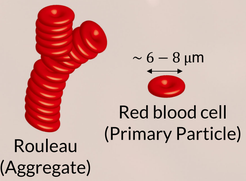
A Rheological Constitutive Model for Human Blood via Population Balances

Soham Jariwala, Jeffrey S. Horner, Antony N. Beris, Norman J. Wagner
Center for Research in Soft matter & Polymers (CRiSP), Department of Chemical and Biomolecular Engineering, University of Delaware, Newark, Delaware, USA-19716

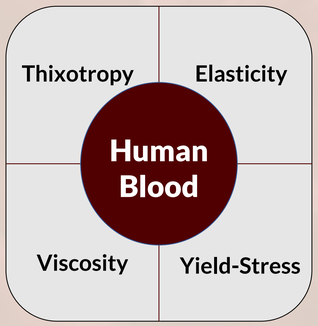
Correspondence: sdj@udel.edu

BACKGROUND AND MOTIVATION:

Human blood is a dense suspension of platelets, white blood cells, red blood cells (RBCs) suspended in plasma along with dissolved proteins. Much of its complex rheology at low deformation rates is a result of RBCs forming coin-stack like aggregates called **rouleaux**.



The kinetics of rouleaux break down and build up due to Brownian motion and shear results in **thixotropic** behavior. Rouleaux also impart **elasticity** and **yield-stress** making human blood a **Thixotropic-Elasto-visco-plastic** fluid.



A more predictive microstructure-rheology relationship could enable us to probe diseases and develop new health diagnostic tools based on changes in the blood rheology.

METHODS:

We use **population balances** to describe the kinetics of rouleaux formation using particle-based theories.

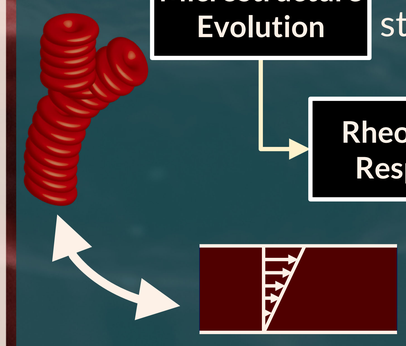
Key Assumptions:

- RBCs and Rouleaux are approximated as spheres and fractals, respectively.
- Aggregation is based on Smoluchowski kernel.
- Breakage is assumed to be binary and uniform, described using model proposed by Spicer and Pratsinis.
- Dynamic arrest is modeled using a hyperbolic cut-off function.

$$\beta(\phi_a) \equiv \tanh\left(2.65\frac{\phi_{max}-\phi_a}{\phi_{max}-\phi_p}\right)$$

Some advantages of this approach:

- The model uses physiologically relevant parameters such as **RBC size** and **hematocrit**
- Physically meaningful parameters like **fractal dimension** and **stability ratio**, that can be validated independently can be obtained through fitting the model to experiments.



Model summary

The model is adapted from coarse-grained population balance model for shear flows developed by Mwasame *et al.* [1] using method of moments.

Microstructure Evolution

Population balance equation describes how aggregate volume fraction (ϕ_a) changes with time due to Brownian motion and shear. The equation is coarse-grained using monodisperse closure and written in terms of zeroth moment of the aggregate size distribution (ν_0), or the number density. Highlighted parameters need to be obtained using data fitting

$$\frac{d\nu_0}{dt} = \underbrace{-2\beta\left(\frac{k_B T\phi_p}{2\mu W\pi a_p^3}\right)\nu_0^2}_{\text{Brownian aggregation}} \underbrace{-4\beta\alpha\left(\frac{\phi_p}{\pi}\right)|\dot{\gamma}|\nu_0^{2-3/d_f}}_{\text{Shear aggregation}} + \underbrace{b_o|\dot{\gamma}|^2\left(\nu_0^{1-1/d_f}-\nu_0\right)}_{\text{Breakage}}$$

$$\phi_a = \phi_p \nu_0^{1-3/d_f} \quad \text{Aggregate volume fraction}$$

$$\phi_h = \phi_a\left(\frac{R_h}{R_a}\right)^3 \quad \text{Hydrodynamic volume fraction}$$

Rheological variables

Red blood cells deform at high-shear rates that results in shear thinning that is captured **by Cross-like term** in viscosity.

Elasticity of rouleaux can be estimated using volume fraction (ϕ_a).

$$\mu(\phi_h,\dot{\gamma}) = \underbrace{\mu_{\infty,C}\left\{\frac{\left(1+2.5\phi_h+7.6\phi_h^2\right)}{\left(1+2.5\phi_p+7.6\phi_p^2\right)}+c_4\left(\frac{\phi_h-\phi_p}{\phi_{max}-\phi_p}\right)\right\}}_{\text{Suspension contribution}} + \underbrace{\left(\frac{\mu_{0,C}-\mu_{\infty,C}}{1+\tau_c|\dot{\gamma}|}\right)}_{\text{Shear-thinning (Cross-like term)}}$$

$$G_{Network}(\phi_a) = G_o\left(\frac{\phi_a-\phi_p}{\phi_{max}-\phi_p}\right)^{\frac{1}{3-d_f}}$$

$$\frac{d\gamma_e}{dt} = \begin{cases}\dot{\gamma}\left(1-\dfrac{\gamma_e}{\tau\dot{\gamma}}\right) & |\gamma_e|<|\tau\dot{\gamma}| \\ 0 & |\gamma_e|=|\tau\dot{\gamma}|\end{cases}, \text{ where } \tau = \frac{\gamma_{lin}}{\dot{\gamma}(\phi_a)}\left|\frac{\gamma_{lin}}{\gamma_e}\right|$$

Macroscopic Stress

Shear stress is based on modified Bingham model with additive elastic and viscous contribution.

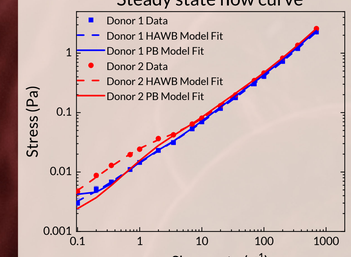
$$\sigma = \underbrace{G_{Network}(\phi_a)\gamma_e(\phi_a)}_{\text{Elastic}} + \underbrace{\mu(\phi_h,\dot{\gamma})\dot{\gamma}}_{\text{Viscous}}$$

RESULTS:

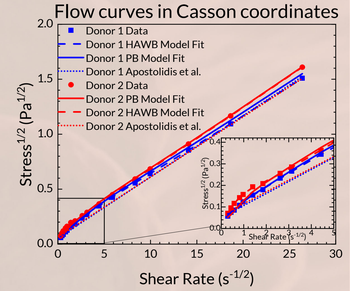
The model was fit to one **steady-state** and four **unidirectional large amplitude oscillatory shear (UD-LAOS)** whole blood measurements carried out by Horner *et al.* [2] for two donors.

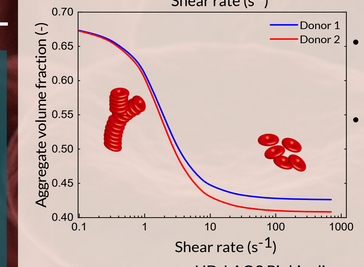
Data fitting: Parallel tempering algorithm developed by Armstrong *et al.* [3] was used to fit the model to rheological data set.

Steady state flow curve



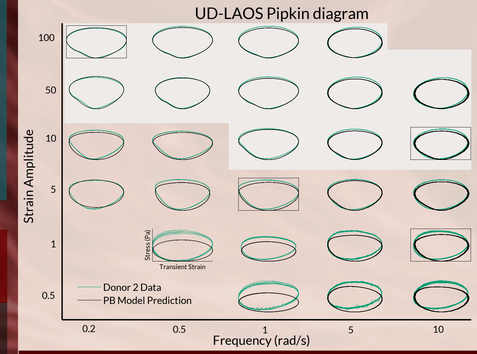
Flow curves in Casson coordinates





- The aggregate volume fraction approaches the hematocrit at high shear rates.
- Fractal dimension from fits ($d_f \sim 1.3 - 1.7$) makes intuitive sense for rouleaux as they may form branches

UD-LAOS Pipkin diagram



Model is reasonably accurate at wide range of shear-rates, especially at physiologically relevant ones (highlighted)

Parameter description		Donor 1		Donor 2		Method
		Best Value	Average value	Best Value	Average value	
a_p	RBC radius	2.5 μm	(–)	2.5 μm	(–)	Physical Estimate
ϕ_{max}	Max. packing fraction	0.68	(–)	0.68	(–)	Physical Estimate
ϕ_p	Hematocrit	0.426	(–)	0.408	(–)	Measured [2]
G_0	Equilibrium modulus	0.173 Pa	(–)	0.164 Pa	(–)	Independent Fit [2]
σ_y	Yield stress	2.03 mPa	(–)	3.17 mPa	(–)	Independent Fit [2]
$\mu_{0,C}$	Zero-shear viscosity	7.82 mPa s	(–)	8.56 mPa s	(–)	Independent Fit [2]
$\mu_{\infty,C}$	Infinite-shear viscosity	3.07 mPa s	(–)	3.50 mPa s	(–)	Independent Fit [2]
τ_C	Time-constant for isolated RBCs	0.0383 s	(–)	0.0361 s	(–)	Independent Fit [2]
W	Stability ratio	175.7	107.7 ± 67.48	165.8	75.2 ± 43.6	Fit
α	Collision efficiency	0.722	0.617 ± 0.113	0.50	0.65 ± 0.16	Fit
b_0	Breakage constant	0.976 s	0.776 ± 0.203 s	0.596 s	0.848 ± 0.135 s	Fit
d_f	Fractal dimension	1.647	1.672 ± 0.097	1.319	1.421 ± 0.162	Fit
R_h/R_a	Porosity	0.915	0.900 ± 0.037	0.808	0.723 ± 0.131	Fit
c_4	Suspension viscosity correction	2.3	4.9 ± 5.2	2.6	12.1 ± 10.9	Fit

CONCLUSION:

We demonstrate that human blood rheology can be accurately modeled and *predicted* using population balance modeling of the rouleaux using existing colloidal physics models. This research opens the possibility for using rheology as a medical diagnostic tool.

REFERENCES:

[1] P.M. Mwasame, A.N. Beris, R.B. Diemer, and N.J. Wagner, AIChE J. 63, 517 (2017).
[2] J.S. Horner, M.J. Armstrong, N.J. Wagner, and A.N. Beris, J. Rheol. 62, 577 (2018).
[3] M.J. Armstrong, A.N. Beris, N.J. Wagner, AIChE J. 63, 1937. (2017)

ACKNOWLEDGEMENT:

The authors would like to thank the **National Science Foundation (NSF)** for funding through awards CBET 1510837 and CBET 1804911