, Adv. Chem. Phys. **140**, 89 (2008);

G. Gompper, T. Ihle, D.M. Kroll, and R.G. Winkler, Adv. Polym. Sci. **221**, 1 (2009)

Particle-Based Mesoscale Hydrodynamics (MPC & DPD)

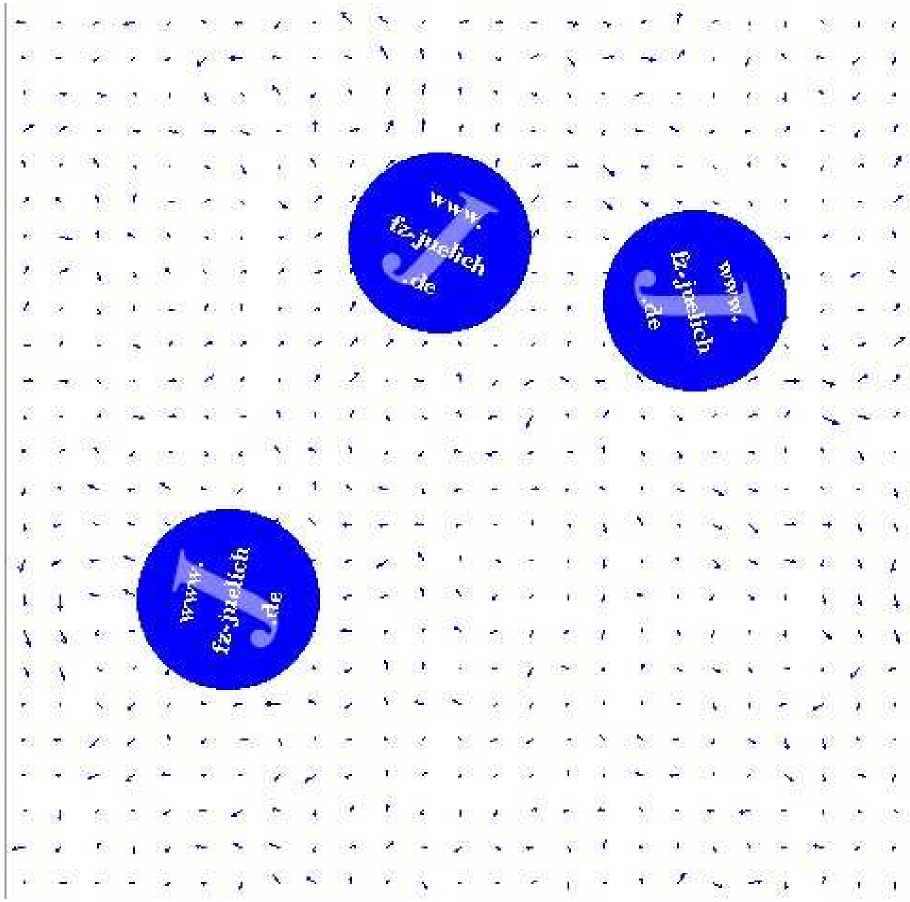
Some applications:

- Vesicles in flow
- Red blood cells in flow
- Microswimmers
- Rod-like colloids in shear flow
- Colloid sedimentation
- Semi-dilute polymer solutions
- Polymers in microchannels
- Star polymers in flow



Do it Yourself — Colloidal Hydrodynamics

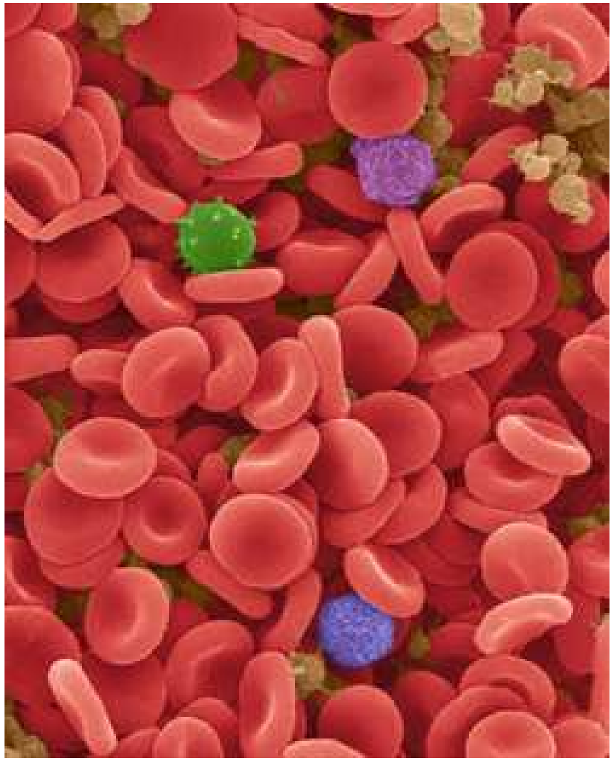
Get a feeling for hydrodynamic interactions: Interactive Simulations

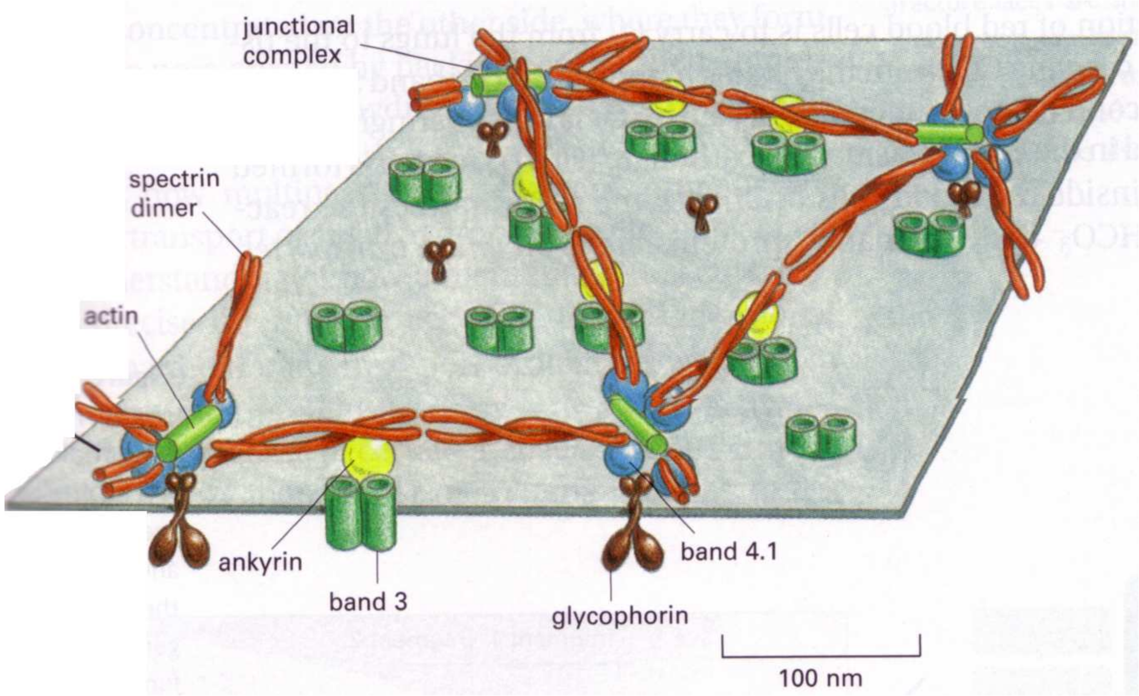


See webpage:

http://www.fz-juelich.de/ics/ics-2/EN/Forschung/HydrodynamicsSimulation/_node.html

Red Blood Cell Membrane

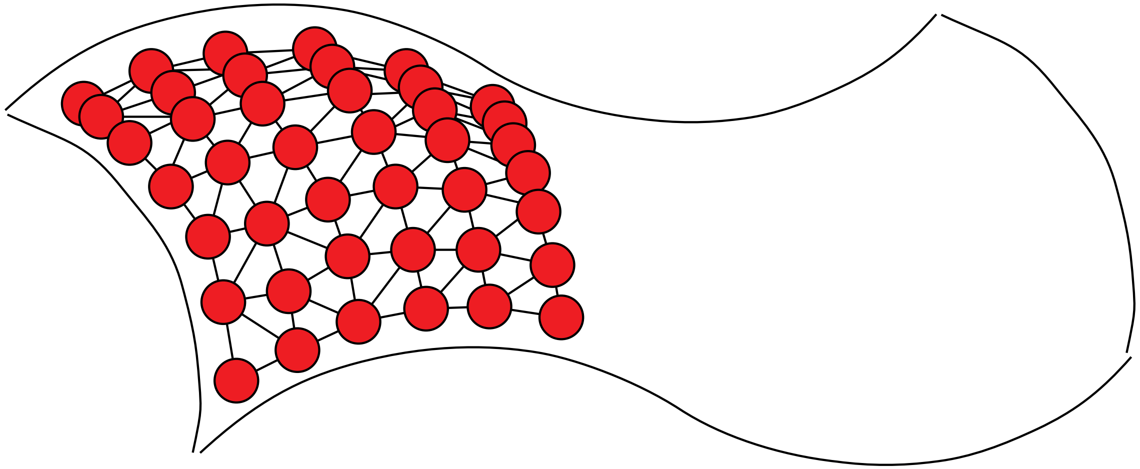




- Spectrin network induces shear elasticity μ of composite membrane
- Elastic parameters: $\kappa/k_BT = 50$, $\mu R_{rbc}^2/k_BT = 5000$

Simulations of Membranes

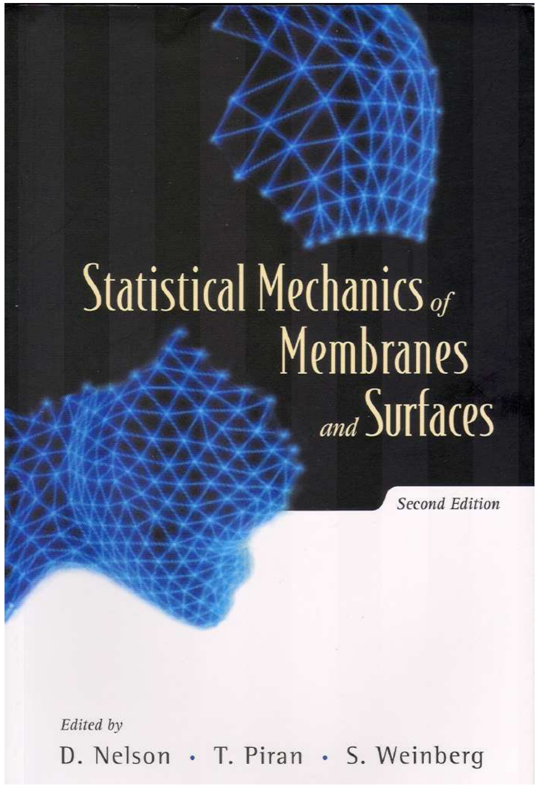
Dynamically triangulated surfaces



Hard-core diameter σ

Tether length L: $\sigma < L < \sqrt{3}\,\sigma$

--> self-avoidance



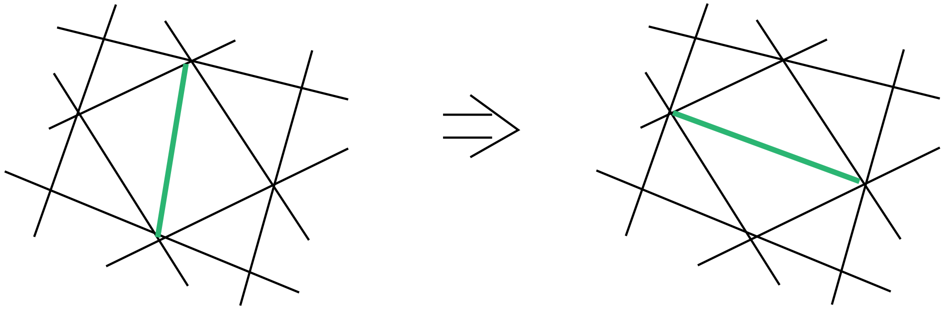
Statistical Mechanics of Membranes and Surfaces

Second Edition

Edited by

D. Nelson · T. Piran · S. Weinberg

Dynamic triangulation:



G. Gompper & D.M. Kroll (2004)

Membrane Hydrodynamics

Interaction between membrane and fluid:

- Streaming step:

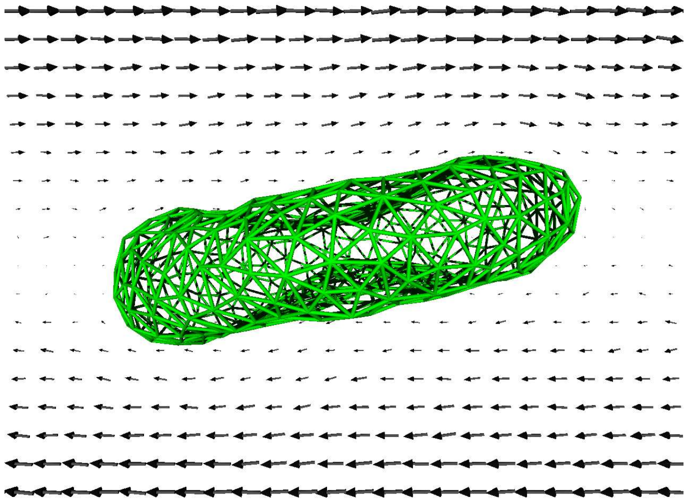
  bounce-back scattering of solvent particles on triangles

- Collision step:

  membrane vertices are included in MPC collisions

implies impenetrable membrane

with no-slip boundary conditions.

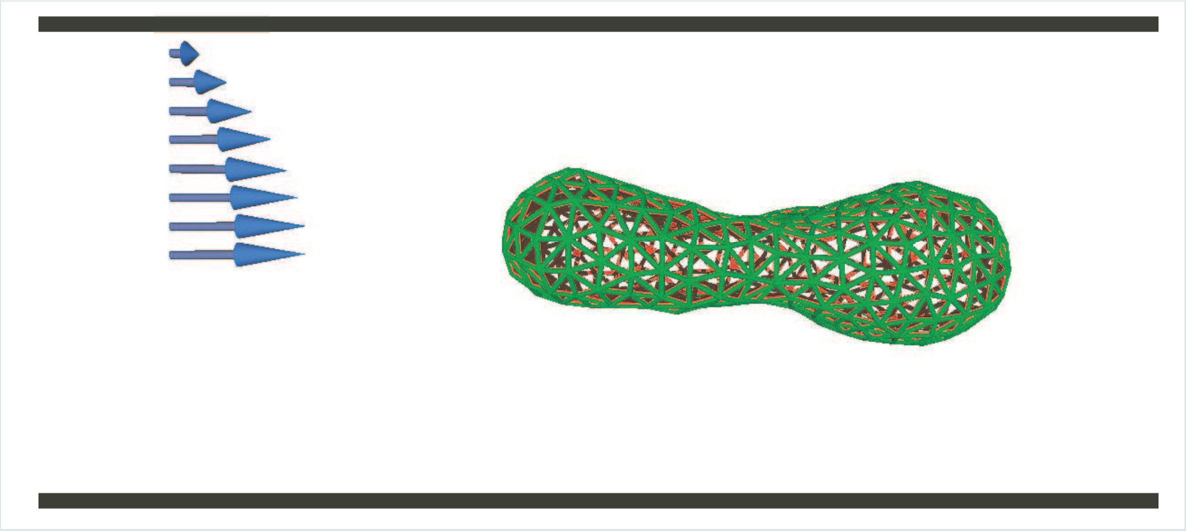


H. Noguchi and G. Gompper, Phys. Rev. Lett. **93** (2004); Phys. Rev. E **72** (2005);

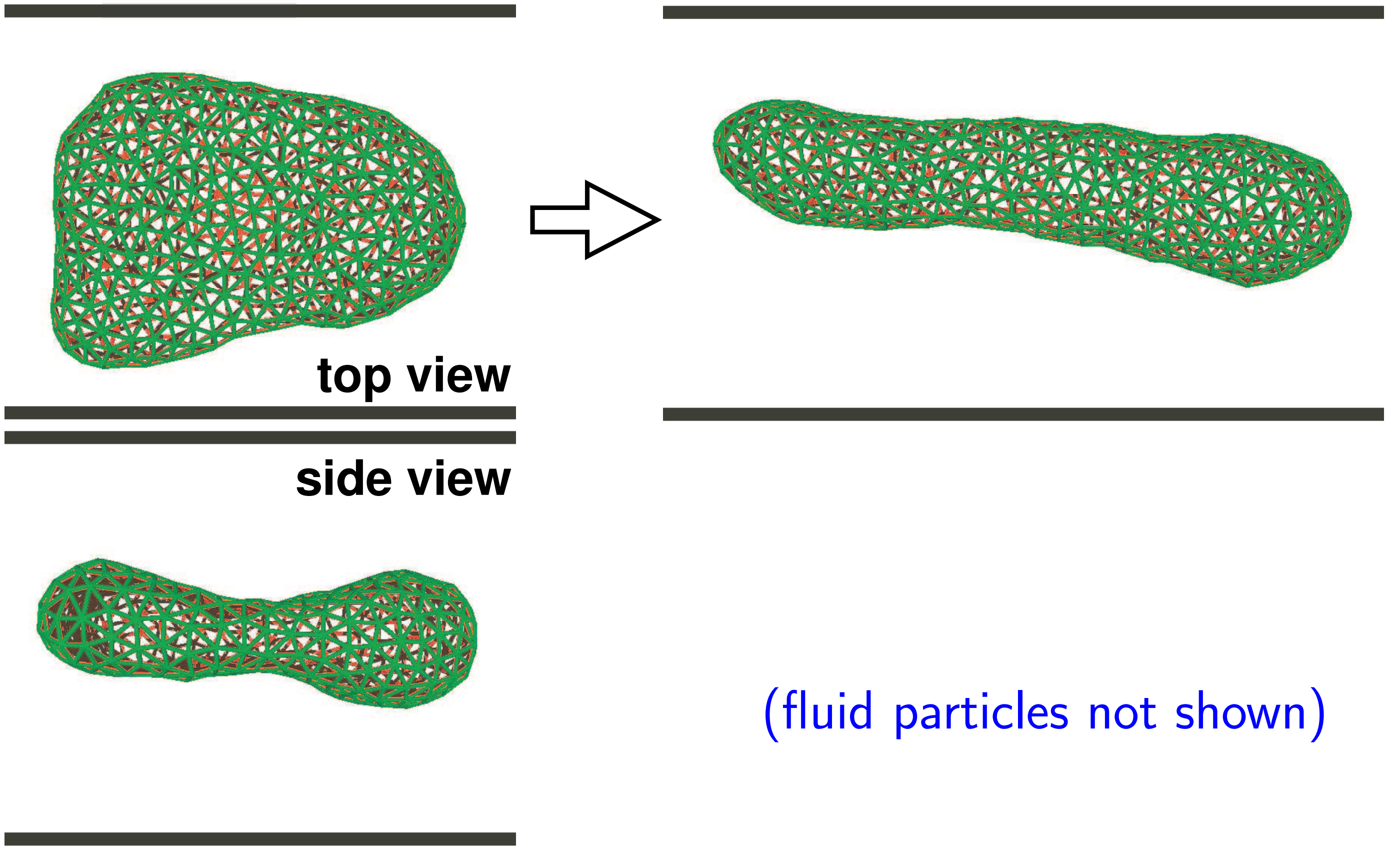
D.A. Fedosov, B. Caswell, G.E. Karniadakis, Biophys. J. **98**, 2215 (2010)

Membrane Hydrodynamics

Single Red Blood Cell in Capillary Flow



Capillary Flow: Fluid Vesicles



(fluid particles not shown)

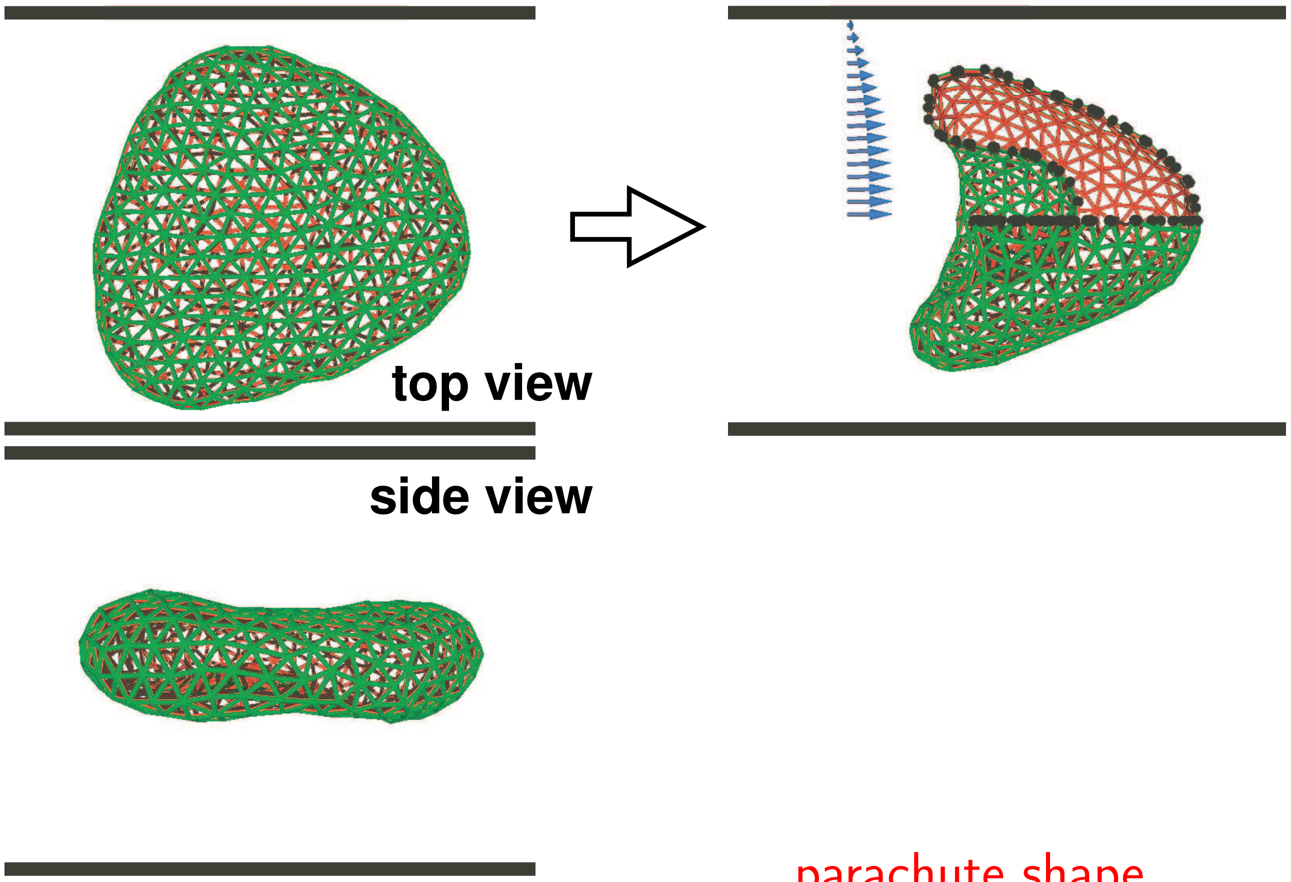
- small flow velocities: vesicle axis perpendicular to capillary axis ⟶ no axial symmetry!
- discocyte-to-prolate transition with increasing flow

H. Noguchi and G. Gompper, Proc. Natl. Acad. Sci. USA **102** (2005)

Capillary Flow: Elastic Vesicles

Elastic vesicle:

- curvature and shear elasticity $(\kappa = 20\, k_B T,\ \mu = 110\, k_B T / R_{rbc}^2)$
- model for red blood cells



parachute shape

Capillary Flow: Elastic Vesicles

Elastic vesicle:

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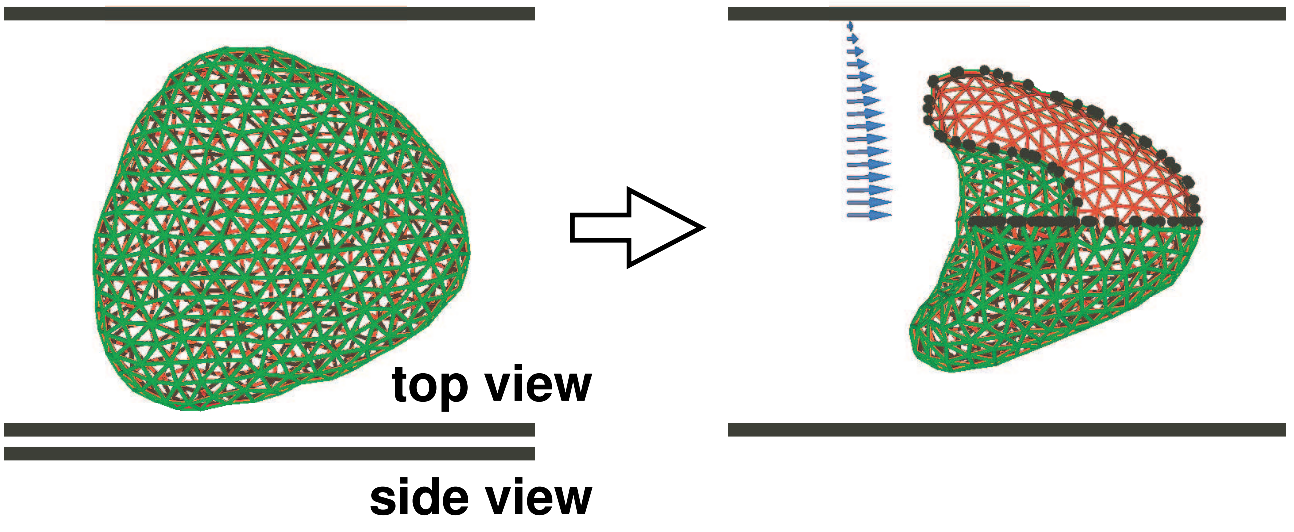
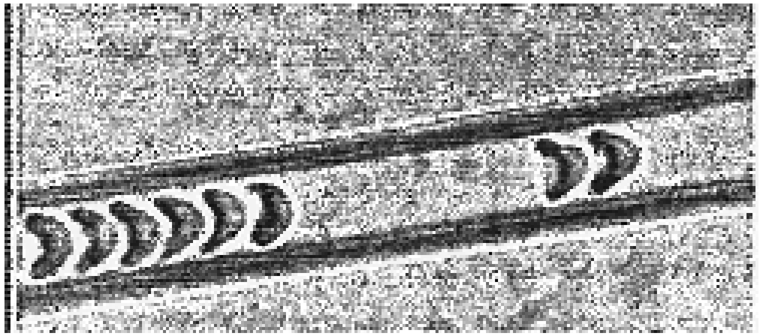
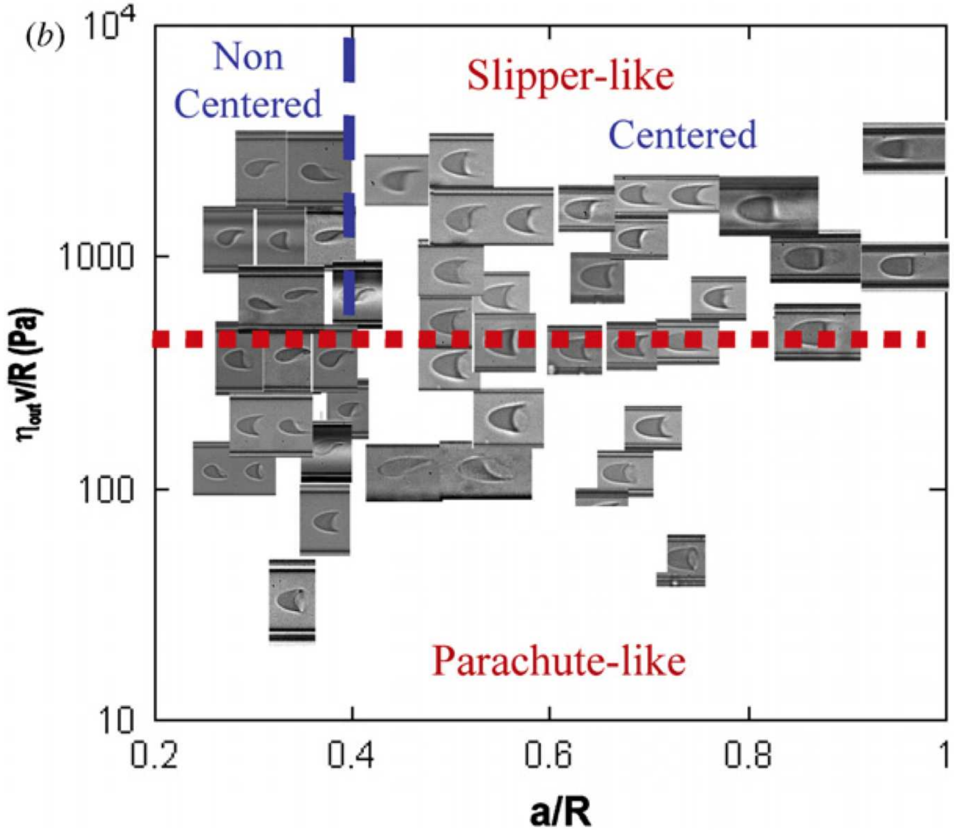
- model for red blood cells





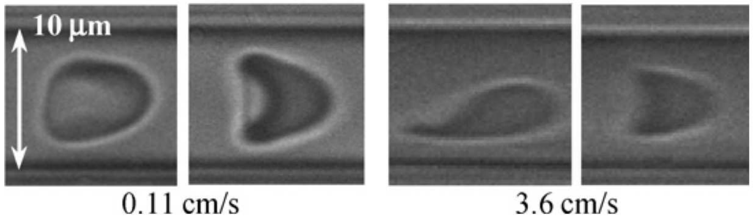
Tsukada et al., Microvasc. Res. **61** (2001)

Capillary Flow: Recent Experiments



M. Abkarian, M. Faivre, R. Horton, K. Smisttrup, C.A. Best-Popescu, and H.A. Stone, Biomed. Mater. **3**, 034011 (2008)

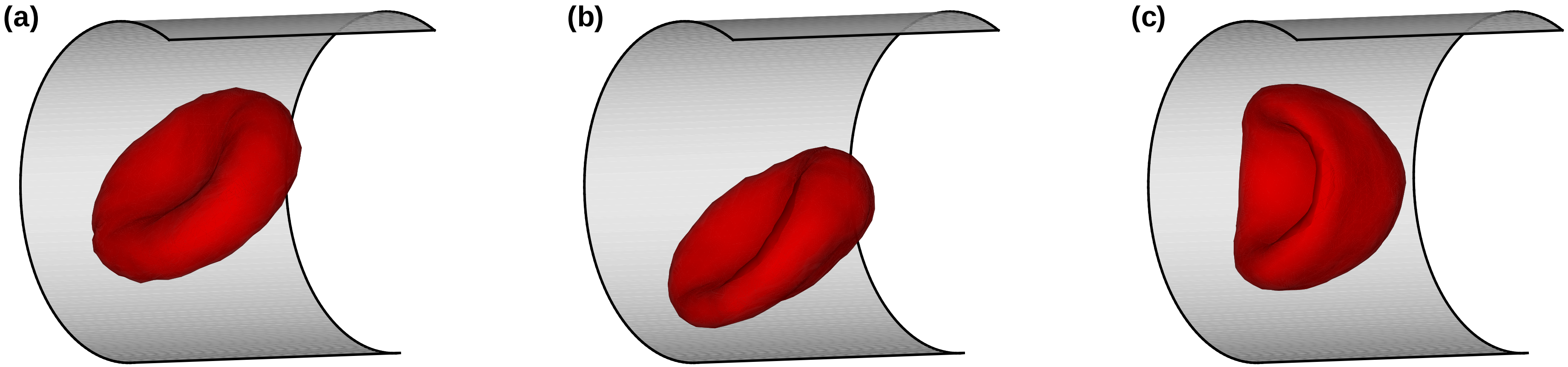
Very high flow velocities $\sim$ 10 cm/s



G. Tomaiuolo, M. Simeone, V. Martinelli, B. Rotoli, and S. Guido, Soft Matter **5**, 3736 (2009)

Short channels 4-5 mm

Capillary Flow: Simulations (DPD) in Three Dimensions

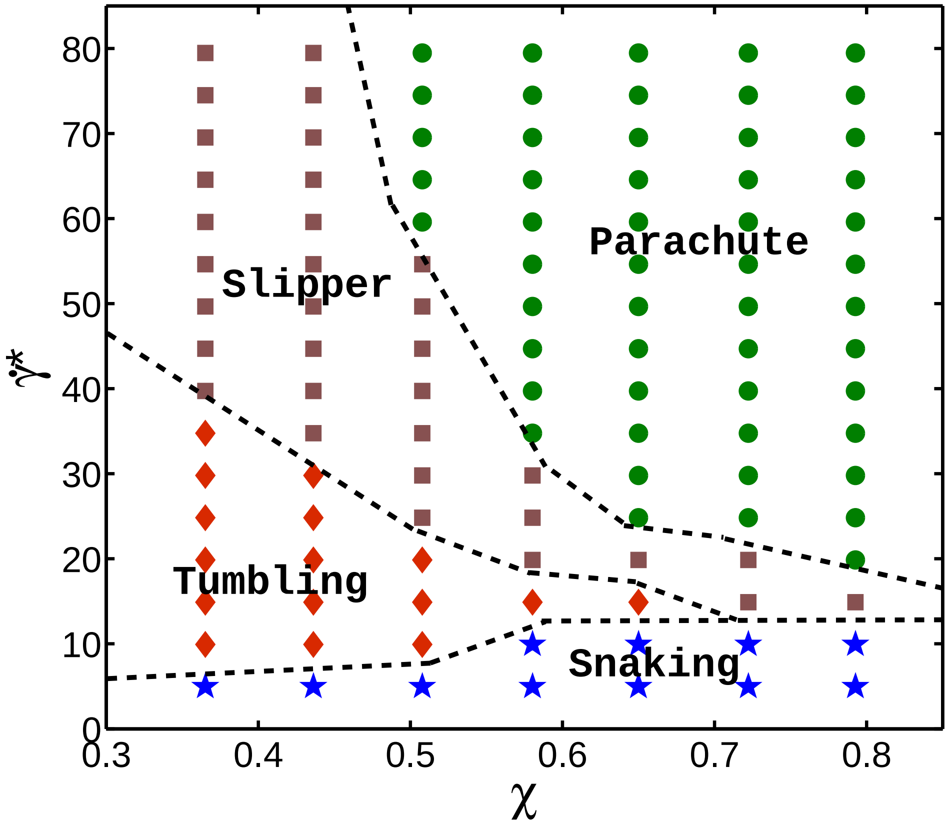


Snaking discocyte ($\dot{\gamma}^* = 5$) Swinging slipper ($\dot{\gamma}^* = 25$) Parachute ($\dot{\gamma}^* = 60$)

D.A. Fedosov, M. Peltomäki, and G. Gompper, submitted (2013)

Capillary Flow: Simulations (SDPD) in Three Dimensions

Phase diagram:



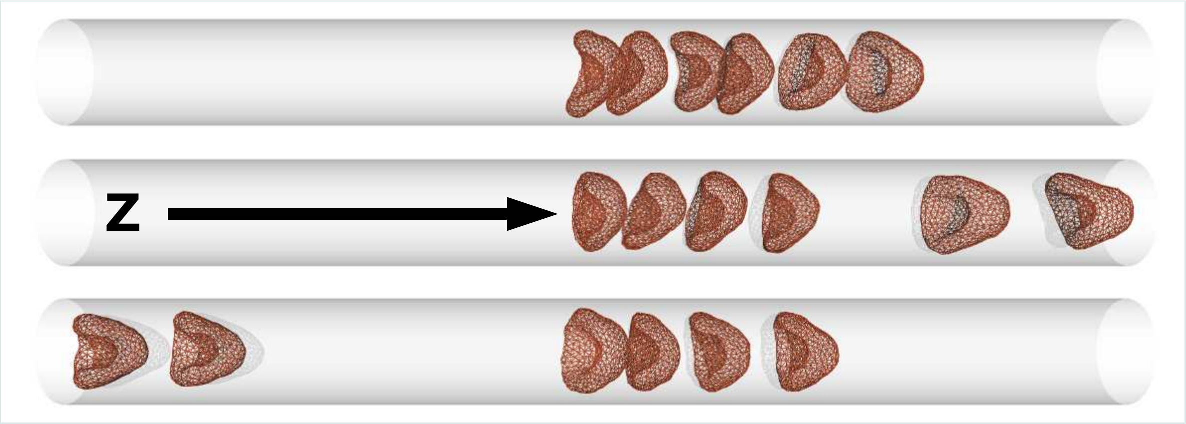
New features:

- Tumbling discocyte
- Swinging dynamics of slipper
- "Confined slipper" suppressed
- Parachure dominating at strong confinement

D.A. Fedosov, M. Peltomäki, and G. Gompper, submitted (2013)

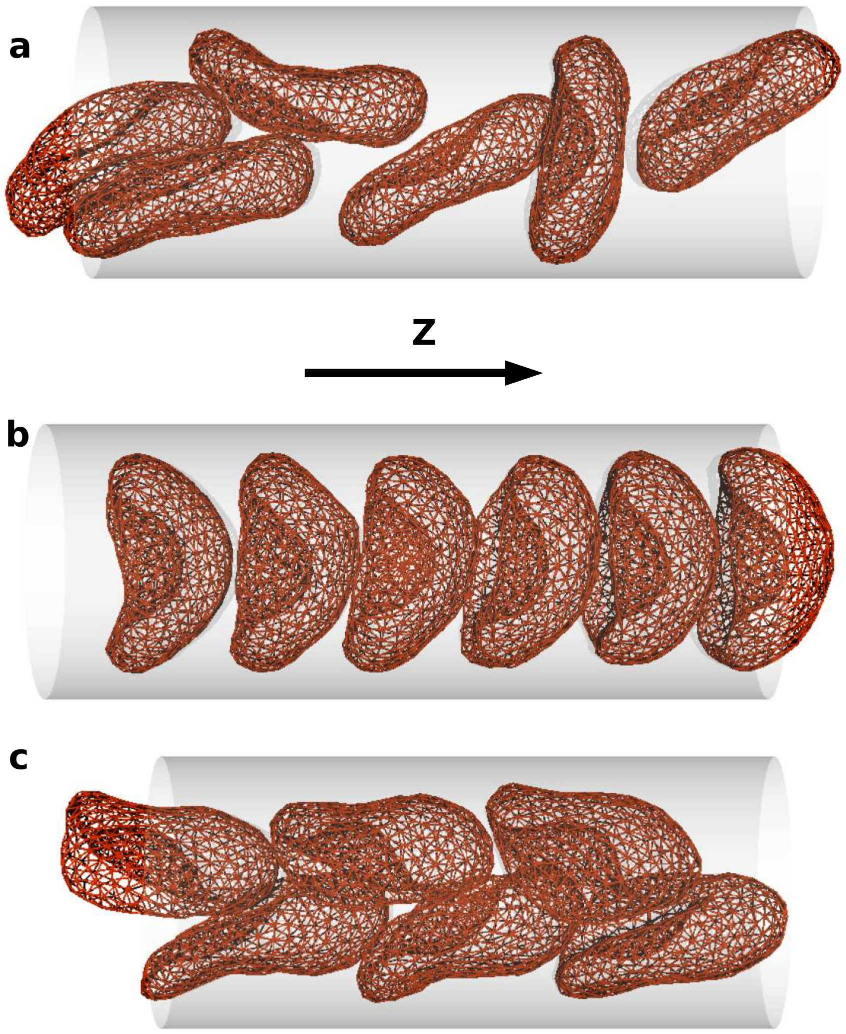
Membrane Hydrodynamics

Several Red Blood Cells in Capillary Flow



RBC Clustering & Alignment in Flow

High hematocrit H_T:



disordered discocyte

aligned parachute

zig-zag slipper

J.L. McWhirter, H. Noguchi, G. Gompper, Proc. Natl. Acad. Sci. **106** (2009)

RBC Clustering & Alignment in Flow

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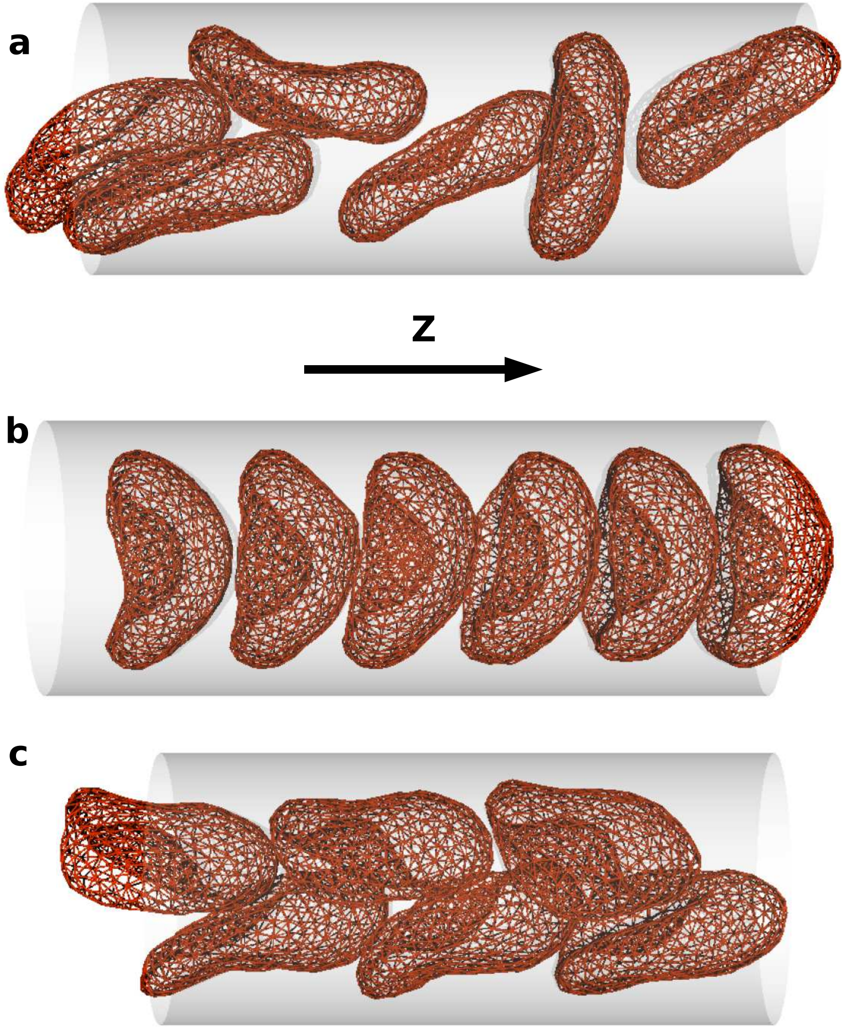
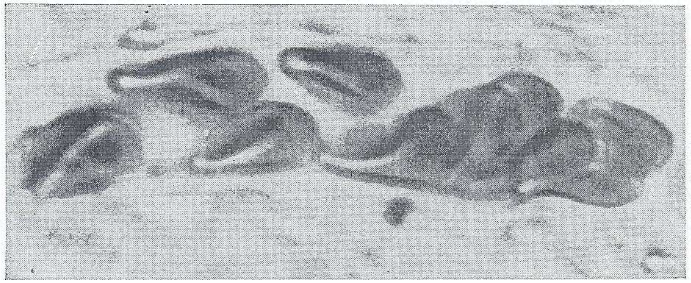


disordered discocyte

aligned parachute

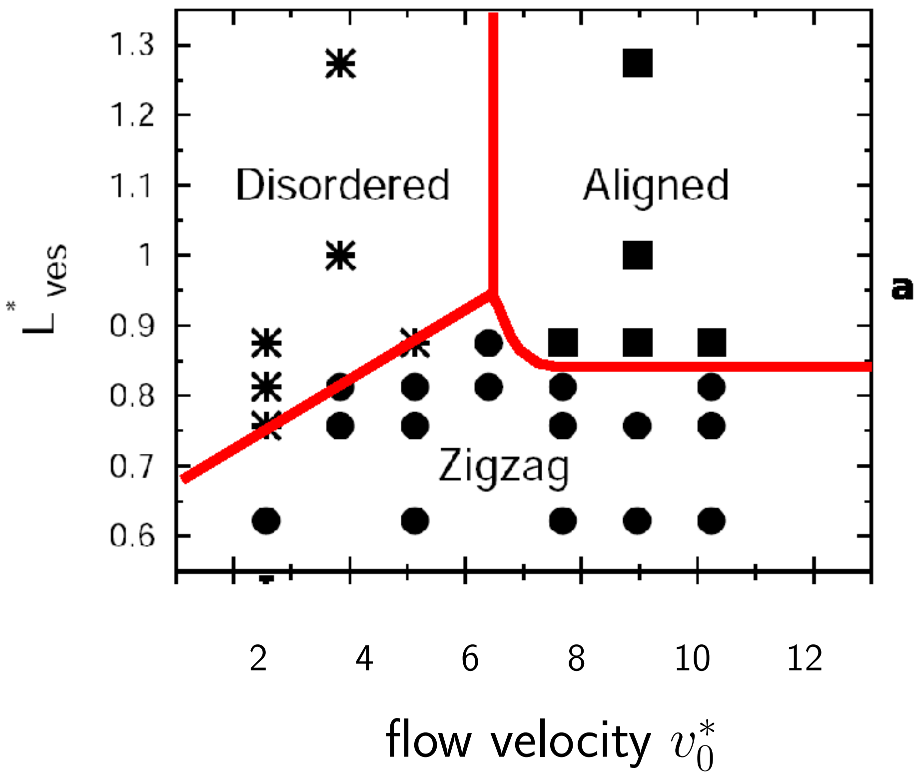
zig-zag



Skalak, Science (1969)

Clustering & Alignment in Flow

Phase diagram for capillary radius $R_{cap} = 4.6\mu m$ ($\chi = 0.71$):



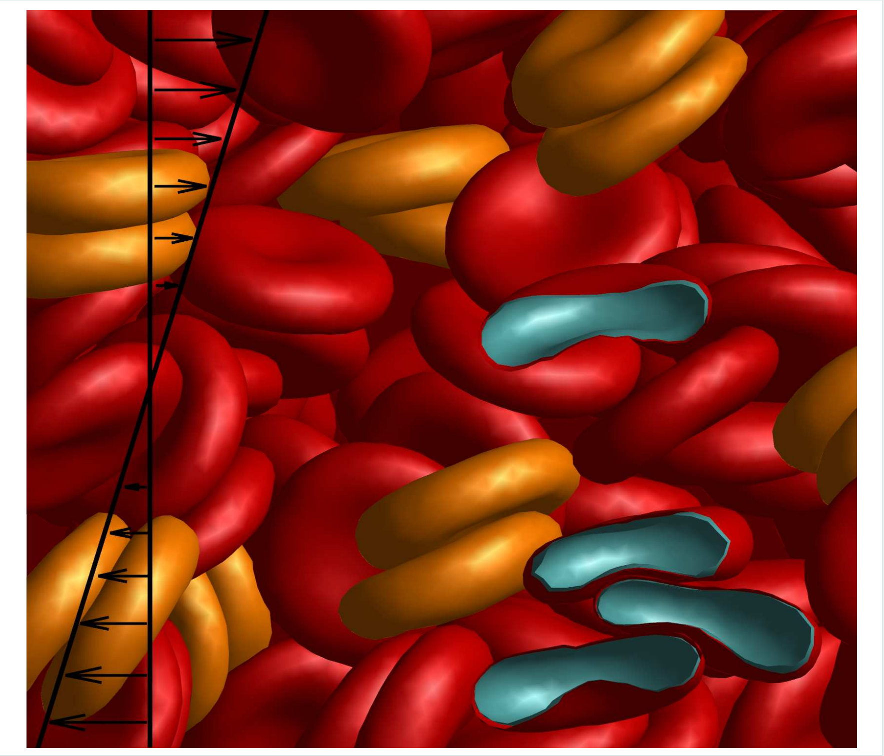
Hematocrit $H_T = 0.28/L^*_{ves}$

Transition to zig-zag phase despite higher flow resistance than aligned-parachute phase!

J.L. McWhirter, H. Noguchi, G. Gompper, Proc. Natl. Acad. Sci. **106** (2009)

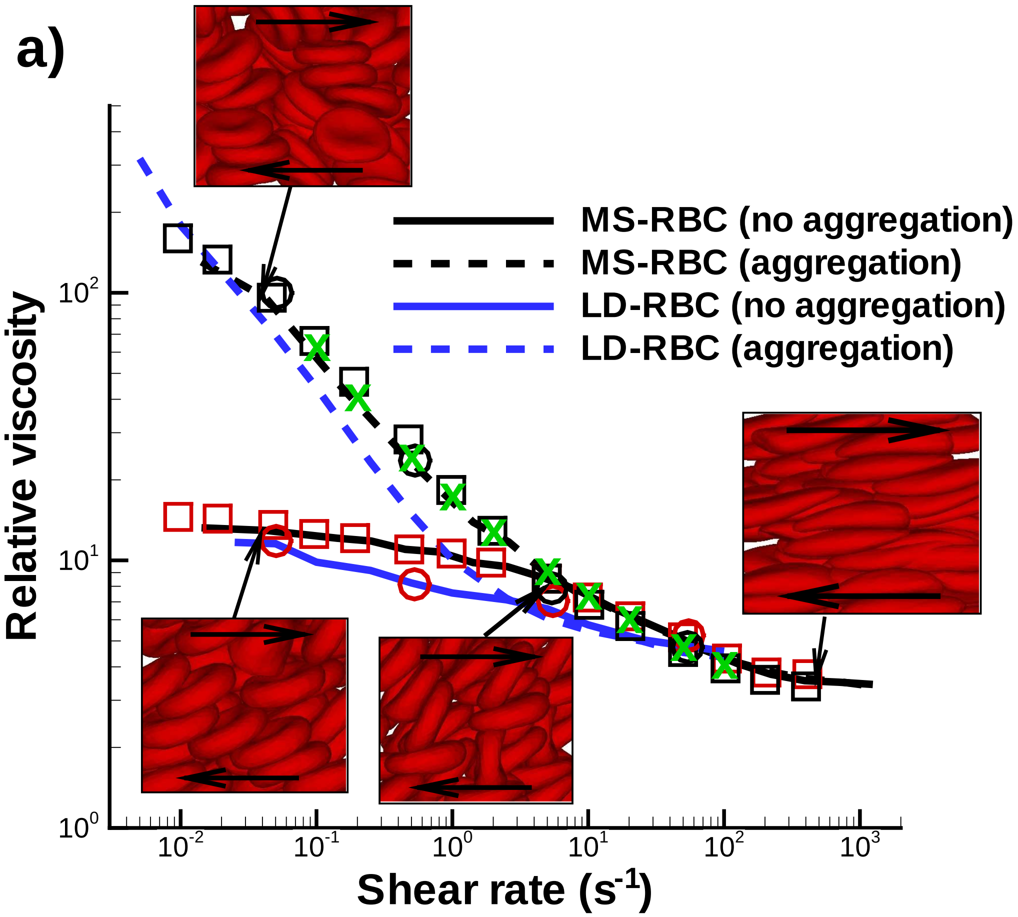
Membrane Hydrodynamics

Blood Rheology



Blood Viscosity (DPD)

Blood viscosity at physiological conditions (hematocrit 45%)



Experiments:

○ Chien et al., Science (1967)

☐ Skalak et al., JBE (1981)

no attraction:

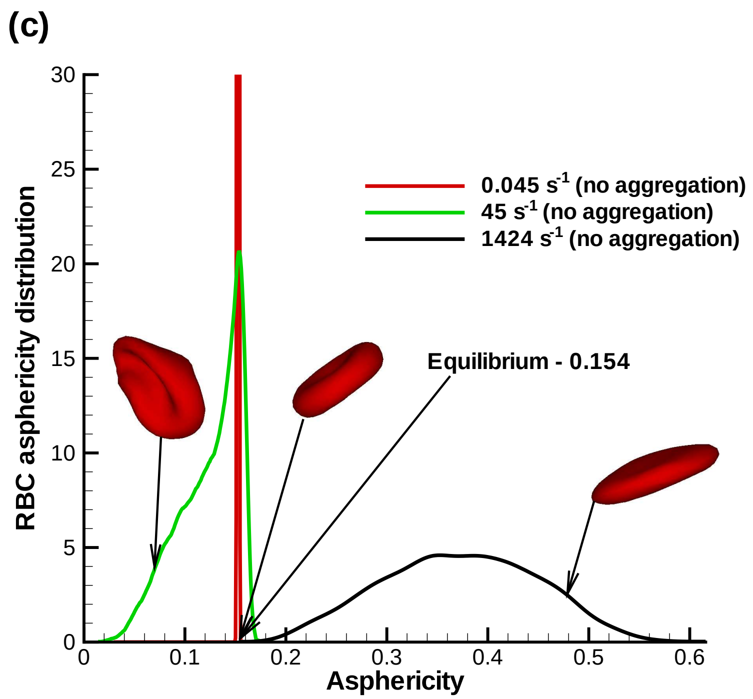
without fibrinogen

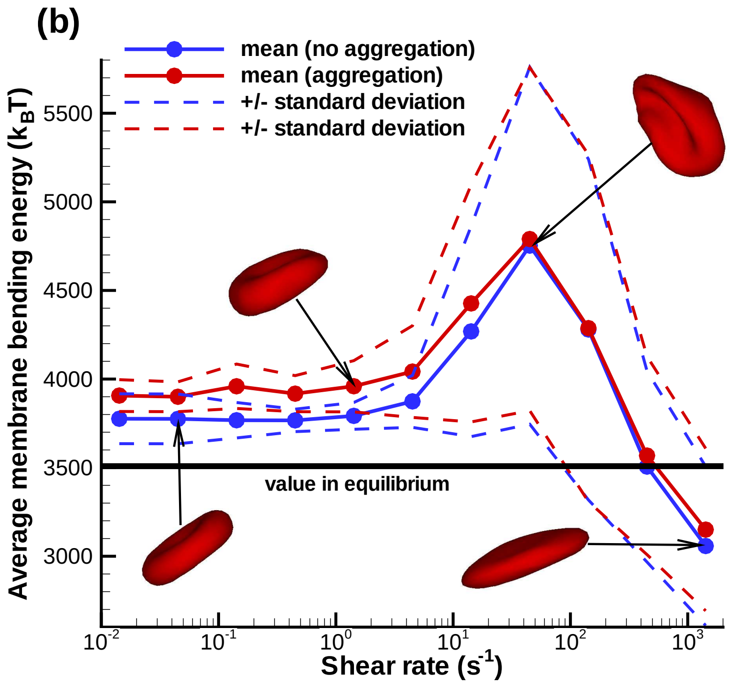
aggregation: whole blood

D.A. Fedosov, W. Pan, B. Caswell, G. Gompper, G.E. Karniadakis, Proc. Natl. Acad. Sci. USA **108** (2011)

Blood Viscosity (DPD)

- Two shear-thinning regimes: attraction / deformation dominated
- Estimate attraction strength: shear stress $\simeq 0.02 Pa$; force $\simeq 2 pN$
- Blood cells: shape and energy





D.A. Fedosov, W. Pan, B. Caswell, G. Gompper, G.E. Karniadakis, Proc. Natl. Acad. Sci. USA **108** (2011)

Summary

- Mesoscale simulation techniques are powerful tool to bridge the length- and time-scale gap in complex fluids
- Mesoscale simulations well suited for hydrodynamics of embedded particles: colloids, polymers, vesicles, RBCs, microswimmers
- Single red blood cell in capillary flow: swinging, tumbling, and snaking dynamics
- Several red blood cell in capillary flow: various flow-induced arrangements
- Red blood cells in shear flow: roleaux formation, shear thinning

Review Blood-Flow Simulations:

D.A. Fedosov, H. Noguchi, G. Gompper, Biomech. Model. Mech. Biol., advance online (2013)

Acknowlegments

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Sebastian Messlinger

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