Non-Newtonian Rheology in Blood
Circulation

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Abstract

Blood is a complex suspension that demonstrates several non-Newtonian rheological characteristics such as deformation-rate dependency, viscoelasticity and yield stress. In this paper we outline some issues related to the non-Newtonian effects in blood circulation system and present modeling approaches based mostly on the past work in this field.

Keywords: hemorheology; hemodynamics; blood properties; biorheology; circulatory system; fluid dynamics; non-Newtonian; shear thinning; yield stress; viscoelasticity; thixotropy.
1 Introduction

Blood is a heterogeneous multi-phase mixture of solid corpuscles (red blood cells, white blood cells and platelets) suspended in a liquid plasma which is an aqueous solution of proteins, organic molecules and minerals. The rheological characteristics of blood are determined by the properties of these components and their interaction with each other as well as with the surrounding structures. The blood rheology is also affected by the external physical conditions such as temperature; however, in living organisms in general, and in large mammals in particular, these conditions are regulated and hence they are subject to minor variations that cannot affect the general properties significantly [1]. Other physical properties, such as mass density, may also play a role in determining the blood overall rheological conduct. The rheological properties of blood and blood vessels are affected by the body intake of fluids, nutrients and medication [2–5], although in most cases the effect is not substantial except possibly over short periods of time and normally does not have lasting consequences.

The viscosity of blood is determined by several factors such as the viscosity of plasma, hematocrit level, blood cell distribution, and the mechanical properties of blood cells [6–8]. The blood viscosity is also affected by the applied deformation forces, extensional as well as shearing, and the ambient physical conditions. While the plasma is essentially a Newtonian fluid, the blood as a whole behaves as a non-Newtonian fluid showing all signs of non-Newtonian rheology which includes deformation rate dependency, viscoelasticity, yield stress and thixotropy. Most non-Newtonian effects originate from the red blood cells due to their high concentration and distinguished mechanical properties such as elasticity and ability to aggregate forming three-dimensional structures at low deformation rates [1, 9].

Deep understanding of the blood rheology, which includes its non-Newtonian characteristics, is important for both diagnosis and treatment. Looking into the
existing biological literature and comparing to the non-biological literature, such as earth science studies, it is obvious that the non-Newtonian phenomena in the blood circulation has not been given sufficient attention in the biological studies. One reason is the complexity of the biological systems which makes the consideration of non-Newtonian effects in blood circulation more difficult to handle. Hence, to simplify the flow models and their computational implementation, blood is generally assumed Newtonian and these effects are ignored. The obvious difficulties in observation, experimentation and measurement related to \textit{in vivo} blood flow add another complicating factor. Moreover, apart from some rare and extreme pathological states, the non-Newtonian effects in blood flow are relatively mild as compared to the non-Newtonian effects exhibited by typical polymeric systems for instance. This makes the approximation of blood as a Newtonian fluid an acceptable assumption and not far from reality in a significant part of the circulatory system under normal conditions.

Many theoretical, numerical, experimental and clinical studies of non-Newtonian effects in blood circulation have been conducted in the last few decades. However, there is no general approach in tackling this problem in a systematic way based on a unified vision. Almost all the past studies focus on individual problems and deal with the existing non-Newtonian phenomena within a limited local context. The current study, which is basically a brief overview of this subject, is trying to deal with the non-Newtonian blood rheology in general as applied to all levels of the circulation system.

2 Non-Newtonian Characteristics

As indicated already, blood is a complex non-Newtonian fluid showing various signs of non-Newtonian rheology such as shear thinning [10], yield stress [7, 11–15] and viscoelasticity [1, 12, 13, 16–19]. The blood is also characterized by a distinctive
thixotropic behavior [9, 20] revealed by the appearance of hysteresis loops during shearing cycles [20–22]. These non-Newtonian properties do not affect the flow patterns inside the flow paths and the fluid transportation only but they also affect the mechanical stress on the blood vessel walls and the surrounding tissues [23] especially in cases of irregular lumen geometry like stenosed arteries [24–26]. The mechanical stress on the vessel wall and tissue is not only important for its direct mechanical impact, especially when sustained over long periods of time, but it can also contribute to the commencement and advancement of long term lesions such as forming sediments inside the vessel wall [27]. The non-Newtonian properties, like viscoelasticity, have also an impact on other transport phenomena such as pulse wave propagation in arteries [17].

Non-Newtonian effects in general are dependent on the magnitude of deformation rates and hence they can exist or be enhanced at certain flow regimes such as low shear rates [19, 28]. The non-Newtonian effects are also influenced by the type of deformation, being shear or elongation [15]. The impact of the non-Newtonian effects can be amplified by a number of factors such as pathological blood rheology and flow in stenosed vessels and stents [29–32]. An interesting finding of one study [33] is that although flow resistance and wall shear stress increases as the size of stenosis increases for a given rheological model, the non-Newtonian nature of blood acts as a regulating factor to reduce the resistance and stress and hence contribute to the body protection. In this context, shear thinning seems to have the most significant role in facilitating blood flow through stenotic vessels.

Blood is a predominantly shear thinning fluid, especially under steady flow conditions, and this property has the most important non-Newtonian impact [7, 19, 23, 34]. Shear thinning is not a transient characteristics; moreover it is demonstrated at most biological flow rates [34] although it is more pronounced at low deformation regimes. Shear thinning rheology arises from disaggregation of the
red blood cells with increasing shear rate [35]. This same reason is behind the observed thixotropic blood behavior as shearing forces steadily disrupt the structured aggregation of blood cells with growing deformation time. The origin of other non-Newtonian effects can also be traced back to the blood microstructure as will be discussed next.

The viscoelastic nature of blood basically arises from its corpuscular microstructure. Viscoelastic properties originate from the red blood cells, which are distinguished by their pronounced elastic deformability [35, 36] associated with the ability to aggregate forming three-dimensional structures known as rouleaux [29]. The aggregation is mostly demonstrated at low shear rates and hence non-Newtonian behavior in general and viscoelasticity in particular are more pronounced at these regimes of low deformation [1, 6, 37]. The viscoelastic effects are magnified, if not activated, by the pulsatile nature of blood flow. The viscoelastic effects in blood circulation should not be limited to the viscoelastic properties of the blood itself but also to the viscoelastic (or elastic depending on the adopted model) properties of the blood vessels and the porous tissue through which the blood is transported [38]. This can be justified by the fact that all these effects are manifested by the blood circulation and hence they participate, affect and affected by the circulation process. An interaction between the viscoelastic behavior of blood with that of the vessel wall and porous tissue is unavoidable consequence.

Blood also demonstrates yield stress although there is a controversy about this issue [1, 24]. Yield stress arises from the aggregation of red blood cells at low shear rates to form the above-mentioned three-dimensional micro-structures (rouleaux) that resist the flow [1, 7, 39]. Studies have indicated that yield stress is positively correlated to the concentration of fibrinogen protein in blood plasma and to the hematocrit level [16, 24, 36, 40]. Other factors, such as the concentration of minerals, should also have a contribution. Many of the blood rheological characteristics
in general, and non-Newtonian in particular, are also controlled or influenced by the fibrinogen level [39]. The yield stress characteristic of blood seems to vanish or become negligible when hematocrit level falls below a critical value [16]. Yield stress contributes to the blood clotting following injuries and subsequent healing, and may also contribute to the formation of blood clots (thrombosis) and vessel blockage in some pathological cases such as strokes. The value of yield stress, as reported in a number of clinical and experimental studies, seems to indicate that it is not significant and hence it has no tangible effect on the flow profile (and hence flow rate) at the biological flow ranges in large and medium size blood vessels [24]. However, it should have more significant impact in the minute capillaries and some porous structures where flow at very low shear rates occurs. The magnitude of yield stress and its effect could be aggravated by certain diseased states related to the rheology of blood, like polycythemia vera, or the structure of blood vessels such as stenoses.

As a shear thinning fluid, blood is also characterized by a thixotropic behavior, which is confirmed experimentally by a number of studies [9], due to the intimate relation between these two non-Newtonian properties [22]. This may also explain a possible controversy about the thixotropic nature of blood [41] as the thixotropic-like behavior may be explained by other non-Newtonian characteristics of blood. Despite the fact that thixotropy is a transient property, due to the pulsative nature of the blood flow the thixotropic effects may have long term impact on the blood circulation. This equally applies to the time-dependent effects of viscoelasticity. Thixotropy is more pronounced at low shear rates with a long time scale. The effect, however, seem to have a less important role in blood flow than other non-Newtonian effects such as shear thinning [34], and this could partly explain the limited amount of studies dedicated to this property. The thixotropic behavior of blood is very sensitive to the blood composition and hence it can demonstrate big
variations between different individuals and under different biological conditions [9].

It should be remarked that time dependent effects in general, whether thixotropic or viscoelastic in nature or of any other type, should be expected in the flow of blood due to a number of reasons. One reason is the pulsatility of blood flow and the rapid change in the deformation conditions during the systolic-diastolic cardiac cycle. Another reason is the rapid change in the shear magnitude between one part of the system to another part, i.e. high shear rate in the arteries to lower shear rates in the capillaries, porous tissue and venous part [42]. A third reason is the irregular shape, such as bends and converging-diverging formations, of the blood flow conduits [43, 44] which activates or accentuates time-dependent effects. A fourth reason is the difference in the deformation rates between the ventricular systole and diastole. The last reason may explain the indication of one study [7] that the non-Newtonian effects are more important at diastole than systole since the shear rates during diastole are expected to be lower than those at systole.

Another remark is that most of the reported non-Newtonian rheological parameters, as well as many other physical properties of blood, are obtained from in vitro measurements and hence they are subject to significant errors as an indicator to the in vivo values due to the difference in ambient conditions as well as the experimental requirements and procedures, such as using additives to preserve and fluidize the blood samples, that can introduce significant variations on the blood properties. Moreover, the reported values could be highly dependent on the measurement method [8]. The differences between the individual subjects and their conditions like dietary intake prior to measurement [3], most of which are difficult to control or quantify, should add to the uncertainties and fluctuations. Hence, most of these values should be considered with caution especially when used for in vivo and patient-specific modeling and investigation.
3 Modeling non-Newtonian Effects

Blood is a complex non-Newtonian fluid and hence reliable modeling of blood flow in the circulation system should take into account its non-Newtonian characteristics. Several non-Newtonian rheological models have been used to describe the blood rheology; these models include Carreau-Yasuda [7, 10, 23, 25, 45–53], Casson [4, 7, 8, 13, 16, 24, 28, 32, 33, 40, 49, 53–55], power law [1, 7, 19, 25, 33, 53, 56], Cross [47–49, 53, 57], Herschel-Bulkley [8, 26, 51, 58, 59], Oldroyd-B [1, 35, 37, 60], Que-mada [4, 49, 53, 61], Yeleswarapu [50, 52, 62], Bingham [24], Jeffrey [63], Eyring-Powell [64], and Ree-Eyring [4]. Other less known fluid models [30] have also been used to describe the rheology of blood. A quick inspection of the blood literature reveals that the most popular models in non-Newtonian hemorheologic and hemodynamic modeling are Carreau-Yasuda and Casson.

Blood is also modeled as a Newtonian fluid [1, 25, 28, 56] which is a good approximation in many circumstances such as the flow in large vessels at medium and high shear rates under non-pathological conditions [55]. As there is no sudden transition from non-Newtonian to Newtonian flow as a function of shear rate, there is no sharply-defined critical limit for such a transition [62] and hence this remains a matter of choice which depends on a number of objective and subjective factors. However, there seems to be a general consensus that the shear rate range for which non-Newtonian effects are considered significant is \( \lesssim 100 \text{ s}^{-1} \) [6, 24, 39, 53, 56]; above this limit the blood is generally treated as a Newtonian liquid.

No single model, Newtonian or non-Newtonian, can capture all the features of the blood complexities [62] and hence different models are used to represent different characteristics of the blood rheology. These models, whether Newtonian or non-Newtonian, obviously have significant differences and hence they can produce very different results [50, 52, 57]. The results also differ significantly between Newtonian and non-Newtonian models in most cases [48, 53]. The non-Newtonian
models vary in their complexity and ability to capture different physical phenomena.

Diverse methods have been used in modeling and simulating non-Newtonian effects in blood rheology; these include analytical [13, 26, 59, 63], stochastic [32, 55, 65–67], and numerical mesh methods; such as finite element [23, 38, 46, 57, 68], finite difference [24, 30, 31, 37, 52, 60], finite volume [1, 7, 28, 47, 48, 52, 53], and spectral collocation methods [37, 60].

As indicated previously, most, if not all, non-Newtonian characteristics arise from the blood microstructure and particularly the concentration, distribution and mechanical properties of the red blood cells. For example, the viscoelastic properties of blood originate from the mechanical properties of the suspended cells and their capability of elastic deformation and structural formation, while the thixotropic properties arise from steady disaggregation of blood cells over prolonged shearing time. Interestingly, the majority of the rheological models used to describe the blood rheology are bulk phenomenological models of empirical nature with little consideration, if any, to its highly influential micro-structure. Hence, more structurally-based models, such as those based on molecular dynamics, are required to improve the description and modeling of the blood rheological behavior.

4 Non-Newtonian Effects in Circulation Subsystems

Because the impact of the non-Newtonian effects is highly dependent on the shape and size of the flow conduits, different non-Newtonian rheological behavior, and hence different flow modeling approaches, should apply to the different parts of the circulatory system. Different approaches are also required because of the difference in the nature of the blood transportation processes in these parts, such as large
scale bulk flow in the large vessels as opposite to perfusion or diffusion in the porous tissue.

We can identify three types of circulatory subsystems in which non-Newtonian effects should be analyzed and modeled differently: large blood vessels which mainly apply to arteries and veins, small blood vessels which broadly include capillaries and possibly arterioles, and porous tissue such as the myocardium and muscles in general. The distinction between large and small vessels is not clear cut as it depends on the nature of the flow phenomenon under consideration and the associated circumstances. However, the distinctive feature that should be used as a criterion to differentiate between these two categories of blood vessels in this context is the validity of the continuum approximation as applied to the blood where in the large vessels this approximation is strictly held true while in the small vessels it approaches its limits as some non-continuum phenomena start to appear.

In the following subsections we outline general strategies for modeling non-Newtonian effects in the circulation subsystems.

4.1 Large Vessels

In large vessels, which include large cavities such as the ventricles and atria inside the myocardium as well as the large arteries and veins, the blood essentially behaves as a Newtonian fluid. One reason is that the blood in such large lumens and cavities is normally exposed to a relatively high shear rates and hence the non-Newtonian effects which are basically induced at low shear rates die out [35]. Also at this large scale the blood appears as a homogeneous continuum medium with diminishing effect of blood cell aggregation [45]. The interaction between the blood cells with their pronounced elastic properties is also minimal at this scale. However, in some pathological situations, non-Newtonian effects are important even in the big cavities and large vessels and therefore they should be considered in the flow
model. This may also be true in some non-pathological situations in which the non-Newtonian effects can be critical to the observed phenomena.

It should be remarked that the non-Newtonian effects in the venous part of the circulatory system should be more important than the arterial part due to the lower deformation rates in the former than the latter as this seems to be an accepted fact in the hemodynamic studies. However, we did not find a proper discussion about this issue in the available literature. The difference in the blood composition in these two parts; due for example to the difference in concentration of substances like nutrients, oxygen and metabolic wastes; should also affect the non-Newtonian rheology in these two subsystems and introduce more complications in modeling blood flow especially in large vessels. Like the previous issue, we did not find an explicit discussion to this issue in the available literature. Another remark is that certain parts of the large vessels network can contain spots of low shear rates such as bends and bifurcation junctions [7, 24] and hence non-Newtonian effects in large vessels could be significant in some cases where these spots play an exceptionally important role in the blood flow due to a diseased case for instance.

Several mathematical and computational models have been used to describe the flow of blood in large individual vessels. These models include the elastic one-dimensional Navier-Stokes and the rigid Hagen-Poiseuille for Newtonian fluids, as well as many other non-Newtonian rheological models such as Cross and Carreau-Yasuda, as discussed previously is section 3. The characteristics of blood flow in large single vessels are obtained from these mathematical models either analytically or numerically, e.g. through the use of finite element or finite difference techniques. Most of the employed non-Newtonian fluid models are generalized Newtonian models and hence they do not account for history-dependent elastic or thixotropic effects. Also, the analytical non-Newtonian models generally apply to rigid tubes only although there are some attempts in this context to extend Poiseuille flow to
4.1 Large Vessels

elastic vessels with non-Newtonian rheology [59]. Numerical methods may also be used to extend the non-Newtonian models to elastic vessels.

With regards to the flow in vascular networks of large vessels, the main models used to describe and simulate blood flow are the one-dimensional Navier-Stokes finite element model for elastic networks [69, 70] and the Hagen-Poiseuille model for rigid networks [71]. Both of these models are Newtonian although the second may be extended to Poiseuille-like non-Newtonian flow through the inclusion of time-independent non-Newtonian effects using a vessel-dependent non-Newtonian effective viscosity which is computed and updated iteratively to reach a consistent flow solution over the whole network [15, 72–74]. Based on a non-thorough inspection of the available literature, there seems to be no extension to the traditional one-dimensional Navier-Stokes distensible network model [69, 75, 76] to incorporate non-Newtonian effects. In fact we did not find serious attempts in the available literature to extend the Navier-Stokes equation in general (whether one-dimensional or multi-dimensional, for rigid or elastic conduits) to account for non-Newtonian effects, although there are attempts to incorporate non-Newtonian effects numerically into Navier-Stokes flow models [77, 78]. The Navier-Stokes equation with its nonlinearity is sufficiently complex to be solved for Newtonian flow in most cases let alone with the added complexities and nonlinearities introduced by the non-Newtonian rheology.

With regards to the one-dimensional Navier-Stokes distensible model for single vessels and networks, we propose two possible general approaches for extending this model to account for non-Newtonian effects. One approach is to accommodate these effects in the fluid viscosity as parameterized by the viscosity friction coefficient $\kappa$. A second possible approach is to incorporate these effects in the flow profile as described by the momentum flux correction factor $\alpha$ in the one-dimensional model [69, 70]. For the network, the second approach is based on
defining a vessel-dependent $\alpha$ field over the whole network. A similar viscosity field may also be required for the first approach as well.

4.2 Small Vessels

Non-Newtonian effects are generally more pronounced in small flow ducts, such as capillaries, than in large ducts like arteries due to several reasons such as the deterioration of the continuum assumption at small scales especially for complex dispersed systems like blood. In such vessels the continuum approximation reaches its limit and the effect of blood cell aggregation with their interaction with the vessel wall becomes pronounced. This activates the non-Newtonian rheological flow modes such as the induction of elastic effects which are associated with the elastic properties of the red blood cells and their structural formation. Also, the non-Newtonian effects of blood are more prominent at low shear rates which are the dominant flow regimes in the small vessels [49]. Hence non-Newtonian rheological effects should be considered in modeling, simulating and analyzing the flow of blood in small vessels.

4.3 Porous Tissue

The commonly used approach in modeling blood perfusion in living tissue is to treat the tissue as a spongy porous medium and employ Darcy law [22, 68, 79–82] which correlates the volumetric flow rate to the pressure gradient. There are several limitations in the Darcy flow model in general and in its application to the blood flow through biological tissue in particular, and hence remedies have been proposed and used to improve the model. Since this law is originally developed for the flow through rigid porous media, modified versions are normally used to account for elasticity as required for modeling biological tissue [68, 83]. Other limitations include neglecting edge effects and the restriction imposed by the laminar low
velocity assumption on which the Darcy flow is based. The former may be overcome by employing the boundary term in the Brinkman equation while the latter can be eliminated through the use of the Forchheimer model which incorporates a high-velocity inertial term [80].

Since Darcy law in its original formulation is based on the Newtonian flow assumptions, non-Newtonian rheology is generally ignored in the modeling of blood perfusion through porous tissue. There have been several extensions and modifications to the Darcy law to include non-Newtonian effects in the flow of fluids in general, and polymers in particular, through rigid non-biological porous media. These attempts include, for example, viscoelastic models [84–87], Herschel-Bulkley [88], power law [89, 90], Blake-Kozeny-Carman [91], as well as other non-Newtonian prototypes [92, 93]. Pore scale network modeling has also been used to accommodate various non-Newtonian effects; such as shear thinning, yield stress and viscoelasticity; in the flow of polymers through rigid porous media [14, 18, 72–74, 94–97]. Similarly, other computational techniques, such as stochastic lattice Boltzmann [98, 99], have been tried to simulate and investigate the non-Newtonian effects of the flow through rigid porous media in non-biological studies. However, it seems there is hardly any work on modeling the non-Newtonian effects in the blood flow through living tissues by incorporating these effects into the distensible Darcy flow model.

To conclude, non-Newtonian effects in the blood perfusion through porous tissue are not negligible in general due to the existence of fluid shearing and extensional forces which activate non-Newtonian rheology. As the deformation rates in this type of transportation is normally low, and considering the small size and tortuous converging-diverging shape of the porous space inside which the blood perfuses, non-Newtonian rheological effects are expected to be significant. Non-Newtonian rheological effects associated with other fluid transport phenomena,
such as diffusion, could be negligible in such porous space due to the absence of shearing and extensional forces as a result of lack of large scale fluid bulk movement in these micro- and nano-scale phenomena. However, the causes underlying the non-Newtonian rheology should affect these transport phenomena as well, although more serious investigations are required to reach any definite conclusion about these issues. The existing literature is, unfortunately, limited in this scope [100, 101].

5 Conclusions

Blood is essentially a non-Newtonian suspension. Its complex rheological non-Newtonian behavior is largely influenced by its microstructure which, through the essentially viscous water-based Newtonian plasma combined with the effect of aggregation, deformation and orientation of the suspended blood cells with their distinguished elastic and three-dimensional structural formation properties, can show diverse non-Newtonian effects at various shear rate regimes and through different flow conduit structures although these effects are more pronounced at certain flow regimes and in particular structures.

Blood rheological properties, and its mechanical characteristics in general, are affected by several factors such as the type and magnitude of deformation rate, hematocrit level and protein concentration. Because blood is a suspension, its properties can be strongly influenced by the shape and size of its flow conduits. The non-Newtonian effects of blood can be accentuated by certain pathological conditions such as hypertension and myocardial infarction.

Apart from some extreme diseased states where the non-Newtonian effects play an exceptionally important role in the fluid transport phenomena, the non-Newtonian effects are generally mild in the bulk flow of blood in large vessels. More important influence of non-Newtonian rheology occurs in the flow of blood through
small vessels and in the blood perfusion through porous tissue. Other transport phenomenain, like diffusion, which do not involve bulk flow associated with deformation forces of shearing or extensional type that activate non-Newtonian rheology, should not be affected directly by the non-Newtonian characteristics although the physical causes at the root of the non-Newtonian rheology should have an impact on these processes. More fundamental studies are required to reach specific conclusions about these issues.

Non-Newtonian rheology, such as viscoelasticity, of the blood vessel walls and the spongy porous tissue should also be considered as a contributor to the overall non-Newtonian behavior of blood circulation as these effects are both non-Newtonian and circulatory in nature like the ones demonstrated by the blood itself. The effect of fluid-structure interaction should also be included in analyzing, modeling and simulating of non-Newtonian effects in the blood circulation as it plays an important hemodynamic and hemorheologic role.
References

[1] T. Bodnár; A. Sequeira; M. Prosi. On the shear-thinning and viscoelastic effects of blood flow under various flow rates. *Applied Mathematics and Computation*, 217(11):5055–5067, 2011. 4, 5, 7, 10, 11

[2] K. Breithaupt-Grögler; M. Ling; H. Boudoulas; G.G. Belz. Protective Effect of Chronic Garlic Intake on Elastic Properties of Aorta in the Elderly. *Circulation*, 96:2649–2655, 1997. 4

[3] G.A. Vlastos; C.C. Tangney; R.S. Rosenson. Effects of hydration on blood rheology. *Clinical Hemorheology and Microcirculation*, 28(1):41–49, 2003. 4, 9

[4] A. Marcinkowska-Gapińska; J. Gapinski; W. Elikowski; F. Jaroszyk; L. Kubisz. Comparison of three rheological models of shear flow behavior studied on blood samples from post-infarction patients. *Medical & Biological Engineering & Computing*, 45(9):837–844, 2007. 4, 10

[5] J. Tripette; G. Loko; A. Samb; B.D. Gogh; E. Sewade; D. Seck; O. Hue; M. Romana; S. Diop; M. Diaw; K. Brudey; P. Bogui; F. Cissé; M.D. Hardy-Dessources; P. Connes. Effects of hydration and dehydration on blood rheology in sickle cell trait carriers during exercise. *American Journal of Physiology Heart and Circulatory Physiology*, 299(3):H908–H914, 2010. 4

[6] O.K. Baskurt; H.J. Meiselman. Blood Rheology and Hemodynamics. *Seminars in Thrombosis and Hemostasis*, 29(5):435–450, 2003. 4, 7, 10

[7] C. Fisher; J.S. Rossmann. Effect of Non-Newtonian Behavior on Hemodynamics of Cerebral Aneurysms. *Journal of Biomechanical Engineering*, 131(9):091004(1–9), 2009. 4, 5, 6, 7, 9, 10, 11, 13
[8] B-K. Lee; S. Xue; J. Nam; H. Lim; S. Shin. Determination of the blood viscosity and yield stress with a pressure-scanning capillary hemorheometer using constitutive models. *Korea-Australia Rheology Journal*, 23(1):1–6, 2011. 4, 9, 10

[9] L. Dintenfass. Thixotropy of Blood and Proneness to Thrombus Formation. *Circulation Research*, 11:233–239, 1962. 4, 6, 8, 9

[10] F.J.H. Gijsen; E. Allanic; F.N. van de Vosse; J.D. Janssen. The influence of the non-Newtonian properties of blood on the flow in large arteries: unsteady flow in a 90° curved tube. *Journal of Biomechanics*, 32(6):601–608, 1999. 5, 10

[11] E.W. Merrill; C.S. Cheng; G.A. Pelletier. Yield stress of normal human blood as a function of endogenous fibrinogen. *Journal of Applied Physiology*, 26(1):1–3, 1969. 5

[12] G.B. Thurston. Viscoelasticity of Human Blood. *Biophysical Journal*, 12(9):1205–1217, 1972. 5

[13] C.L. Morris; C.M. Smith II; P.L. Blackshear Jr. A new method for measuring the yield stress in thin layers of sedimenting blood. *Biophysical Journal*, 52(2):229–240, 1987. 5, 10, 11

[14] T. Sochi. Modelling the Flow of Yield-Stress Fluids in Porous Media. *Transport in Porous Media*, 85(2):489–503, 2010. 5, 16

[15] T. Sochi. Non-Newtonian Flow in Porous Media. *Polymer*, 51(22):5007–5023, 2010. 5, 6, 14

[16] E.W. Merrill. Rheology of Blood. *Physiological Reviews*, 49(4):863–888, 1969. 5, 7, 8, 10
[17] Y. Da kang; Y. Yu-bing; L. Zhao-rong. The effects of blood viscoelasticity on the pulse wave in arteries. *Applied Mathematics and Mechanics*, 21(9):1058–1065, 2000. 5, 6

[18] T. Sochi. Pore-scale modeling of viscoelastic flow in porous media using a Bautista-Manero fluid. *International Journal of Heat and Fluid Flow*, 30(6):1202–1217, 2009. 5, 16

[19] R. Revellin; Fr. Rousset; D. Baud; J. Bonjour. Extension of Murray’s law using a non-Newtonian model of blood flow. *Theoretical Biology and Medical Modelling*, 6:1–9, 2009. 5, 6, 10

[20] C.R. Huang; W. Fabisiak. Thixotropic parameters of whole human blood. *Thrombosis Research*, 8:1–8, 1976. 6

[21] H.A. Barnes. Thixotropy – a review. *Journal of Non-Newtonian Fluid Mechanics*, 70(1):1–33, 1997. 6

[22] T. Sochi. Flow of Non-Newtonian Fluids in Porous Media. *Journal of Polymer Science Part B*, 48(23):2437–2467, 2010. 6, 8, 15

[23] J. Chen; X-Y. Lu; W. Wang. Non-Newtonian effects of blood flow on hemodynamics in distal vascular graft anastomoses. *Journal of Biomechanics*, 39:1983–1995, 2006. 6, 10, 11

[24] Z. Lou; W.J. Yang. A computer simulation of the non-Newtonian blood flow at the aortic bifurcation. *Journal of Biomechanics*, 26(1):37–49, 1993. 6, 7, 8, 10, 11, 13

[25] B. Liu; D. Tang. Non-Newtonian Effects on the Wall Shear Stress of the Blood Flow in Stenotic Right Coronary Arteries. *International Conference on Computational & Experimental Engineering and Sciences*, 17(2):55–60, 2011. 6, 10
[26] J.C. Misra; S. Maiti. Peristaltic Pumping of Blood Through Small Vessels of Varying Cross-Section. Journal of Applied Mechanics, 79(6):061003–061021, 2012. 6, 10, 11

[27] A.T. Golpayeghani; S. Najarian; M.M. Movahedi. Numerical simulation of pulsatile flow with Newtonian and non-Newtonian behavior in arterial stenosis. Iranian Cardiovascular Research Journal, 1(3):167–174, 2008. 6

[28] Y. Fan; W. Jiang; Y. Zou; J. Li; J. Chen; X. Deng. Numerical simulation of pulsatile non-Newtonian flow in the carotid artery bifurcation. Acta Mechanica Sinica, 25(2):249–255, 2009. 6, 10, 11

[29] J.F. Stoltz. Hemorheology: pathophysiological significance. Acta Médica Portuguesa, 6(7-8):S4–S13, 1985. 6, 7

[30] T. Ishikawa; L. F.R. Guimaraes; S. Oshima; R. Yamane. Effect of non-Newtonian property of blood on flow through a stenosed tube. Fluid Dynamics Research, 22:251–264, 1998. 6, 10, 11

[31] M.S. Mandal; S. Mukhopadhyay; G.C. Layek. Pulsatile flow of shear-dependent fluid in a stenosed artery. Theoretical and Applied Mechanics, 39(3):209–231, 2012. 6, 11

[32] C. Huang; Z. Chai; B. Shi. Non-Newtonian Effect on Hemodynamic Characteristics of Blood Flow in Stented Cerebral Aneurysm. Communications in Computational Physics, 13(3):916–928, 2013. 6, 10, 11

[33] J.B. Shukla; R.S. Parihar; B.R.P. Rao. Effects of stenosis on non-Newtonian flow of the blood in an artery. Bulletin of Mathematical Biology, 42(3):283–294, 1980. 6, 10

[34] P.K. Mandal. An unsteady analysis of non-Newtonian blood flow through
tapered arteries with a stenosis. *International Journal of Non-Linear Mechanics*, 40(1):151–164, 2005. 6, 8

[35] K. Perktold; G. Karner; A. Leuprecht; M. Hofer. Influence of non-Newtonian Flow Behavior on Local Hemodynamics. *Journal of Applied Mathematics and Mechanics*, 79(S1):187–190, 1999. 7, 10, 12

[36] K.M. Hell; A. Balzereit; U. Diebold; H.D. Bruhn. Importance of blood viscoelasticity in arteriosclerosis. *Angiology*, 40(6):539–546, 1989. 7

[37] G. Pontrelli. Blood flow through a circular pipe with an impulsive pressure gradient. *Mathematical Models and Methods in Applied Sciences*, 10(2):187, 2000. 7, 10, 11

[38] S. Čanić; C.J. Hartley; D. Rosenstrauch; J. Tambača; G. Guidoboni; A. Mikelić. Blood Flow in Compliant Arteries: An Effective Viscoelastic Reduced Model, Numerics, and Experimental Validation. *Annals of Biomedical Engineering*, 34(4):575–592, 2006. 7, 11

[39] R.L. Replogle; H.J. Meiselman; E.W. Merrill. Clinical implications of blood rheology studies. *Circulation*, 36(1):148–160, 1967. 7, 8, 10

[40] C.L. Morris; D.L. Rucknagel; R. Shukla; R.A. Gruppo; C.M. Smith; P. Blackshear Jr. Evaluation of the yield stress of normal blood as a function of fibrinogen concentration and hematocrit. *Microvascular Research*, 37(3):323–338, 1989. 7, 10

[41] P. Davenport; S. Roath. Blood thixotropy. *Journal of Clinical Pathology*, 34(1):106–107, 1981. 8

[42] C. Alonso; A.R. Pries; P. Gaetgens. Time-dependent rheological behavior of blood at low shear in narrow vertical tubes. *American Journal of Physiology - Heart and Circulatory Physiology*, 265(2):H553–H561, 1993. 9
REFERENCES

[43] T. Sochi. The flow of power-law fluids in axisymmetric corrugated tubes. *Journal of Petroleum Science and Engineering*, 78(3-4):582–585, 2011. 9

[44] T. Sochi. Newtonian Flow in Converging-Diverging Capillaries. *International Journal of Modeling, Simulation, and Scientific Computing*, 2013. DOI: 10.1142/S1793962313500116. 9

[45] F.J.H. Gijsen; F.N. van de Vosse; J.D. Janssen. Wall shear stress in backward-facing step flow of a red blood cell suspension. *Biorheology*, 35(4-5):263–279, 1998. 10, 12

[46] F.M.A. Box; R.J. van der Geest; M.C.M. Rutten; J.H.C. Reiber. The Influence of Flow, Vessel Diameter, and Non-Newtonian Blood Viscosity on the Wall Shear Stress in a Carotid Bifurcation Model for Unsteady Flow. *Investigative Radiology*, 40(5):277–294, 2005. 10, 11

[47] A. Jonášová; J. Vimmr. Numerical simulation of non-Newtonian blood flow in bypass models. *Proceedings in Applied Mathematics and Mechanics, 79th Annual Meeting of the International Association of Applied Mathematics and Mechanics, Bremen 2008*, 8(1):10179–10180, 2008. 10, 11

[48] J. Vimmr; A. Jonášová. On the Modelling of Steady Generalized Newtonian Flows in a 3D Coronary Bypass. *Engineering Mechanics*, 15(3):193–203, 2008. 10, 11

[49] Y.H. Kim; P.J. VandeVord; J.S. Lee. Multiphase non-Newtonian effects on pulsatile hemodynamics in a coronary artery. *International Journal for Numerical Methods in Fluids*, 58(7):803–825, 2008. 10, 15

[50] M. Lukáčová-Medviďová; A. Zaušková. Numerical modelling of shear-thinning non-Newtonian flows in compliant vessels. *International Journal for Numerical Methods in Fluids*, 56(8):1409–1415, 2008. 10
REFERENCES

[51] D.S. Sankar; A.I.Md. Ismail. Two-Fluid Mathematical Models for Blood Flow in Stenosed Arteries: A Comparative Study. *Boundary Value Problems*, 2009:1–15, 2009. 10

[52] A. Hundertmark-Zaušková; M. Lukáčová-Medvid’ová. Numerical study of shear-dependent non-Newtonian fluids in compliant vessels. *Computers & Mathematics with Applications*, 60(3):572–590, 2010. 10, 11

[53] M.M. Molla; M.C. Paul. LES of non-Newtonian physiological blood flow in a model of arterial stenosis. *Medical Engineering & Physics*, 34(8):1079–1087, 2012. 10, 11

[54] B. Das; P.C. Johnson; A.S. Popel. Computational fluid dynamic studies of leukocyte adhesion effects on non-Newtonian blood flow through microvessels. *Biorheology*, 37(3):239–258, 2000. 10

[55] J. Boyd; J.M. Buick; S. Green. Comparison of Newtonian and Non-Newtonian Oscillatory Flows Using the Lattice Boltzmann Method. *World Congress on Medical Physics and Biomedical Engineering, IFMBE Proceedings*, 14:3395–3399, 2007. 10; 11

[56] B.M. Johnston; P.R. Johnston; S. Corney; D. Kilpatrick. Non-Newtonian blood flow in human right coronary arteries: transient simulations. *Journal of Biomechanics*, 39(6):1116–1128, 2006. 10

[57] F. Abraham; M. Behr; M. Heinkenschloss. Shape optimization in steady blood flow: A numerical study of non-Newtonian effects. *Computer Methods in Biomechanics and Biomedical Engineering*, 8(2):127–137, 2005. 10, 11

[58] A. Valencia; A. Zarate; M. Galvez; L. Badilla. Non-Newtonian blood flow dynamics in a right internal carotid artery with a saccular aneurysm. In-
ternational Journal for Numerical Methods in Fluids, 50(6):751–764, 2006.

[59] K. Vajravelu; S. Sreenadh; P. Devaki; K.V. Prasad. Mathematical model for a Herschel-Bulkley fluid flow in an elastic tube. Central European Journal of Physics, 9(5):1357–1365, 2011. 10, 11, 14

[60] G. Pontrelli. Pulsatile blood flow in a pipe. Computers & Fluids, 27(3):367–380, 1998. 10, 11

[61] B. Das; G. Enden; A.S. Popel. Stratified multiphase model for blood flow in a venular bifurcation. Annals of Biomedical Engineering, 25(1):135–153, 1997. 10

[62] F. Yilmaz; M.Y. Gundogdu. A critical review on blood flow in large arteries; relevance to blood rheology, viscosity models, and physiologic conditions. Korea-Australia Rheology Journal, 20(4):197–211, 2008. 10

[63] N.S. Akbar; S. Nadeem. Simulation of Variable Viscosity and Jeffrey Fluid Model for Blood Flow Through a Tapered Artery with a Stenosis. Communications in Theoretical Physics, 57(1):133–140, 2012. 10, 11

[64] J. Zueco; O.A. Bég. Network numerical simulation applied to pulsatile non-Newtonian flow through a channel with couple stress and wall mass flux effects. International Journal of Applied Mathematics and Mechanics, 5(2):1–16, 2009. 10

[65] R. Ouared; B. Chopard. Lattice Boltzmann Simulations of Blood Flow: Non-Newtonian Rheology and Clotting Processes. Journal of Statistical Physics, 121(1-2):209–221, 2005. 11

[66] S.C. Fu; W.W.F. Leung; R.M.C. So. A lattice Boltzmann and immersed
boundary scheme for model blood flow in constricted pipes: Part 1 - steady flow. *Communications in Computational Physics*, 14(1):126–152, 2013.

[67] S.C. Fu; W.W.F. Leung; R.M.C. So. A lattice Boltzmann and immersed boundary scheme for model blood flow in constricted pipes: Part 2 - pulsatile flow. *Communications in Computational Physics*, 14(1):153–173, 2013.

[68] D. Chapelle; J.F. Gerbeau; J. Sainte-Marie; I.E. Vignon-Clementel. A poroelastic model valid in large strains with applications to perfusion in cardiac modeling. *Computational Mechanics*, 46(1):91–101, 2010.

[69] T. Sochi. One-Dimensional Navier-Stokes Finite Element Flow Model. *arXiv:1304.2320*, 2013.

[70] T. Sochi. Flow of Navier-Stokes Fluids in Cylindrical Elastic Tubes. *Submitted*, 2013.

[71] T. Sochi. Comparing Poiseuille with 1D Navier-Stokes Flow in Rigid and Distensible Tubes and Networks. *Submitted*, 2013.

[72] T. Sochi. *Pore-Scale Modeling of Non-Newtonian Flow in Porous Media*. PhD thesis, Imperial College London, 2007.

[73] T. Sochi; M.J. Blunt. Pore-scale network modeling of Ellis and Herschel-Bulkley fluids. *Journal of Petroleum Science and Engineering*, 60(2):105–124, 2008.

[74] T. Sochi. Computational Techniques for Modeling Non-Newtonian Flow in Porous Media. *International Journal of Modeling, Simulation, and Scientific Computing*, 1(2):239–256, 2010.

[75] L. Formaggia; D. Lamponi; A. Quarteroni. One-dimensional models for blood
flow in arteries. *Journal of Engineering Mathematics*, 47(3/4):251–276, 2003.

[76] S.J. Sherwin; V. Franke; J. Peiró; K. Parker. One-dimensional modelling of a vascular network in space-time variables. *Journal of Engineering Mathematics*, 47(3-4):217–250, 2003. 14

[77] X.Y. Xu; M.W. Collins; C.J.H. Jones. A problem-oriented approach to the numerical modelling of haemodynamic problems. *Advances in Engineering Software*, 28(6):365–377, 1997. 14

[78] V. Prokop; K. Kozela. Numerical simulation of Newtonian and non-Newtonian flows in bypass. *Mathematics and Computers in Simulation*, 80(8):1725–1733, 2010. 14

[79] J.M. Huyghe; T. Arts; D.H. van Campen; R.S. Reneman. Porous medium finite element model of the beating left ventricle. *American Journal of Physiology Heart and Circulatory Physiology*, 262(4):H1256–H1267, 1992. 15

[80] A.-R.A. Khaled; K. Vafai. The role of porous media in modeling flow and heat transfer in biological tissues. *International Journal of Heat and Mass Transfer*, 46(26):4989–5003, 2003. 15, 16

[81] O. Coussy. *Poromechanics*. John Wiley & Sons Ltd, 1st edition, 2004. 15

[82] O. Coussy. *Mechanics and Physics of Porous Solids*. John Wiley & Sons Ltd, 1st edition, 2010. 15

[83] W.J. Vankan; J.M. Huyghe; J.D. Janssen; A. Huson; W.J.G. Hacking; W. Schreiner. Finite element analysis of blood flow through biological tissue. *International Journal of Engineering Science*, 35(4):375–385, 1997. 15
REFERENCES

[84] T.J. Sadowski; R.B. Bird. Non-Newtonian flow through porous media I. Theoretical. Transactions of the Society of Rheology, 9(2):243–250, 1965. 16

[85] W.B. Gogarty; G.L. Levy; V.G. Fox. Viscoelastic effects in polymer flow through porous media. SPE 47th Annual Fall Meeting, 8-11 October, San Antonio, Texas, SPE 4025, 1972. 16

[86] M.L. De Haro; J.A.P. Del Río; S. Whitaker. Flow of Maxwell fluids in porous media. Transport in Porous Media, 25(2):167–192, 1996. 16

[87] A.A. Garrouch. A Viscoelastic model for polymer flow in reservoir rocks. SPE Asia Pacific Oil and Gas Conference and Exhibition, 20-22 April, Jakarta, Indonesia, SPE 54379, 1999. 16

[88] T.F. Al-Fariss; K.L. Pinder. Flow of a shear-thinning liquid with yield stress through porous media. SPE 13840, 1984. 16

[89] A. Fadili; P.M.J. Tardy; J.R.A. Pearson. A 3D filtration law for power-law fluids in heterogeneous porous media. Journal of Non-Newtonian Fluid Mechanics, 106(2):121–146, 2002. 16

[90] M.A. Al-Nimr; T.K. Aldoss. The effect of the macroscopic local inertial term on the non-Newtonian fluid flow in channels filled with porous medium. International Journal of Heat and Mass Transfer, 47(1):125–133, 2004. 16

[91] W. Kozicki; C. Tiu. A unified model for non-Newtonian flow in packed beds and porous media. Rheologica Acta, 27(1):31–38, 1988. 16

[92] L. Kondic; P. Palffy-Muhoray; M.J. Shelley. Models of non-Newtonian Hele-Shaw flow. Physical Review E, 54(5):R4536–R4539, 1996. 16

[93] L. Kondic; M.J. Shelley; P. Palffy-Muhoray. Non-Newtonian Hele-Shaw Flow
and the Saffman-Taylor Instability. *Physical Review Letters*, 80(7):1433–1436, 1998. 16

[94] K.S. Sorbie; P.J. Clifford; E.R.W. Jones. The Rheology of Pseudoplastic Fluids in Porous Media Using Network Modeling. *Journal of Colloid and Interface Science*, 130(2):508–534, 1989. 16

[95] X. Lopez. *Pore-scale modelling of non-Newtonian flow*. PhD thesis, Imperial College London, 2004. 16

[96] M.T. Balhoff. *Modeling the flow of non-Newtonian fluids in packed beds at the pore scale*. PhD thesis, Louisiana State University, 2005. 16

[97] C.L. Perrin; P.M.J. Tardy; S. Sorbie; J.C. Crawshaw. Experimental and modeling study of Newtonian and non-Newtonian fluid flow in pore network micromodels. *Journal of Colloid and Interface Science*, 295(2):542–550, 2006. 16

[98] E.S. Boek; J. Chin; P.V. Coveney. Lattice Boltzmann Simulation of the Flow of Non-Newtonian Fluids in Porous Media. *International Journal of Modern Physics B*, 17:99–102, 2003. 16

[99] S.P. Sullivan; L.F. Gladden; M.L. Johns. Simulation of power-law fluid flow through porous media using lattice Boltzmann techniques. *Journal of Non-Newtonian Fluid Mechanics*, 133(2-3):91–98, 2006. 16

[100] S. Kumar; S.N. Upadhyay. Laminar Flow Dissolution and Diffusion in Non-Newtonian Fluid. *Industrial & Engineering Chemistry Fundamentals*, 19(1):75–79, 1980. 17

[101] P.T. Cummings; B.Y. Wang; D.J. Evans; K.J. Fraser. Nonequilibrium molecular dynamics calculation of self-diffusion in a non-Newtonian fluid subject to
a Couette strain field. *Journal of Chemical Physics*, 94(3):2149–2158, 1991.