Migration of hard particles in suspension of soft particles flowing in a tube

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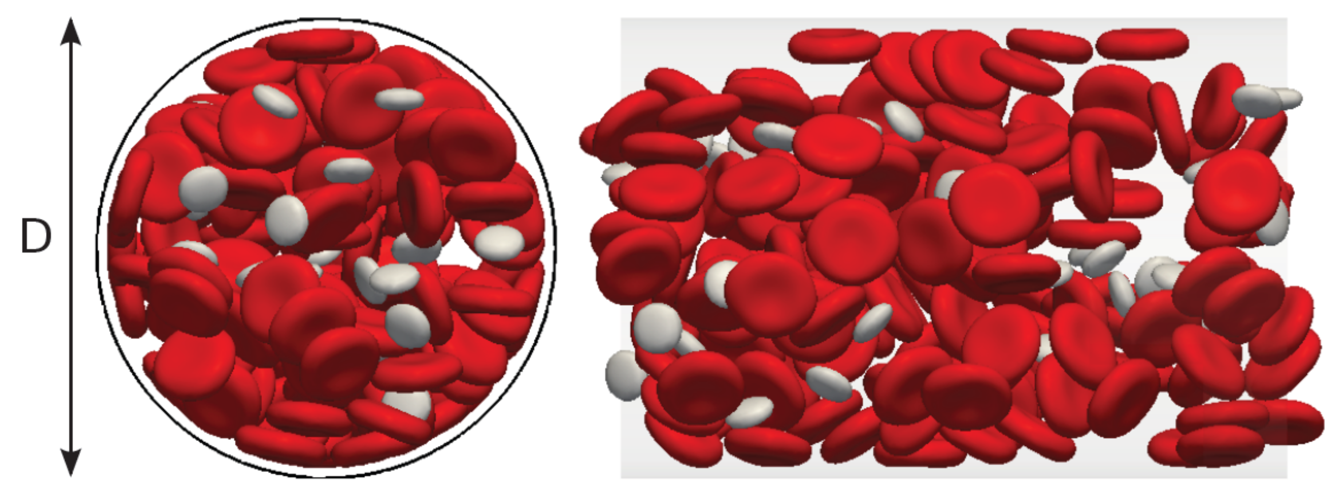

Georgia Tech
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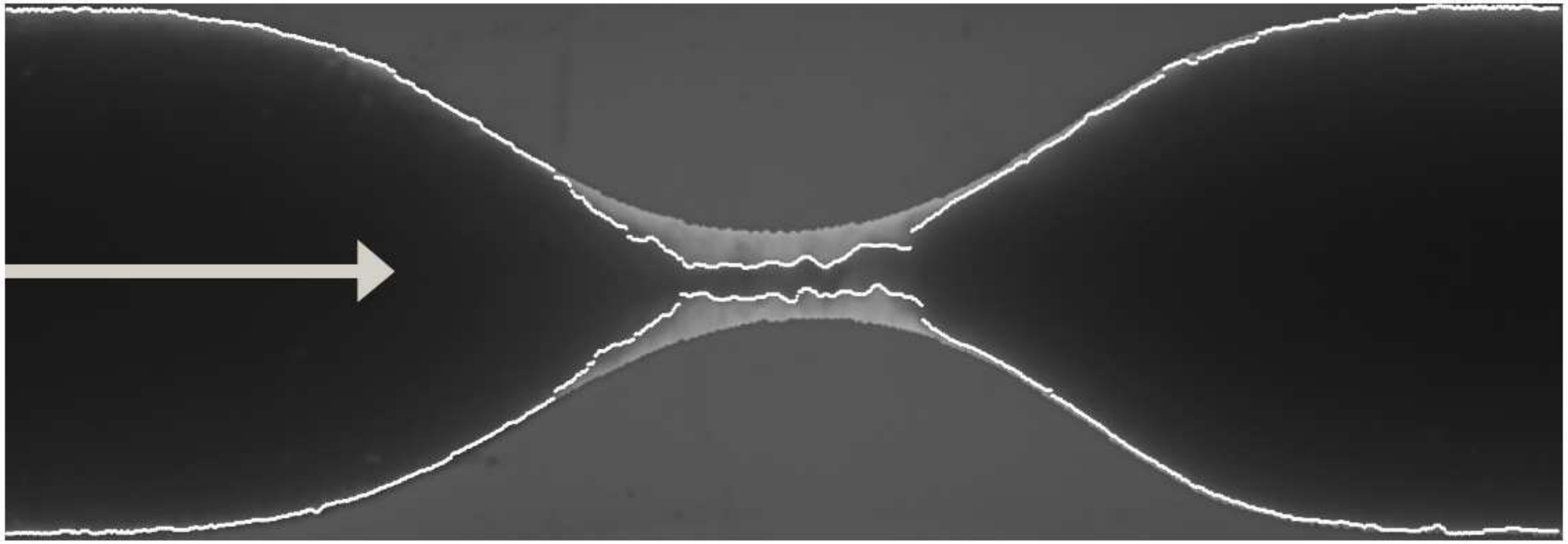
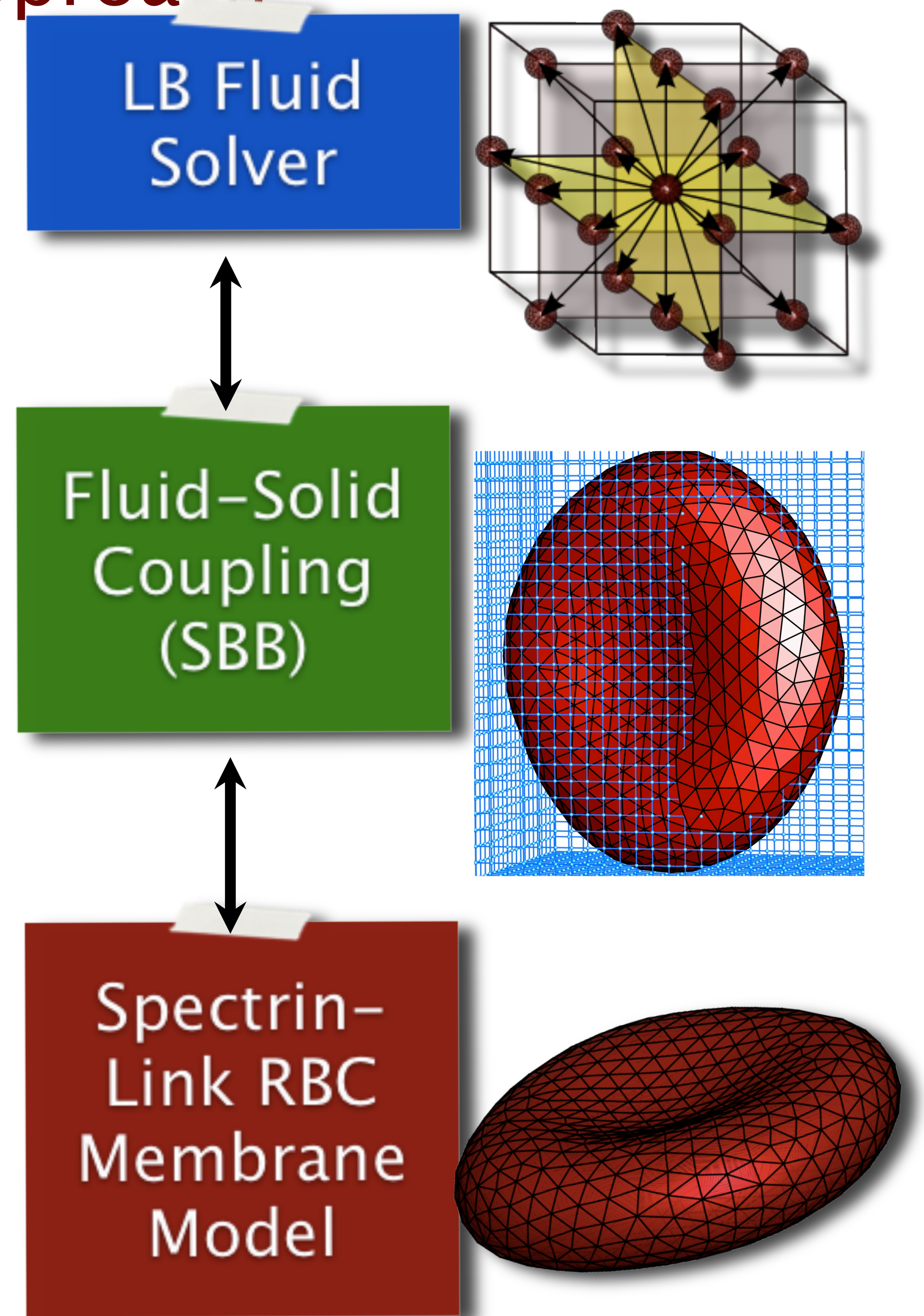
An *in vitro* thrombosis model – platelet transport rate

- *In vitro* thrombosis model $\Rightarrow$
  platelet accumulation rate $\sim 1.5 \times 10^6$ platelets/min
- Platelet transport rate with Brownian diffusivity $\ll$ platelet accumulation rate



Thrombosis formed after 7 minutes of blood perfusion in a 85% stenosed section of a 1.5mm ID glass tube (Bark D, PhD thesis 2010)

Computational Approach



- Fluid domain is solved in 3-D with the D3Q19 lattice-Boltzmann method using a single relaxation time BGK operator.

- RBC deformations are modeled using a coarse-grained spectrin-link method.

- Fluid-Particle interactions are done with the standard "bounce-back" (SBB) boundary condition.

- Particle-Particle and Particle-Boundary interactions are computed with a sub-grid-scale contact model or adhesion-contact model.

Aidun, Lu, & Ding, *J Fluid Mech*, 373, 1998.
Reasor, Clausen, & Aidun, *Inter J Num Meth Fluids*, 2011.

Lattice–Boltzmann Method

Derived from the discretized Boltzmann equation, i.e., a discretized version of the Boltzmann equation in velocity space.

Symbols

$\mathbf{e}_i$	Discrete lattice velocity vectors
f_i	Particle distribution
$f_i^{(eq)}$	Equilibrium particle distribution
$\mathbf{x}$	Cartesian coordinate
t	Time
τ	Single relaxation time

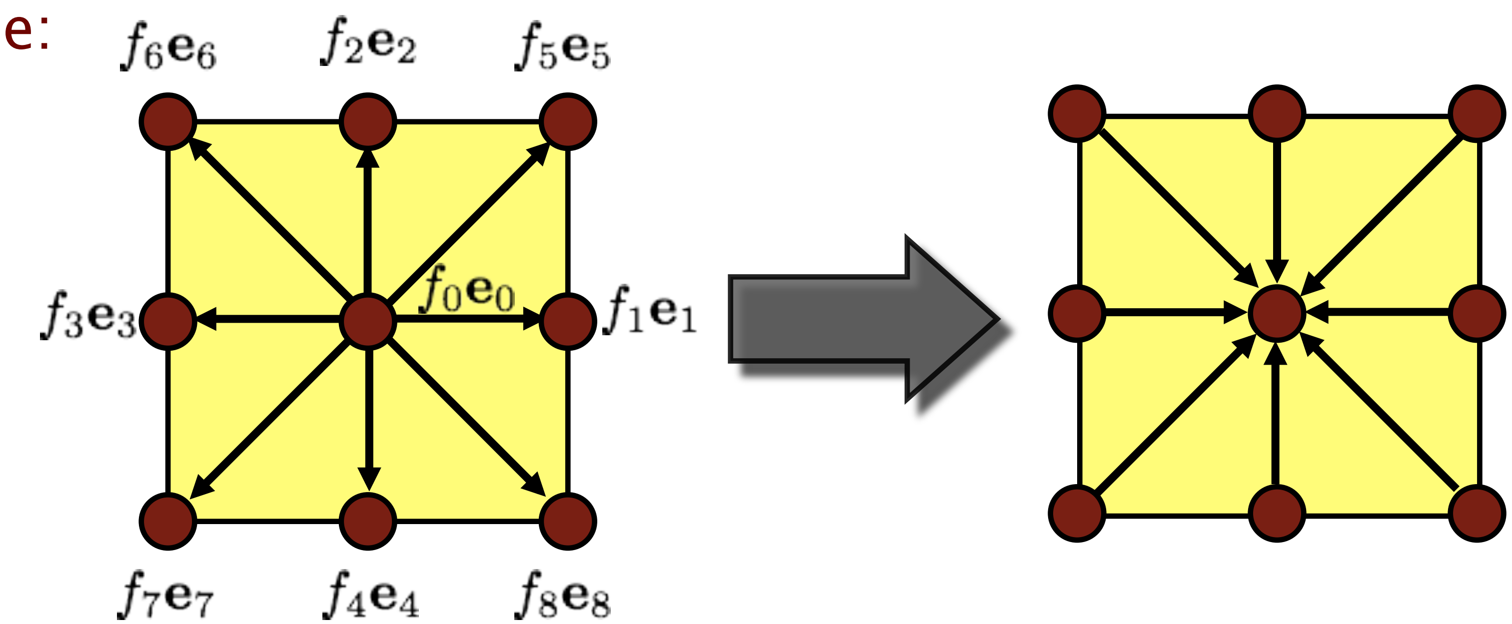
lattice Boltzmann Equation with BGK Collision Operator (E-LB for large Re)

$$f_i(\mathbf{x}+\mathbf{e}_i, t+1) - f_i(\mathbf{x}, t) = -\frac{1}{\tau}[f_i(\mathbf{x}, t) - f_i^{(eq)}(\mathbf{x}, t)]$$

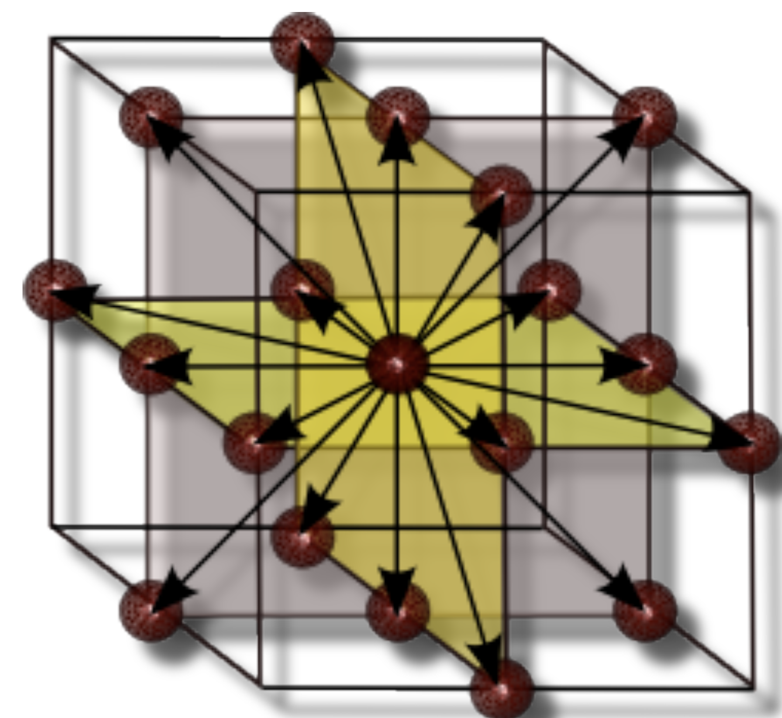
D2Q9 Lattice:

Streaming

Collision



D3Q19 Lattice



Aidun & Clausen, Annual Rev. Fluid Mech., 42, 2010

Lattice–Boltzmann Method

Equilibrium Distribution Function

$$f_i^{(eq)}(\mathbf{x},t) = w_i\rho\left[1 + \frac{1}{c_s^2}(\mathbf{e}_i\cdot\mathbf{u}) + \frac{1}{2c_s^4}(\mathbf{e}_i\cdot\mathbf{u})^2 - \frac{1}{2c_s^2}u^2\right]$$

Macroscopic Fluid Properties

Density

$$\sum_i^Q f_i^{(eq)}(\mathbf{x},t) = \rho$$

Velocity

$$\frac{1}{\rho}\sum_i^Q f_i^{(eq)}(\mathbf{x},t)\mathbf{e}_{i\alpha} = u_\alpha$$

Pressure

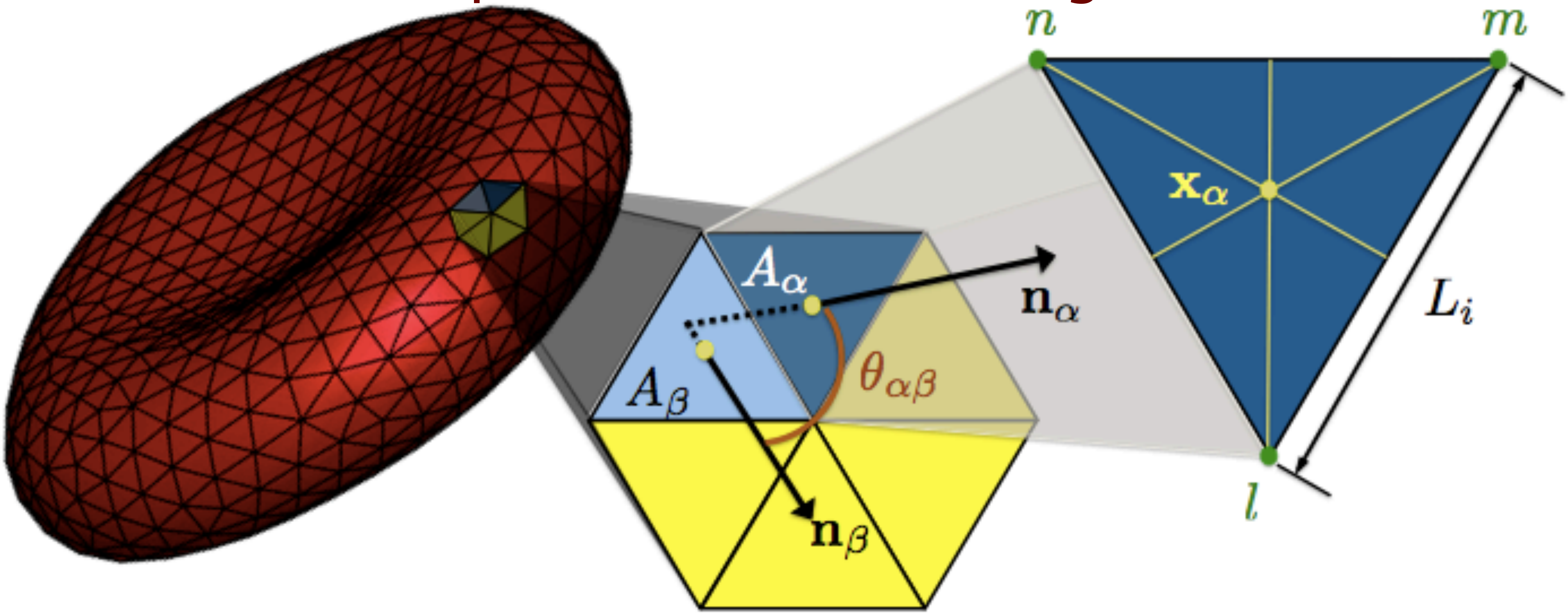
$$\sum_i^Q f_i^{(eq)}(\mathbf{x},t)\mathbf{e}_{i\alpha}\mathbf{e}_{i\beta} = c_s^2\rho\delta_{\alpha\beta} + \rho u_\alpha u_\beta$$

Symbols

c_s	Pseudo sound speed
$\mathbf{e}$	Discrete lattice velocity vectors
$f_i^{(eq)}$	Equilibrium distribution
$\mathbf{x}$	Cartesian coordinate
$\mathbf{u}$	Macroscopic velocity
t	Time
w_i	Lattice weights
$\delta_{\alpha\beta}$	Dirac delta
ν	Kinematic viscosity
ρ	Density
τ	Single relaxation time

Aidun & Clausen, Annual Rev. Fluid Mech., 42, 2010

Spectrin-Link Modeling

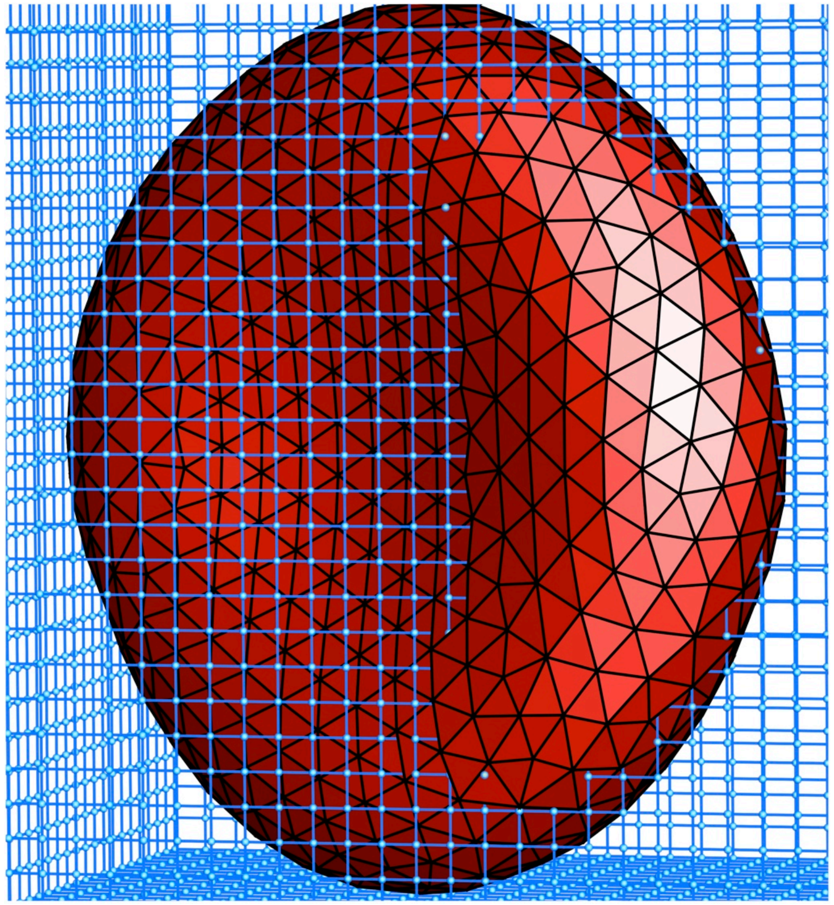


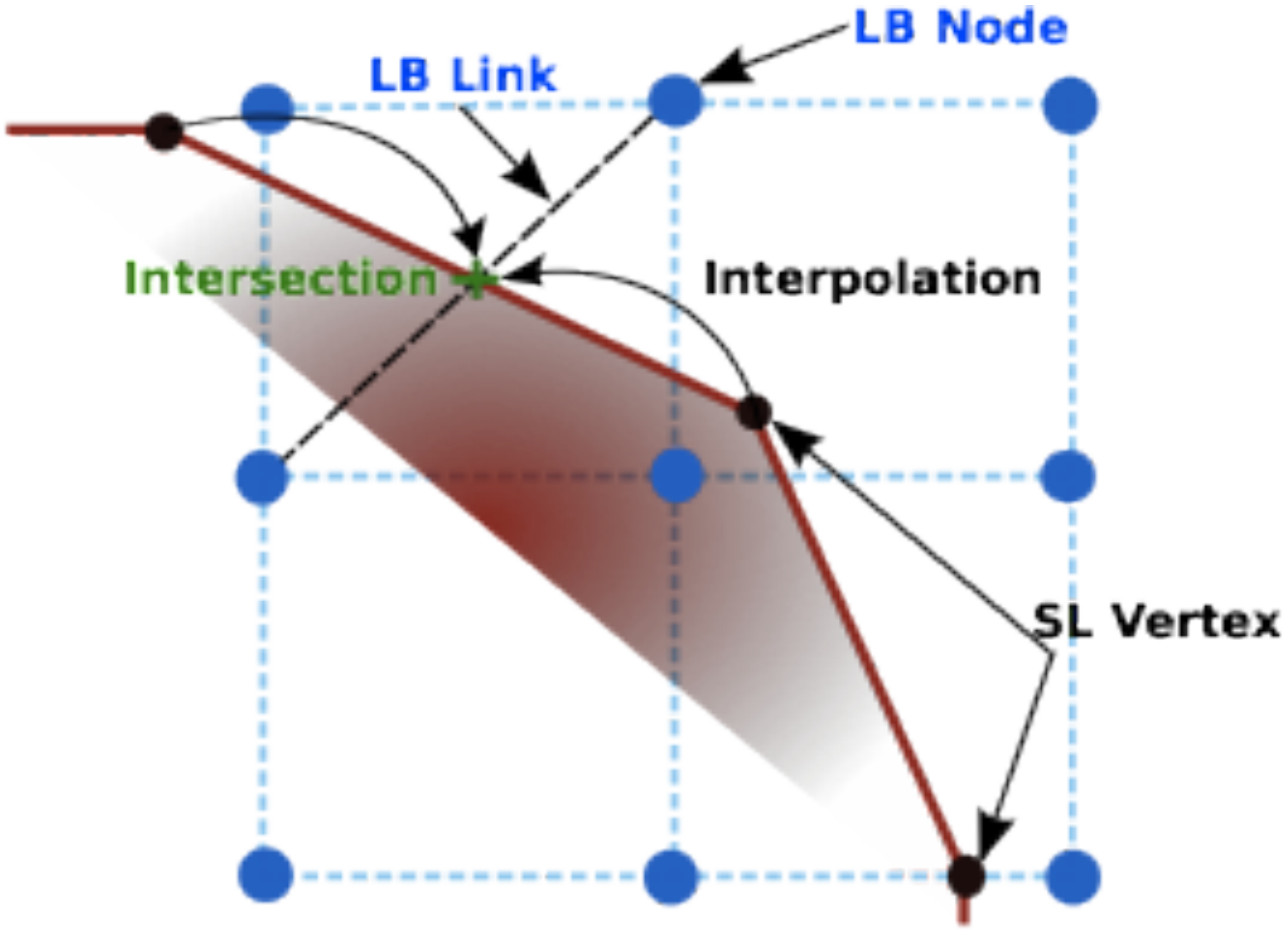
Geometric Description

Vertices	$\{\mathbf{x}_n, n \in 1 \ldots N\}$	**Area**	$A_\alpha = \frac{1}{2}\lvert(\mathbf{x}_m - \mathbf{x}_l) \times (\mathbf{x}_n - \mathbf{x}_l)\rvert$
Link Lengths	$L_i = \lvert\mathbf{x}_m - \mathbf{x}_n\rvert$	**Total Area**	$A_{\text{total}} = \sum_{\alpha\in\Pi} A_\alpha$
Centroid	$\mathbf{x}_\alpha = \frac{1}{3}(\mathbf{x}_l + \mathbf{x}_m + \mathbf{x}_n)$	**Total Volume**	$\Omega_{\text{total}} = \sum_{\alpha\in\Pi}(\mathbf{x}_\alpha \cdot \mathbf{n}_\alpha)A_\alpha$
Angle	$\theta_{\alpha\beta} = \cos^{-1}(\mathbf{n}_\alpha \cdot \mathbf{n}_\beta)$	**Normal**	$\mathbf{n}_\alpha = [(\mathbf{x}_m - \mathbf{x}_l) \times (\mathbf{x}_n - \mathbf{x}_l)]/2A_\alpha$

Li, Dao, Lim, & Suresh, Biophysical J., 88, 2005.
Dao, Li, & Suresh, Mat. Sci. Engr. C-BioS., 26, 2006.
Fedosov, Caswell, Karniadakis, Comp Meth Applied Mech & Eng, 2010

LB-SL Coupling: Fluid-Solid Interaction





- Momentum is conserved across the interface
- Stress on interior fluid and exterior fluid is equal
- Identical to the no-slip BC
- First-order accurate in space due to SL face not at midpoint

Particle Distribution Adj.

$$f_i(\mathbf{x}, t+1) = f_{i'}(\mathbf{x}, t^+) + 6\rho w_i \mathbf{u}_b \cdot \mathbf{e}_i$$

Traction Force on RBC/Platelet

$$\mathbf{f}^{(b)}(\mathbf{x} + \frac{1}{2}\mathbf{e}_{i'}, t) = -2\mathbf{e}_i[f_{i'}(\mathbf{x}, t^+) + 3\rho w_i \mathbf{u}_b \cdot \mathbf{e}_i]$$

Aidun, Lu, & Ding. JFM, 373, 1998 – LBM for suspension of hard particles
MacMeccan, Clausen, Neitzel, & Aidun. J. Fluid Mech., 618, 2009 – soft particles
Reasor, Clausen, & Aidun. Inter. J. Num. Meth. Fluids, online, 2011– LBM for RBC
Aidun and Clausen, Annual Rev. Fluid Mech., 2010

Dimensionless Parameters (I)

RBC Capillary Number: Inertia vs. Shear Deformation

$$Ca_{\mathrm{G}} \equiv \frac{\mu\dot{\gamma}a}{G}$$

G membrane shear modulus

a RBC radius

μ plasma dynamic viscosity

$\dot{\gamma}$ shear rate experienced by the RBC

RBC Reynolds Number: Inertia vs. Viscous Effects

$$Re_{\mathrm{RBC}} \equiv \frac{\rho\dot{\gamma}a^2}{\mu}$$

ρ plasma density

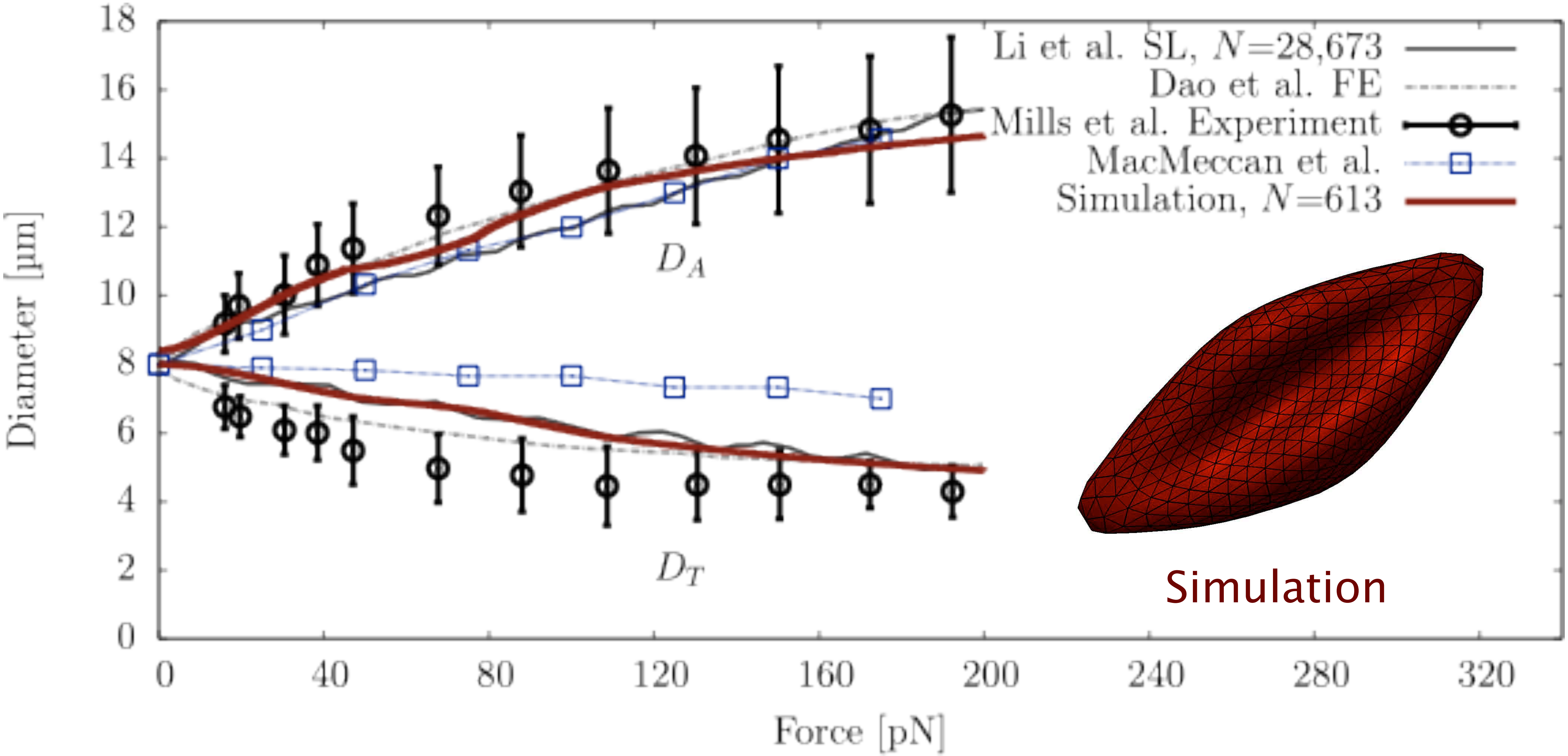
Tube Reynolds Number: Inertia vs. Viscous Effects

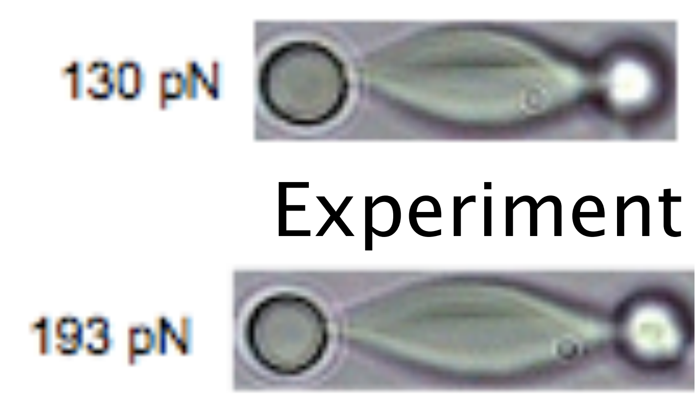
$$Re_t \equiv \frac{\rho\bar{u}D}{\mu}$$

$\bar{u}$ average velocity

D tube diameter

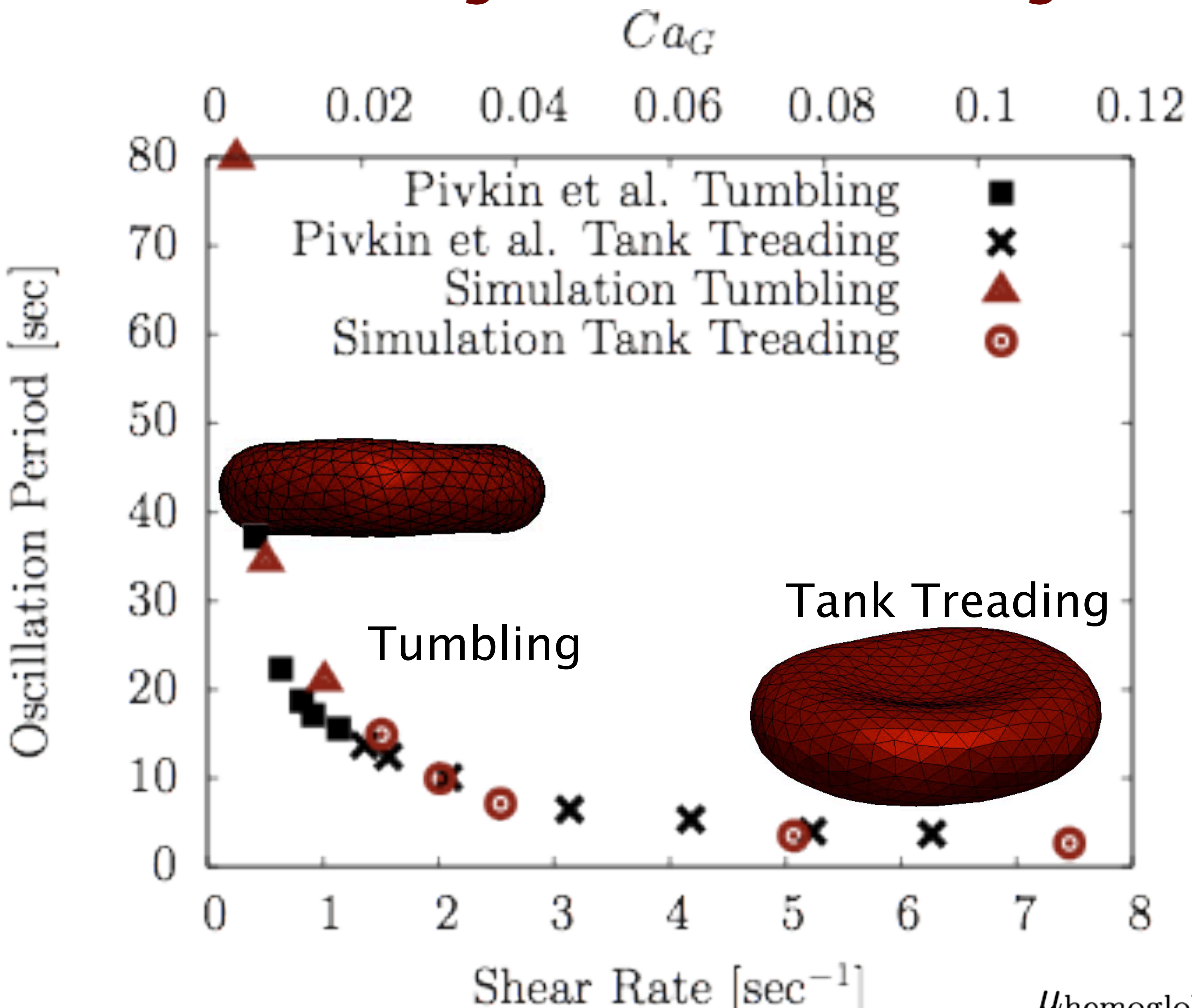
Validation: Optical Tweezer Experiment





Li et al., Biophys. J., 88, May 2005.
Dao et al., Mat. Sci. Engr. C-BioS., 26, 2006.
Mills et al., MCB, 1(3), 2004.
MacMeccan, et al., J. Fluid Mech., 618, 2009.
Reasor et al., Inter. J. Num. Meth. Fluids, 2011.

Tumbling and Tank Treading



$$\lambda = \frac{\mu_{\text{hemoglobin}}}{\mu_{\text{dextran}}} = \frac{6}{22} = 0.28$$

Pivkin & Karniadakis. *Phys. Rev. Lett.*, 101(118105), 2008.
Reasor, Clausen, & Aidun. *Int J Num Meth Fluids*, online, 2011.

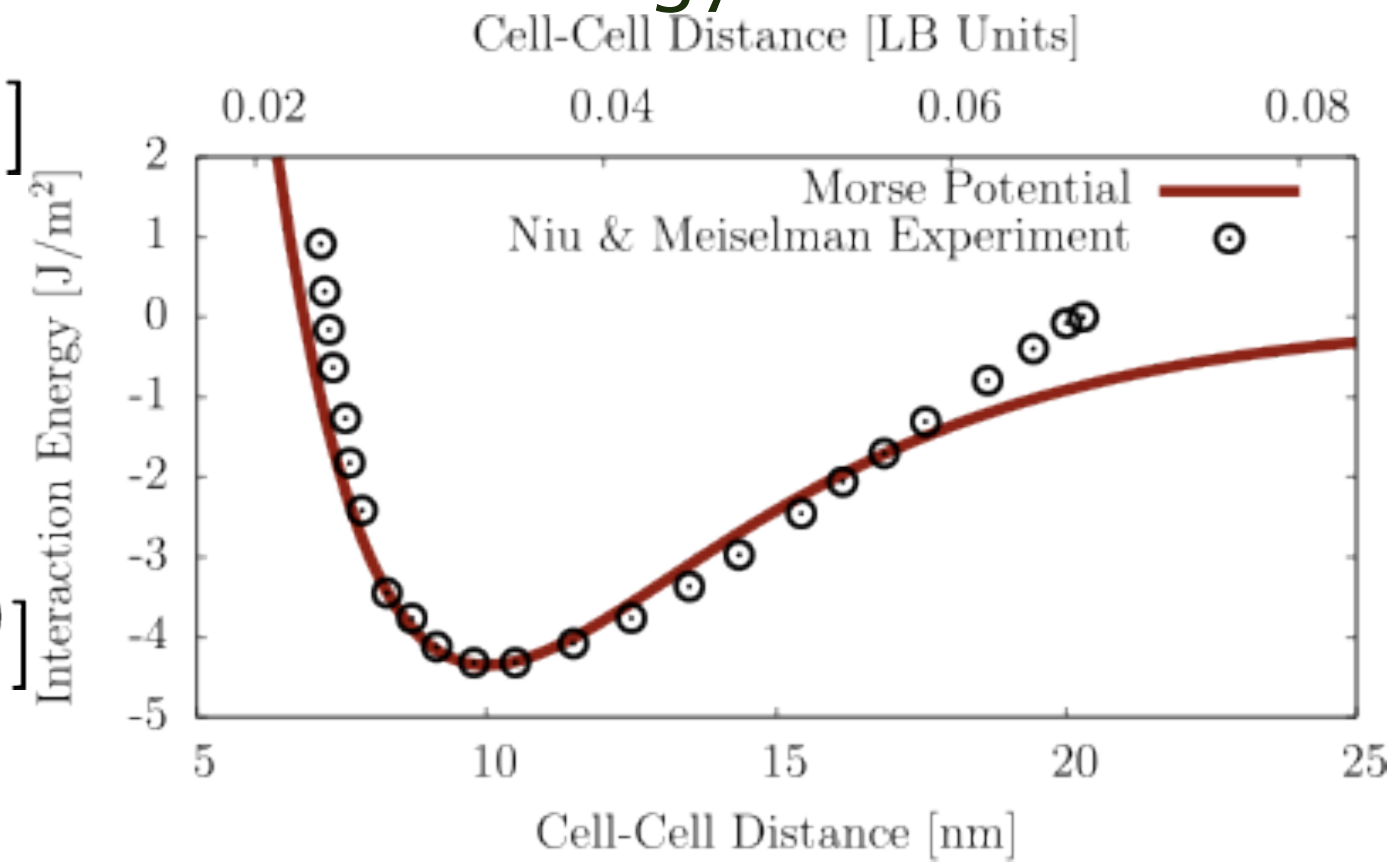
Contact & Adhesion: Morse Potential and Force

The Morse potential mimics the interaction energy between RBCs.

$$\phi(x) = D_e[e^{2\beta(x_0-x)} - 2e^{\beta(x_0-x)}]$$

$$f(x) = -\frac{\partial\phi(x)}{\partial x}$$

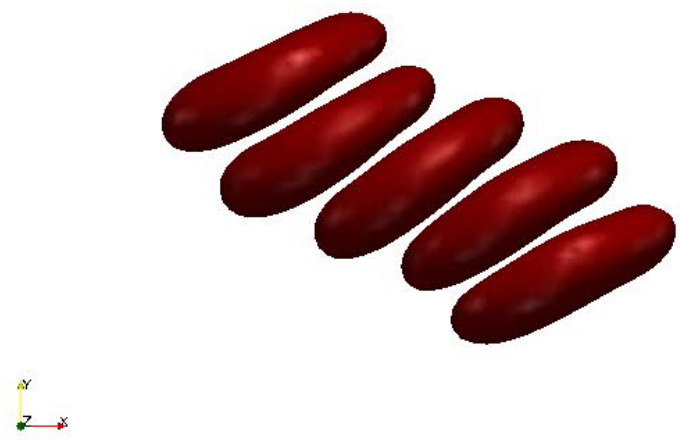
$$f(x) = 2D_e\beta[e^{2\beta(x_0-x)} - e^{\beta(x_0-x)}]$$



Repulsive Force
(contact prevents overlap)

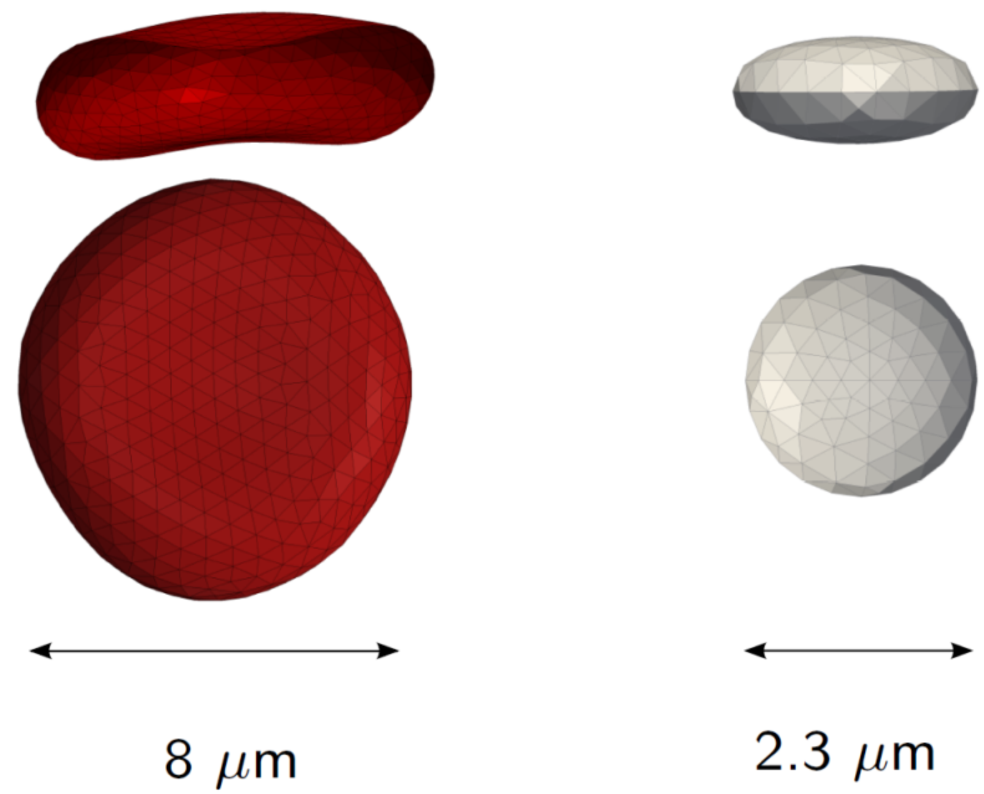
Adhesion Force
(mimics cell-cell bonding)

"The basic behavior of the interaction forces between two RBCs is simply illustrated as the weak attractive and strong repulsive forces at far and near distances."



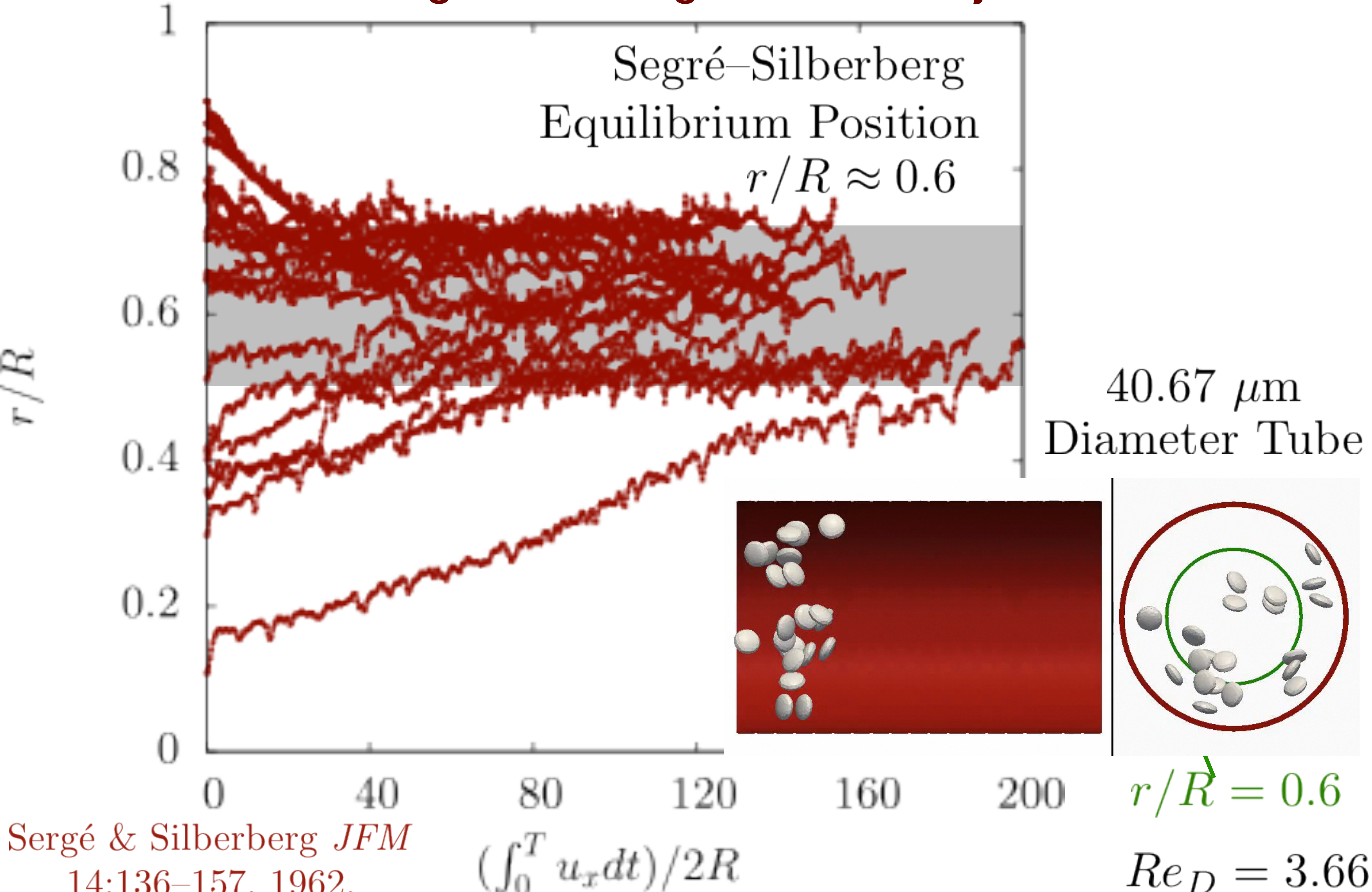
Neu & Meiselman, Biophys. J., 83:2482-2490, 2002.
Liu, Zhang, Wang & Liu, Int. J. Num. Meth. Fluids, 46:1237-1252, 20(
Aidun & Clausen, Annual Rev. Fluid Mech., 42, 2010
Reasor, Clausen, & Aidun, *Inter J Num Meth Fluids*, 2011.

Platelet modeling



radius (µm)	~5.5	~2.7
Shear modulus (µN/m)	~2	~2.9 x 10
shape	Biconcave disks (AR ~2.7)	Oblate spheroid (AR ~2.7)

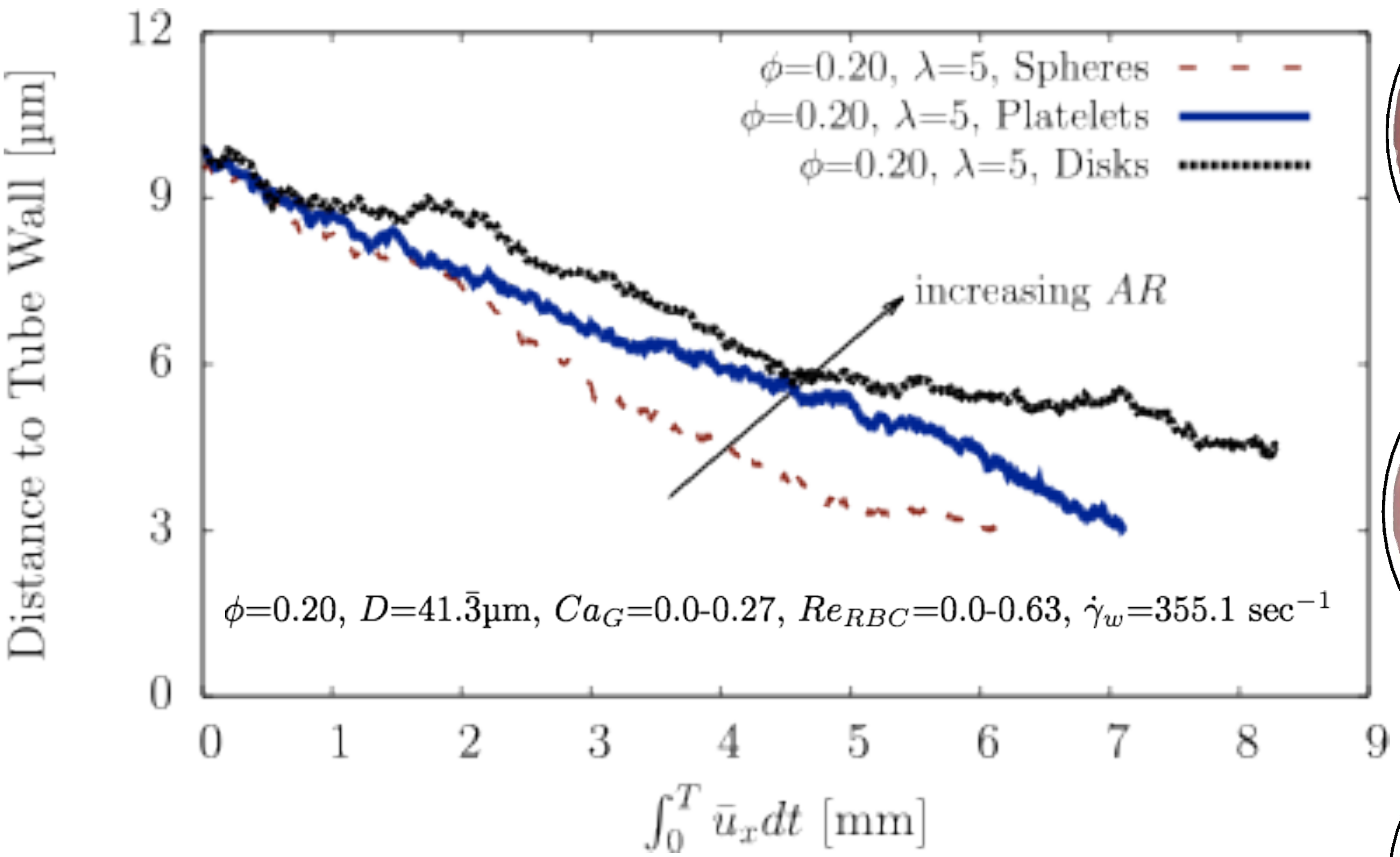
Platelet Migration: Single Phase Trajectories

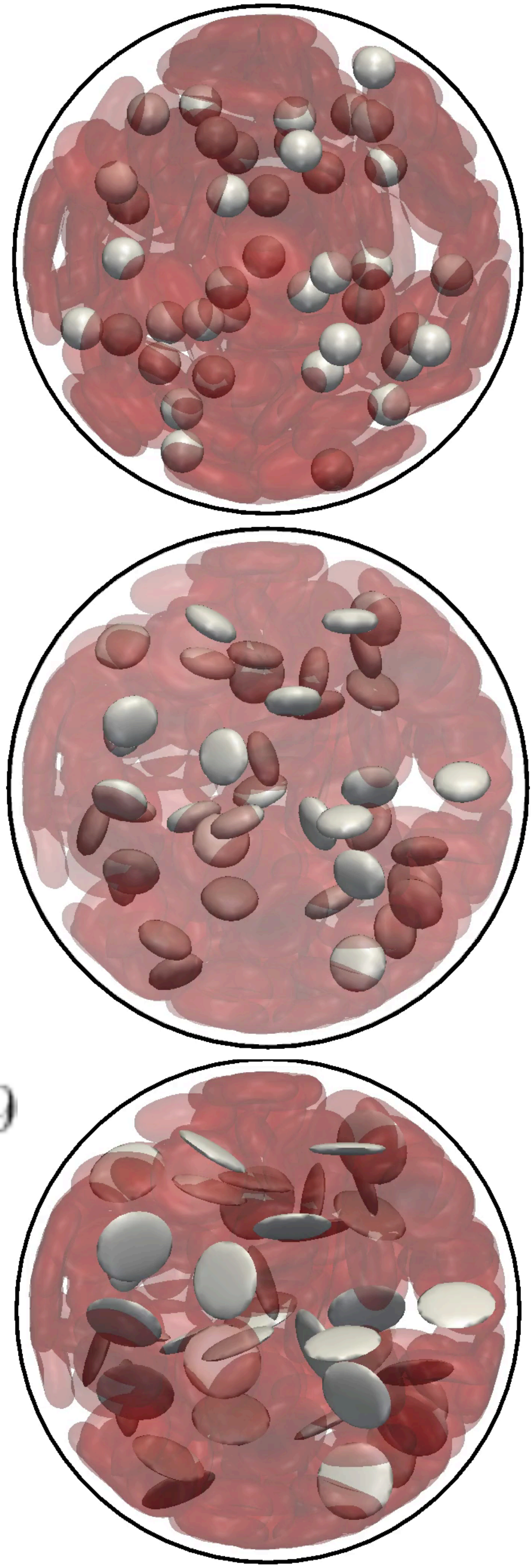


Sergé & Silberberg *JFM* 14:136–157, 1962.

Reasor, Mehrabadi, Ku, and Aidun, *Annals of Biomedical Engineering*, 41(2):238-49, 2013

Platelet Margination: Shape Dependence



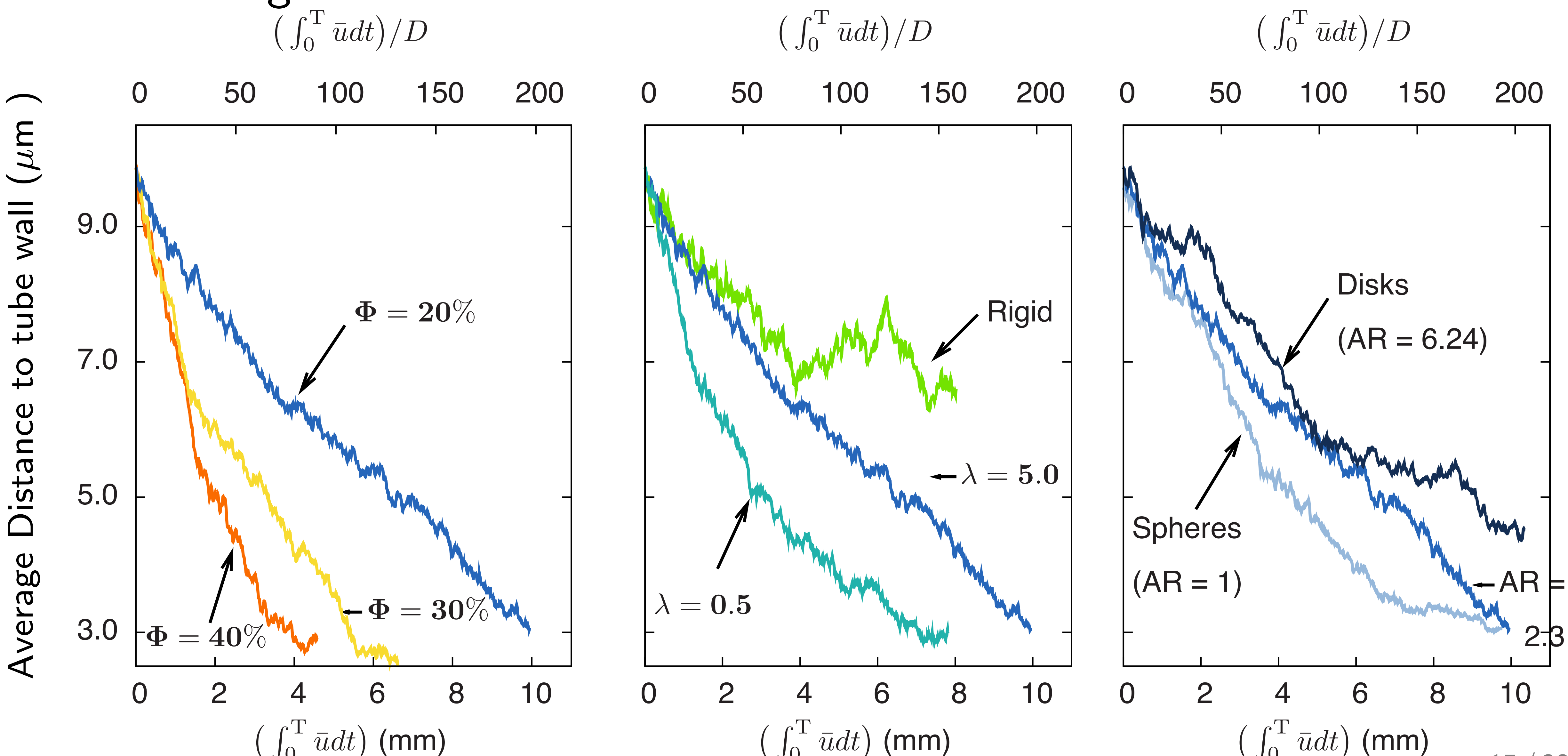


Aidun & Clausen, Annual Rev. Fluid Mech., 42, 2010
Reasor, Clausen, & Aidun, *Inter J Num Meth Fluids*, 2011.
Reasor, Mehrabadi, Ku, and Aidun, *Annals of Biomedical Engineering*, 41(2):238-49, 2013

Effect of ϕ, λ and shape on platelet margination rate

Simulations in $41.\bar{3}$ μm D tubes (Reasor et al.):

- Increasing ϕ (20%–40%) $\Rightarrow$ increase of margination rate
- Increasing λ (0.5–∞) $\Rightarrow$ decrease of margination rate
- Increasing platelet aspect ratio (1–6.2) $\Rightarrow$ decrease of margination rate

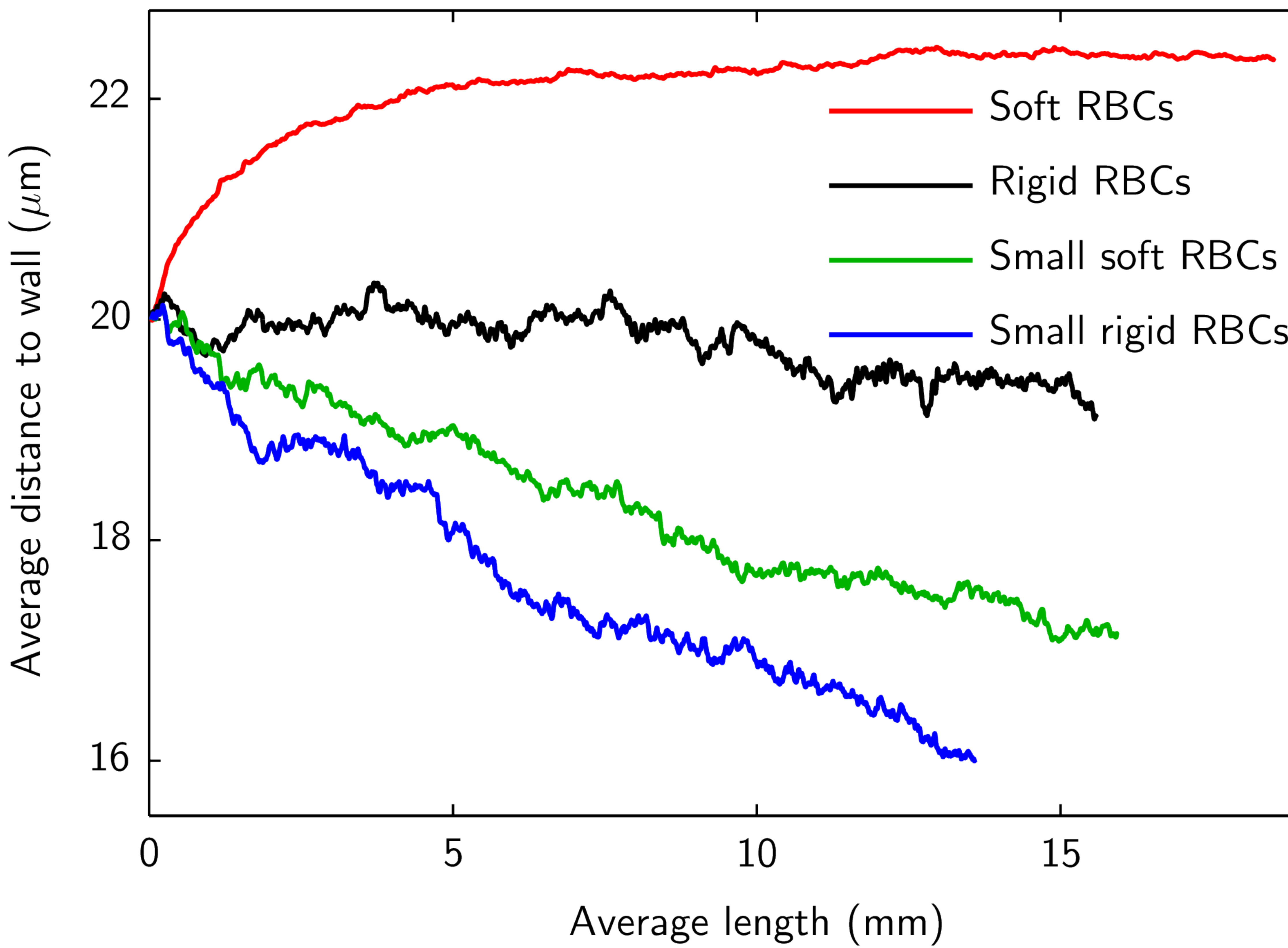


Reasor, Mehrabadi, Ku, and Aidun, *Annals of Biomedical Engineering*, 41(2):238-49, 2013

The cause of platelet margination

- Test cases:
  - Rigid RBCs
  - Small soft RBCs
  - Small rigid RBCs
- Simulation parameters:
  - H $= 40\ \mu$m
  - $\phi = 20$ %
  - $\lambda = \frac{\mu_{\text{in}}}{\mu_{\text{out}}} = 5$
  - $\dot{\gamma}_w = 490\ s^{-1}$
  - $\text{Re}_{\text{RBC}} = \frac{\rho \dot{\gamma} a^2}{\mu} =$ 0-0.0035
  - $\text{Ca}_G = \frac{a \dot{\gamma} \mu}{G} =$ 0-0.27

Effect of size and deformability on margination rate



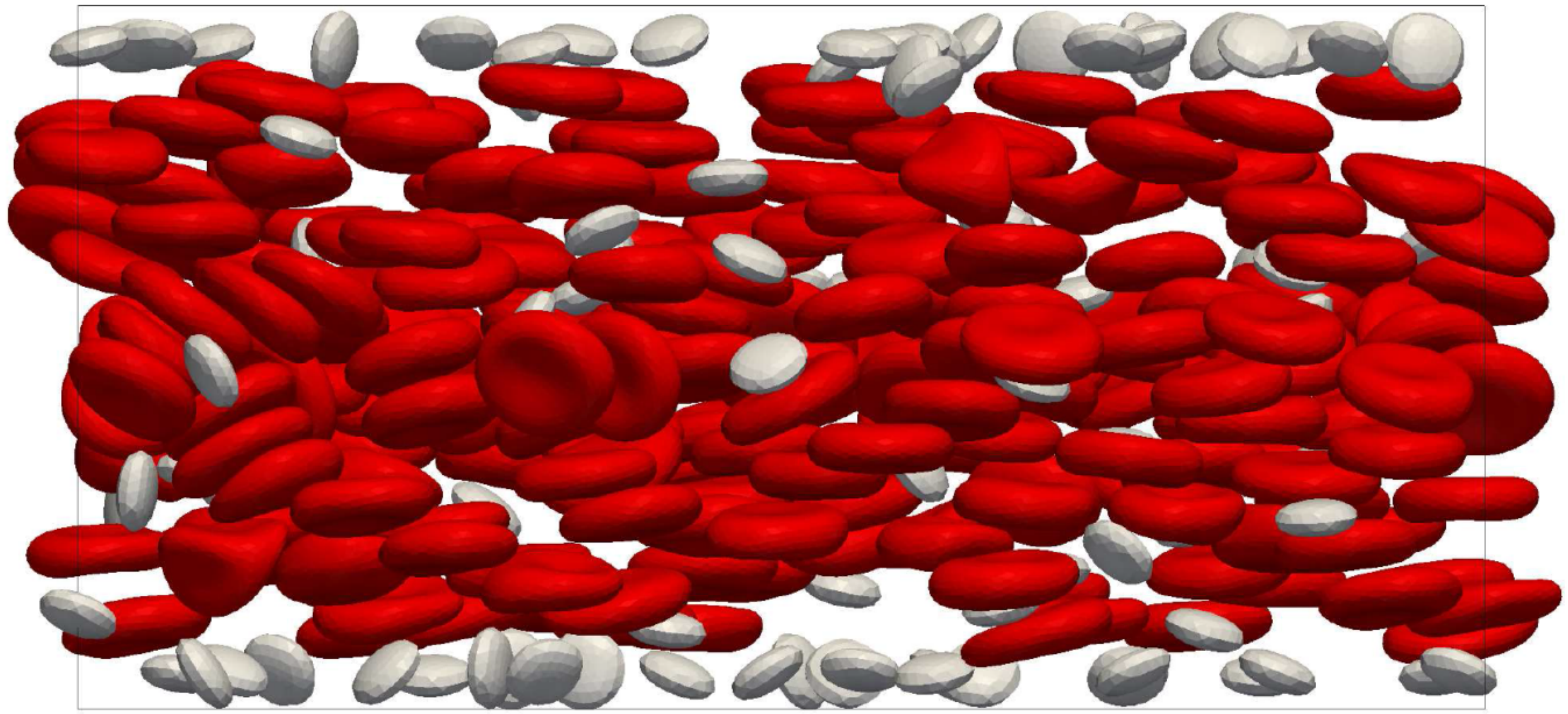
Effect of shear rate on margination rate

Simulation parameters:

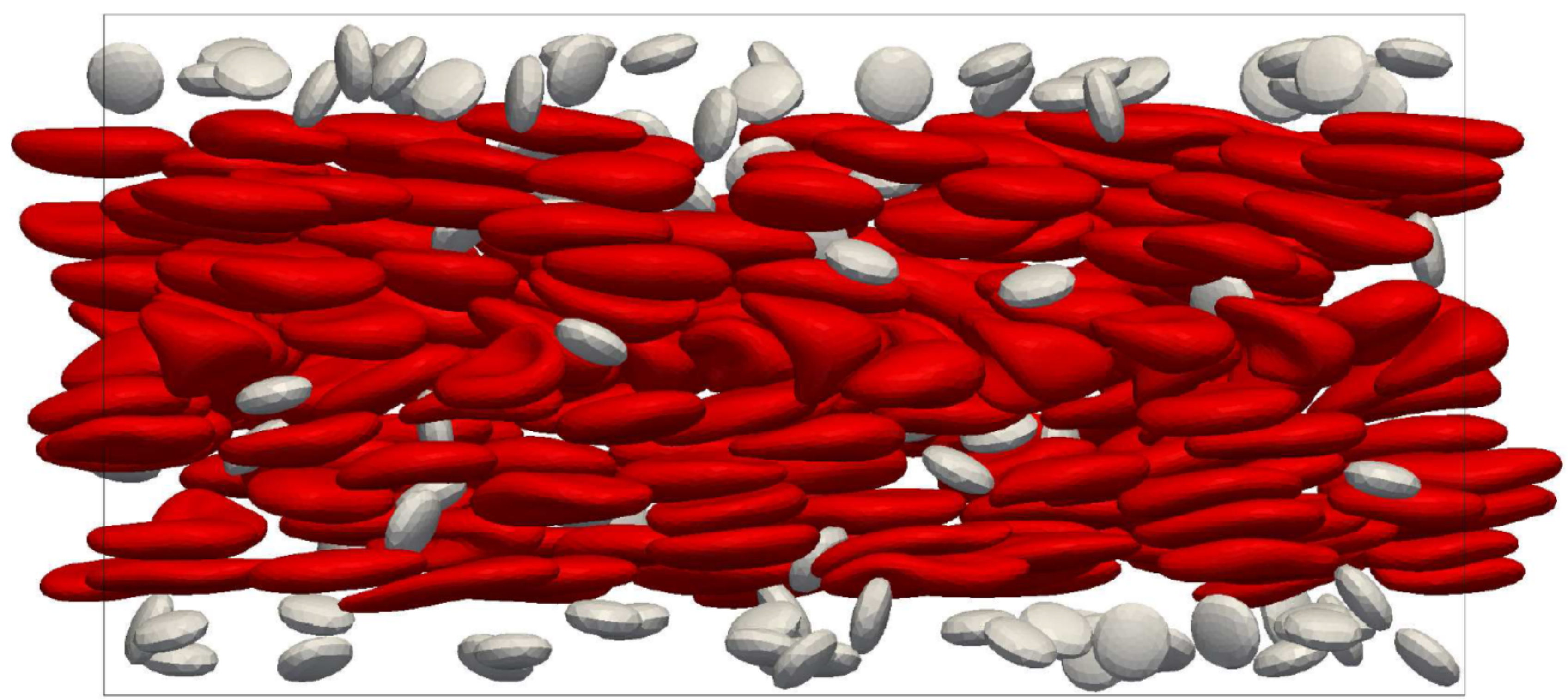
- $H = 40\ \mu m$
- $\phi = 20\ \%$
- $\lambda = \frac{\mu_{in}}{\mu_{out}} = 5$
- $\dot{\gamma}_w = 1000\text{–}20{,}000\ s^{-1}$

Effect of shear rate on skimming layer thickness

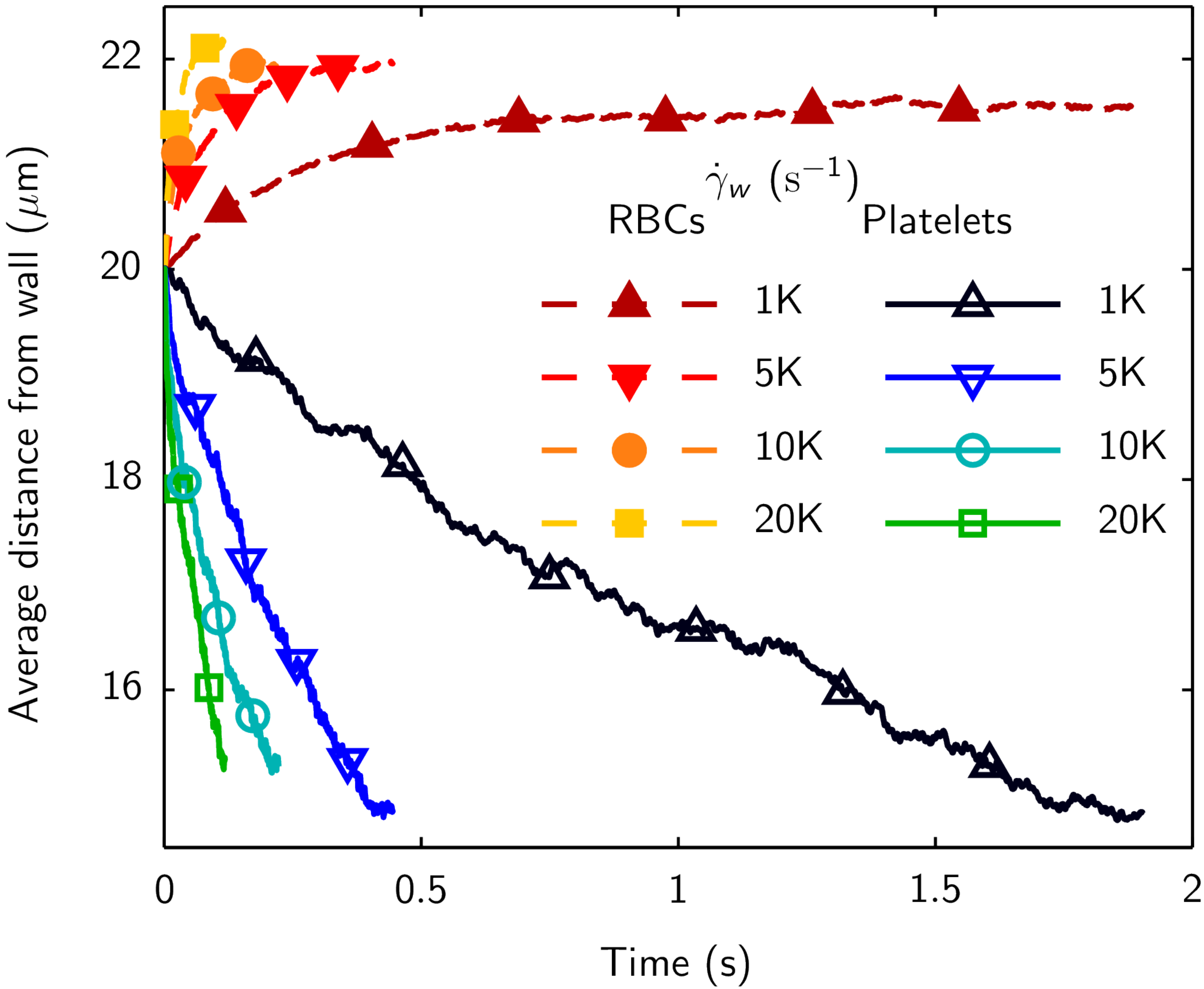
$\dot{\gamma}_w$=1000 s^{-1}



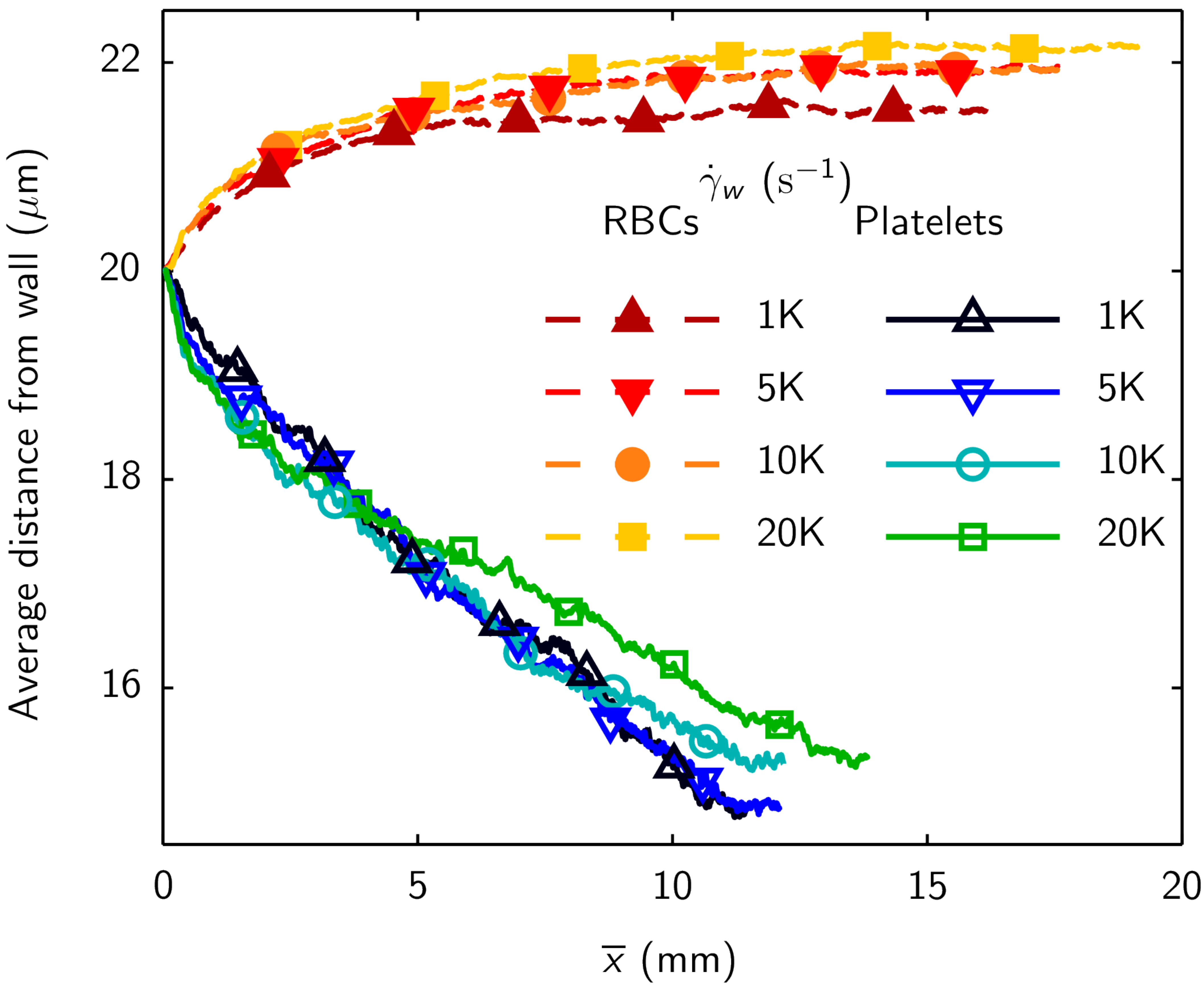
$\dot{\gamma}_w$=20,000 s^{-1}



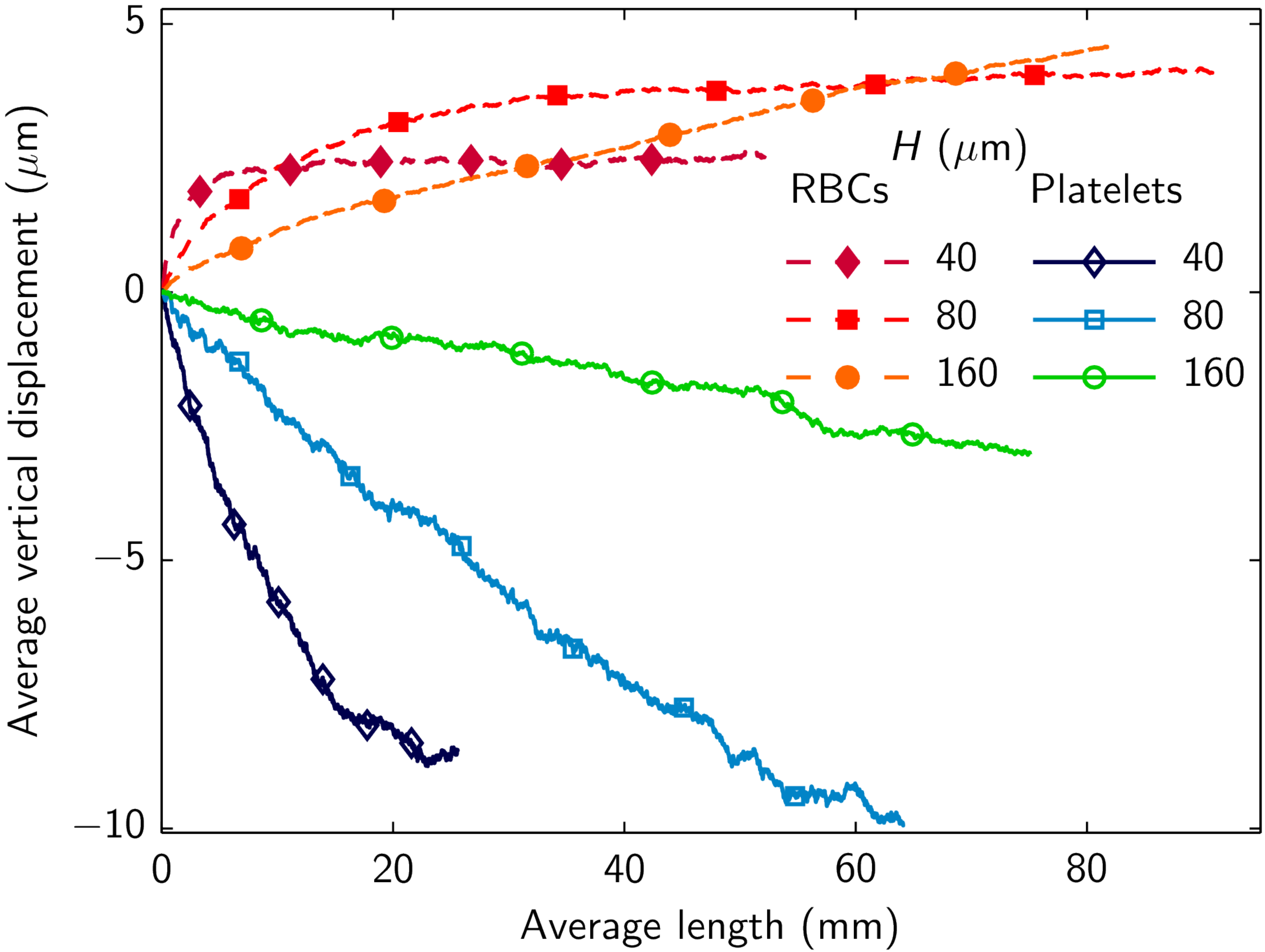
Effect of shear rate on margination rate



Effect of shear rate on margination rate



Effect of channel size on margination rate



Margination length scale

- Average distance traveled by particles due to diffusion in time t:

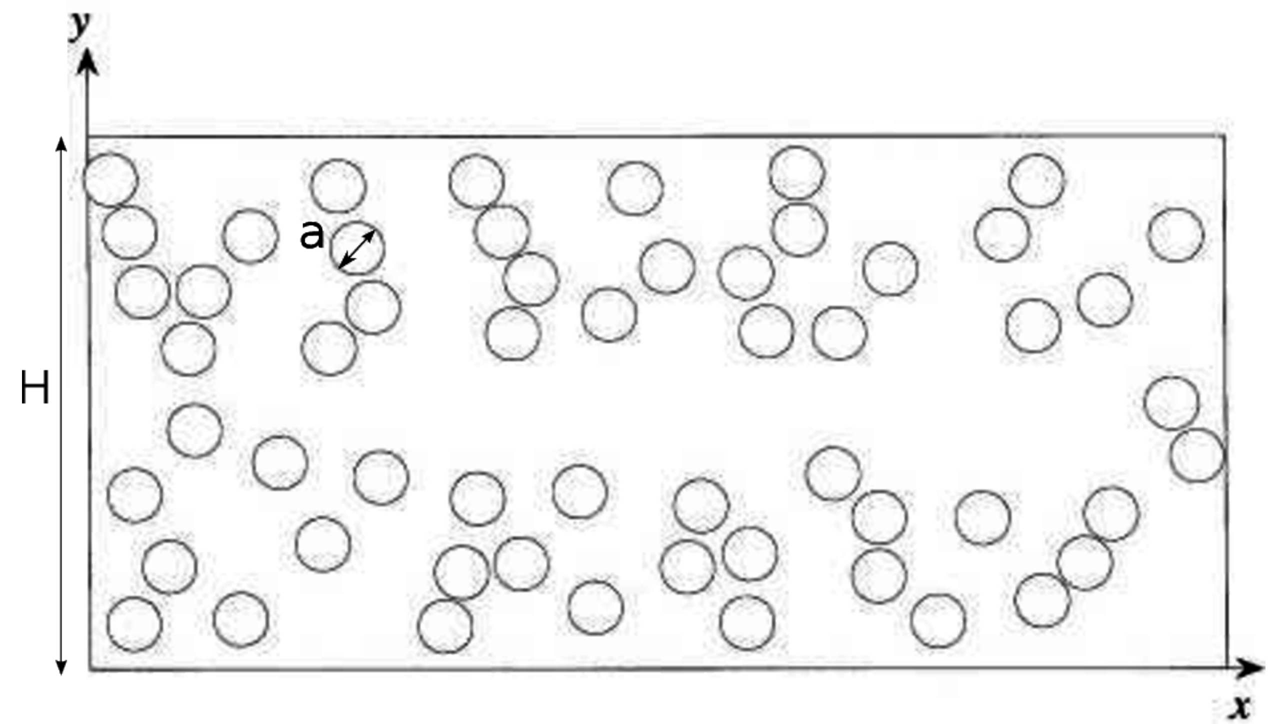
$$y = 2\sqrt{Dt}$$

- Assuming time to reach stead state is:

$$t_{ss} = H^2/4D$$

- shear-induced diffusivity:

$$D = d(\phi)\dot{\gamma}a^2$$

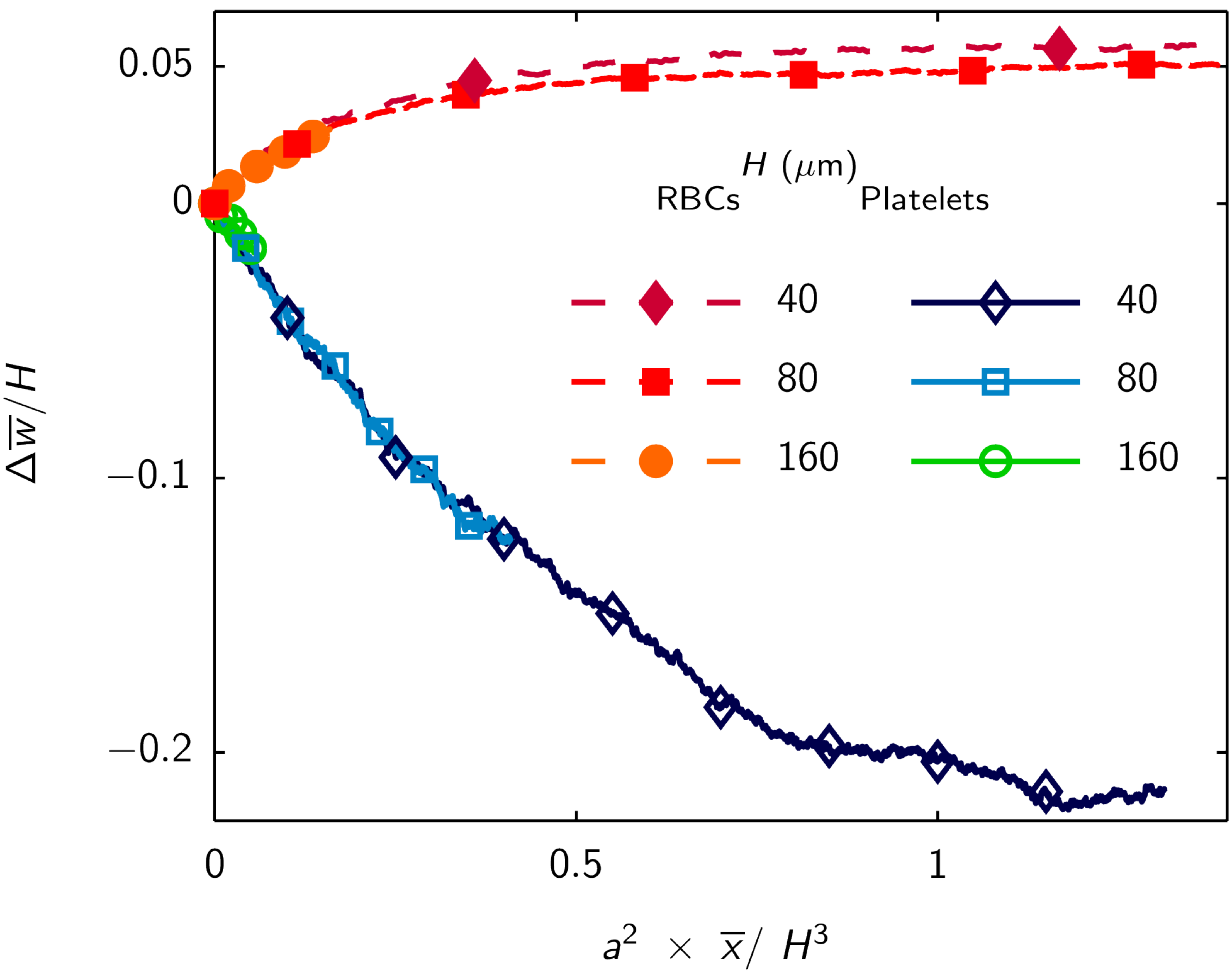


- Estimating average shear rate by $3U/H$

- Margination/migration length scale:

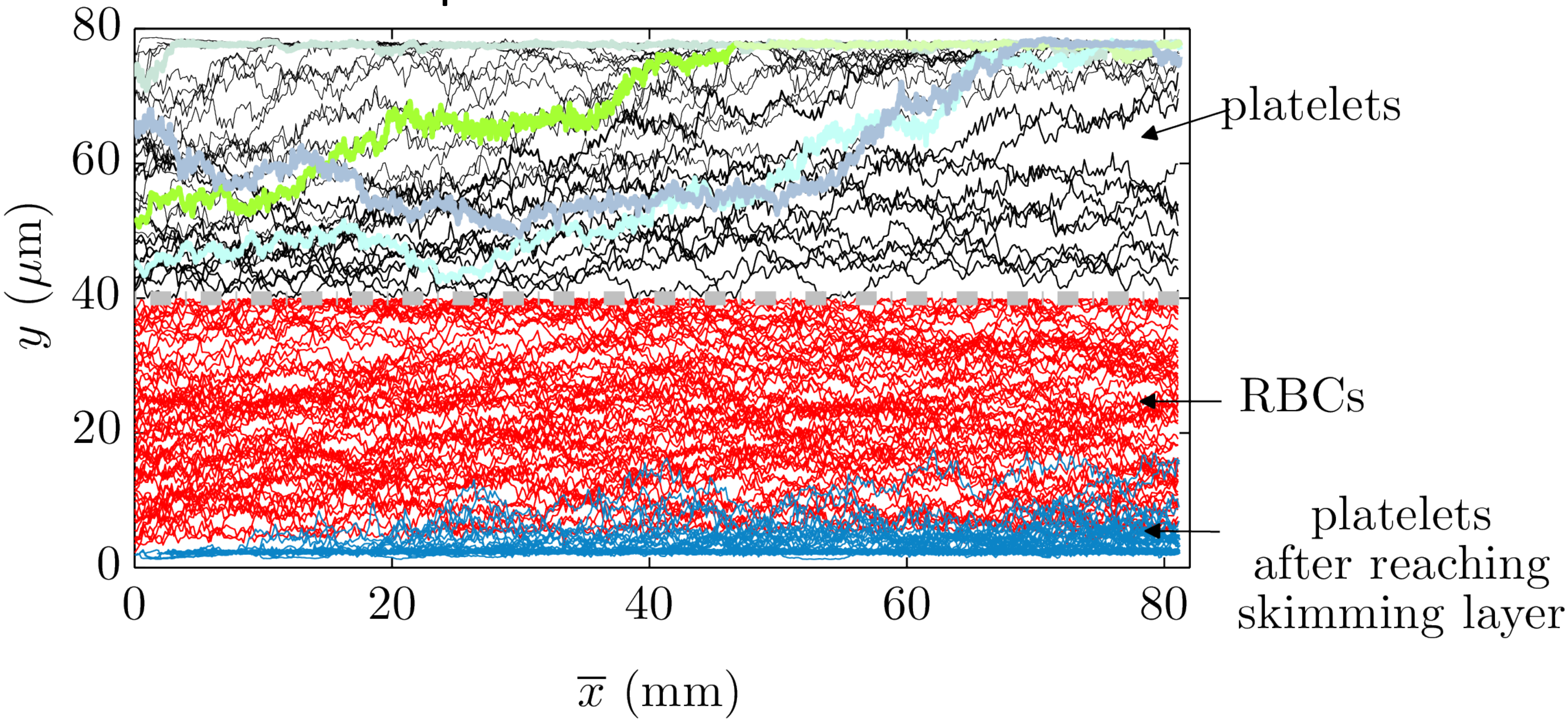
$$L \sim \frac{1}{12d(\phi)}\left(\frac{H}{a}\right)^2 H$$

Effect of channel size on margination length



Drift force or trapped platelets?

- Average time before reentering the cell-laden region
  > 1000× average platelet time step between jumps
- Platelets stay in the RBC-free layer
  ⇒ 'sink' boundary at the edge of the RBC-free layer
- Diffusion + 'sink' boundary
  ⇒ net drift of platelets to the walls



The diffusion with 'sink' boundary (DSB) model

- Continuum mass transfer equation in the *y* direction in the cell-laden region:

$$\frac{\partial P(y,t)}{\partial t} + \cancelto{0}{v_y} \frac{\partial P(y,t)}{\partial y} = \frac{\partial}{\partial y}\left(D_{yy}(y) \frac{\partial P(y,t)}{\partial y} \right), \delta < y < H - \delta$$

- 'Sink' BC at the RBC-free layer edge:

$$P(\delta, t) = P(H-\delta, t) = 0.$$

- DSB model requires δ and $D_{yy}(y)$

P	platelet concentration
v_y	Lateral flow velocity
$D_{yy}(y)$	Platelet lateral diffusion
δ	RBC-free layer thickness

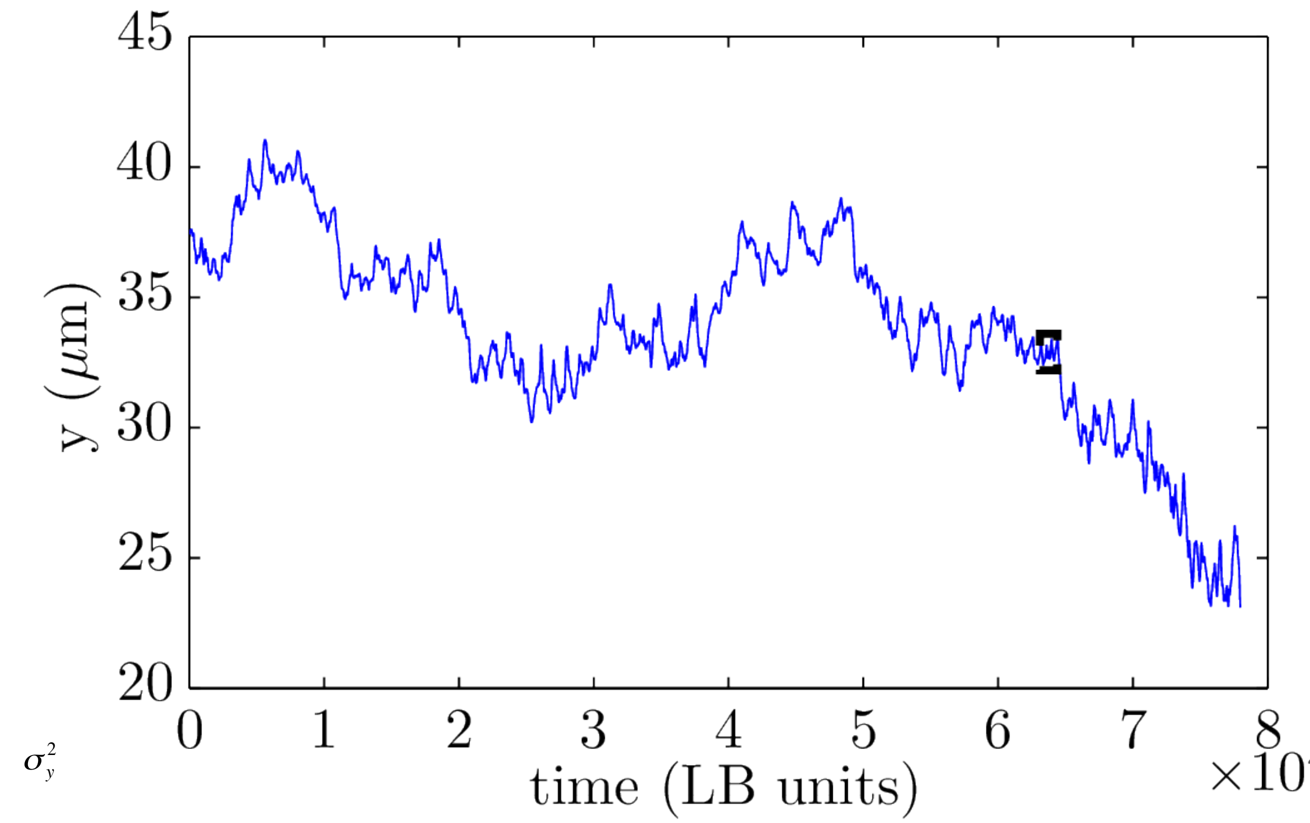
Effective diffusivity of platelets

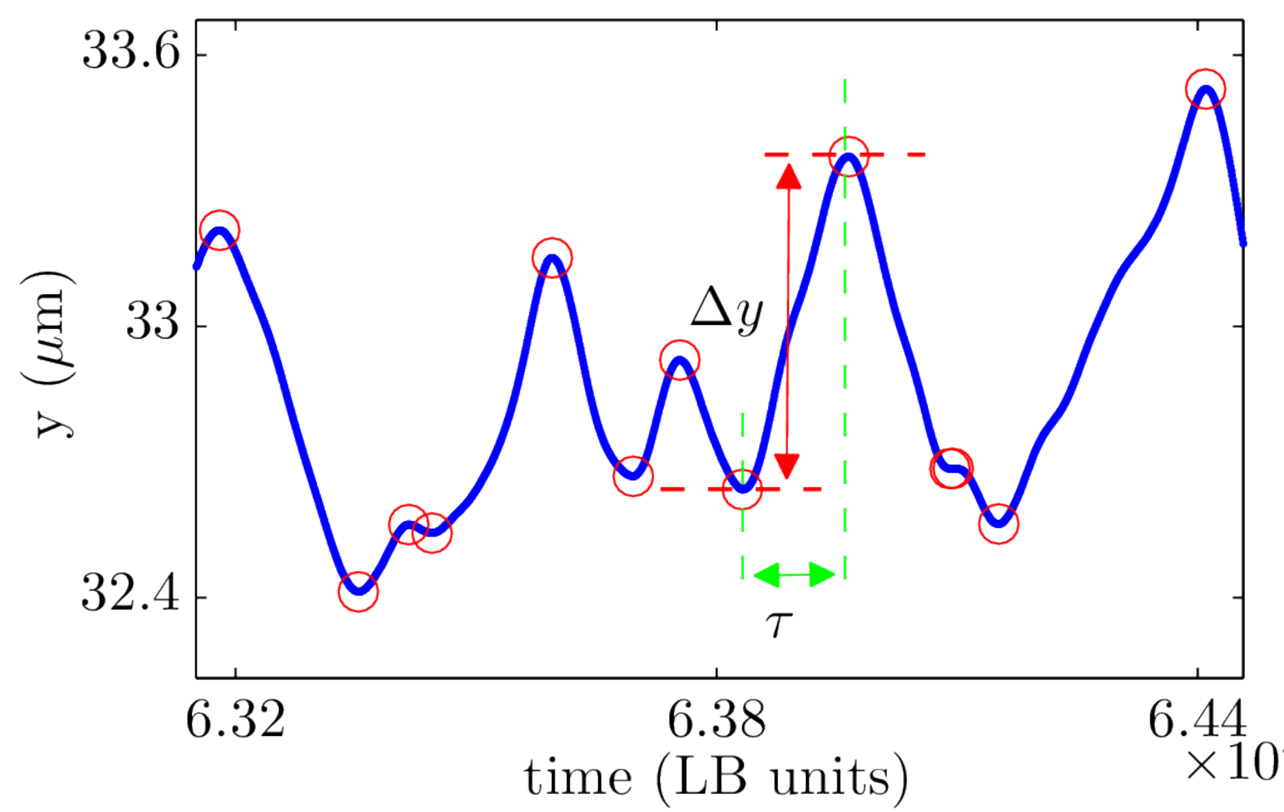
- Effective diffusivity in the *y* direction:

$$D_{yy}(y) = \frac{\langle \sigma_y^2(y) \rangle}{2\langle \tau(y) \rangle},$$

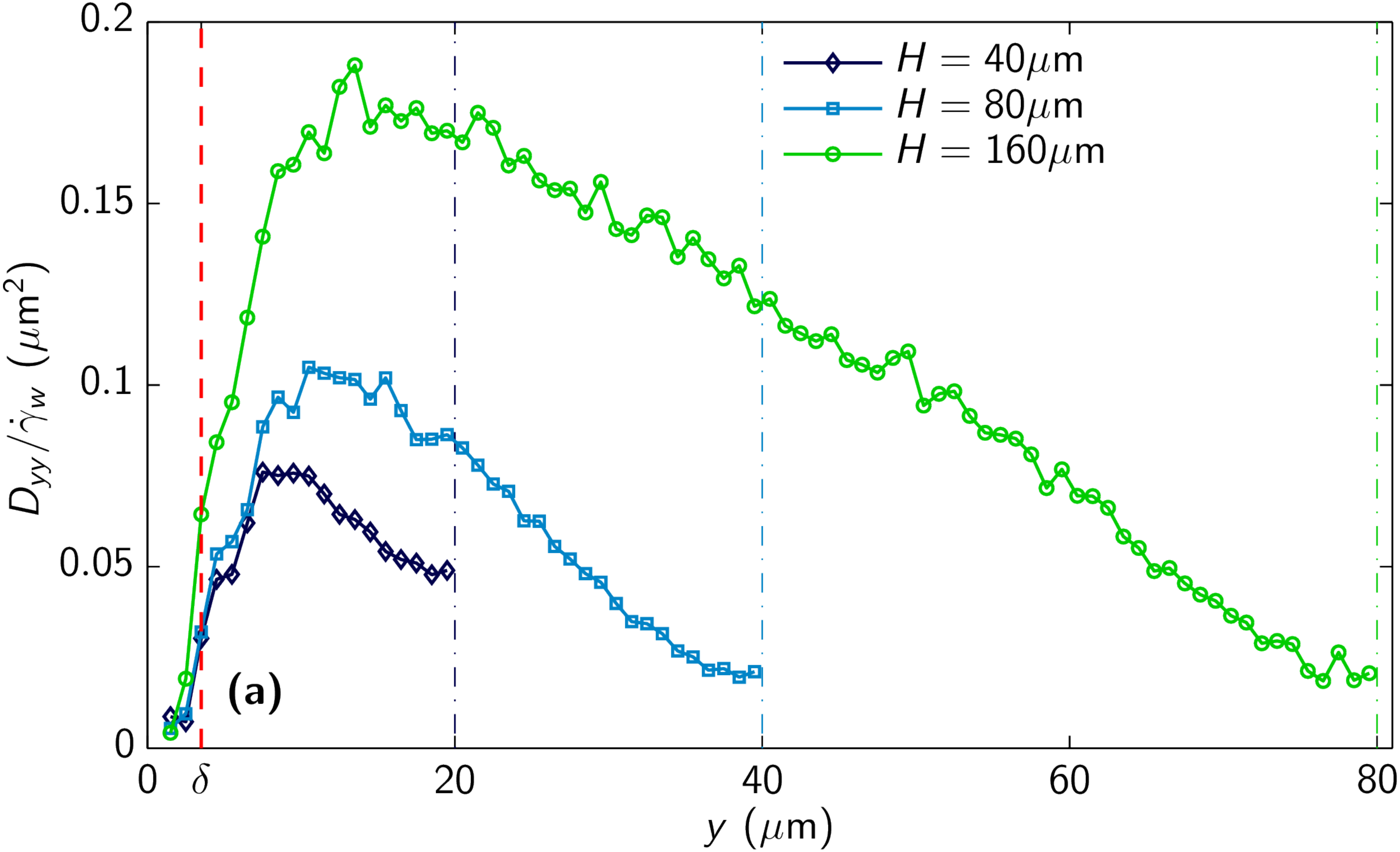
where

- τ, time step between collisions
- $\Delta y(y)$ is step size in lateral travel
- $\langle \sigma_y^2(y) \rangle$ is time average of variance of the step size

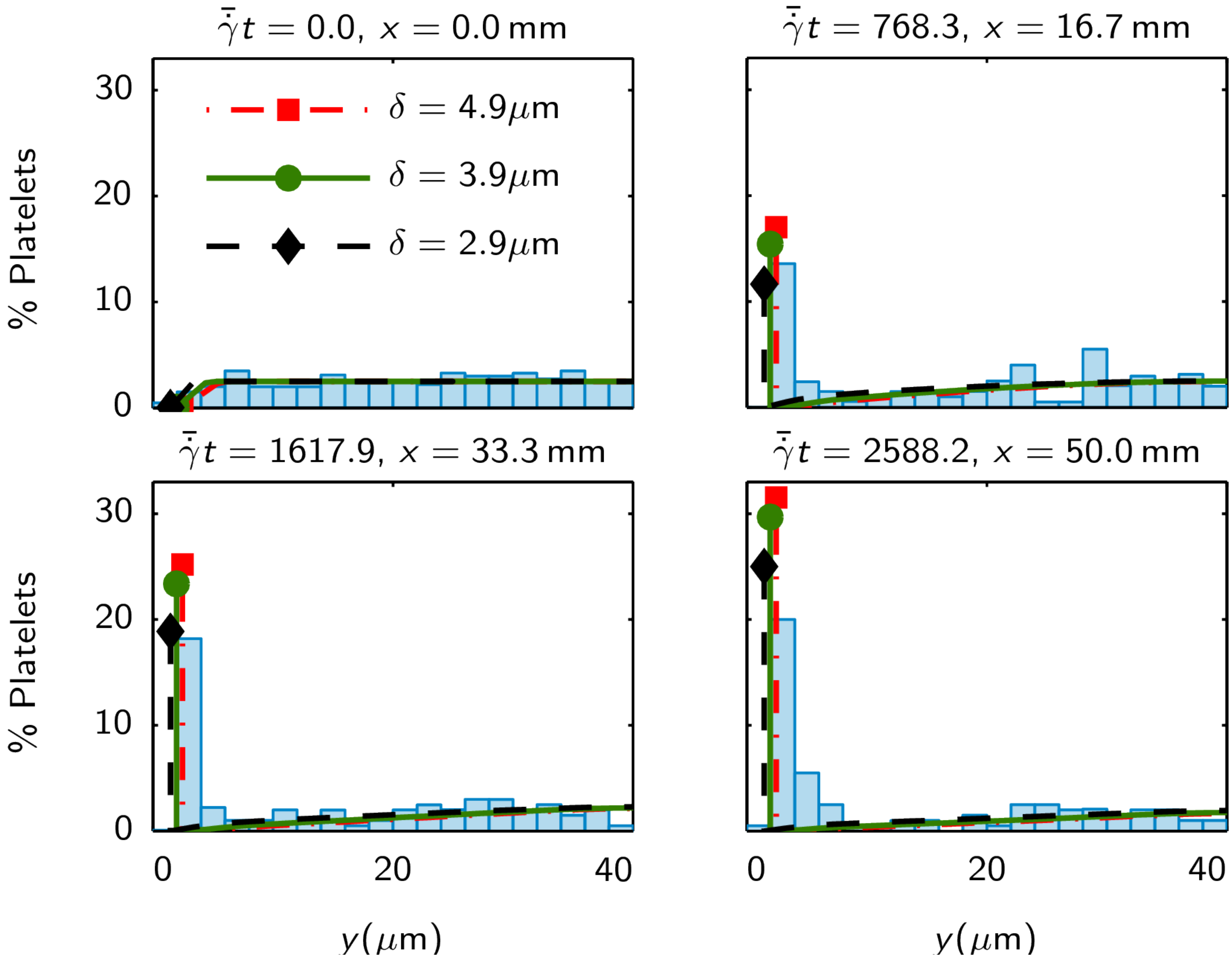




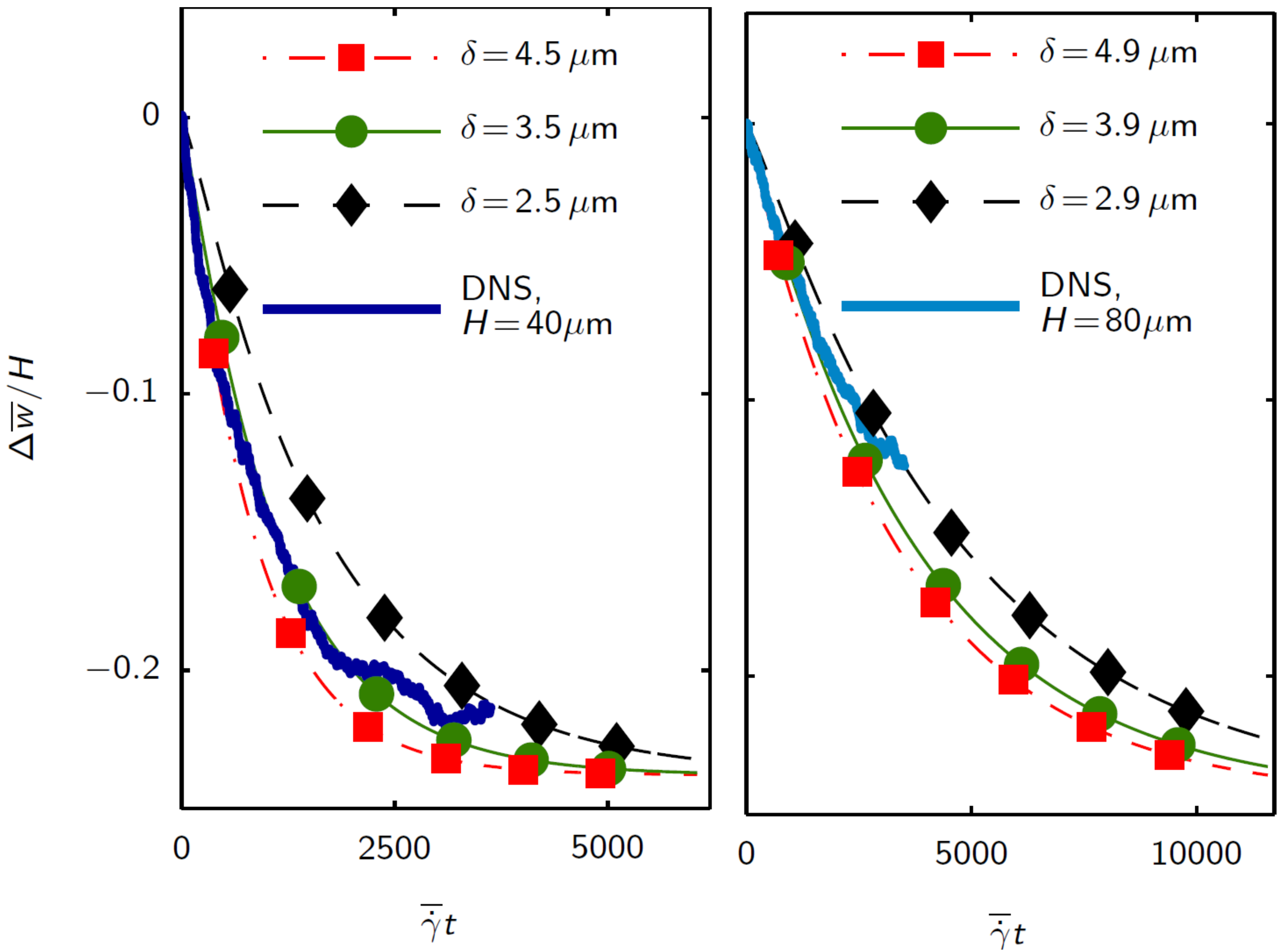
Effective diffusivity of platelets



Comparison of DNS and DSB results (H = 80 µm)

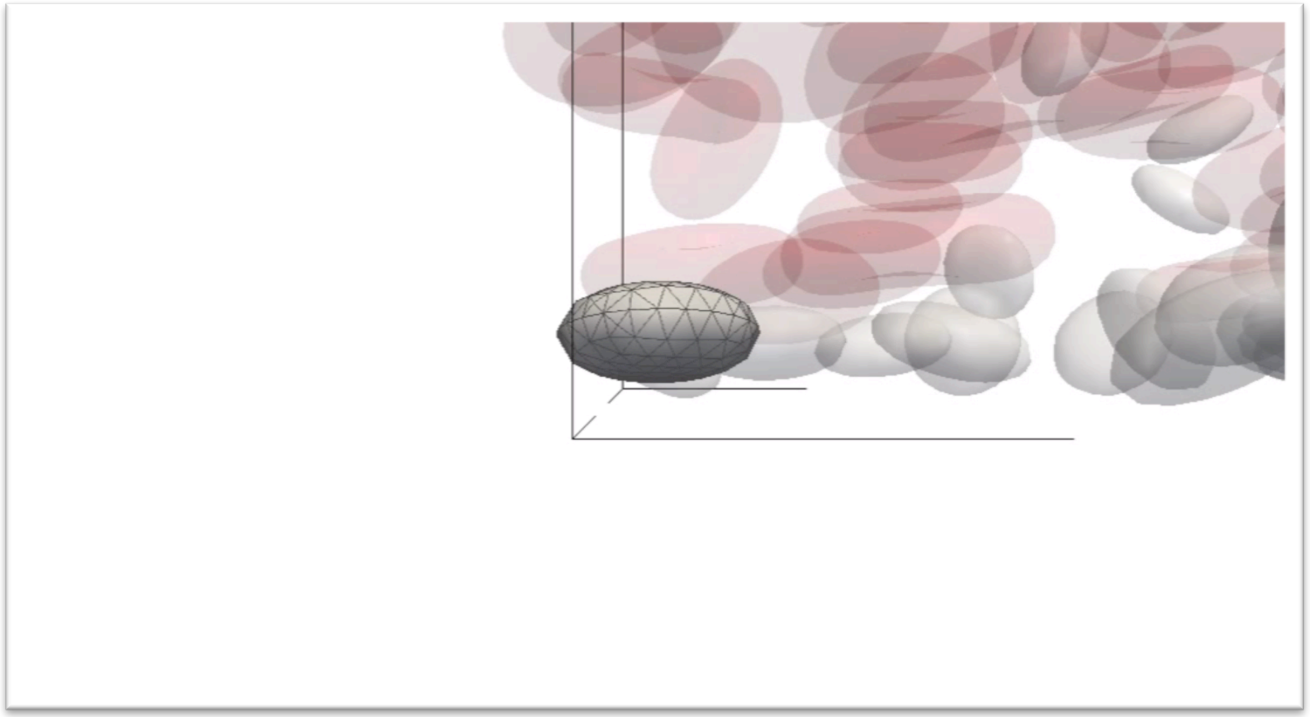


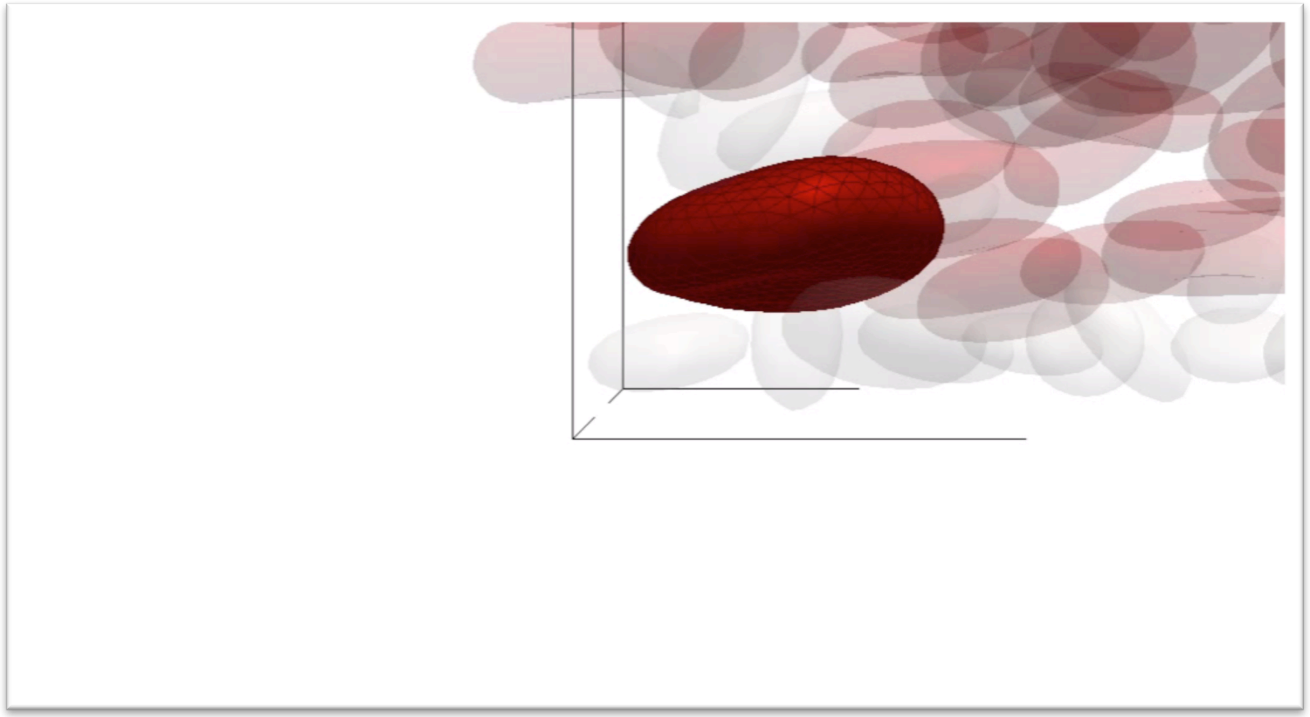
Comparison of direct simulations and DSB results



Why do platelets get trapped in the RBC-free layer?

- Low effective diffusion of platelets in the RBC-free layer
- Low drift from wall compared to RBCs:
  - RBCs tank thread while platelets tumble
- Heterogeneous pair collisions between RBCs and platelets (Kumar et al., 2011)





H = 40 µm, Φ = 20%, 280 s^{-1}

Summary

In small vessels, the time scale for RBC migration is much smaller than time scale for platelet migration; therefore, platelet margination is not 'governed' by inward RBC migration

Rate of margination increases with hematocrit, decreases with viscosity ratio (λ from 0.5 to ∞) and platelet aspect ratio

Shear rate does not 'significantly' influence rate of platelet margination

Margination in a confined channel flow scales with shear-induced diffusion scale

Results show that in small vessels, outward platelet migration is based on *RBC-enhanced self-diffusion*

Accumulation is due to entrapment in the RBC-depleted region at the boundary