Low Shear Rate Rheology of Horse and Human Blood:
Experimental, Theoretical, and Machine Learning Investigation of Rouleaux

Sean Farrington
Advisors: Dr. Norman J. Wagner and Dr. Antony N. Beris
Committee Members: Dr. Alexandra V. Bayles, Dr. Abraham M. Lenhoff, and Dr. Matthew J. Armstrong

August 15th, 2025, at 0930
366 Colburn Laboratory | https://udel.zoom.us/j/99541501345 | Password: Blood

---

Hemorheology is the study of blood flow dynamics with the mechanical stresses and kinematics involved. The rheological properties of blood are linked to many cardiovascular diseases such as diabetes, sickle cell anemia, thrombosis, and hypertension. This connection makes hemorheology applicable as a potential diagnostic tool for cardiovascular diseases, which are the leading cause of death in the United States. Human blood contains red blood cells, white blood cells, platelets, and thousands of plasma proteins, which provide numerous functions including oxygen, nutrient, and waste material transport. The red blood cells are deformable, non-spherical, disc-like particles with a tendency to aggregate into coin-stack shaped structures (known as rouleaux) at low shear rates. The extreme complexity presented by this concentrated suspension of red blood cells gives rise to unique and nuanced rheological behaviors such as plasticity, thixotropy, and viscoelasticity with significant variability even among healthy people. *This dissertation achieves a detailed and careful analysis of low shear rate transient rheometry induced by rouleaux, quantitative correlations between physiology and rheology via machine learning, and the development of a new approach to measure the yield stress and low shear viscosity in a microfluidic device*.

A more complete, detailed description of low shear rate phenomena where rouleaux exist is provided in this dissertation. The first measurements of both steady shear and transient rheology for red blood cell resuspensions under conditions that control for rouleaux demonstrates quantitative evidence for the rheological signature caused by rouleaux. One anomalous transient phenomenon known as the step-down transience at low shear rates is unequivocally prescribed to rouleaux behavior in this work. The mechanism of this step-down transience is found to be more likely one involving a wall-induced migration layer instead of sedimentation, as was suggested in literature. Those results are independently confirmed with experiments that apply a two-fluid shear model to low shear viscometry and through optical microfluidic measurements.

A substantial achievement documented in this dissertation is a machine learning approach that improves the correlation of blood physiology to rheological parameters. This correlation utilizes the most detailed, standardized dataset on blood samples collected from 22 healthy donors, which was recently developed through previous work within our research group. These correlations of physiology to rheology can be used in a variety of medical applications, such as a priori implementation of rheology parameters into blood flow simulations, which are a step towards personalized medicine. The successful steady shear correlations of the Casson model parameters to hematocrit and fibrinogen substantially improves pre-existing analytical relations that were developed using old data from literature, which were collected without standardization. Thanks to those correlations, a healthy range for rheological parameters is also developed that can immediately be used for potential pathological condition diagnosis. Also, an extension

of this work to other physiological factors led to the discovery of a new physiological parameter correlated to the Casson yield stress (mean corpuscular hemoglobin). Correlations with a more detailed thixo-elasto-viscoplastic (TEVP) model known as t-ESSTV could not reveal statistically significant correlations even with a principal component approach that included many more physiological variables. Generating synthetic data for that TEVP model shows that a minimum of 75–100 more data points are needed to expect robust correlations between physiology and t-ESSTV parameters. The poor correlations with the current limited data size of n=22 (the largest in existence) indicate that larger blood rheology datasets with more variability are needed and simpler, more physically relevant, models should be developed.

Finally, useful progress toward the development of a miniaturized low shear rate blood rheometer promises to improve portability, reduce sample size, and decrease time for measurement. Successful development of low shear rate viscosity measurement in a microfluidic device is achieved, although there are limitations in measurement accuracy that must be overcome. A new, direct optical measurement of the yield stress is developed in this work, which is accurate compared to the apparent Casson yield stress values obtained from rheometry. This optical yield stress measurement may be a robust technique for early development of blood rheology microfluidics in diagnostics, but significant validation will be required.

The results of this research deliver insight into the connection between the microscopic physiological complexity, rouleaux behavior, and bulk fluid dynamics of blood in terms of rheology, wall-induced migration, and microfluidic flow. This insight provides a next step in the future application of blood rheology for personalized medicine and can be extended to provide connections to diseases like hypertension, anemia, and various cardiac events. The quantitative connection between healthy physiology and rheology developed here already provides a healthy range of rheology parameters to help interpret rheology for the screening of potential diseases. Additionally, this connection provides a means for a priori determination of rheology in personalized blood flow simulations that could be used to improve the accuracy of flow simulations used in surgery or in better modeling of thrombosis development.