Blood is a dense suspension primarily of red blood cells (RBCs), but also white blood cells and platelets, suspended in an aqueous plasma containing various dissolved proteins, hormones, electrolytes, and gases. The microscopic interactions between constituents gives rise to a complex, viscoplastic, and thixotropic rheological behavior. Much of this complex rheological behavior arises from the tendency of RBCs to stack into linear, coin stack aggregates called rouleaux at low shear rates. Additionally, at high shear rates, the RBCs can deform from the flow field, giving rise to additional viscoelasticity and a less pronounced shear thinning behavior. Due to the multitude of competing interactions and potential measurement complications associated with handling living fluids, the existing understanding of hemorheology is limited.

A significant achievement of this dissertation is a more complete measurement of the transient rheology of blood. Such experimental results are enabled through a statistically validated measurement procedure designed to ensure reproducibility. An original rheometric protocol, mimicking the in vivo flow profile and known as unidirectional large amplitude oscillatory shear (UD-LAOS), is employed throughout to achieve an understanding of the complex material properties. Moreover, a framework is provided for interpreting such tests for general fluids. A new constitutive model is developed, which incorporates thixotropy and viscoelasticity with inherent connections to the underlying microstructure. The full capability of the model is demonstrated for a variety of experimental, transient shear protocols. Furthermore, the model is extended to a three-dimensional, inhomogeneous framework that can be efficiently implemented in hemodynamic simulations through complex geometries.

From the newly acquired measurements, constituting the most comprehensive hemorheological dataset currently available, a discussion is initiated on how blood changes across donors, as well as across species. These changes are quantified in terms of experimental “fingerprints” in the aforementioned specially designed transient experiments for blood: UD LAOS. For human blood, physiological parameters, such as the hematocrit, total cholesterol
concentration, and fibrinogen concentration, are shown to correlate strongly with the rheological parameters, correlations which could not be fully realized previously due to the lack of available data. Across species, more significant variation is observed, despite a near-constant makeup. Particularly, blood from some species exhibits strong shear thinning behavior, while blood from other species exhibits an almost constant viscosity. This interesting result is explored, and a new allometric scaling relation is identified for the low shear blood viscosity across species. The observed relation is hypothesized to arise from a maintenance of wall shear stress in the circulatory system across species.

The results presented throughout this thesis, for the first time, fully connect the macroscopic rheology of blood to the underlying microstructure through a theoretical basis supported by precise measurements. This connection can be pertinent for early disease detection and general health monitoring as numerous diseases, such as hypertension, sickle cell anemia, and diabetes, have been shown to affect the rheology of blood. Understanding interspecies hemorheological changes elucidates the biophysical mechanisms governing human blood rheology and heightens the existing understanding about how biofluid material properties scale across species – an understanding that can be critical for intravenous drug scaleup. Furthermore, the derived constitutive equations for hemorheology can significantly improve the accuracy of existing hemodynamics simulations, which are used in various applications including drug delivery, bypass surgery, and medical device design.