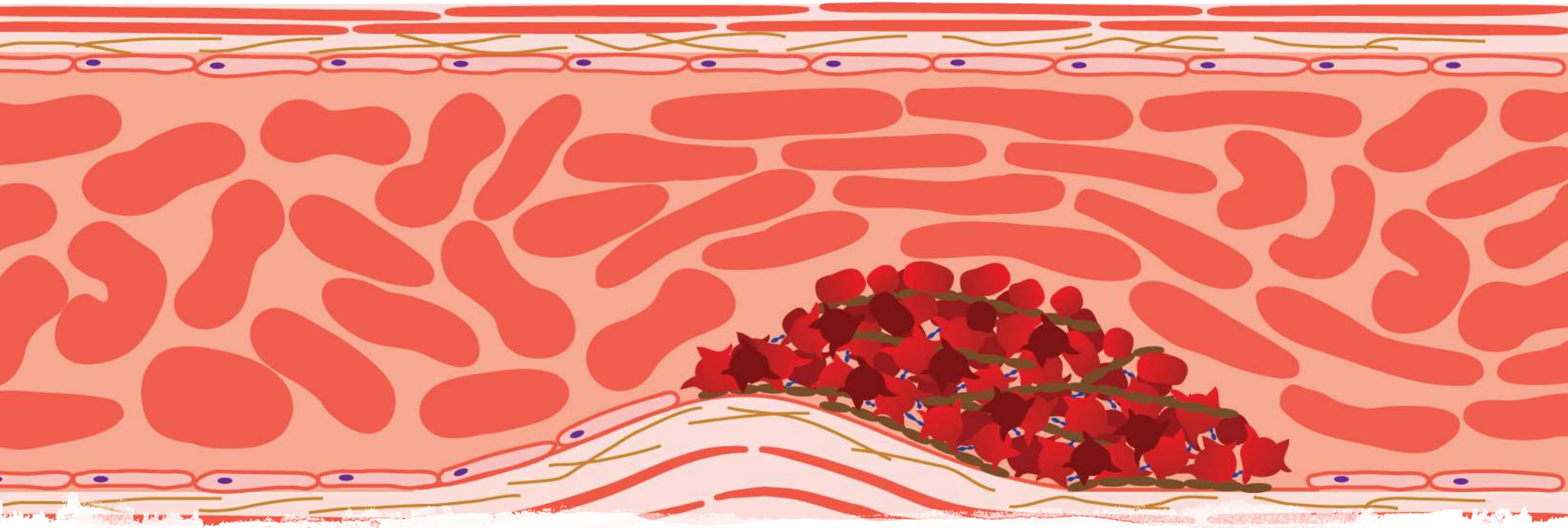

Multi-Scale Investigation of High Shear Rate Thrombus Formation

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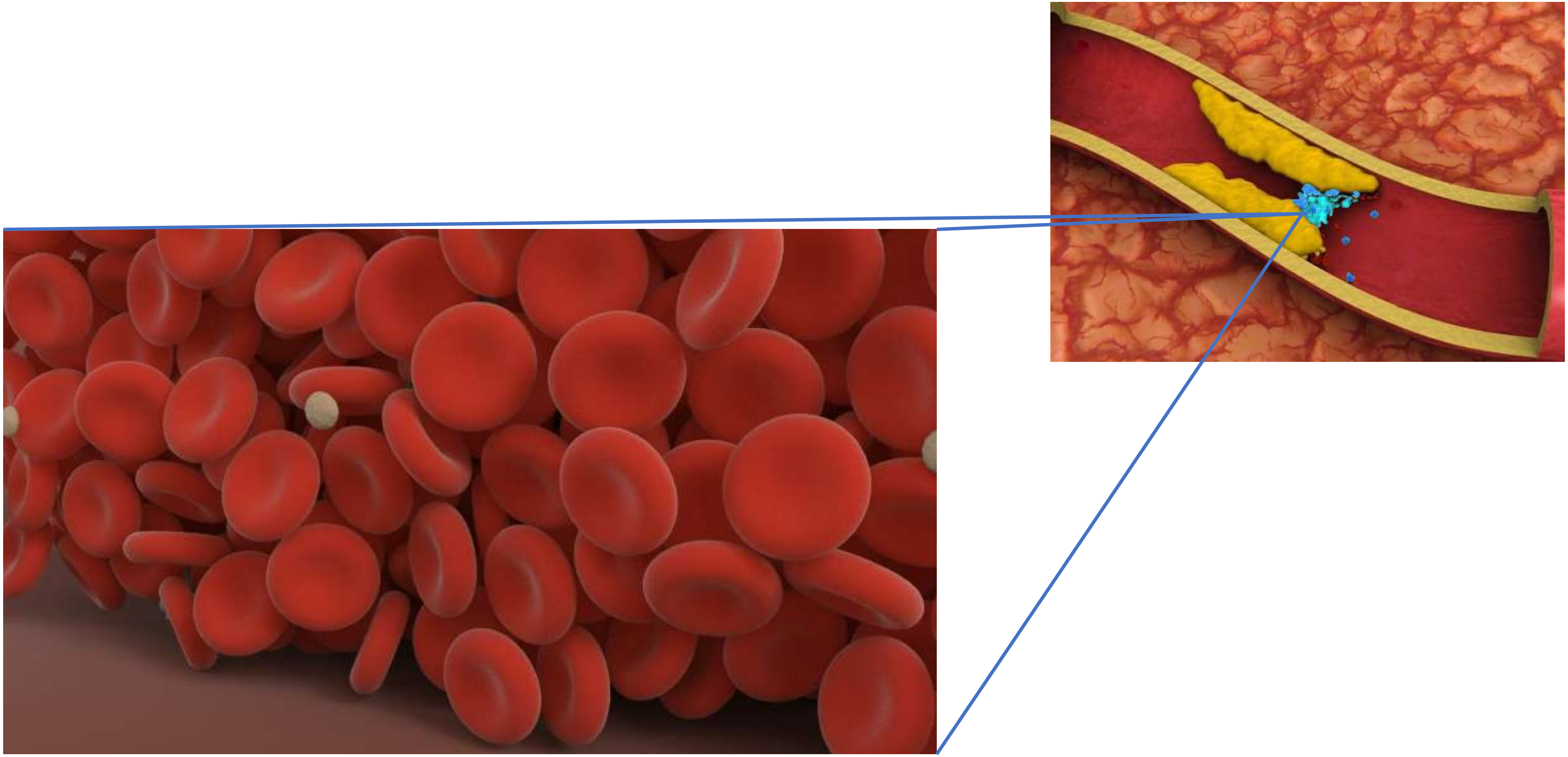
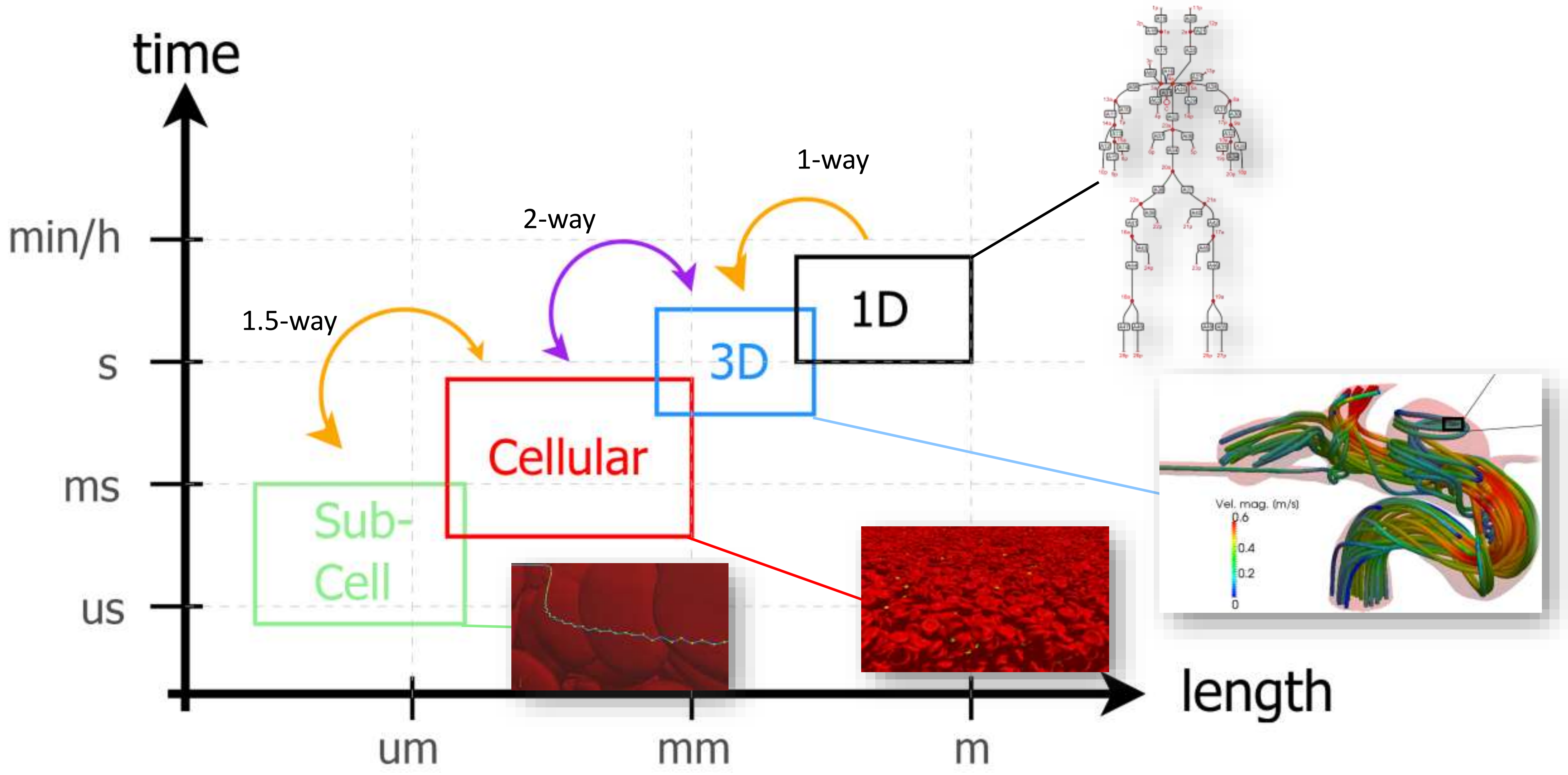
High shear-rate thrombus formation



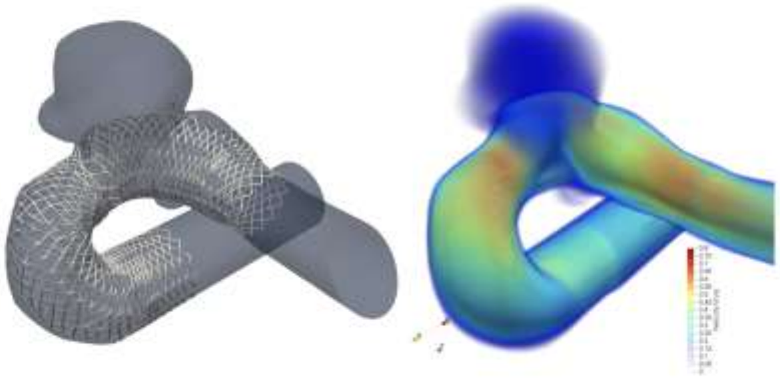
Scale-separation map



HemoCell
cellular

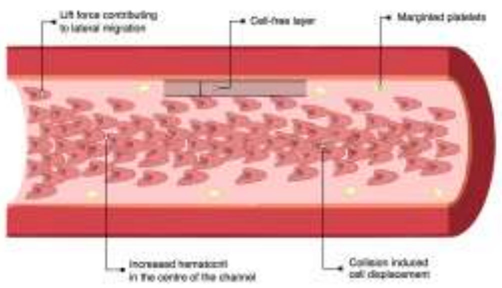
Závodszky, et al. (2017) Fontiers in Physiology, 8, 563
Závodszky, et al. (2017) Procedia Comput Sci.108,159.
Alowayyed et al. (2018) Journal of Comp. Sci., 24, 1-7.
Czaja et al. (2018) J. Royal Society Interface 2018.0485.
de Haan et al. (2018) Applied Sciences, 8(9), 1616.
van Rooij, et al. (2019) J. Royal Society Interface, accepted
Tarksalooyeh, et al. (2019) Procedia Comput Sci., accepted
Tarksalooyeh et al. (2018) Computers & Fluids, 172, 312-317.
Mountrakis et al. (2016) EPL (Europhysics Letters) 114.1: 14002.
Mountrakis, et al. (2015) Journal of Computational Science 9 : 45.
Hoekstra et al. (2016). Phil. Trans. R. Soc. A. 374

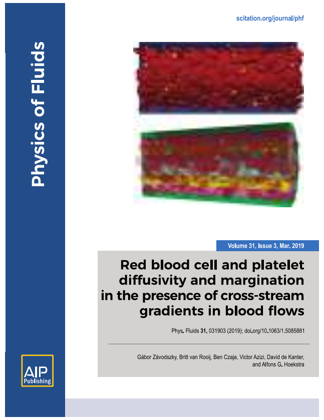
HemoFlow
macroscopic



Závodszky, et al.. (2013). Int. J. of Heat and Fluid Flow, 44, 276
Závodszky, et al.. (2015). Journal of theoretical biology 368. 95-101
Csippa, et al. (2018). Computers in biology and medicine 103: 244-251.
Závodszky, et al. (2019). Int. J. for Num. M. in Bio. Eng., under review

rheoModel
coarse-grained





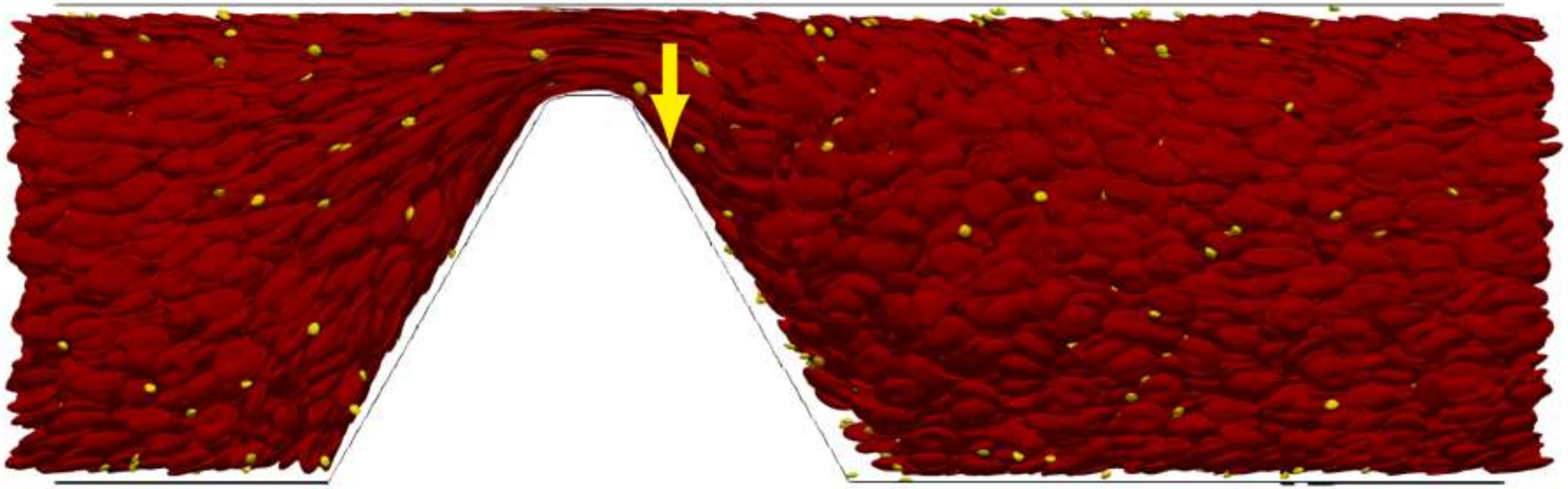
Závodszky, et al. (2019) Physics of Fluids, 31 (3), 031903

+ vWF model
Under development

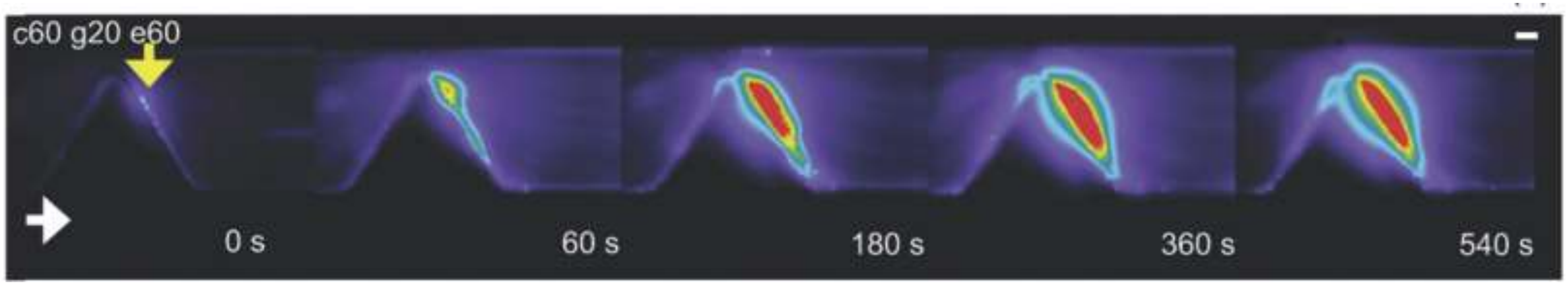
+ CEPAC
Under development

Cellular modeling – shear conditions

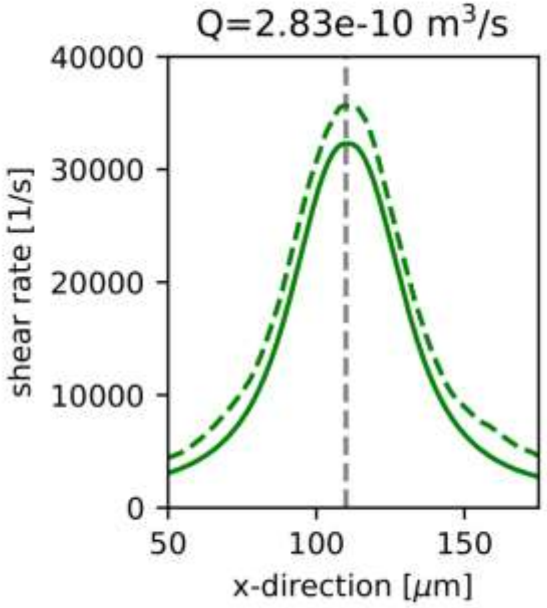
vs. continuum flow model

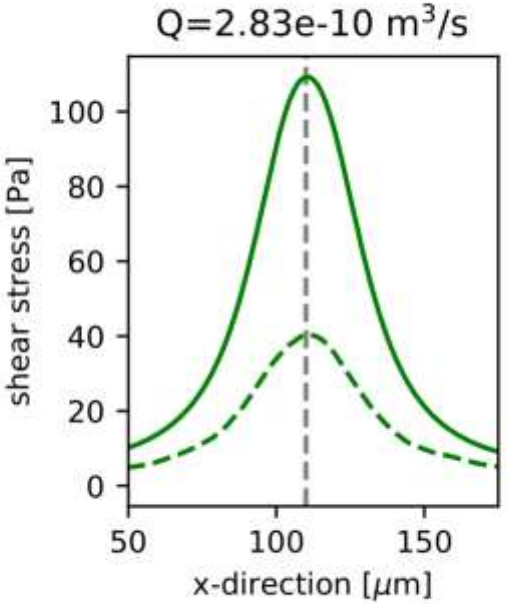


van Rooij, et al. (2019) J. Royal Society Interface, accepted



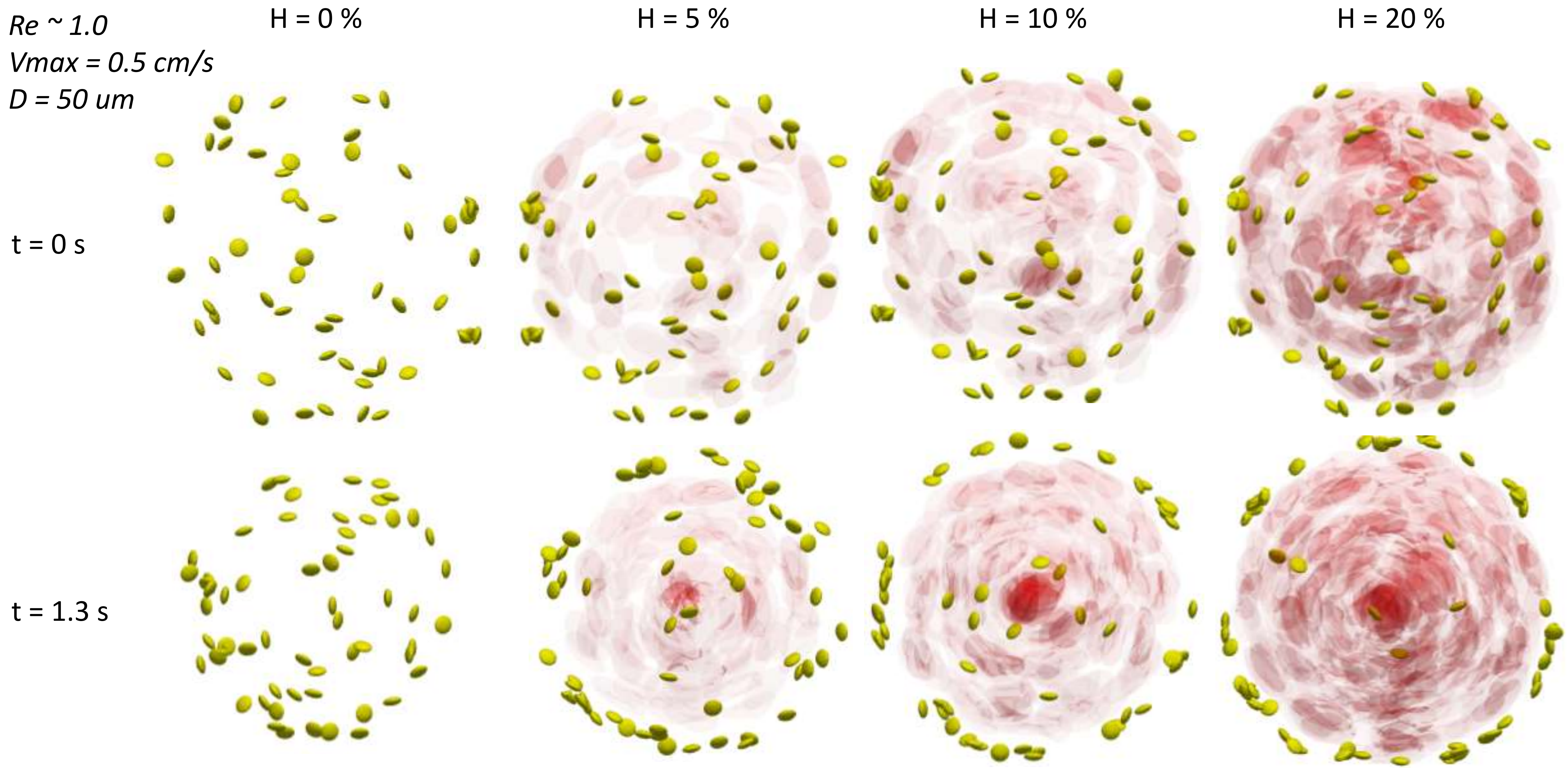
Tovar-Lopez and Nesbitt et al., Lab Chip, 2010, 10, 291-302





Cellular modeling - platelet margination

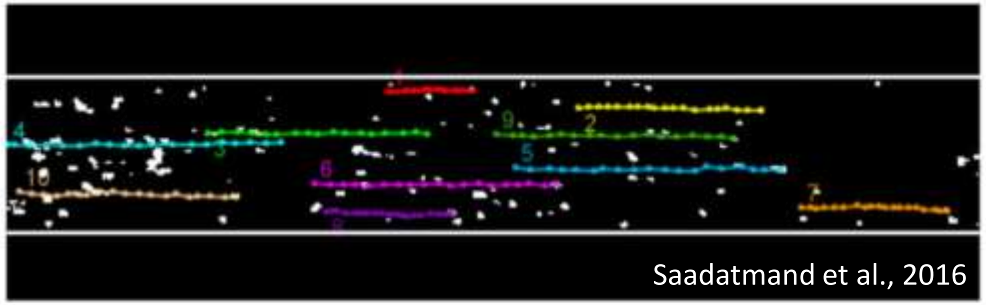
Re ~ 1.0
Vmax = 0.5 cm/s
D = 50 um



Margination from cell pair collisions

Experiment:

- Following both RBC and small tracer particle trajectories
- Straight channel flow



Experiment:
Drr_RBC = **1.2e-8** cm^2/s

Simulation (using the same parameters) with [HemoCell]:

HemoCell:
Drr_RBC = **1.15e-8** cm^2/s

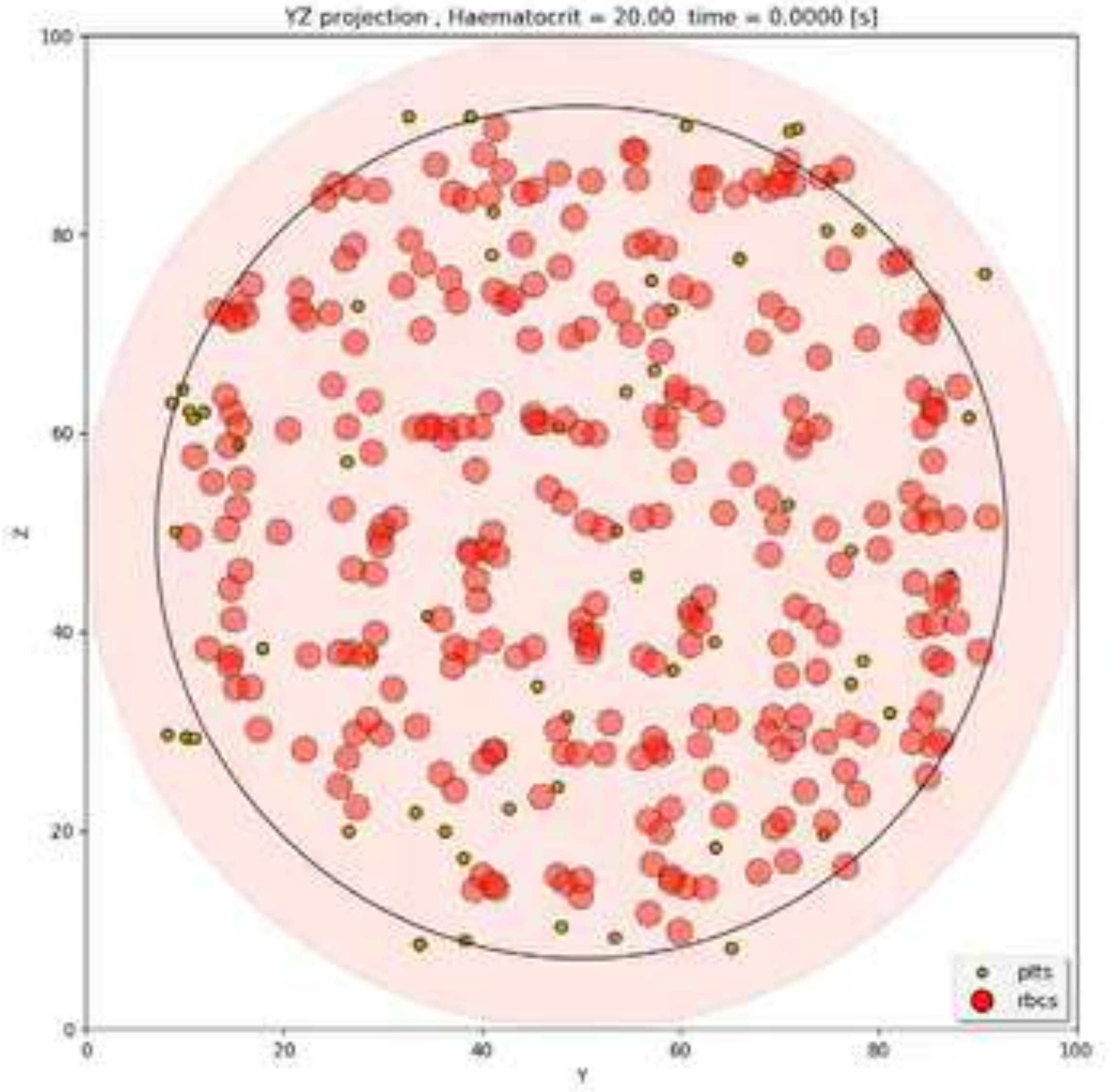
Cell radial dispersion:

$$D_{rr} = \frac{1}{N}\sum_{i=1}^{N} \frac{\langle (R_{i,r}(t) - R_{i,r}(0))^2 \rangle}{2t}$$

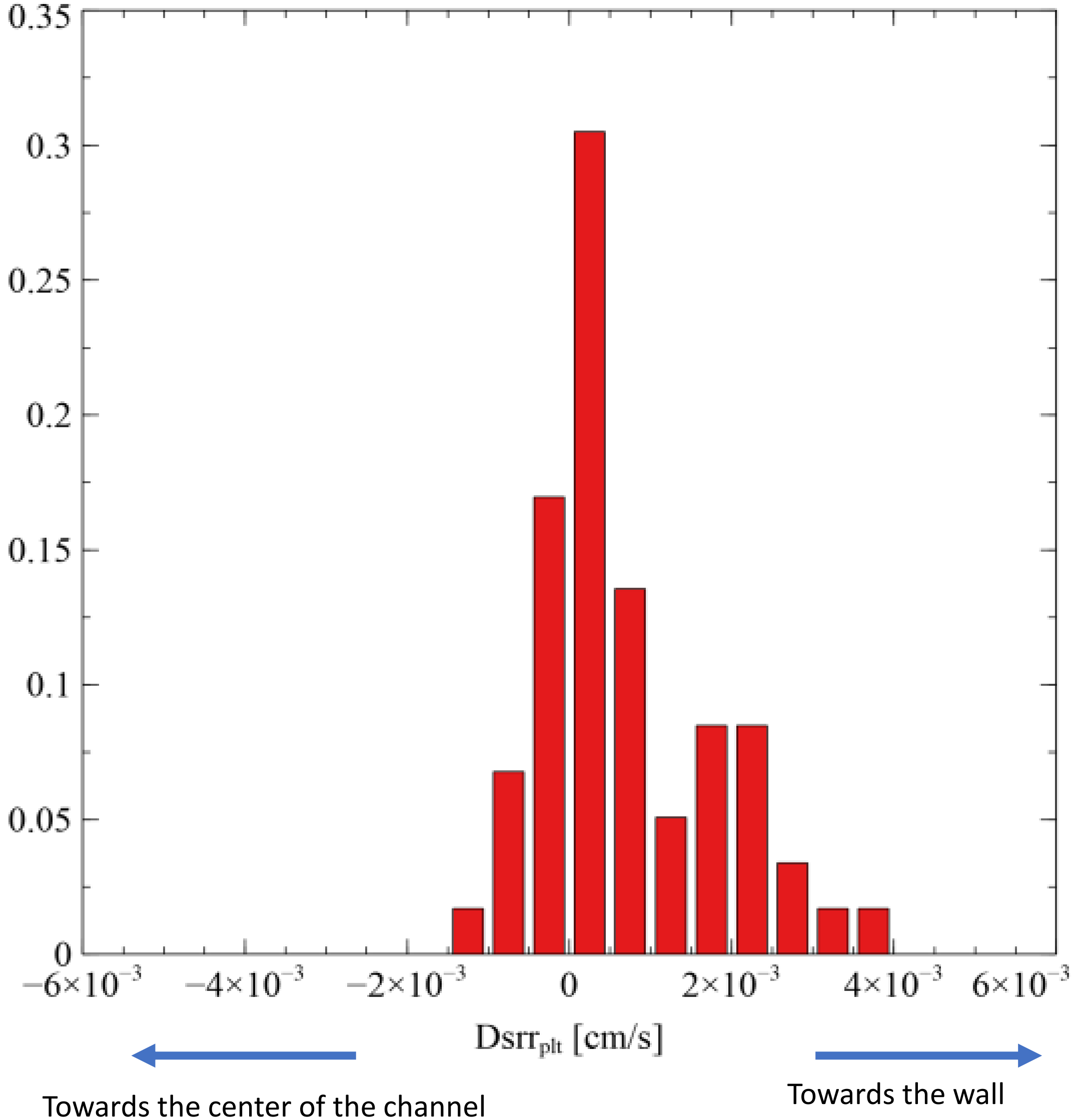
Cell radial drift velocity:

$$D_{srr} = \frac{1}{N}\sum_{i=1}^{N} \frac{\langle R_{i,r}(t) - R_{i,r}(0) \rangle}{t}$$

Preferential diffusivity

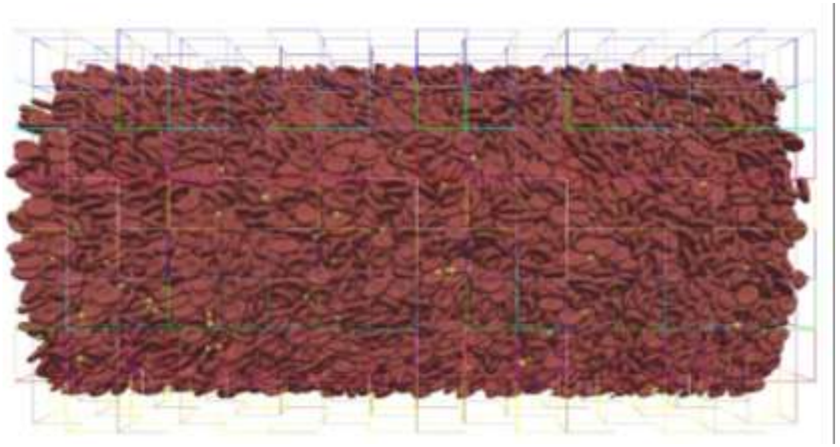


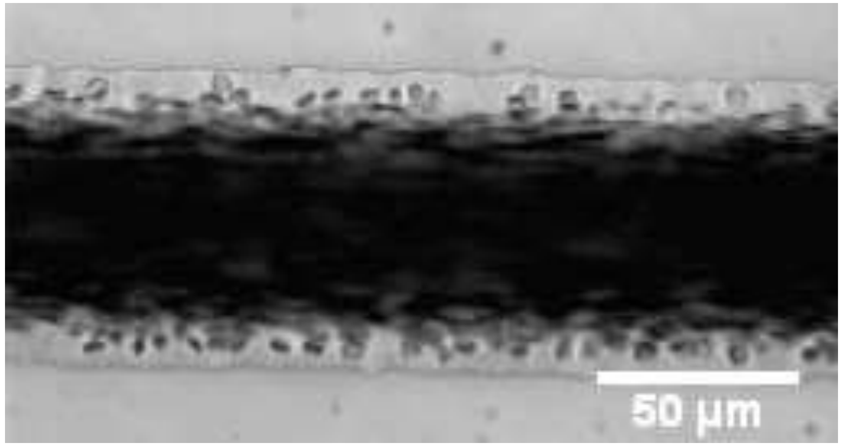
Video: David de Kanter



Coarse-grained model from statistics

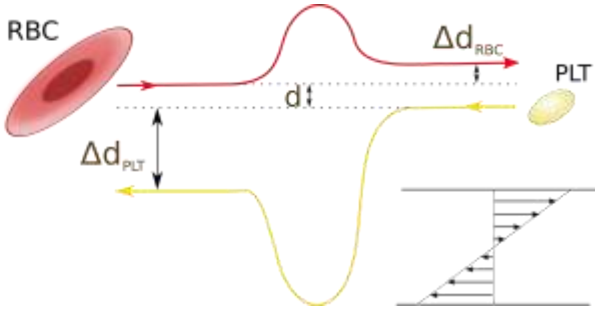
22 x





D = 50..70 um
H = 7% ... 36%
Re = 0,04 ... 2,0

→ Extract various parameters in a statistical sense in 242 points.



Závodszky, et al. (2019) Physics of Fluids

$$\frac{\partial \Phi}{\partial t} = -\frac{\partial}{\partial r}\left[V(r)\Phi - D(r)\frac{\partial \Phi}{\partial r}\right]$$

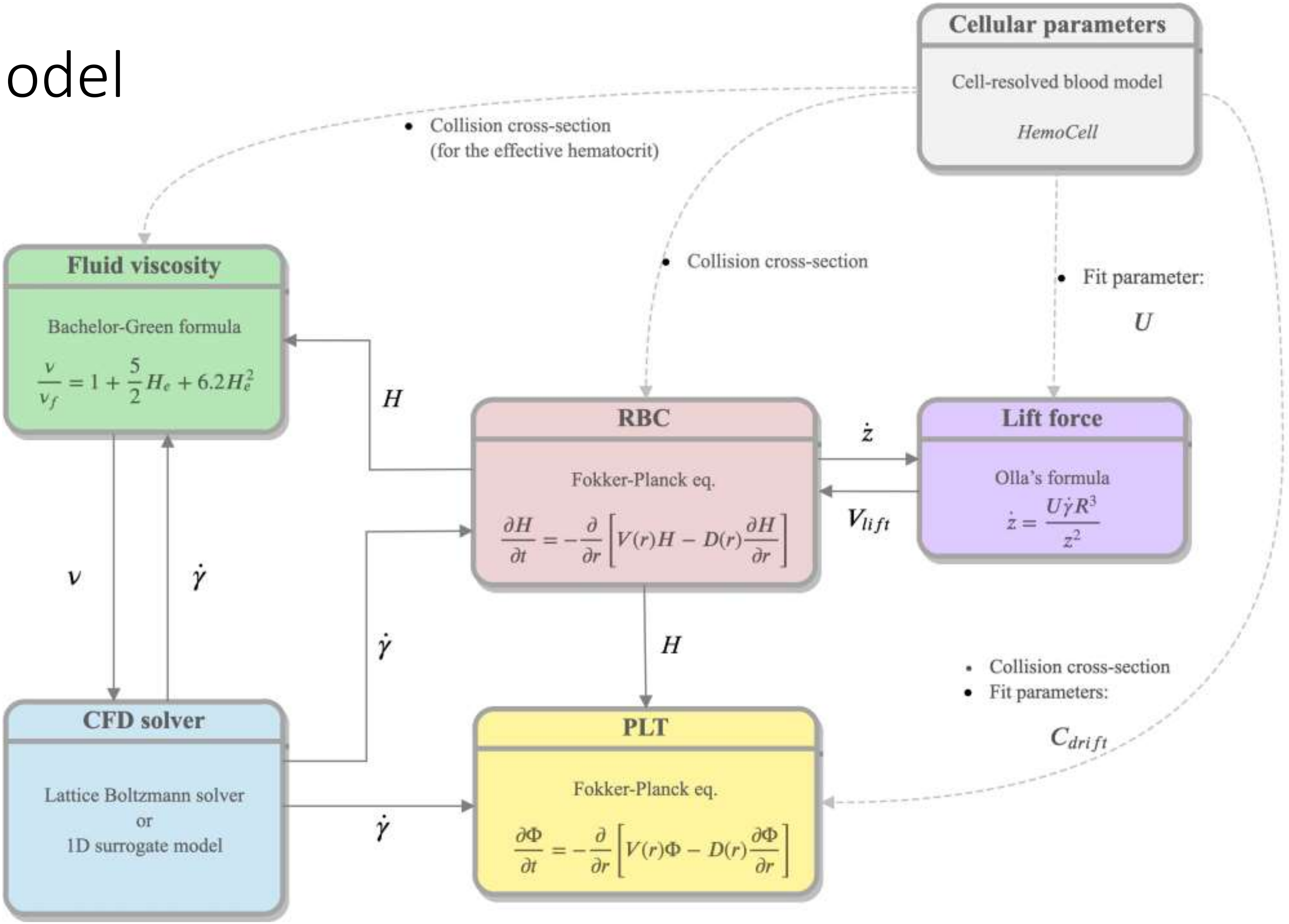
$$V_{lift} = -\frac{U\dot{\gamma}R^3}{z^2}$$

$$V_{asym} = -C * a(\dot{\gamma})^2 * \dot{\gamma} * \frac{\partial H}{\partial r}$$

$$D_{self} = C * a(\dot{\gamma})^2 * \dot{\gamma} * H$$

$$D_{saturation} = C * H^2$$

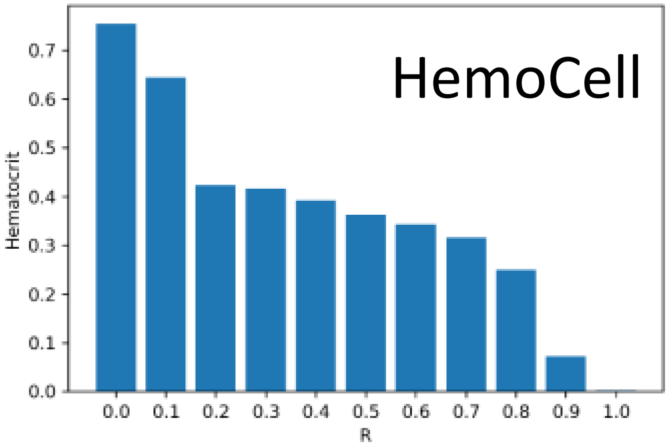
rheoModel



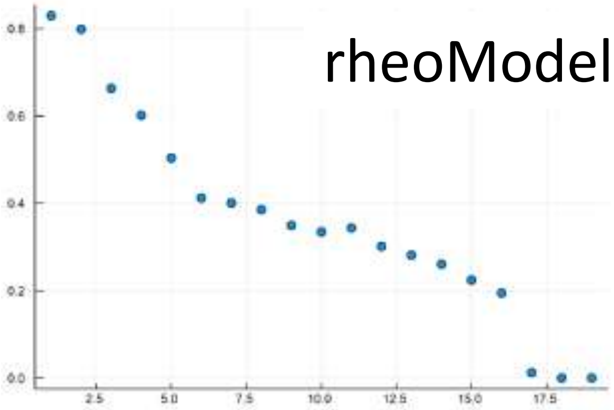
Cellular parameters
Cell-resolved blood model
HemoCell
• Collision cross-section
(for the effective hematocrit)
• Collision cross-section
• Fit parameter:
U
Fluid viscosity
Bachelor-Green formula
$\frac{\nu}{\nu_f} = 1 + \frac{5}{2}H_e + 6.2H_e^2$
H
RBC
Fokker-Planck eq.
$\frac{\partial H}{\partial t} = -\frac{\partial}{\partial r}\left[V(r)H - D(r)\frac{\partial H}{\partial r}\right]$
$\dot{z}$
V_{lift}
Lift force
Olla's formula
$\dot{z} = \frac{U\dot{\gamma}R^3}{z^2}$
ν
$\dot{\gamma}$
$\dot{\gamma}$
H
• Collision cross-section
• Fit parameters:
C_{drift}
CFD solver
Lattice Boltzmann solver
or
1D surrogate model
$\dot{\gamma}$
PLT
Fokker-Planck eq.
$\frac{\partial \Phi}{\partial t} = -\frac{\partial}{\partial r}\left[V(r)\Phi - D(r)\frac{\partial \Phi}{\partial r}\right]$

rheoModel vs. experiments

Radial distribution of cells in a vessel
(D=50um, H=36%, Re=1.5, t=1 s)

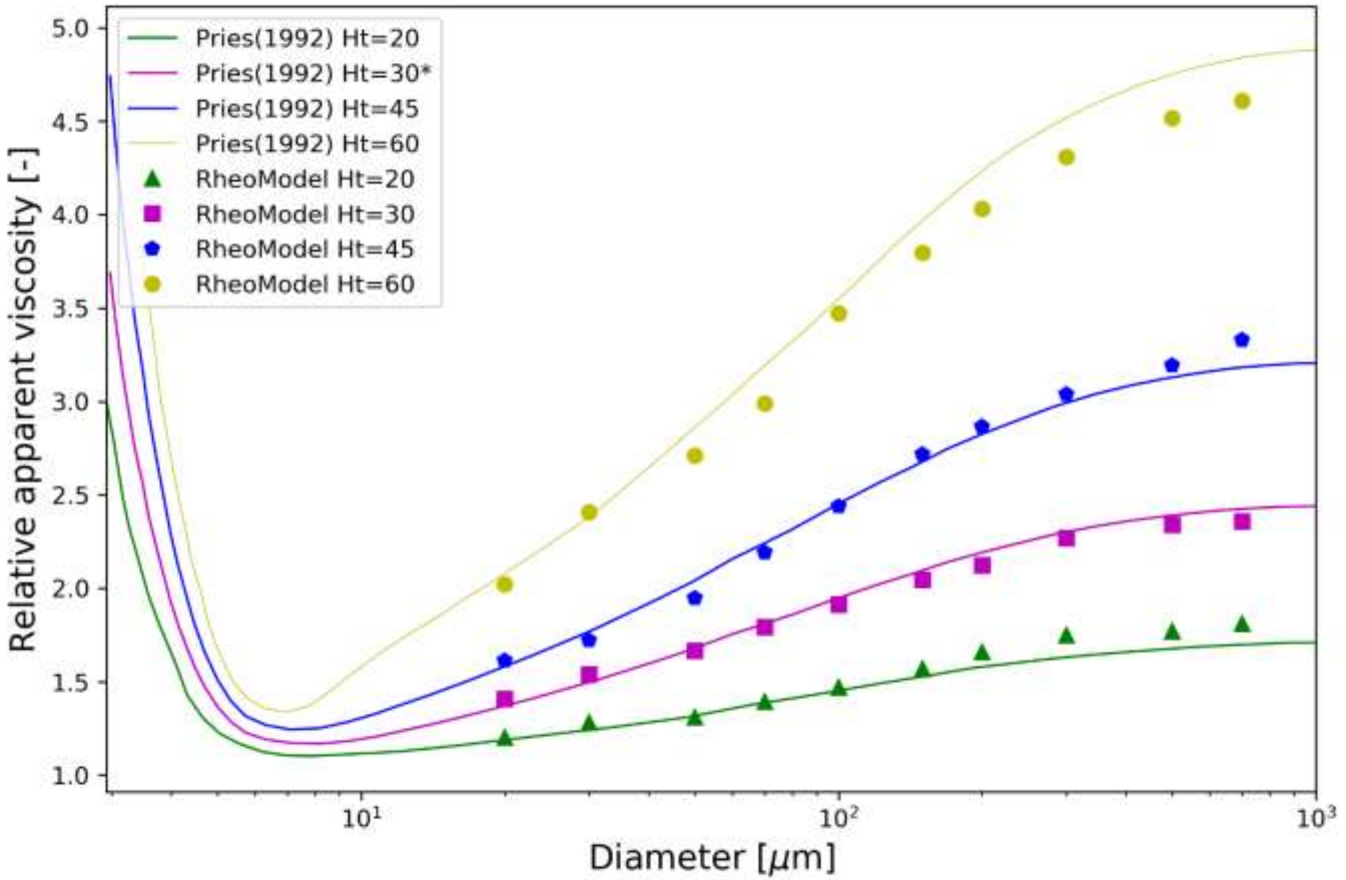


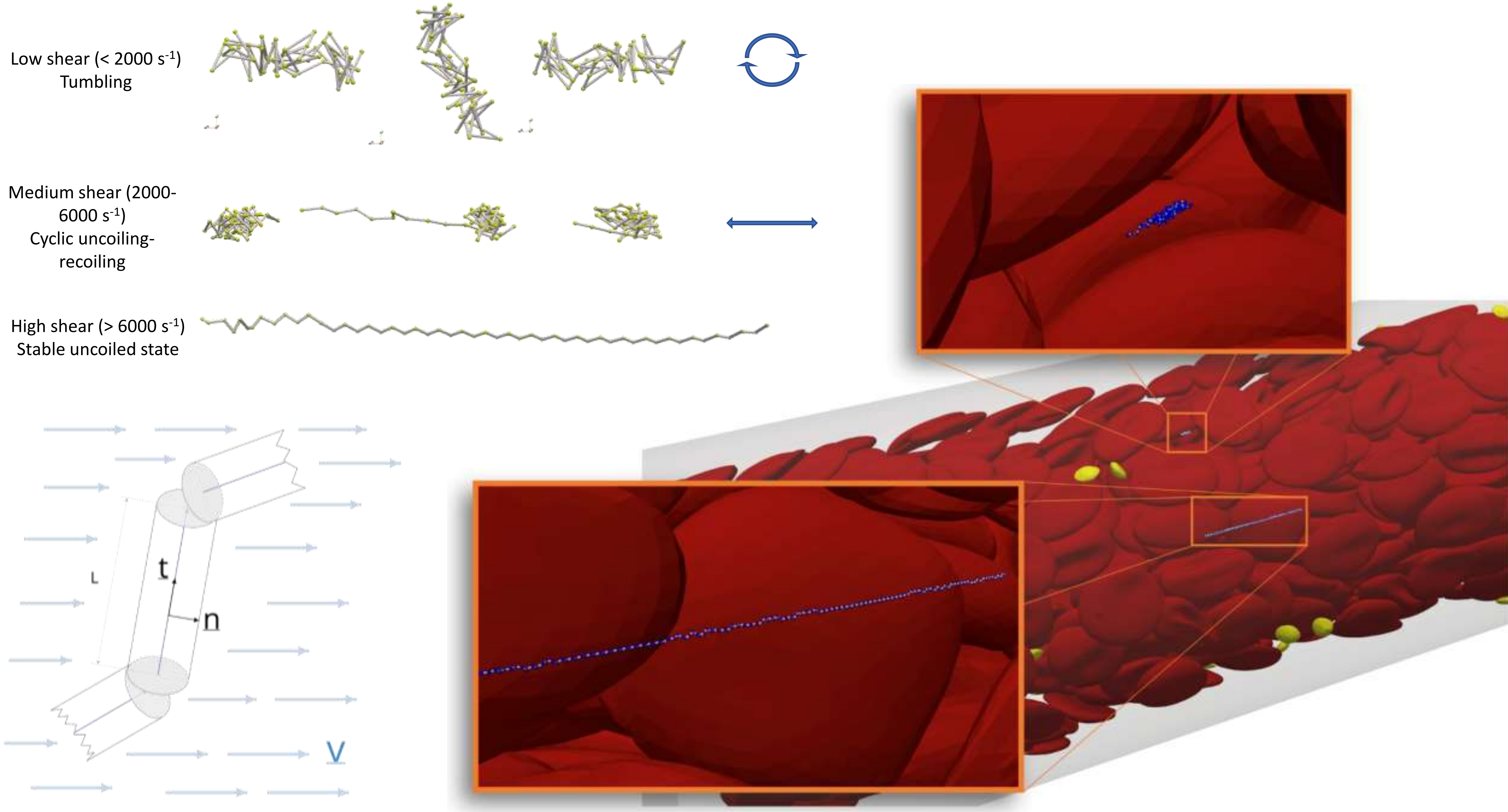
Computation: 9 days on 128 cores (Cartesius)



Computation: ~5 s on my notebook

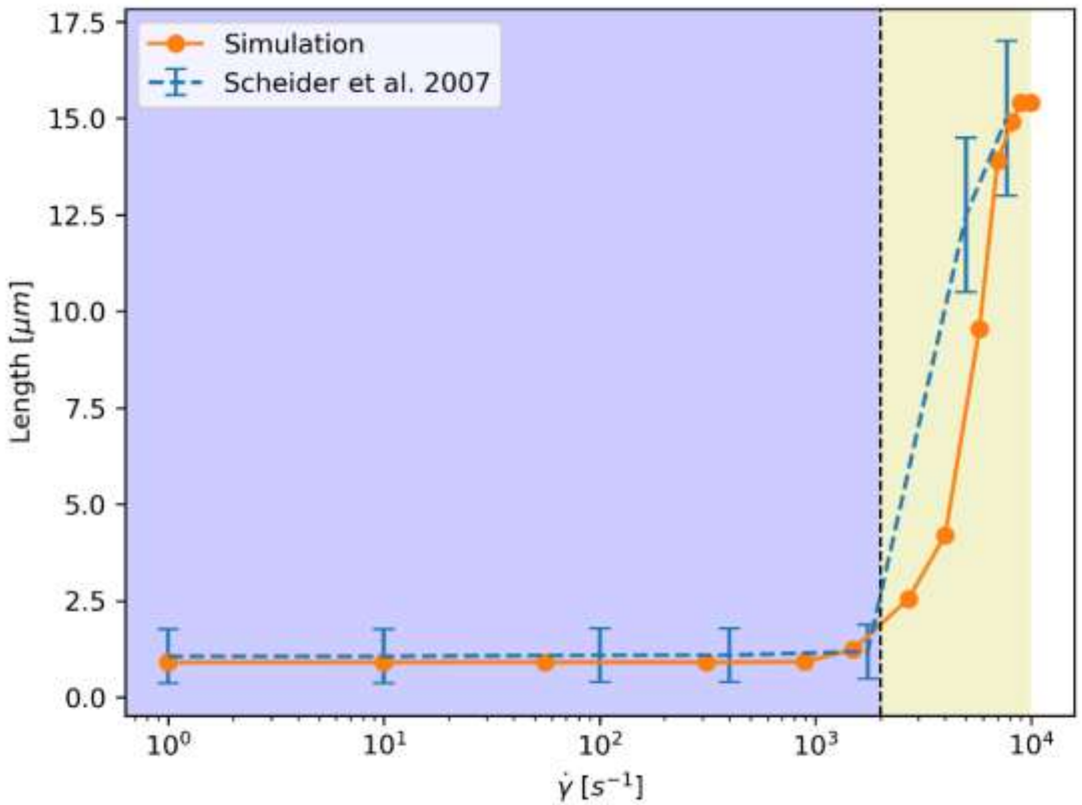
Viscosity of blood in a vessel section




Low shear (< 2000 s^{-1})
Tumbling
Medium shear (2000-6000 s^{-1})
Cyclic uncoiling-recoiling
High shear (> 6000 s^{-1})
Stable uncoiled state
L
t
n
V

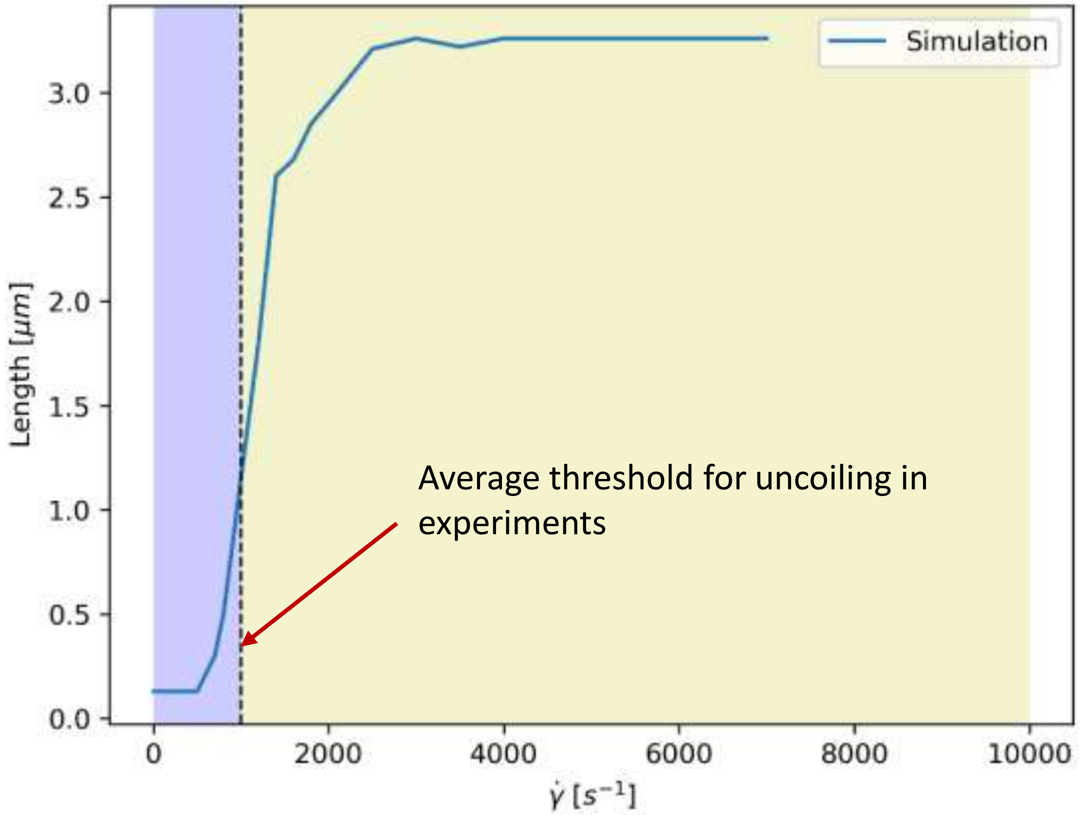
vWF mechanical model

Uncoiling in pure shear flow



Comparison to: Schneider et al. (2007), *PNAS*

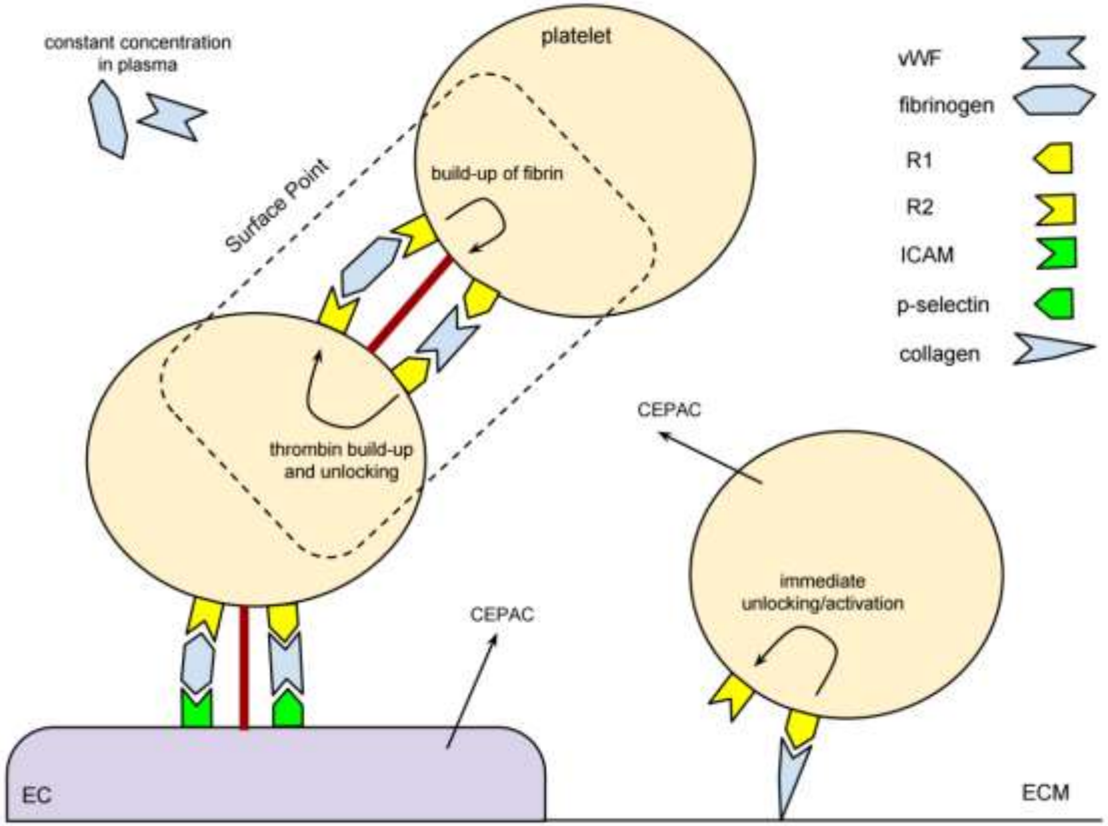
Uncoiling in shear flow while head fixed to wall



Comparison to: Fu et al. (2017), *Nature Communications*

Note: the spherical chain representation cannot match both with the same parameters.
Conclusion: allowing the elements of the chain to change alignment compared to the flow might be important.

CEPAC - Combined Effect for Pro- and Anti-coagulants



R1 receptor → weak bonds

- Platelet receptor to vWF: Gp Ib/Ia [~25000 on a platelet]
- Integrin receptor to vWF: αIIbβ3 [~50000 on a platelet]
- Platelet receptor to collagen: Gp VI (+Gp Ia/IIa) [~4000 on platelet]

⇩

Platelet adhesion and rolling over surface

More important in arteries (>500 s-1) and arterioles (1000-1800 s-1) than in veins (<200 s-1)

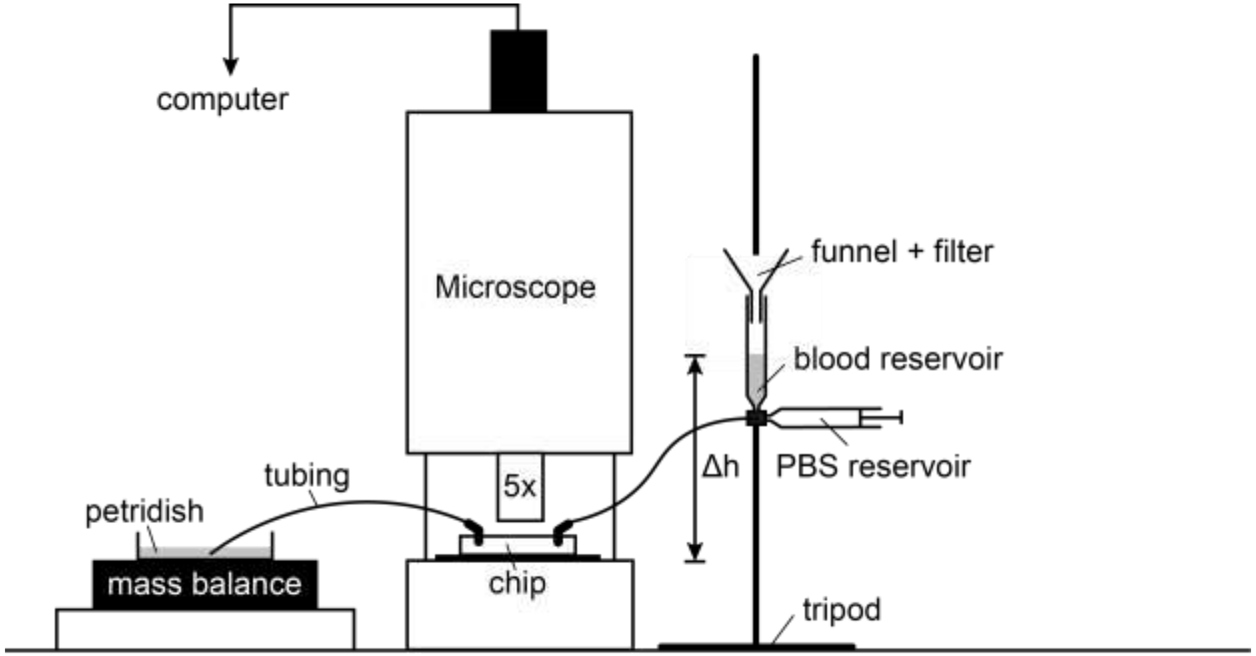
R2 receptor → strong bonds

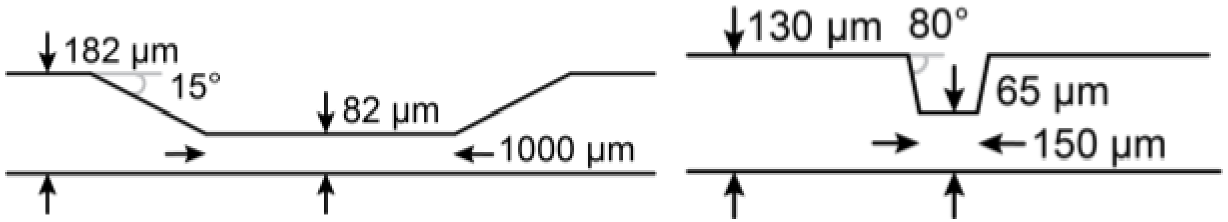
- Integrin receptor to fibrinogen: αIIbβ3 [~50000 on a platelet]
- Integrin receptor to collagen via vWF: α2β1 [~1000-4000 on a platelet]

⇩

Platelet aggregation

First target experiments

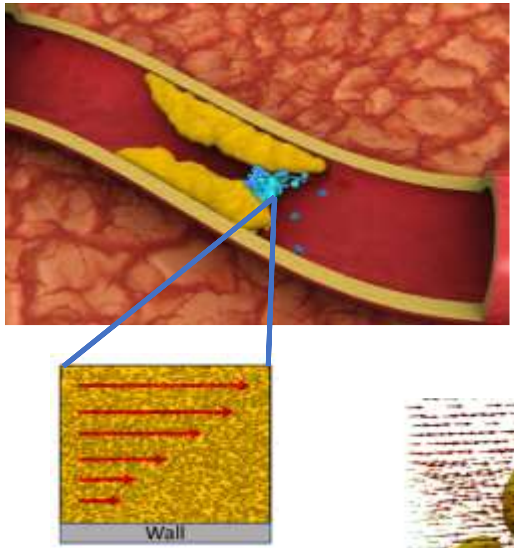


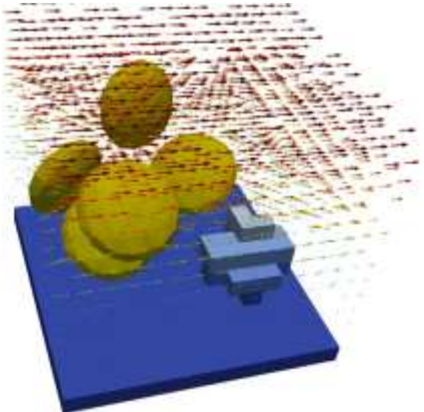


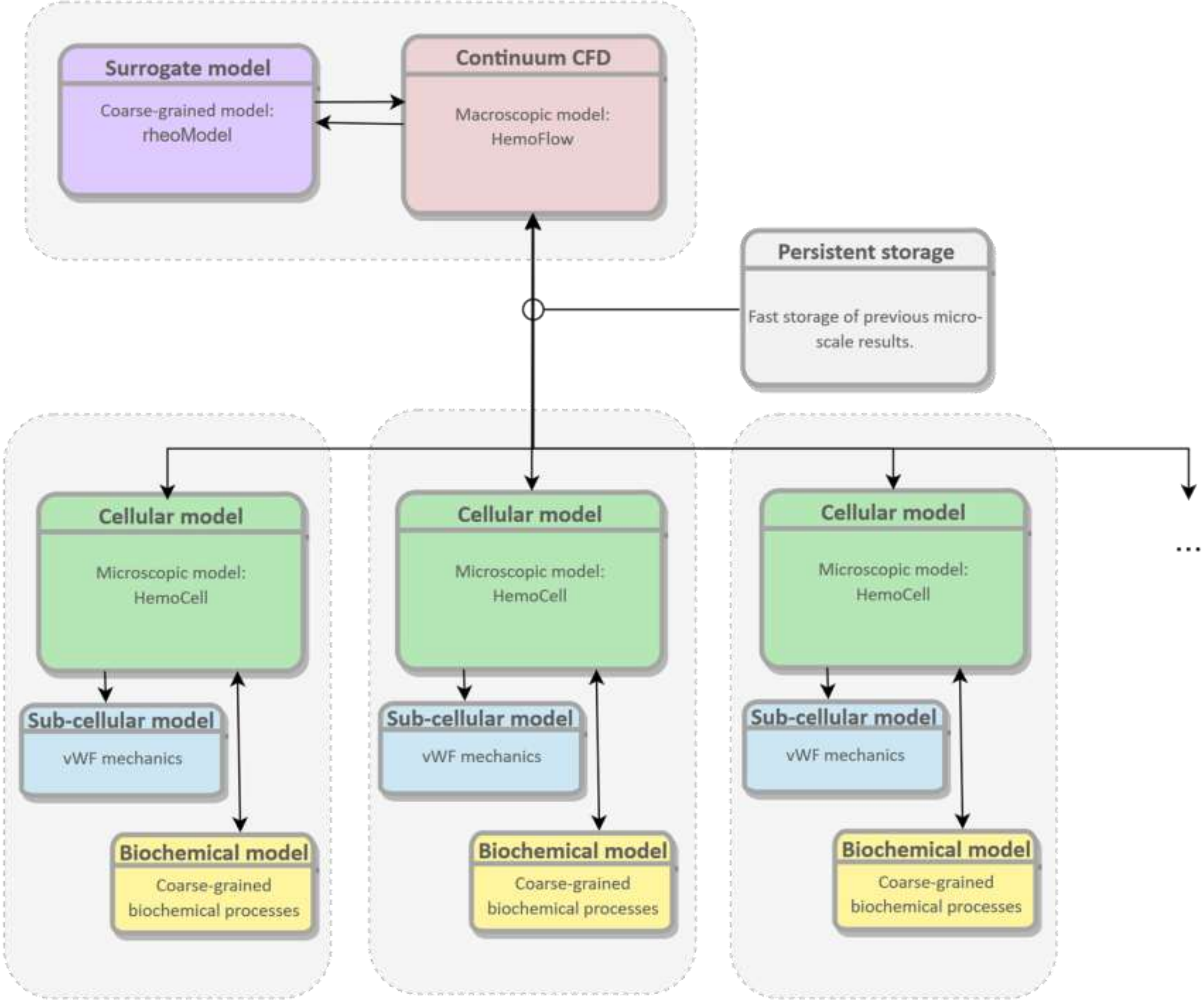
Britt van Rooij

HemoScale

Model level

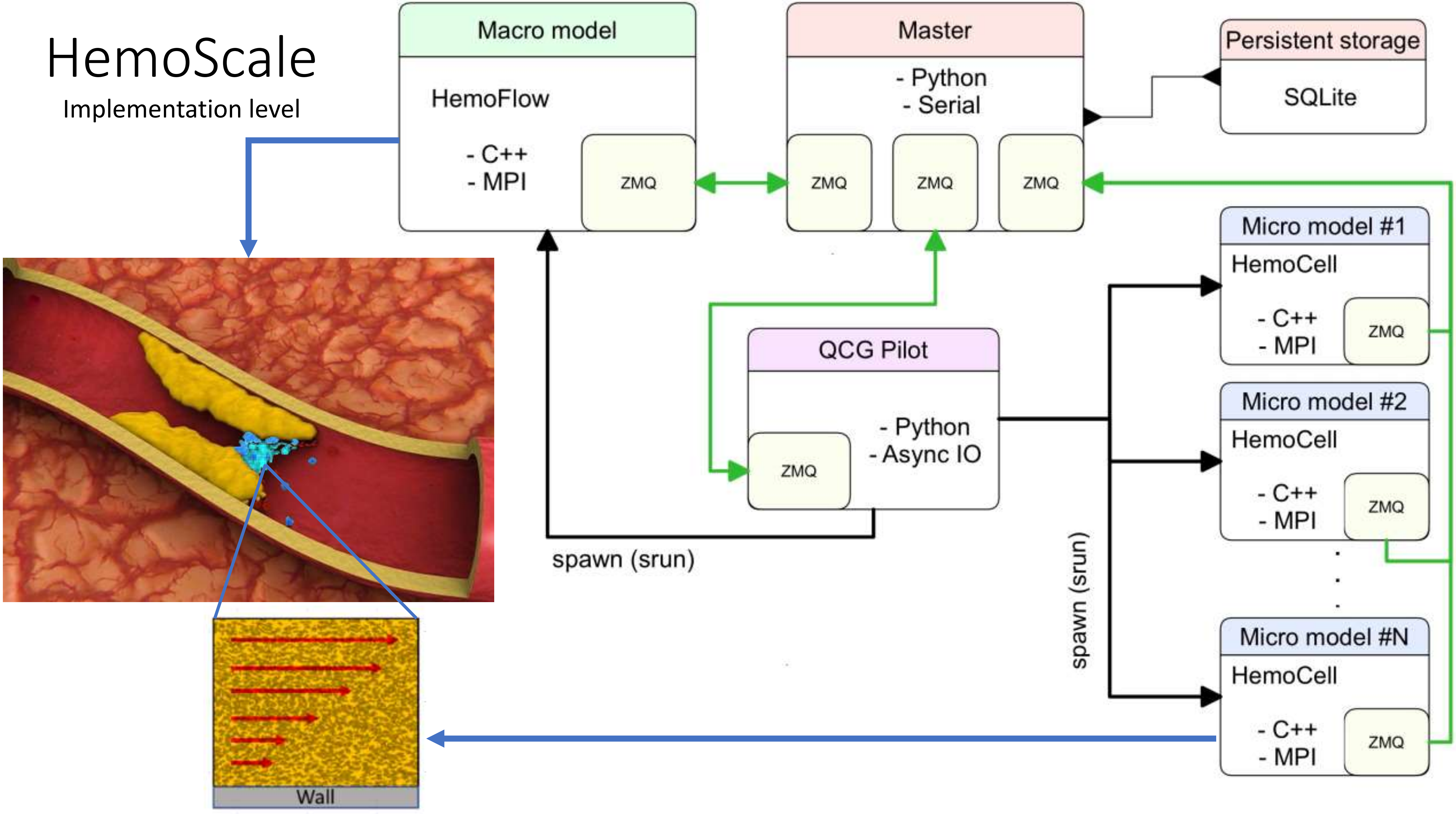






HemoScale

Implementation level



Thank you for your attention!

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Computing Patterns for High Performance Multiscale Computing

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