

# Recent advancements to characterize human blood via thixo-visco-elasto-plastic modeling

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## Abstract

In the previous several years there has been much progress in developing more accurate thixo- lasto- visco- plastic rheological models that can be used to mechanically characterize human blood. In theory as the thixo-elasto-visco-plastic (TEVP) model accuracy and predictive capability improves, the parameterization, as well as insights and parametric correlations will also improve. This will allow researchers to determine the healthy, average values for each rheological parameter, as well as left and right limits (2-standard deviations in either direction from average) respectively. It is understood that the mechanical characterization can be vastly improved by using Series of Physical Process framework that can further explore the viscous (liquid-like) and elastic (solid-like) properties along with the TEVP model parameterization.

**Keywords:** Thixotropy, Viscoelasticity, Rheology, Hemorrheology

Blood consists of three chief components: platelets, red blood cells (RBCs), and white blood cells. When at rest or exposed to a low shear rate, the suspended RBCs aggregate into coin stack-like structures called “rouleaux.” The rouleaux form as a function of the stress or shear rate applied to the blood fluid as well as other blood components such as fibrinogen [1,2]. The formation and destruction of these rouleaux are reversible, per the evolution of shear rate magnitude [3,4].

In aggregate, the presence of rouleaux acts to increase blood viscosity, by adding more surface area ‘resisting’ flow. This forms an aspect of blood’s complex properties such as viscoelasticity and viscoplasticity. While the thixotropic property, or microstructure, is also a direct result of rouleaux evolution. Viscoelasticity describes the dual viscous and elastic character of the material while viscoplasticity implies the existence of a yield stress threshold below above which the material ceases to elastically deform and, instead, undergoes irreversible shattering, stretching or change. Thixotropy, however, describes the influence of fluid material microstructure on a time-dependent increasing, decreasing or steady shear rates respectively. While blood’s viscoplasticity and thixotropy are functions of the formation of rouleaux aggregates, the individual contribution of solitary RBCs also contributes a viscoelastic response to the system [5-9]. Rouleaux contributions to blood’s total viscoelastic behavior, along with other complex behavior, can be most easily observed at low shear rates below  $10 \text{ s}^{-1}$  [10-12]. However, similar contributions from individual, non-agglomerated RBCs correspond to relatively shorter relaxation times, leading to a steady-state viscosity that exhibits notable shear thinning at shear rates between  $10\text{-}1000 \text{ s}^{-1}$ . Characterizing the complexity of such flow phenomena requires the use of models capable of reconciling blood’s thixotropic characteristics with the spectrum of viscoelastic features [5-8,11-19].

Human blood TEVP models of rheological data have seen significant development in the recent years [20-32]. It is crucial to note the necessity of including thixotropy and the two, separate viscoelastic timescales; one for the contribution of the blood plasma and solitary RBCs and the other for rouleaux evolution. To approach a full description of blood’s mechanical behavior, it is vital to account for the yield stress and viscoelasticity of microstructure *via* its history-dependence. In crafting any model three distinct timescale differentials must be used to ultimately describe the three key transient phenomena governing blood’s rouleaux aggregation and disaggregation: a) a rouleaux agglomeration timescale; b) a rouleaux disintegration timescale; and c) a Brownian build-up timescale. To characterize the evolving state of microstructure more precisely throughout shear evolutions, a kinetic rate expression is included, featuring a nondimensional parameter describing structure. This

parameter ranges from 0, indicating no rouleaux accumulations, to 1, representing full agglomeration [16-19].

The Enhanced Thixotropic Viscoelastic (ETV) model developed in this effort is a variant of the ethixo-mHAWB model, where the plastic contribution to strain rate is replaced with the total strain rate in the expression representing rouleaux viscoelastic contribution [7,8,20-26]. While the aforementioned modifications have little effect on predictive abilities, they facilitate the use of theories of plasticity to improve ETV via the two additional alterations: a) the adoption of a new elastic-viscoelastic formulation to express the elastic and viscoelastic stress contributions of blood rouleaux, creating the Enhanced Structural Stress Thixotropic Viscoelastic (ESSTV) variant; and b) the casting of ETV or ESSTV in full tensor form, leading to the  $\tau$ -ETV and  $\tau$ -ESSTV models [20,22]. This small change has vastly improved both the fitting and predictive capability of these TEVP models. Our modeling approach is as follows: first fitting several model parameters to steady state then simultaneously fitting the remaining parameters via three step-up and three step-down shear rate tests. With the tensorial versions of the models all the parameters are fit together. We then have used the full set of model parameters to gauge a model's efficacy by predictions of small, large and uni-directional oscillatory shear flow. The parameters are fit with a parallel tempering algorithm, in Matlab using the data directly from the rheometer. All our tactics, techniques and procedures for obtaining the rheological data and fitting the parameters can be found here [23-32].

With best parameters for each donor, along with the physiological data from the labs, one can construct a correlation matrix to analyze correlations of significance. This informs how the hematocrit, fibrinogen, cholesterol, etc. effect the mechanical properties of human blood and whether this is significant. From here the oscillatory shear flow is analyzed to separate the elastic and viscous signature. At the high strain amplitudes typically, blood is completely liquified, and this has been corroborated with a decrease in the elasticity, as observed with the transient elastic modulus. The transient moduli are computed via Series of Physical Processes (SPP), whereby the instantaneous partial derivative of strain with respect stress at each data point is the elastic transient modulus, and the instantaneous partial derivative of shear rate with respect to stress at each data point is the viscous transient modulus. These values are determined using the Frenet-Serret framework [33].

Overall, the parameterization of the rheological models with more accurate fitting and predictive capability and mechanical analysis with SPP allows for more detailed, and deeper rheological characterization of human blood [33]. These methodologies incorporated together will allow for a more nuanced understanding of and explanation of the interactions of the evolving rouleaux with the overall mechanical signatures both elastic and viscous of human blood.

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