Modeling Blood Flow in Microcirculation: An In Vitro Study Using Capillary Microchannels

Maya Salame[1] and Marianne Fenech[1]

[1] Department of Mechanical Engineering, University of Ottawa, Ottawa, Canada

Abstract— **Microcirculatory blood flow is influenced by complex non-Newtonian properties, including shear-thinning behavior and the presence of a cell-free layer (CFL), a plasma-rich zone near vessel walls caused by hydrodynamic forces. Existing rheological models, such as Newtonian, Power Law, and Carreau, capture certain aspects of blood properties but fail to fully describe its dynamic flow characteristics. This study introduces the Core-Plasma Model, which combines Newtonian and non-Newtonian elements to represent the RBC core and CFL as a two-phase system. Evaluation across microchannel sizes and hematocrits highlights the Core-Plasma Model's superiority in capturing velocity profiles and shear dynamics, particularly in channels with larger CFLs. The Core-Plasma Model stands out as a promising tool for advancing microscale hemodynamic predictions and understanding microvascular flow.**

Keywords— **blood flow modeling, microcirculation, capillary microchannels, hematocrit, cell-free layer**

INTRODUCTION

Blood flow in the microcirculation exhibits a complex non-Newtonian behavior, primarily driven by shear-thinning properties. A key feature of this flow is the formation of a cell-free layer (CFL) near the vessel walls in small-diameter vessels such as arterioles, venules, and capillaries. Shear rate, defined as the velocity gradient perpendicular to the flow direction, plays a crucial role in this process. Hydrodynamic forces push red blood cells (RBCs) toward the flow center, leaving a plasma-rich region near the walls. As a result, the CFL is characterized by a reduced or absent concentration of RBCs, which influences both blood rheology and microvascular function. [1; 2; 3]. The Newtonian Model assumes constant viscosity and fails to account for shear-thinning behavior, whereas non-Newtonian models address blood viscosity variations. The Power Law Model effectively captures shear-thinning at intermediate shear rates but fails to account for viscosity plateaus. In contrast, the Carreau Model spans the full range of shear-thinning by asymptotically approaching constant viscosities at extreme shear rates [4; 1]. While the Double-Parameter Power Fit is a commonly employed fitting method, it does not constitute a true rheological model where we can extract fluid properties [5]. These existing models struggle to fully capture the dynamic behavior observed in blood flow. In this study, we propose a new Core-Plasma Model. The Core-Plasma Model represents blood as a two-phase system, integrating Newtonian and non-Newtonian dynamics to describe the RBC core and the surrounding CFL. The objective of this study is to assess the performance of this Model in accurately capturing blood properties and achieving optimal fits for evaluating shear dynamics.

MATERIALS AND METHODS

Blood Samples: Blood samples were collected from healthy donors (University of Ottawa, Ethics File No. H-03-19-3441). After centrifugation, the buffy coat and plasma were removed, leaving packed RBCs. The RBCs were washed with Phosphate Buffered Saline (PBS) to remove residual plasma and platelets. Washed RBCs were resuspended in PBS or autologous plasma at hematocrit levels of 5%, 10%, 15%, and 20%, verified using a CritSpin Micro-Hematocrit Centrifuge (CritSpin, Thermo Fisher Scientific Inc., China). A suspension stabilizing solution of PBS, OptiPrep® (Sigma Aldrich, Ref. D1556), and glucose was used to prevent sedimentation. **Microchannel Fabrication:** Borosilicate glass capillaries (VitroCom, MA, USA) of 25 μm and 50 μm diameters were used as microchannels. Capillaries were cut to size, attached to a custom 3D printed enclosure, and mounted on a glass slide. Channels were submerged in 99% glycerol to reduce light refraction and improve imaging clarity. To minimize RBC adhesion, channels were coated with a PLL-PEG solution [6]. **Experimental Setup:** Figure 1 outlines the experimental setup. A Flow EZ pressure controller (Fluigent, France) regulated blood flow through the microchannels. Flow rates were monitored in real-time using Fluigent OxyGEN software. **Velocity Profile Aquisition:** Micro-Particle Image Velocimetry (μPIV) was employed to capture velocity profiles, using a 532 nm Nd:YAG laser and

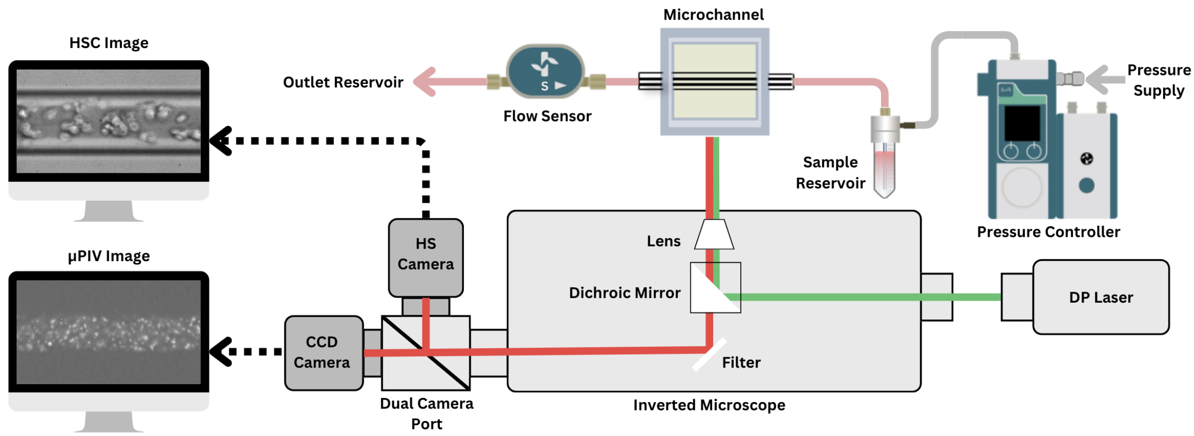

Fig. 1: Schematic of the experimental setup, including the pressure and flow controller, microchannel setup, and imaging components for both High-Speed Camera (HSC) and Micro-Particle Image Velocimetry (μPIV) analysis.

a CCD camera (LaVision, Germany) coupled with a fluorescent microscope (20× objective, Zeiss, Germany). Fluorescent tracer particles illuminated by the laser visualized flow, and measurements were recorded at the channel center plane to ensure accuracy. **Cell Free Layer Acquisition:** For each flow rate setting, the high-speed camera captured a set of 200 images of the flow with an exposure time of 0.1 ms. These images were then imported into a Matlab application designed for image processing to obtain the CFL thickness, developed by [7]. This measurement is defined as the optical cell-free layer (δ_o). In contrast, the hydrodynamic cell-free layer (δ_h) is derived from shear rate profiles, representing the region near the vessel wall with minimal velocity gradients.

BLOOD MODELING

Rheological Models

The Newtonian Model assumes constant viscosity, with velocity defined as:

$$u(r) = \frac{\Delta P}{4\mu L}(R^2 - r^2), \tag{1}$$

where ΔP is the pressure drop, μ is the viscosity, L is the channel length, R is the vessel radius, and r is the radial position [1]. While straightforward, this Model fails to account for the shear-thinning properties of blood.

For non-Newtonian fluids like blood, the Power Law Model captures shear-thinning behavior:

$$u(r) = \left(\frac{\Delta P}{2KL}\right)^{1/n} \frac{n}{n+1}\left(R^{(n+1)/n} - r^{(n+1)/n}\right), \tag{2}$$

where K is the consistency index, and n is the flow behavior index [1]. While effective at intermediate shear rates, this Model struggles to represent viscosity plateaus.

The Carreau Model overcomes this limitation by describing viscosity variations across a broad range of shear rates, asymptotically approaching constant values at low and high shear rates:

$$\eta(\dot{\gamma}) = \eta_\infty + (\eta_0 - \eta_\infty)\left[1 + (\lambda_c\dot{\gamma})^2\right]^{(n-1)/2}, \tag{3}$$

where η_0 and η_∞ are viscosities at zero and infinite shear rates, λ_c is the time constant, and $\dot{\gamma}$ is the shear rate [1]. This makes the Carreau Model particularly suited for capturing the full rheological spectrum of blood flow.

Building on these frameworks, the Core-Plasma Model was developed to incorporate both Newtonian and non-Newtonian elements, representing blood as a two-phase system. It describes the layered flow structure consisting of a cell-rich core and a plasma-rich CFL (δ), where μ_p is the plasma viscosity:

$$u(r) = \begin{cases} \frac{\Delta P}{4\mu_p L}(r^2 - R^2), & r \geq (R-\delta) \\ \left(\frac{\Delta P}{2K_{cp}L}\right)^{\frac{1}{n_{cp}}} \frac{n_{cp}}{n_{cp}+1}\left[r^{\frac{n_{cp}+1}{n_{cp}}} - (R-\delta)^{\frac{n_{cp}+1}{n_{cp}}}\right] & \\ \quad + \frac{\Delta P}{4\mu_p L}\left[(R-\delta)^2 - R^2\right], & r < (R-\delta) \end{cases} \tag{4}$$

Fitting Models

To improve velocity profiling, a Double-Parameter Power Fit was introduced. Unlike rheological models, this purely fitting model incorporates distinct shape factors (k_1 and k_2) to adjust the curvature and steepness of the velocity profile:

$$u(r) = V_{\max}\left(1 - k_1\left(\frac{r}{R}\right)^2\right)\left(1 - \left(\frac{r}{R}\right)^{k_2}\right), \quad (5)$$

where $V_{\max}$ represents the maximum velocity. While this Model cannot extract fluid properties, it provides an effective means of capturing distinct flow characteristics in the core and CFL regions [1; 4].

Shear Rate Computation

Shear rates ($\dot{\gamma}$) were computed numerically from experimental data and theoretically from the derivation of the models. The relationship is described as the gradient of velocity (v) across the channel height (y):

$$\dot{\gamma} = \frac{\partial v}{\partial y}. \quad (6)$$

RESULTS AND DISCUSSION

Shear Rate at Discontinuity

The shear rate profiles revealed a distinct transition between the core region, dominated by RBCs, and the CFL near the channel walls, as exemplified in Figure 2. The δ_o thickness was measured to be approximately 18 μm and δ_h approximately 19 μm. The magnitudes of δ_o and δ_h are generally comparable across channel sizes and hematocrit levels. However, δ_h slightly underestimates the CFL thickness in 50 μm channels, likely due to the enhanced sensitivity of δ_o to subtle RBC distributions at larger scales [2; 1].

Velocity Profiles and Model Performance

The velocity profiles and the performance of rheological models are illustrated in Figure 3. The top panel displays the experimental velocity profile alongside the fitted models, while the bottom panel presents the corresponding root-mean-square (RMS) velocity values. Figure 4 further compares the RMS errors for velocity and shear rate predictions across both channel sizes and suspending fluids. The Double-Parameter Power Fit achieved the best velocity profile fitting

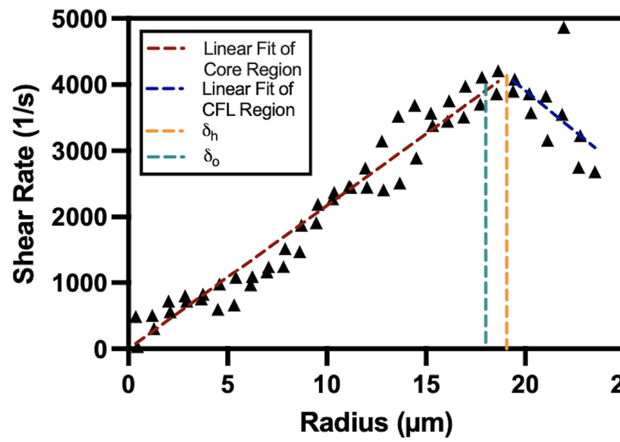

Fig. 2: Shear rate profile for a 15% hematocrit suspension in plasma at 180 mBar flow pressure through a 50 μm microchannel. The shear rate discontinuity indicates the boundary between the RBC-dominated core region and the δ_h. A dashed line highlights the corresponding δ_o thickness, providing a visual comparison of the two methodologies.

across all channel sizes, effectively capturing both the core flow and the CFL transition regions through its distinct shape factors. However, it is not a rheological model derived from physical laws. The Core-Plasma Model demonstrated strong performance, particularly in the 50 μm channel, where the larger CFL allowed for a more accurate representation of the layered flow structure. In contrast, the Core-Plasma Model struggled in the 25 μm channel, exhibiting higher RMS errors. The Carreau, Power Law, and Newtonian Models provided reasonable fits but lacked the adaptability to fully capture the dynamics at the CFL boundary. The Core-Plasma Model's reduced accuracy in the 25 μm channel was likely due to the smaller CFL and higher RBC density, which limited its ability to model this two-phase transition [2; 4].

CONCLUSION

The Core-Plasma Model is the most optimal rheological representation of blood flow, effectively capturing the complexity of microcirculatory systems. However, limitations such as discrepancies between δ_h and δ_o measurements, as well as the oversimplifications inherent in linear fitting approaches, underscore the need for further refinement in modeling techniques. These insights not only enhance our understanding of blood flow behavior but also contribute to advancements in biomedical applications, including drug delivery optimization leveraging the CFL, the development of di-

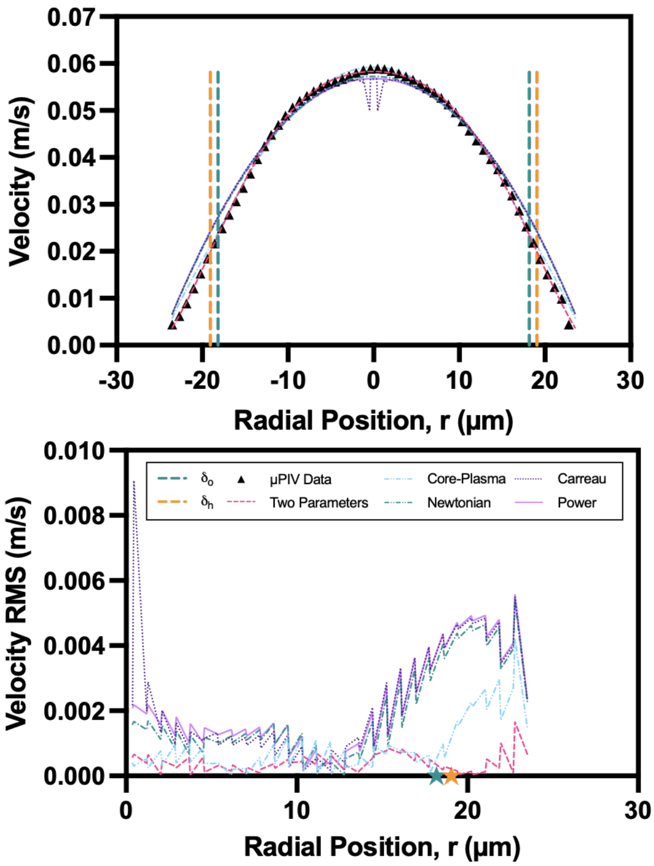

Fig. 3: (Top) Velocity profile and (Bottom) velocity Root-Mean-Square (RMS) for blood flow in a 50 μm microchannel at 180 mBar pressure and 15% hematocrit suspended in plasma. Experimental data (black triangles) are compared with fitted Models (Newtonian, Power Law, Double-Parameter Power Fit, Carreau, and Core-Plasma). The boundaries of the δ_h and the δ_o are indicated.

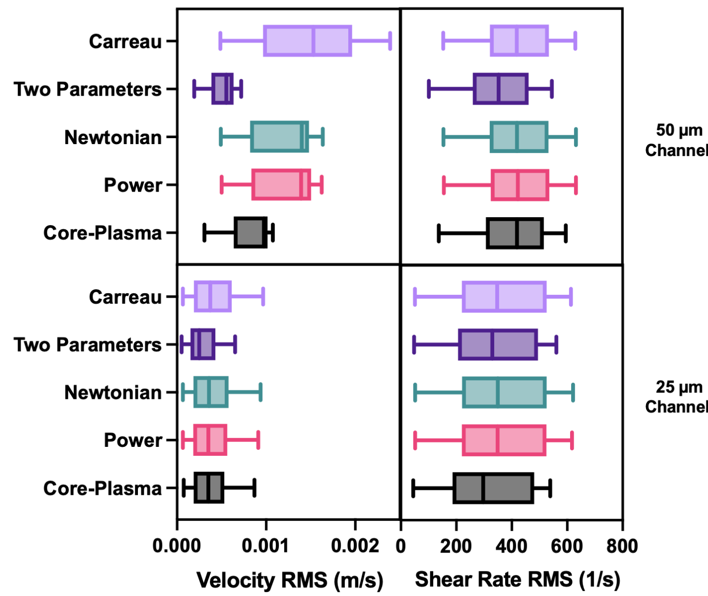

Fig. 4: Root-Mean-Square (RMS) errors for velocity (top) and shear rate (bottom) predictions in 25 μm and 50 μm microchannels, comparing the performance of various rheological models across different fluid suspensions.

agnostic microfluidic devices, and the study of pathological conditions in the microvasculature.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

ACKNOWLEDGMENTS

This work was financially supported by the Natural Sciences and Engineering Research Council of Canada (NSERC).

REFERENCES

[1] M. Fenech and L. Haya, "Blood flow mechanics," in *Cardiovascular Mechanics*, CRC Press, 2018.

[2] D. Fedosov, B. Caswell, A. Popel, and G. Karniadakis, "Blood flow and cell-free layer in microvessels," *Microcirculation*, vol. 17, pp. 615–628, November 2010.

[3] A. R. Pries and T. W. Secomb, "Rheology of the microcirculation," *Clinical Hemorheology and Microcirculation*, vol. 29, no. 3–4, pp. 143–148, 2003.

[4] R. Mehri, C. Mavriplis, and M. Fenech, "Red blood cell aggregates and their effect on non-newtonian blood viscosity at low hematocrit in a two-fluid low shear rate microfluidic system," *PLOS ONE*, vol. 13, p. e0199911, July 2018.

[5] K. L. Pitts and M. Fenech, "Micro-particle image velocimetry for velocity profile measurements of micro blood flows," *Journal of Visualized Experiments (JoVE)*, p. 50314, Apr. 2013.

[6] C. Chartrand, A. V. Le, and M. Fenech, "Microparticle image velocimetry for blood flow in thick round glass micro-channels: Channel fabrication and velocity profile characterization," *MethodsX*, vol. 10, p. 102110, January 2023.

[7] M. Fenech, A. V. Le, M. Salame, O. Gliah, and C. Chartrand, "Semi-automated red blood cell core detection in blood micro-flow," *Microvascular Research*, vol. 147, p. 104496, May 2023.

Author: Maya Salame
Insitute: University of Ottawa
Country: Canada
Email: msala029@uottawa.ca