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1 **A fractional nonlocal approach to nonlinear blood flow in**
2 **small-lumen arterial vessels**

3 **Gioacchino Alotta · Mario Di Paola · Francesco**
4 **Paolo Pinnola · Massimiliano Zingales**

5
6 Received: date / Accepted: date

7 **Abstract** The behavior of human blood flowing in arteries is still an open topic for its
8 multi-phase nature and heterogeneity. In large arterial vessels the well-known Hagen-
9 Poiseuille law, which main assumption is that the blood is Newtonian, is considered
10 acceptable. In small arterial vessels, instead, this law does not reproduce experimen-
11 tal results that show non-parabolic profiles of velocity across the vessel diameter. For
12 capillary vessels the Casson model of fluids that is nonlinear is used in place the
13 Newton law, resulting in nonlinear governing equations and difficulties in mathemat-
14 ical manipulation. For these reasons an alternative approach is proposed in this paper.
15 Starting from the micro-mechanics of blood, the Hagen-Poiseuille model is enriched
16 with long-range interactions that simulate the interactions of non-adjacent fluid vol-
17 ume elements due to the presence of red blood cells and other dispersed cells in the
18 plasma. These nonlocal forces are defined as linearly dependent on the product of
19 the volumes of the considered elements and on their relative velocity. Moreover, as
20 the distance between two volume elements increases, the nonlocal forces are scaled
21 through an attenuation function; if this function is chosen as a power law of real
22 order of the distance between the volume elements, an operator related to the frac-
23 tional derivative of relative velocity appears in the resulting governing equation. It is

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1 shown that the fractional Hagen-Poiseuille law is able to reproduce experimentally
2 measured profiles of velocity with a great accuracy, moreover as the dimension of the
3 vessel increases, nonlocal forces become negligible and the proposed model reverts
4 to the classical Hagen-Poiseuille model.

5 **Keywords** Blood flow · nonlocal fluid · Mesoscale approach · fractional model

6 **1 Introduction**

7 The rheological behavior of blood has been investigated from the nineteenth century
8 and it is still an open debate. Indeed the characteristic of blood flow inside vessels
9 strongly affects stresses that are transmitted by the blood to the vessels themselves;
10 in a biomechanics context, stresses on the vessels may be determinant for some ar-
11 terial widespread diffused diseases such as aneurysm or for consequences of arterial
12 stenosis. For these reasons, analytical models capable to accurately predict the main
13 features of blood flow inside human arteries are essential in order to better understand
14 the mechanisms of appearance of aneurysms and consequence in blood supply down-
15 stream the aneurysm or a stenosis; moreover, an accurate description of blood flow
16 is essential in order to allow the definition of medical protocols able to predict the
17 evolution of an aneurysm on the basis of medical images. The first model for blood
18 flow inside arterial vessels is the well-known Hagen-Poiseuille (HP) law [1], derived
19 assuming Newtonian fluid and providing parabolic profile of velocity along the diam-
20 eter of a circular vessel; this model has proven to be reliable for large arterial vessels
21 [1,2]. For capillary arterial vessels experimentally measured profiles of velocity are
22 not parabolic [3], hence the HP model is not suitable for this kind of problem. In
23 the case of capillary vessels the Casson model is certainly more reliable of the HP;
24 this law considers a nonlinear relationship between shear stress and shear rate with
25 the introduction of the concept of yield stress of the fluid that leads to a nonlinear
26 governing equation and piece-wise profile of velocity across the vessel diameter. The
27 Casson law provides results in good agreement with experimental observations, how-
28 ever mathematical manipulations are not straightforward due to the nonlinearity and
29 the model is not obtained on physical evidences on the mechanics of blood flow. An
30 alternative and effective approach to nonlinear modeling of blood is represented by
31 the nonlocal approach.

32 Nonlocal mechanics, both in terms of gradients [4,5,6,7] or integrals [8,9,10] of the
33 state variables of the problem, has proved to be effective in modeling a wide range
34 of solid mechanics problems such as wave dispersion, shear bands as well as strain
35 localization in mechanical interfaces [11,12], but also to take into account for hetero-
36 geneity in the medium at hands. In the context of fluid mechanics, nonlocal theories
37 have been proposed to capture the motion of fluids in microvessels or in order to
38 perform efficient simulation of fluid with dispersion [13,14,15,16,17,18]. In the ap-
39 proaches available in literature, however, the nonlocal interactions are not constructed
40 on solid mechanical basis. For the above-mentioned reasons, in this paper an alter-
41 native mesoscale approach is proposed. The model is based on the HP law that is
42 enriched with nonlocal forces mutually exerted by non-adjacent fluid elements; these
43 forces are transmitted to relatively long distance by relatively large cells, mainly Red

1 Blood Cells (RBC). These long-range interactions are constructed as volume viscous
 2 forces scaled by an attenuation function that decreases the forces mutually exerted by
 3 two non-adjacent volume elements as the distance between them increases; the ap-
 4 proach is analogous of that successfully used in various micro/nanomechanics prob-
 5 lems [19,20,21,22,23,24]. As a consequence in the governing equation an integral
 6 representing these additional forces appears; it is shown that if the attenuation func-
 7 tion is chosen as a power law of the distance between two volume elements, the inte-
 8 gral representing non local forces is closely related to a fractional derivative operator
 9 [25,26] (or it is exactly a fractional derivative if unbounded domains are considered).
 10 The advantage of this formulation is that the governing equation remains linear and
 11 comparison with experimentally observed velocity profiles along capillary vessels di-
 12 ameter shows very good agreement, with lower root mean square error in comparison
 13 with Casson model. The model is able to automatically reverts to the classical Hagen-
 14 Poiseuille law when the vessel is not capillary, indeed as the diameter of the vessel
 15 increases nonlocal forces become negligible. Moreover it is shown that the model
 16 is able to numerically reproduce the shear thinning behavior of blood observed in
 17 rotating viscometer.

18 2 Governing equation of nonlocal flow

19 In this section the equations governing the fluid motion are briefly described. In Sec.
 20 2.1 the Navier-Stokes equations for Newtonian incompressible fluids are recalled,
 21 while in Sec. 2.2 the gradient and integral approaches to nonlocality are briefly de-
 22 scribed and finally the proposed mechanically based approach to nonlocality is intro-
 23 duced in Sec. 2.3.

24 2.1 Navier-Stokes equations (local)

25 The dynamic equilibrium of a generic fluid element is completely described by en-
 26 forcing the linear momentum balance and the balance of mass. The equation of the
 27 linear momentum balance, describing the dynamic equilibrium of a fluid element,
 28 may be written as follows:

$$\rho(\mathbf{x},t)\mathbf{f}(\mathbf{x},t) - \frac{D\rho(\mathbf{x},t)\mathbf{v}(\mathbf{x},t)}{Dt} + \text{div}\mathbf{T}(\mathbf{x},t) = 0 \quad (1)$$

29 where $\rho(\mathbf{x},t)$ is the density, $\mathbf{f}(\mathbf{x},t)$ is the volume forces vector, $\mathbf{v}(\mathbf{x},t)$ is the velocity
 30 vector, D/Dt is the total derivative operator, $\mathbf{T}(\mathbf{x},t)$ is the Cauchy stress tensor, \mathbf{x} is
 31 the position vector and t is the time. Eq. (1) is a set of three coupled partial differential
 32 equations in the unknown fields $\mathbf{v}(\mathbf{x},t)$, $\mathbf{T}(\mathbf{x},t)$ and $\rho(\mathbf{x},t)$; they describe the dynamic
 33 equilibrium along three mutually orthogonal directions.

34 To the purpose of solving the system in Eq. (1) the constitutive behavior of the fluid
 35 at hands must be introduced. In particular, the Navier-Stokes equation are related
 36 to incompressible Newtonian fluid. From the incompressibility hypothesis descends
 37 that $\rho(\mathbf{x},t) = \rho$. A Newtonian fluid is such that the deviatoric component of the stress

1 tensor is directly proportional to the strain rate tensor $\dot{\boldsymbol{\epsilon}}_D$ and for this reason the stress
2 tensor may be written as in the following:

$$\mathbf{T}(\mathbf{x}, t) = p(\mathbf{x}, t)\mathbf{I} + 2\mu\dot{\boldsymbol{\epsilon}}_D(\mathbf{x}, t) \quad (2)$$

3 where the first term of the rhs is the volumetric part of the stress tensor and the
4 second term is the deviatoric part, p is the pressure, \mathbf{I} is the identity matrix and μ
5 is the dynamic viscosity. The strain rate tensor $\dot{\boldsymbol{\epsilon}}_D$ may be written in terms of the
6 velocity field $\mathbf{v}(\mathbf{x}, t)$ by means of the compatibility equations as follows:

$$\dot{\epsilon}_{D,ij} = \frac{1}{2} \left(\frac{\partial v_i}{\partial x_j} + \frac{\partial v_j}{\partial x_i} \right) - \frac{\dot{\theta}}{3} \delta_{ij}; \quad i, j = 1, 2, 3; \quad (3)$$

7 being $\dot{\epsilon}_{D,ij}$ the element in the i -th row and the j -th column of $\dot{\boldsymbol{\epsilon}}_D$, v_i the i -th com-
8 ponent of the velocity vector, x_i the i -th axis in the coordinate system and $\dot{\theta}$ the
9 volumetric strain rate. By inserting Eq. (2) and Eq. (3) into Eq. (1) and taking into
10 account of the incompressibility condition the Navier-Stokes equations are obtained
11 in the following form:

$$\rho \frac{D\mathbf{v}(\mathbf{x}, t)}{Dt} - \nabla p(\mathbf{x}, t) - \mu \nabla^2 \mathbf{v}(\mathbf{x}, t) - \rho \mathbf{f}(\mathbf{x}, t) = 0 \quad (4)$$

12 in the unknown velocity field $\mathbf{v}(\mathbf{x}, t)$ and in the unknown pressure field $p(\mathbf{x}, t)$. In
13 order to obtain the solution, it is necessary to enforce the balance of mass that, for
14 incompressible fluids, reads:

$$\operatorname{div} \mathbf{v} = 0 \quad (5)$$

15 that is commonly known as *continuity equation*. Note that Eq. (5) has been also con-
16 sidered in the substitution of the compatibility equations inside the linear momentum
17 balance Eq. (1). The Navier-Stokes equations are the basis of the fluid mechanics,
18 however they are not satisfactory in describing multiphase or microstructured fluid
19 such as the blood. For this reason researchers of the field have made a great effort in
20 the last decades in order to formulate models capable to predict more accurately the
21 blood behavior.

22 2.2 Nonlocal models

23 In the last decades many nonlocal models have appeared in literature with appli-
24 cations both in the field of solid mechanics and in field of fluid mechanics. These
25 models may be subdivided into two main categories, that are gradient or weak non-
26 local models and integral or strong nonlocal models. We will briefly recall both kind
27 of nonlocal models in the following.

28 In gradient nonlocal models the stress tensor is the sum of the Cauchy stress and of
29 the second order gradient of the stress; the constitutive law may be written as follows:

$$\boldsymbol{\sigma}(\mathbf{x}, t) = \mathbf{T}(\mathbf{x}, t) - \nabla^2 \mathbf{T}(\mathbf{x}, t) l_c^2 \quad (6)$$

30 where $\boldsymbol{\sigma}(\mathbf{x}, t)$ is the total stress tensor, while $\nabla^2 \mathbf{T}(\mathbf{x}, t)$ is the so-called higher order
31 stress tensor that is the work conjugate of the strain gradient (for solid or strain rate

1 gradient for fluid) tensor that represents the nonlocal part of the stress tensor and l_c is
 2 a specific internal scale. Constitutive models of the type of Eq. (6) have been applied
 3 successfully in the study of many engineering problems, such as nonlocal effects,
 4 dislocation kinematics, the formation of shear bands and also during the plastic de-
 5 formations of metals and to eliminate singularities at dislocation lines and crack tips
 6 [27]. Mathematical manipulations in presence of the constitutive equation (6) is very
 7 cumbersome, then many authors have put their effort to obtain simplified formula-
 8 tions able to reproduce the same results of Eq. (6) (see for example [28]). Recently,
 9 microstructured fluid have been investigated in the context of gradient models of me-
 10 chanics [29] introducing a nonlocal model of Herschal-Bulkey relation that reads in
 11 our particular study:

$$\langle |t_{rz}| - l_c^2 \frac{d^2 |t_{rz}|}{dr^2} - \tau_0 \rangle = \mu^{1/n} |\dot{\gamma}_{rz}|^n \quad (7)$$

12 where $\langle x \rangle = \frac{x+|x|}{2}$ is the positive operator, n is a non-Newtonian dependence on the
 13 material flow rate, τ_0 is the initial yield stress, t_{rz} is the shear stress in the direction
 14 of the fluid flow (z), r is the radial coordinate and γ_{rz} is the shear strain. The flow
 15 transport equation in Eq. (7) is a nonlocal gradient generalization of linear nonlocal
 16 approach ([27]) with the introduction of a nonlocal stress as ($\tau_0 = 0$, $n = 1$):

$$t_{rz} - l_c^2 \frac{d^2 t_{rz}}{dr^2} - \tau_0 = \mu \dot{\gamma}_{rz} = \mu \frac{dv_z}{dr} \quad (8)$$

17 being v_z the velocity in the flow direction, that can be compared with the well-known
 18 stress gradient approaches to nonlocal solid mechanics in 1D reading [28]:

$$t_{rz}^{(l)} + t_{rz}^{(nl)} = E \gamma_{rz} \quad (9)$$

19 where E is the elastic modulus and the nonlocal stresses $t_{rz}^{(nl)} = -l_c^2 \frac{d^2 t_{rz}}{dr^2}$ is related
 20 to the local contribution by the second order gradient operator. The constitutive as-
 21 sumption in Eq. (8) may be considered in the balance equation to yield, upon the
 22 integration, the velocity profile of the microstructured fluid [14, 15, 29].

23 In integral models the equilibrium of a solid or fluid elements involves terms depend-
 24 ing on the integral over the domain of the strain (or strain rate for the case of fluid).
 25 The first to propose such a kind of strong nonlocal model was Eringen [8] regarding
 26 solid mechanics problems and many modifications appeared in literature after the pa-
 27 per [8] in order to adapt it to various engineering and physical problems. A general
 28 integral nonlocal model may be written as follows:

$$\boldsymbol{\sigma}(\mathbf{x}, t) = \mathbf{T}(\mathbf{x}, t) + \int_V g(\mathbf{x} - \boldsymbol{\xi}) \boldsymbol{\epsilon}(\boldsymbol{\xi}, t) d\boldsymbol{\xi} \quad (10)$$

29 where $g(\cdot)$ is the Kroner-Eringen attenuation function, \mathbf{x} and $\boldsymbol{\xi}$ are the positions of
 30 the interacting volume elements and $\boldsymbol{\epsilon}$ is the strain tensor. Eq. (10) is particularized
 31 for nonlocal elasticity. Integral approach to fluids nonlocality have been proposed in
 32 recent papers (see e.g. [18]) assuming that the relations among the shear stress and
 33 shear strain are of the type of Eq. (10) where the strain tensor $\boldsymbol{\epsilon}$ has been substi-
 34 tuted with the strain rate tensor $\boldsymbol{\epsilon}_D$. Examples of strong nonlocality applied to fluid

1 mechanics can be also found in [13,14,15]. Despite the wide diffusion of integral
 2 nonlocal elasticity and viscosity models, they show mathematical inconsistencies as
 3 bounded domains are considered [19]; indeed in this case the presence of nonlocal
 4 interactions involves the appearance of constitutive boundary conditions that violate
 5 the equilibrium [30].
 6 These considerations push toward a different approach to nonlocal viscosity model
 7 as proposed in the next sections.

8 2.3 Mechanically based nonlocality

9 In the last years the authors of the present paper developed an alternative approach
 10 to nonlocal models described above for nonlocal-elasticity [19,21,22,23,24]. In this
 11 approach, the nonlocal forces are constructed on a mechanical basis by inserting in
 12 the model long-range springs such that non-adjacent volume elements mutually ex-
 13 change forces due to relative motion. In the case of fluids, the mechanics of long-
 14 range interactions is assumed Newtonian and the resultant of nonlocal viscous forces
 15 applied (see Fig. 1) to a generic volume element reads:

$$\mathbf{f}_v^{(nl)}(\mathbf{x}, t) = \int_V \mathbf{f}_v^{(nl)}(\mathbf{x}, \boldsymbol{\xi}, t) = dV(\mathbf{x}) \int_V \mathbf{G}_v(\mathbf{x} - \boldsymbol{\xi}) (\mathbf{v}(\boldsymbol{\xi}, t) - \mathbf{v}(\mathbf{x}, t)) dV(\boldsymbol{\xi}) \quad (11)$$

16 where $\mathbf{f}_v^{(nl)}(\mathbf{x}, \boldsymbol{\xi}, t)$ is the nonlocal viscous force applied to volume element located
 17 at \mathbf{x} due to the relative velocity with the volume element located at $\boldsymbol{\xi}$, $\mathbf{G}_v(\mathbf{x} - \boldsymbol{\xi}) =$
 18 $g(\mathbf{x} - \boldsymbol{\xi}) [\mathbf{I} - \mathbf{J}(\mathbf{x}, \boldsymbol{\xi})]$, being $g(\mathbf{x}, \boldsymbol{\xi})$ the attenuation function and $\mathbf{J}(\mathbf{x}, \boldsymbol{\xi})$ the Jacobi
 19 directional tensor which components are written as $J_{kj}(\mathbf{x}, \boldsymbol{\xi}) = i_k(\mathbf{x}, \boldsymbol{\xi}) i_j(\mathbf{x}, \boldsymbol{\xi})$, where
 20 $i_k(\mathbf{x}, \boldsymbol{\xi})$ is the k -th component of the unit vector in the direction $(\mathbf{x} - \boldsymbol{\xi})$ defined as:

$$i_k(\mathbf{x}, \boldsymbol{\xi}) = \frac{(\xi_k - x_k)}{|\mathbf{i}(\mathbf{x}, \boldsymbol{\xi})|} \quad (12)$$

The attenuation or decay function $g(\mathbf{x} - \boldsymbol{\xi})$ is a symmetric and real function that de-
 cays with the distance.

In the case of the human blood the nonlocal forces in Eq. (11) are introduced for its
 multiphase nature and the tendency to self organize in a microstructure. Such a kind
 of microstructures are mainly constituted by RBCs that are considered to be the most
 responsible for the non-Newtonian behavior of blood. Indeed they aggregates into
 the so-called Rouleaux formations (see Fig. 2); moreover, RBCs have the tendency
 to migrate toward the center of the arterial vessels (Fahereus-Lindqvist wall effect,
 see Fig. 3). In small arterial vessels these two phenomena are able to modify the
 whole blood behavior, while in large arterial vessels their influence is negligible. This
 fact highlights the size-dependent behavior of the blood flow. In order to perform
 reliable and computationally efficient biomechanical simulations for cardiovascular
 applications, the blood domain is considered homogeneous and its heterogeneity and
 microstructure is accounted by means of the long-range viscous forces introduced in
 Eq. (11). Indeed the simulation of liquid phase and corpuscle require high computa-
 tional efforts.

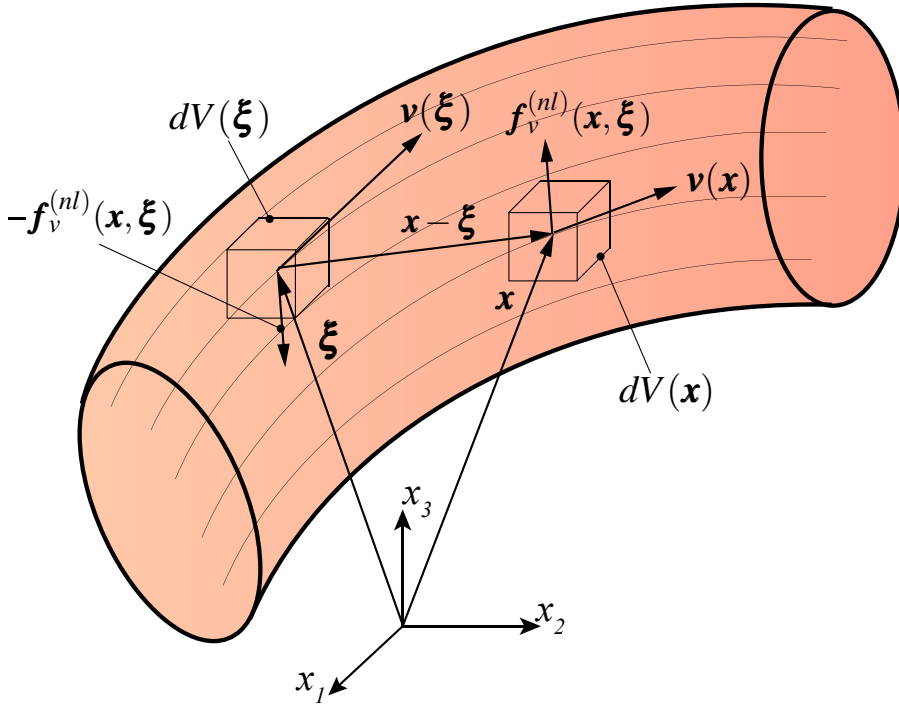


Fig. 1 Nonlocal forces mutually exerted by two non-adjacent volume forces are proportional to the difference of velocity vectors.

The nonlocal Navier-Stokes equations are written starting from the linear momentum balance, by including the local constitutive behavior Eq. (2), introducing the non local forces of Eq. (11) and taking into account incompressibility condition as:

$$\rho \left(\frac{\partial \mathbf{v}(\mathbf{x}, t)}{\partial t} + \mathbf{v}(\mathbf{x}, t) \cdot \nabla \mathbf{v}(\mathbf{x}, t) \right) - \nabla p(\mathbf{x}, t) - \mu \nabla^2 \mathbf{v}(\mathbf{x}, t) + \int_V \mathbf{G}_v(\mathbf{x} - \boldsymbol{\xi}) (\mathbf{v}(\boldsymbol{\xi}, t) - \mathbf{v}(\mathbf{x}, t)) dV(\boldsymbol{\xi}) - \rho \mathbf{f}(\mathbf{x}, t) = 0 \quad (13)$$

- 1 Eq. (13) corresponds to Eq. (4) with the additional integral terms representing the
- 2 resultant of nonlocal forces. Inspection of Eq. (13) reveals that the nonlocal force
- 3 between two volume elements is defined in the direction of the component of the
- 4 vector $[\mathbf{v}(\boldsymbol{\xi}, t) - \mathbf{v}(\mathbf{x}, t)]$ perpendicular to $(\mathbf{x} - \boldsymbol{\xi})$.

5 3 Mesoscale model of the Poiseuille flow

In this section Eq. (13) is particularized to the case of the 1D axisymmetric flow in stationary conditions. Let us consider a cylindrical volume $V = AL$, where L is the length in the direction of the axis of the cylinder and A the cross sectional area of the

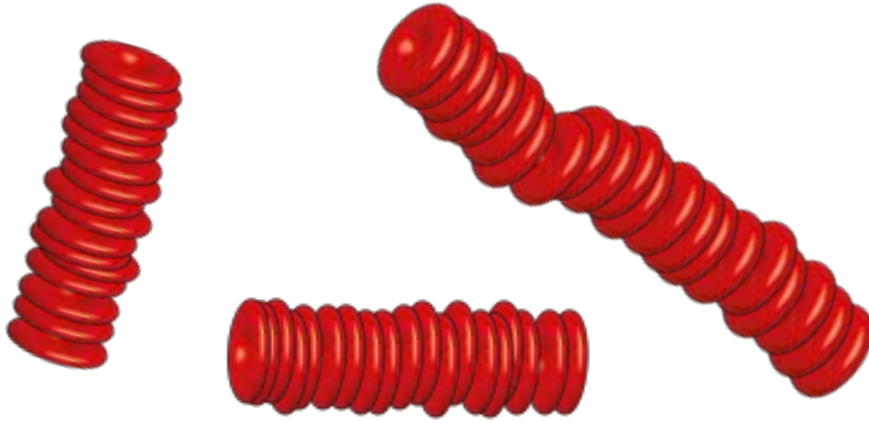


Fig. 2 Rouleaux formations.

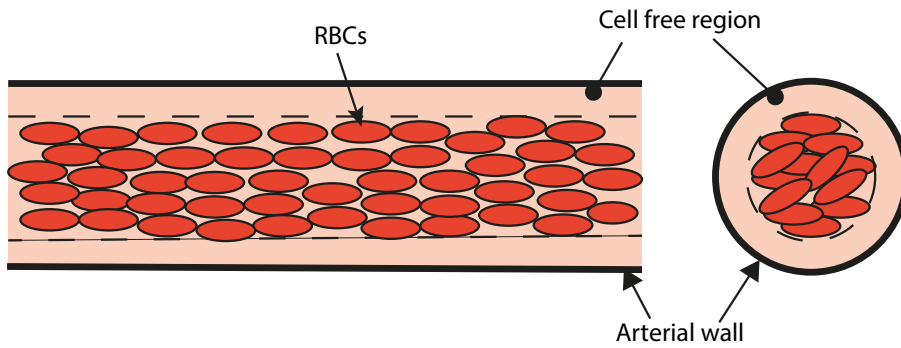


Fig. 3 Fahraeus-Lindqvist wall effect.

considered domain. Volume V is referred to a cylindrical coordinate system (r, θ, z) as reported in Fig. 4 and let us assume that a pressure drop of $\Delta p = p(r, \theta, 0) - p(r, \theta, L)$ is applied at the two sides of the cylinder. In such circumstances the linear momentum balance on a volume element Fig. 4b along the flux direction (z) reads:

$$[t_{zz}(r, \theta, z + \Delta z) - t_{zz}(r, \theta, z)] r \Delta \theta \Delta r + [t_{\theta z}(r, \theta + \Delta \theta, z) - t_{\theta z}(r, \theta, z)] \Delta z \Delta r + t_{rz}(r + \Delta r, \theta, z)(r + \Delta r) \Delta z \Delta \theta - t_{rz}(r, \theta, z) r \Delta z \Delta \theta = \frac{D\rho v_z}{Dt} r \Delta z \Delta \theta \Delta r \quad (14)$$

- 1 being ρ the fluid density $\rho(r, \theta, z, t)$ and $\frac{D}{Dt}$ the total derivative operator. Eq. (14) may
- 2 be rewritten, after some straightforward manipulations, as:

$$\frac{\partial t_{rz}}{\partial r} + \frac{t_{rz}}{r} + \frac{1}{r} \frac{\partial t_{\theta z}}{\partial \theta} + \frac{\partial t_{zz}}{\partial z} = \frac{D\rho v_z}{Dt} \quad (15)$$

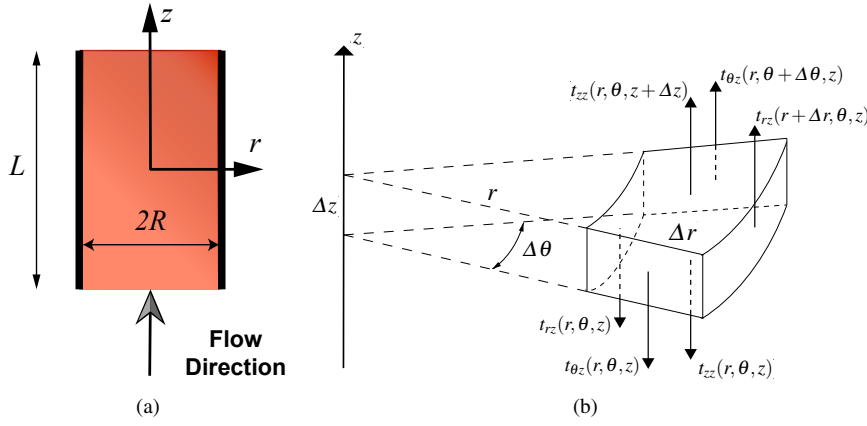


Fig. 4 Blood vessel model.

1 Under the assumptions of axisymmetric flow and stationary flow ($D\rho v_z/Dt = 0$) the
 2 balance equation in Eq. (15) yields:

$$\frac{\partial t_{rz}}{\partial r} + \frac{t_{rz}}{r} = -\frac{\partial t_{zz}}{\partial z} = -\frac{\Delta p}{L} \quad (16)$$

3 where we assumed that the pressure gradient is constant from $z = 0$ to $z = L$. Eq. (16)
 4 is a differential equation in the unknown shear stress $t_{rz}(r)$; in order to be solved it
 5 is necessary to enforce the rheological behavior, that in the case of Newtonian fluid
 6 reads:

$$t_{rz} = \mu \frac{\partial v_z}{\partial r} = \mu \frac{\partial}{\partial t} \frac{\partial u_z}{\partial r} = \mu \dot{\gamma}_{rz} \quad (17)$$

7 where $\dot{\gamma}_{rz}$ is the shear rate, that is the rate of the change of the displacement $u_z = u_z(r)$
 8 of the generic particle inside the control volume. Eq. (17) is a constitutive equation
 9 that relates the shear stress to the shear rate in the actual configuration of the fluid,
 10 and, after substitution, we get:

$$\mu \frac{d^2 v_z}{dr^2} + \frac{\mu}{r} \frac{dv_z}{dr} = -\frac{\Delta p}{L} \quad (18a)$$

$$v_z(-R) = 0; \quad v_z(R) = 0 \quad (18b)$$

12 being R the radius of the cylinder, that may be solved with the additional boundary
 13 conditions in Eq. (18b) for the velocity at the border of the domain to yield:

$$v_z(r) = \frac{R^2 - r^2}{4\mu} \frac{\Delta p}{L} \quad (19)$$

14 that describes a parabolic velocity profile along the diameter of the considered circu-
 15 lar cross-section. It is to emphasize that the equation in Eq. (18a) may be obtained
 16 directly by particularizing Eq. (4).

3.1 Small capillary vessels

In small-diameter vessels the experimental evidences [3] show a strong deviation from the parabolic profile predicted by assuming the Newtonian constitutive equation. Such a discrepancy, observed at the beginning of the fifties of last century is probably due to Fahreus-Lindqvist effect (Fig. 3) and Rouleaux formations (Fig. 2) already described in the previous section. The constitutive model capable to reproduce the experimental measured velocity profiles is the so-called Casson model, that reads:

$$\sqrt{t_{rz}(r)} = \sqrt{\tau_0} + \sqrt{\mu} (\dot{\gamma}_{rz})^{1/2} \quad (20)$$

Eq. (20) is a nonlinear relationship between shear stress and shear rate. If $\tau_0 = 0$ it reverts to the Newtonian model of Eq. (17). Introducing Eq. (20) into the balance equation in Eq. (16), a nonlinear governing equation is obtained:

$$-\frac{\Delta p}{L} = \frac{1}{r} \left[\tau_0 + \mu \frac{du_z}{dr} + 2\sqrt{\tau_0\mu} \left(\frac{du_z}{dr} \right)^{\frac{1}{2}} \right] + \frac{d^2 u_z}{dr^2} \left[\mu + 2\sqrt{\tau_0\mu} \left(\frac{du_z}{dr} \right)^{-\frac{1}{2}} \right] \quad (21)$$

The solution to Eq. (21) is a piece-wise velocity profile that may be expressed in the form:

$$u_z(r) = \frac{R^2}{4\mu} \left\{ \frac{\Delta p}{L} \left[1 - \left(\frac{r}{R} \right)^2 \right] - \frac{8}{3} \left(\frac{2\tau_0 \Delta p}{R L} \right)^{\frac{1}{2}} \times \right. \\ \left. \left[\left(1 - \frac{r}{R} \right)^{\frac{3}{2}} \right] + \frac{4\tau_0}{R} \left(1 - \frac{r}{R} \right) \right\} \quad |r| > r_y \quad (22a)$$

$$u_z(r) = u_z(r_y) \quad |r| \leq r_y \quad (22b)$$

where $r_y = (2\tau_0 L) / \Delta p$. From the inspection of Eq. (22) we find that in the central part of the vessel, the velocity is constant; this is related to the fact that in the region $-r_y \leq r \leq r_y$ the yield stress τ_0 is not exceeded, hence the velocity gradient is zero. The Casson model is satisfying in the reproduction of non-Newtonian velocity profiles, however it has the disadvantage to be nonlinear, hence mathematical manipulations are not straightforward except that for simple problems (see e.g. [2]), such as the case of the Poiseuille flow studied in this section. Moreover the concept of shear yield stress, in the authors opinion, does not reflect the real mechanics of the blood flow, that is not a visco-plastic fluid but it is a multiphase medium. For these reasons, in the next sections an alternative approach is proposed.

3.2 Mesoscale approach to blood circulation in small-size arterial vessels

In this section the nonlocal blood flow model is introduced starting from simple observations regarding the mechanics of blood. In particular two main facts are taken into account:

- the blood is multiphase material, which contains a fluid part, the plasma, and many different solid parts, such as RBCs that are the larger and more influent cells;

1 – the blood is strongly heterogeneous, indeed the presence of the Fahraues-Lindqvist
 2 wall effect (see Fig. 3) and Rouleaux formations(see Fig. 2) make the concentra-
 3 tion of RBCs larger at the center of the vessels than at the sides; as a consequence
 4 if the dimensions and the position of a representative volume are changed, differ-
 5 ent situations may be found.

6 In order to take into account of these peculiarities without really modelling all the
 7 phases contained in the blood, it is possible to adopt a *mesoscale approach*. In this
 8 manner, the blood is considered as a homogeneous fluid and the presence of RBCs
 9 and fibrinogen is taken into account by inserting in the governing equations long-
 10 range forces mutually exerted by non-adjacent fluids elements. The reason to intro-
 duce these forces is readily understandable if Fig. 5 is closely inspected. Indeed when

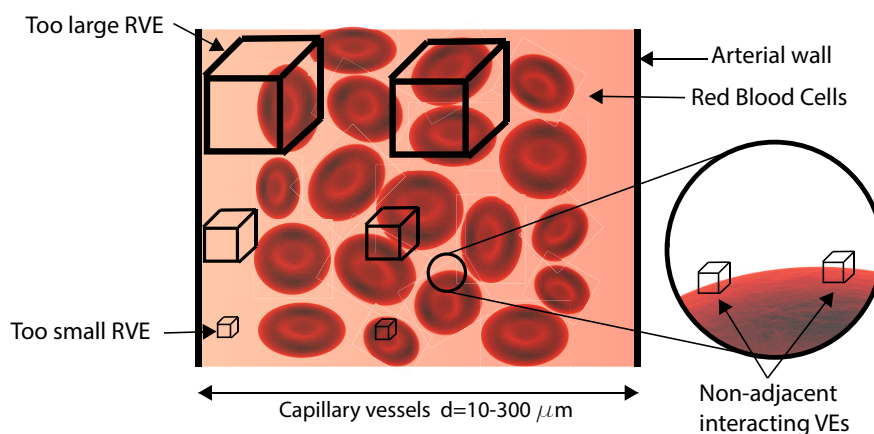


Fig. 5 Heterogeneity and multiphase nature of blood. In the circle, two non-adjacent fluid elements mutually exchange forces because of the presence of the RBC.

11 the dimension of the vessel is comparable to the average dimension of RBCs, that is
 12 about $7.5 \mu\text{m}$, a Representative Volume Elements (RVE) that is suitable for the di-
 13 mension of the domain is too small because it is not really representative of all hetero-
 14 geneity of the blood; on the contrary, an RVE sufficiently large to be representative of
 15 the heterogeneous nature of blood is too large because its dimensions are of the same
 16 order of magnitude of the domain dimension. Then, in the framework of a mesoscale
 17 approach, if two very small volume elements are taken on the boundary of a RBC, it
 18 is reasonable to think that they interact because of the presence of the RBC itself, and
 19 their interaction is modeled here as a nonlocal viscous force. In particular nonlocal
 20 forces are thought as linearly depending on the product between the two interacting
 21 volumes and their relative velocity; moreover the long-range forces are weighted by
 22 an attenuation function that decreases the force magnitude as the distance between
 23 the two elements increases. Under these assumptions the force mutually exerted by
 24 two non-adjacent volume elements may be written as follows for a one-dimensional
 25

1 problem (see Fig. 6):

$$F_{ki} = \mu_{ki} \Delta V_k \Delta V_i (v_i - v_k) \quad (23)$$

2 where ΔV_k and ΔV_i are the volume of the two fluid elements, while v_k and v_i are
 3 the velocities of the fluid elements; μ_{ki} is a viscous coefficient that varies with the
 4 distance d_{ki} through an appropriate attenuation function $g(\cdot)$, that is $\mu_{ki} = \mu_{NL} g(d_{ki})$,
 5 being μ_{NL} a nonlocal viscosity parameter of the model. The nonlocal viscosity μ_{NL} ,
 6 together with the attenuation function $g(\cdot)$, governs the entity of long-range viscous
 7 forces. It may be thought as the nonlocal counterpart of the local viscosity μ . For fixed
 8 local viscosity μ and attenuation function $g(\cdot)$ a larger value of μ_{NL} implies a larger
 9 intensity of nonlocal interactions compared with the local ones and then a major
 10 deviation from the local behavior of the fluid. Its physical meaning may be defined
 11 with the following parallelism: as the local viscosity fluid μ reflects the capability
 12 of the fluid volume to “drag” adjacent volume elements, the nonlocal viscosity μ_{NL}
 13 quantifies the capability of the fluid volume to “drag” non-adjacent volume elements.
 The resultant of nonlocal forces on the element k may be written as follows:

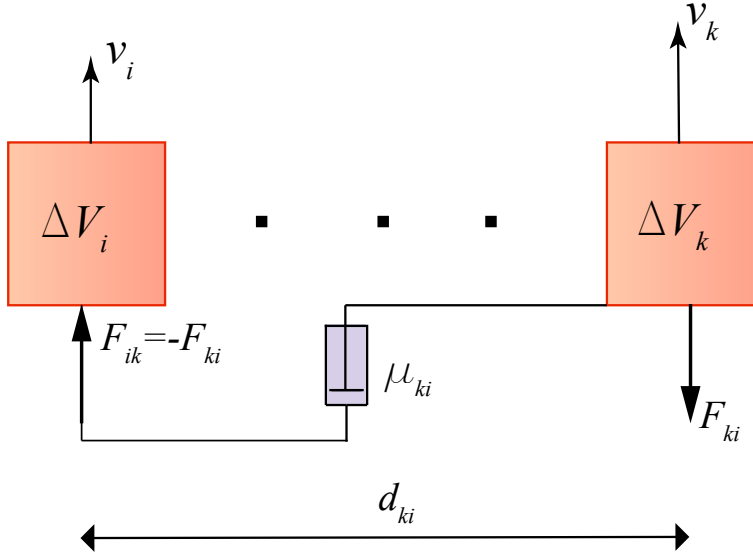


Fig. 6 Nonlocal forces mutually exerted by the two volume elements i and k in a one-dimensional problem.

14

$$F_k = \mu_{NL} \Delta V_k \sum_{i=1}^N \Delta V_i g(d_{ki}) (v_i - v_k) \quad (24)$$

15 being N the number of element in which the domain is discretized. If we refer to
 16 the two dimensional domain of Fig. 7 in axisymmetric conditions, the resultant of
 17 nonlocal forces on the k -th volume element may be written as:

$$F_k = \mu_{NL} \Delta V_k \sum_{i=1}^{N_r} \sum_{j=1}^{N_\theta} \Delta V_{ij} g(d_{k,ij}) (v_{ij} - v_k) \quad (25)$$

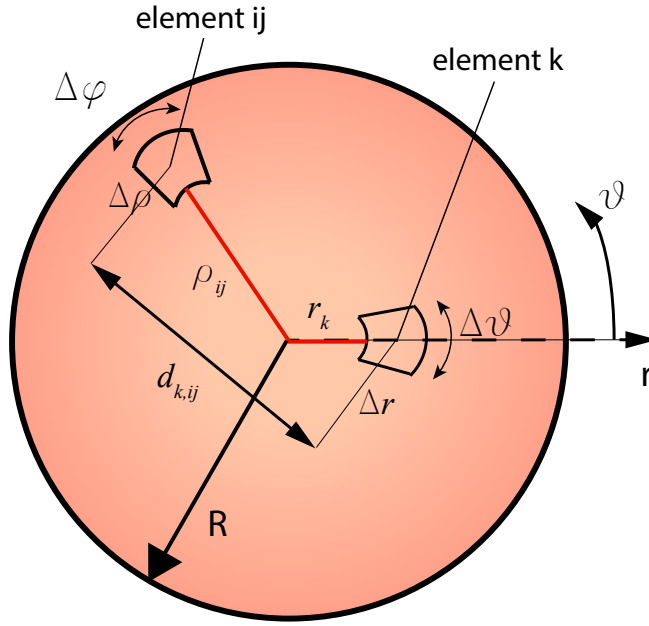


Fig. 7 Two dimensional axisymmetric domain (cross section of the circular vessel).

1 where:

$$\Delta V_k = r_k \Delta r \Delta \theta L \quad \Delta V_{ij} = \rho_{ij} \Delta \rho \Delta \varphi L \quad (26)$$

2 are the volumes of the two considered fluid elements and N_r and N_θ are the number
3 of elements in which the radial and circumferential directions have been discretized,
4 respectively. By taking the limits for $\Delta V_k \rightarrow 0$ and $\Delta V_{ij} \rightarrow 0$, the double sum reverts
5 to a double integral as:

$$F(r) = \mu_{NL} \int_0^R \int_0^{2\pi} g(d_{r\theta,\rho\varphi}) (v(\rho) - v(r)) \rho d\varphi d\rho \quad (27)$$

6 where the dependence of F , $v(r)$ and $v(\rho)$ from the angular coordinates θ and φ has
7 intentionally been omitted because the problem is axisymmetric, while for obvious
8 geometric reasons the same can not be done for $g(d_{r\theta,\rho\varphi})$, being $d_{r\theta,\rho\varphi}$ the distance
9 between two generic volume elements. As for the attenuation function, typical forms
10 are exponential, power law or Gaussian; in this study a power law attenuation function
11 in the form:

$$g(d_{r\theta,\rho\varphi}) = \frac{1}{(d_{r\theta,\rho\varphi})^{2+\alpha}} \quad (28)$$

12 has been selected; in Eq. (28) $d_{r\theta,\rho\varphi} = \sqrt{\rho^2 + r^2 - 2\rho r \cos \varphi}$ and α is a parameter
13 governing the velocity of decaying of the entity of long-range interactions as the
14 distance increases; with these assumptions the governing equation is obtained as:

$$-\frac{\Delta p}{L} = \mu \left(\frac{1}{r} \frac{dv(r)}{dr} + \frac{d^2 v(r)}{dr^2} \right) + \mu_{NL} L \int_0^R \int_0^{2\pi} \frac{(v(\rho) - v(r))}{(\rho^2 + r^2 - 2\rho r \cos \varphi)^{\frac{2+\alpha}{2}}} \rho d\varphi d\rho \quad (29)$$

1 which may be labelled as *Fractional Hagen-Poiseuille* (FHP) law, since the integral
 2 term is strictly related to the Marchaud fractional derivative in polar coordinates (see
 3 Appendix and [26,31]). From a rigorous point of view a proper fractional operator
 4 is not present in Eq. (29). Indeed in a bounded domain, as in the considered applica-
 5 tion, a properly said fractional operator would involve additional non integral terms,
 6 as in the case of Eqs. (37) of the Appendix (for one-dimensional problem). From a
 7 mechanical point of view these additional terms have not correspondence, except if
 8 we admit the presence of long-range viscosity connecting volume elements with the
 9 frontier, analogously to the approach followed in [32] in the case of nonlocal elastic-
 10 ity. However in our mechanical representation these long-range interactions between
 11 volume elements and the bounds of the domain are not present and then the addi-
 12 tional terms related to fractional derivative in bounded domain do not appear. But
 13 if the domain was unbounded, the integral in Eq. (29) would be a two-dimensional
 14 Central Marchaud fractional derivative (see Appendix) in polar coordinates and for
 15 this reason we feel that the present formulation may be labeled as “fractional”.
 16 The solution of such a problem in analytical form is not straightforward and it may
 17 be found for a restricted class of problem, such as very simple geometry with no real
 18 engineering relevance (e.g. unbounded domains); however, accurate solutions may be
 19 easily found by discretizing the domain and the governing equation with a finite dif-
 20 ference approximation. The advantage on the use of the proposed approach compared
 21 with the gradient or Eringen integral approaches is that the boundary conditions can
 22 be enforced as in a problem involving a classical local fluid [19]; then the boundary
 23 conditions are exactly the same of those in Eq. (18b) that in the context of a finite dif-
 24 ference approximation are enforced in a straightforward manner. In the next section,
 25 Eq. (29) is used in order to fit experimental data and the simulate velocity profiles in
 26 a small arterial vessel.

27 3.3 Best fitting of model parameters

28 In [3] results of measurements of velocity profiles on arterioles of rabbit mesentery
 29 have been reported. The data refers to arterioles with diameter size in the range 17-
 30 32 μm . In this study data obtained on a 32 μm diameter vessels (Fig. (3) of Ref.
 31 [3]) have been used in order to calibrate parameters of the HP model, the Casson
 32 model and the proposed fractional nonlocal model. For the HP and the Casson mod-
 33 els the least squares method has been used in order to calibrate the mechanical pa-
 34 rameters. For the FHP model, since analytical solution for the Poiseuille flow is
 35 not available, the parameters have been calibrated by means of an iterative proce-
 36 dure. In this procedure the discretized version of Eq. (29) has been solved numeri-
 37 cally several times with different set of parameters. At the end of the procedure, the
 38 adopted parameters are those that minimize the Root Mean Square Error (RMSE)
 39 between experimental data and theoretical curve. More specifically, the procedure
 40 has been developed through three refinement steps. In the first one the following
 41 range values of the moduli have been explored: $\mu = (5 \div 1000) \times 10^{-4} \text{ Pa s}$ and
 42 $\mu_{NL} = (5 \div 1000) \times 10^{-7} \text{ N s/mm}^{6-\alpha}$. The moduli have been progressively increased
 43 by $\Delta\mu = 5 \times 10^{-4} \text{ Pa s}$ and $\Delta\mu_{NL} = 5 \times 10^{-7} \text{ N s/mm}^{6-\alpha}$, respectively. The low-

est values were chosen in a way such that magnitude of the maximum velocity in the theoretical profile was about some tenths larger than the maximum experimental velocity. As for the order α , in the first refinement step it has been varied in the range $\alpha = 0 \div 1$ at intervals $\Delta\alpha = 0.05$. In the second refinement step the mechanical parameters have been varied with smaller interval in smaller ranges around the values giving the minimum RMSE in the previous step. The same has been done when passing from the second to the third step. The procedure of each refinement step was completely automatic and performed by means of a custom subroutine in Matlab [33]. Between one refinement step and the successive the range and the interval amplitude of parameters have been updated manually. Results of the best fitting are reported in Table 1 and theoretical curves are contrasted with experimental data in Fig. 8. From this figure it is evident that the classical Hagen-Poiseuille model is

Table 1 Parameters obtained by the best-fitting procedure for the HP, Casson and NLHP model.

Model	μ (Pa s)	τ_0 (Pa)	μ_{NL} (Ns/mm $^{6-\alpha}$)	α
HP	1.23×10^{-2}	–	–	–
Casson	2.45×10^{-3}	1.79	–	–
FHP	5.36×10^{-3}	–	7.8×10^{-5}	0.042

not capable of simulating the blood flow in small arterial vessels; the Casson and the proposed fractional nonlocal models, instead, are suitable for simulate the characteristics flattened velocity profiles that are experimentally observed. Some differences, however, may be highlighted between these last two models. While the Casson model has two different behaviors along the diameter, the latter provides a velocity profile that varies very gradually. In order to numerically assess the accuracy of the three models, the RMSE is used. This quantity is defined as:

$$RMSE = \sqrt{\frac{\sum_i^n (v_T(x_i) - v_{m,i})^2}{n}} \quad (30)$$

where n is the number of velocity data along the diameter, v_T is the theoretical velocity and v_m is the measured velocity. In Table 2 the RMSEs of the three models are compared. From Table 2 it may be concluded that the proposed nonlocal model

Table 2 Comparison of the RMSEs obtained with the three models HP, Casson and FHP.

Model	RMSE
HP	0.6644
Casson	0.4486
FHP	0.3937

represents an improvement, in terms of accuracy, of results obtained with the Casson model. Then we can state that the proposed nonlocal model is a linear model that is capable to simulate an apparent nonlinearity in the blood behavior. Moreover, it can

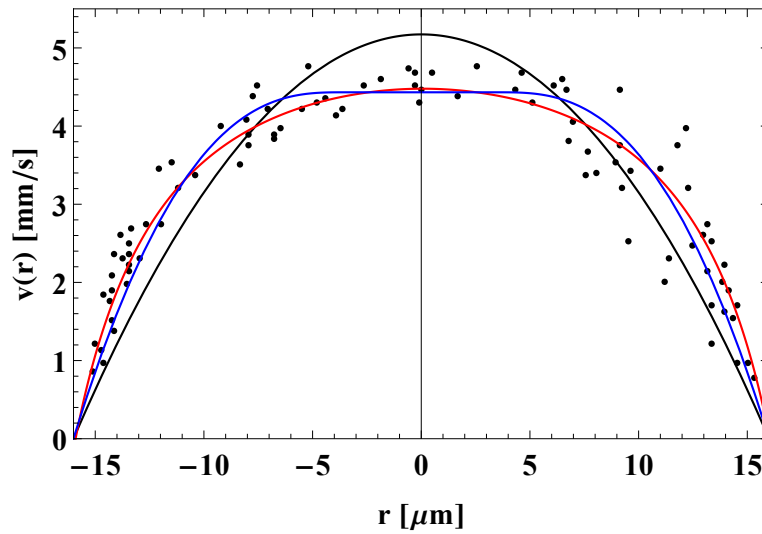


Fig. 8 Comparison between theoretical velocity profile and experimental data (black dots). HP model black line, Casson model blue line, FHP model red line.

1 be easily verified that another desirable feature of the proposed model is that as the
 2 diameter of the vessel increases, nonlocal forces become negligible and the model
 3 reverts to the classical Hagen-Poiseuille model. The proposed model, indeed, is size
 4 dependent. In order to highlight this concept, in Fig. 9 velocity profiles obtained for
 5 different values of the diameter dimensions are compared. Each profile is normalized
 6 with respect to the maximum velocity value obtained, for the same diameter value,
 7 with the classical HP model ($v_l(0)$). It is easy to note that for relatively large diameter
 8 the velocity profile tends to the local response, characterized by a parabolic velocity
 9 profile. In contrast, as the diameter of the vessel decreases, the velocity profile be-
 10 comes flatter and the ratio between the maximum non-local velocity magnitude and
 11 the maximum local velocity magnitude becomes smaller and tends to unity.

12 **4 Shear thinning of blood in coaxial cylinder viscometer**

13 An important feature of the rheological behavior of blood is the so-called shear thin-
 14 ning. This effect has been observed experimentally from decades and it regards the
 15 decrease of apparent viscosity of blood for increasing shear rate. It is widely believed
 16 that the shear thinning of blood is due mainly to the deformability of RBCs ([34]).
 17 This hypothesis is particularly suitable for the mesoscale approach adopted in this
 18 paper; indeed, in [34] measurements in a coaxial cylinder viscometer have been per-
 19 formed with three types of suspension: normal RBC in heparinized plasma, normal
 20 RBC in 11% albumin-Ringer solution and hardened RBC in 11% albumin-Ringer
 21 solution. It has been shown that only the suspension with hardened RBC shows an
 22 almost constant viscosity for varying shear rate, while the other suspensions show a
 23 clear shear thinning effect, especially for normal RBC in plasma (see Fig. 1 of [34])

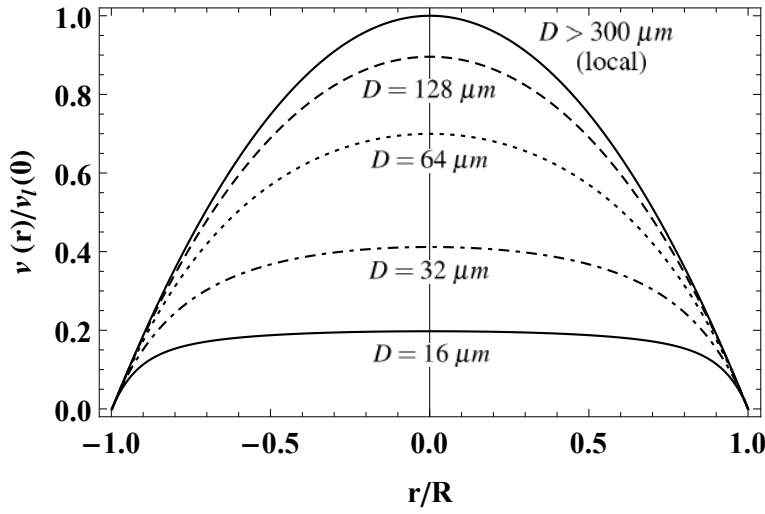


Fig. 9 Size effect of the fractional non-local Hagen-Poiseuille model.

1 In the frame of a mesoscale approach of this work, it is easy to hypothesize a quali-
 2 tative mechanism that, as a consequence of RBC deformability, is responsible of the
 3 shear thinning when blood viscosity is measured in a coaxial cylinder viscometer.
 4 Indeed in such a kind of viscometer the (apparent) shear rate is directly proportional
 5 to the angular velocity of the moving cylinder; the shear rate is apparent because no
 6 assumption has been made on the rheological behavior of blood, then the velocity
 7 profile is implicitly assumed linear and the apparent (constant) shear rate $\dot{\gamma}_a$ is evalu-
 8 ated simply as:

$$\dot{\gamma}_a = \frac{\omega R_i}{R_e - R_i} \quad (31)$$

9 where ω is the angular velocity of the internal cylinder, R_e and R_i are the external
 10 and internal radius of the chamber where the blood is placed for the measurement,
 11 respectively; in Eq. (31) the external cylinder is not rotating. As a consequence of the
 12 fact that the shear rate is apparent, the viscosity values reported in [34] are apparent
 13 as well.

14 The role played by the deformability of RBCs is clearly illustrated in Fig. 10; as
 15 ω increases, the inertial forces increase and as results RBCs migrate to the external
 16 cylinder surface; moreover, as they aggregate to the internal surface of the external
 17 cylinder, they are flattened by inertial forces. The distribution and shape of RBCs are
 18 sensibly different from one value of ω to another and as a consequence macroscopic
 19 rheologic behavior of blood is changed.

20 For these reasons, in the following we reinterpreted the data published in [34] by
 21 using the proposed rheological model. In a coaxial cylinder viscometer the tangential
 22 stress measurement is obtained indirectly from the measure of the torque M_T applied
 23 by the blood to the rotating (internal) cylinder:

$$\tau = \frac{M_T}{2\pi R_i^2 H} \quad (32)$$

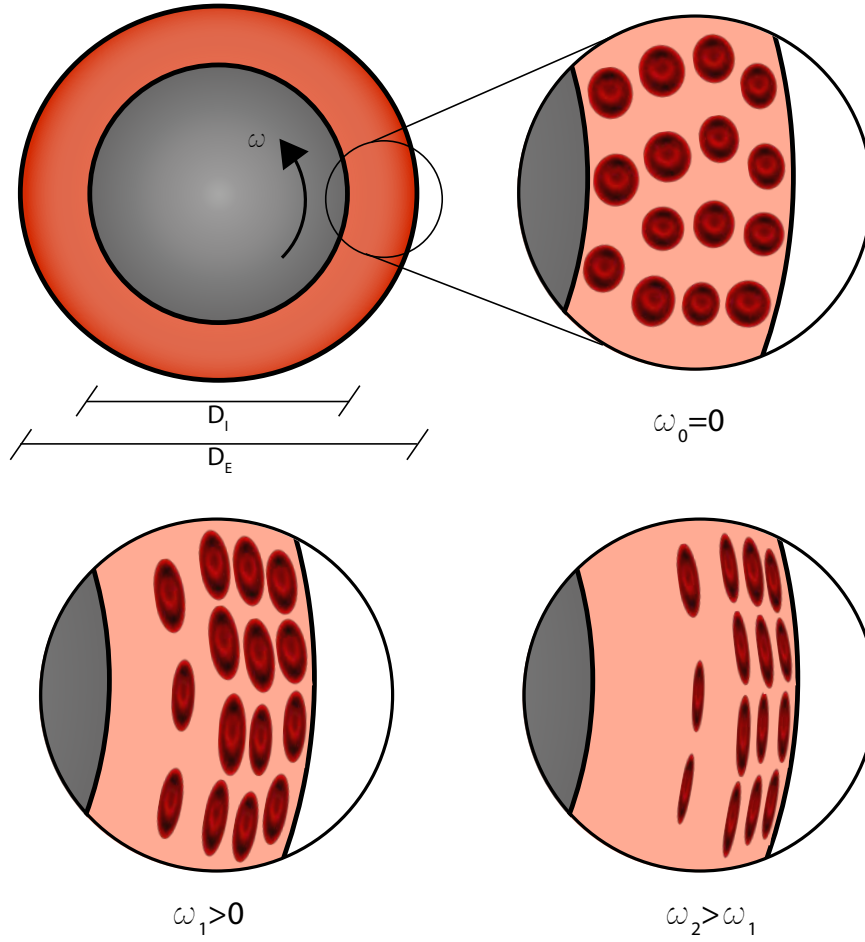


Fig. 10 Mesoscale explanation of the shear thinning of blood in the double cylinder rheometer as a consequence of deformability of RBC.

- 1 being H the height of the internal cylinder. The apparent viscosity is then evaluated
- 2 simply as:

$$\mu_a = \frac{\tau}{\dot{\gamma}_a} \quad (33)$$

- 3 The parameters of the nonlocal model proposed here have been optimized for several
- 4 couples of values of shear rate and viscosity deduced from [34]; the parameters
- 5 have been tuned in such way that for each apparent shear rate value $\dot{\gamma}_a$ the tangential
- 6 stress obtained with the proposed model is equal to the tangential stress obtained
- 7 by multiplying the value of shear rate and viscosity in [34]; to this purpose the data
- 8 related to normal RBC in plasma have been considered. In Fig. 11 the shear stress
- 9 versus the apparent shear strain, obtained from data in [34] is depicted. In order to
- 10 optimize the parameters of the proposed nonlocal model, numerical simulations of

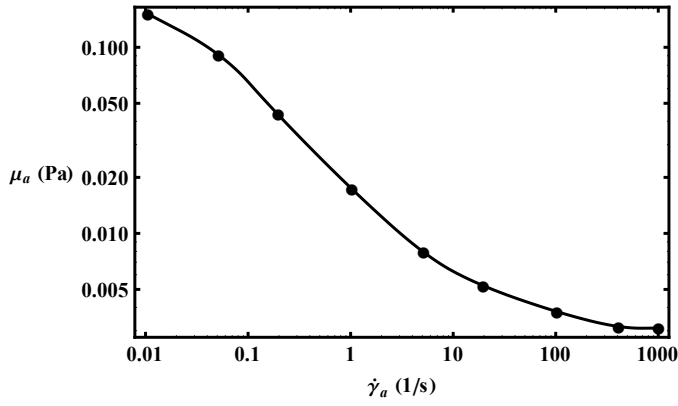


Fig. 11 Apparent viscosity as a function of apparent shear rate experimental data (dots) and proposed nonlocal model (continuous line)

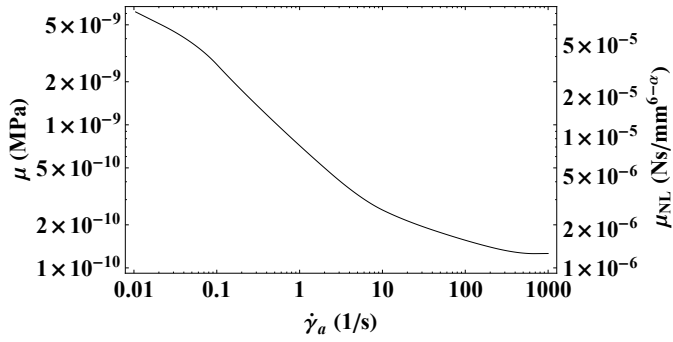


Fig. 12 Local and nonlocal viscosity parameters μ and μ_{NL} as a function of apparent shear rate for the proposed nonlocal model.

1 the conditions inside the coaxial cylinder viscometer have been performed. To this
 2 purpose, the geometry of the viscometer has been considered equal to that of a com-
 3 mercial viscometer, that is $R_i = 17.245$ mm ad $R_e = 18.415$ mm. In the optimization
 4 procedure, only the parameters μ and μ_{NL} have been calibrated, while the parameter
 5 α has been assumed equal to the value obtained by the best fitting procedure based
 6 on the velocity profile data and described in the previous section. For each experi-
 7 mental value coming form the rotating viscometer, the parameters μ and μ_{NL} have
 8 been calibrated iteratively as done in Section 3.3 for the Poiseuille flow. By means
 9 of this optimization procedure, we have been able to reproduce the experimental data
 10 obtained in [34] in terms of apparent shear rate and apparent viscosity, as shown in
 11 Fig. 11. In order to obtain these results, the coefficients μ and μ_{NL} varies with the
 12 apparent viscosity with the same trend of the apparent viscosity, as shown in Fig. 12
 13 (continuous thick line). From the values of Fig. 11 the curve of the shear stress vs the
 14 apparent shear rate have been obtained. Indeed in Fig. 13 the shear stress-apparent

1 shear rate curve obtained for the blood have been contrasted with a linear behavior
 2 tangent to the blood curve at its lowest shear rate value. It is clear that, especially for
 3 low values of the apparent shear rate, the behavior of blood is nonlinear, indeed as
 4 the apparent shear rate increases the shear stress grows less than linearly. In order to
 5 show the capability of the proposed model, in Fig. 13 it is also shown a curve related
 6 to a hypothetical fluid with a shear thickening behavior, that is a behavior opposite to
 7 that of blood.

8 5 Conclusion

9 In this paper a nonlocal model for the blood behavior in small arterial vessels has
 10 been introduced. The model is based on a mesoscale approach in which the presence
 11 of RBCs and other cells dispersed in the blood plasma is neglected but taken into
 12 account in the rheological behavior of blood by adding long-range interactions be-
 13 tween non-adjacent fluid elements in the equilibrium equations. The use of a power
 14 law attenuation function leads to governing equations involving fractional derivatives
 15 in case of unbounded domains or operator closely related to the fractional ones in
 16 case of bounded domains. The model has proved to be very efficient in reproducing
 17 experimental velocity profiles without the need of nonlinearity in the rheological be-
 18 havior. In comparison with existing non local models one important property of the
 19 proposed nonlocal model is that boundary conditions may be enforced as in a local
 20 model. To this stage, the only negative aspect of the proposed formulation is that it
 21 has not been possible to obtain an analytical solution for the considered application
 22 that would be desirable for a straightforward tuning of the mechanical parameters.
 23 However, despite this undesirable feature, in the future the model maybe applied to
 24 more complicated problems and implemented in a CFD context, where the knowl-
 25 edge of analytical solutions is not required.

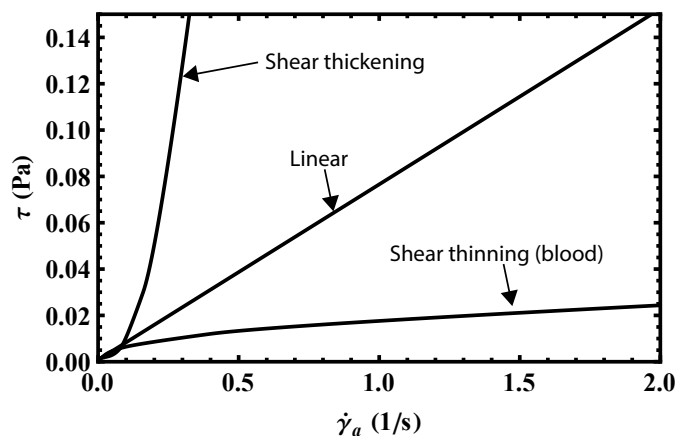


Fig. 13 Shear thinning of blood and hypothetical shear thickening behavior obtained with the proposed model.

1 Appendix - Fractional calculus

2 In this section, a brief introduction to the fundamentals of fractional calculus will be
3 given.

4 Consider the function $f(x)$, $x \in \mathbb{R}$, the left and the right Riemann-Liouville (RL)
5 fractional integral are defined as [25]:

$$(I_+^\alpha f)(x) = \frac{1}{\Gamma(\alpha)} \int_{-\infty}^x \frac{f(\xi)}{(x-\xi)^{1-\alpha}} d\xi \quad (34a)$$

$$(I_-^\alpha f)(x) = \frac{1}{\Gamma(\alpha)} \int_x^\infty \frac{f(\xi)}{(\xi-x)^{1-\alpha}} d\xi \quad (34b)$$

7 while the RL fractional derivative are defined as:

$$(D_+^\alpha f)(x) = \frac{1}{\Gamma(1-\alpha)} \frac{d}{dx} \int_{-\infty}^x \frac{f(\xi)}{(x-\xi)^\alpha} d\xi \quad (35a)$$

$$(D_-^\alpha f)(x) = -\frac{1}{\Gamma(1-\alpha)} \frac{d}{dx} \int_x^\infty \frac{f(\xi)}{(\xi-x)^\alpha} d\xi \quad (35b)$$

9 where $\alpha \in \mathbb{R}$, $0 \leq \alpha \leq 1$ and $\Gamma(\cdot)$ is the Euler gamma function. If $f(x)$ is a continuous
10 function with continuous first derivative, the left and right RL fractional derivatives
11 are coincident with the Marchaud fractional derivatives, that may be written as fol-
12 lows:

$$(\mathbf{D}_+^\alpha f)(x) = \frac{\alpha}{\Gamma(1-\alpha)} \int_{-\infty}^x \frac{f(x) - f(\xi)}{(x-\xi)^\alpha} d\xi \quad (36a)$$

$$(\mathbf{D}_-^\alpha f)(x) = \frac{\alpha}{\Gamma(1-\alpha)} \int_x^\infty \frac{f(x) - f(\xi)}{(\xi-x)^\alpha} d\xi \quad (36b)$$

14 The Marchaud fractional derivatives may be defined also for a bounded domain
15 $0 \leq x \leq L$ as:

$$(\mathbf{D}_{0+}^\alpha f)(x) = \frac{\alpha}{\Gamma(1-\alpha)} \int_0^x \frac{f(x) - f(\xi)}{(x-\xi)^{1+\alpha}} d\xi + \frac{f(x)}{\Gamma(1-\alpha)x^{1+\alpha}} \quad (37a)$$

$$(\mathbf{D}_{L-}^\alpha f)(x) = \frac{\alpha}{\Gamma(1-\alpha)} \int_x^L \frac{f(x) - f(\xi)}{(\xi-x)^{1+\alpha}} d\xi + \frac{f(x)}{\Gamma(1-\alpha)(L-x)^{1+\alpha}} \quad (37b)$$

17 The definitions of Marchaud fractional derivatives related to a single-variable scalar
18 function may be extended to a multi-variable scalar function. The extension is more
19 readable if referred to the Riesz fractional operators. Then it is necessary to introduce
20 Riesz fractional integral $(\bar{I}^\alpha f)(x)$ and derivative $(\bar{D}^\alpha f)(x)$:

$$(\bar{I}^\alpha f)(x) = \nu(\alpha) \int_{-\infty}^\infty \frac{f(\xi)}{|x-\xi|^{1-\alpha}} d\xi = \nu(\alpha) [(I_+^\alpha f)(x) + (I_-^\alpha f)(x)] \quad (38a)$$

$$\begin{aligned} (\bar{D}^\alpha f)(x) &= \nu(-\alpha) \int_{-\infty}^\infty \frac{f(x-\xi) - f(x)}{|\xi|^{1+\alpha}} d\xi = \\ &= \Gamma(1-\alpha)\nu(-\alpha) [(\mathbf{D}_+^\alpha f)(x) + (\mathbf{D}_-^\alpha f)(x)] \end{aligned} \quad (38b)$$

1 where $v(\pm\alpha) = [2\cos(\alpha\pi/2)\Gamma(\pm\alpha)]^{-1}$. The Riesz fractional operator may be gen-
 2 eralized to multivariate scalar function $f(\mathbf{x})$, with $\mathbf{x} \in \mathbb{R}^n$:

$$(\bar{D}^\alpha f)(\mathbf{x}) = \frac{1}{d_{n,\bar{l}}(\bar{\alpha})} \int_{\mathbb{R}^n} \frac{f(\boldsymbol{\xi}) - f(\mathbf{x})}{\|\boldsymbol{\xi} - \mathbf{x}\|^{n+\alpha}} d\boldsymbol{\xi} = \frac{\chi(\bar{\alpha})}{d_{n,\bar{l}}(\bar{\alpha})} [(\mathbf{D}_+^\alpha f)(\mathbf{x}) + (\mathbf{D}_-^\alpha f)(\mathbf{x})] \quad (39)$$

3 where:

$$d_{n,l}(\alpha) = \beta_n(\alpha) \frac{A_l(\alpha)}{\sin(\alpha\pi/2)} \quad (40a)$$

$$\beta_n(\alpha) = \frac{\pi^{1+n/2}}{2^\alpha \Gamma(1+\alpha/2) \Gamma(n+\alpha/2)} \quad (40b)$$

$$A_l(\alpha) = \sum_{k=0}^l (-1)^{k-1} \binom{l}{k} k^\alpha \quad (40c)$$

6 and $\chi_l(\alpha) = -A_l(\alpha)\Gamma(\alpha)$, $\bar{\alpha} = n - 1 + \alpha$, $\bar{l} = n - 1 + l$, $l = \{\alpha\} + 1$ and $\{\alpha\}$ is
 7 the integer part of α . The complete demonstration of Eq. (39) is omitted here for the
 8 sake of brevity; more information can be found in [26].

9 Finally, we briefly introduce the n -dimensional Central Marchaud Fractional Deriva-
 10 tive (CMFD) as:

$$(\mathbf{D}_-^\alpha f)(\mathbf{x}) = \frac{\alpha}{\Gamma(1-\alpha)} \int_{\mathbb{R}^n} \frac{f(\mathbf{x}) - f(\boldsymbol{\xi})}{(\boldsymbol{\xi} - \mathbf{x})^{n+\alpha}} \mathbf{J}_{kj} d\boldsymbol{\xi} \quad (41)$$

11 where $\mathbf{J}_{kj} = \mathbf{i}_k \mathbf{i}_j$ is a Jacoby directional tensor, being \mathbf{i}_k the unit vector associated with
 12 the direction $\mathbf{x} - \boldsymbol{\xi}$. In the specific problem treated in this paper (the Poiseuille flow),
 13 the governing equation written in polar coordinates and in axisymmetric conditions
 14 is basically a scalar governing equation, then the Jacoby tensor reduce to unity. This
 15 means that the power law attenuation function, responsible for the appearance of
 16 fractional operator, reduces in this case to a scalar function. As a consequence, in the
 17 governing equation in Eq. (29), the integral term may be recognized as the integral
 18 part of the Marchaud fractional derivative defined in bounded domain and reported
 19 in Eq. (37). More details can be found in [31].

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21 This study was not founded.

22 Conflict of interest

23 The authors declare that they have no conflict of interest.

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