Article

A simplified model for predicting friction factors of laminar blood flow in small-caliber vessels

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Abstract: The aim of this study is to provide the scientists with a straightforward correlation that can be applied for predicting the Fanning friction factor and consequently the pressure drop during blood flow in small-caliber vessels. Due to the small diameter of the conduit, the Reynolds numbers are low and thus the flow is laminar. The study has been conducted using Computational Fluid Dynamics (CFD) simulations validated with relevant experimental data, acquired using an appropriate experimental set-up. The experiments concern pressure drop measurement during the flow of a blood analogue that follows the Casson model, i.e. an aqueous glycerol solution that contains a small amount of xanthan gum and exhibits similar behavior to blood, in a smooth, stainless steel microtube (L = 50 mm and D = 400 μm). The interpretation of the resulting numerical data led to the proposal of a simplified model that incorporates the effect of the blood flow rate, the hematocrit value (35-55%) and the vessel diameter (300-1800 μm) and predicts, with better than ±10% accuracy, the Fanning friction factor and consequently the pressure drop during laminar blood flow in small-caliber vessels.

Keywords: pressure drop; CFD; Casson fluid; blood; hematocrit; small vessel; microfluidics

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1. Introduction

The flow behavior of non-Newtonian fluid in small-caliber tubes is of high interest in practical applications (e.g. flow, mixing, and separation of various biological species in microchips) [1]. Blood exhibits non-Newtonian behavior, meaning that its viscosity depends on shear rate. The ability of predicting blood flow pressure drop is essential in therapy strategy and the design of surgical repairments and implantable medical devices [2]. The investigation on blood flow in small arteries is of both fundamental interest and practical significance.

Blood is a two-phase suspension of plasma and cells that behaves as a non-Newtonian shear-thinning liquid. The plasma exhibits Newtonian behavior with viscosity ranging from 1.10 to 1.35 mPa.s at 37 C. It comprises of proteins (albumin, globulins and fibrinogen) that represent about 7–8 wt% of plasma, glucose, clotting factors, inorganic ions, dissolved gases, hormones and other substances at low concentration [3]. The most abundant cells are the red blood cells (RBCs) or erythrocytes comprising about 95% of the cellular component of blood while the rest 5% are white cells and platelets. The non-Newtonian shear-thinning character of blood results from the red cells variations in aggregation and deformation, while its viscosity is primarily affected by the volume percentage of red blood cells in blood, i.e. the value of hematocrit.

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The equations that define non-Newtonian flows, although they are well established, they have a high degree of complexity compared to those defined for Newtonian flow [4]. This is why in many papers blood is treated as Newtonian fluid. This assumption although holds practically true for high shear rates, i.e. greater than 1000 s^{-1}, it is not valid for blood flow in small vessels [5], where the Reynolds numbers are low, and the flow is laminar.

The research considering non-Newtonian fluid flow is based on the pioneer work of Metzner & Reed [6] from 1955. According to their approach the same friction factor chart can be used for Newtonian and time-independent non-Newtonian fluids in the laminar or turbulent region, provided that an appropriate effective Reynolds number can be estimated. In this way the problem reduces to the quest of an appropriate effective viscosity, which would relate the behavior of the non-Newtonian fluid to an equivalent one of a hypothetical Newtonian fluid [7]. However, the calculations seem to be complex and rather laborious because the suggested equations must be solved iteratively.

Many models have been developed to describe blood viscosity, e.g. Casson, Hershel-Bulkley, Carreau, Quemada [8]. Chilton & Stainsby [4] suggested a model for Hershel-Bulkley fluids that iteratively calculate the friction factor both in laminar and turbulent flow in pipes, but it does not take into account the effect of hematocrit. Cruz et al. [9] proposed a generalized method for predicting friction factors in fully developed non-Newtonian laminar flow in circular pipes using several viscoelastic models, i.e. Herschel–Bulkley, Bingham, Casson and Carreau–Yasuda. Their method, apart from the fluid velocity, the pipe diameter and the parameters of each rheological models, utilizes an apparent flow behavior index, whose estimation is quite complicated. The most prevalent model for predicting blood viscosity is the Casson model [10] because its constants can be expressed as a function of hematocrit [8] and it is reported that it leads to reliable results [11].

The pressure drop exerted during blood flow depends mainly on the blood vessel diameter and the blood flow rate as well as the hematocrit value [11]. The **aim** of this study is to provide engineers and physicians with a simple straightforward algorithm that can be applied for predicting the pressure losses, or equivalently the Fanning friction factor, during blood flow in small diameter vessels. As experiments are difficult to perform and time consuming, the effect of the various parameters will be evaluated by performing a series of Computational Fluid Dynamics (CFD) simulations, using a previously validated code. Due to the small diameter of the conduit, the corresponding Reynolds numbers are low and consequently the flow can be regarded laminar.

2. Experimental setup and procedure

It is common practice, prior to proceeding with the simulations, to validate the CFD code using data acquired by performing relevant experiments. The experimental set up used for the pressure drop measurements (Figure 1) comprises the test section (Figure 2), two syringe pumps (AL-2000, World Precision Instruments®), a three-way valve and a digital pressure transducer (68035, Cole Palmer).

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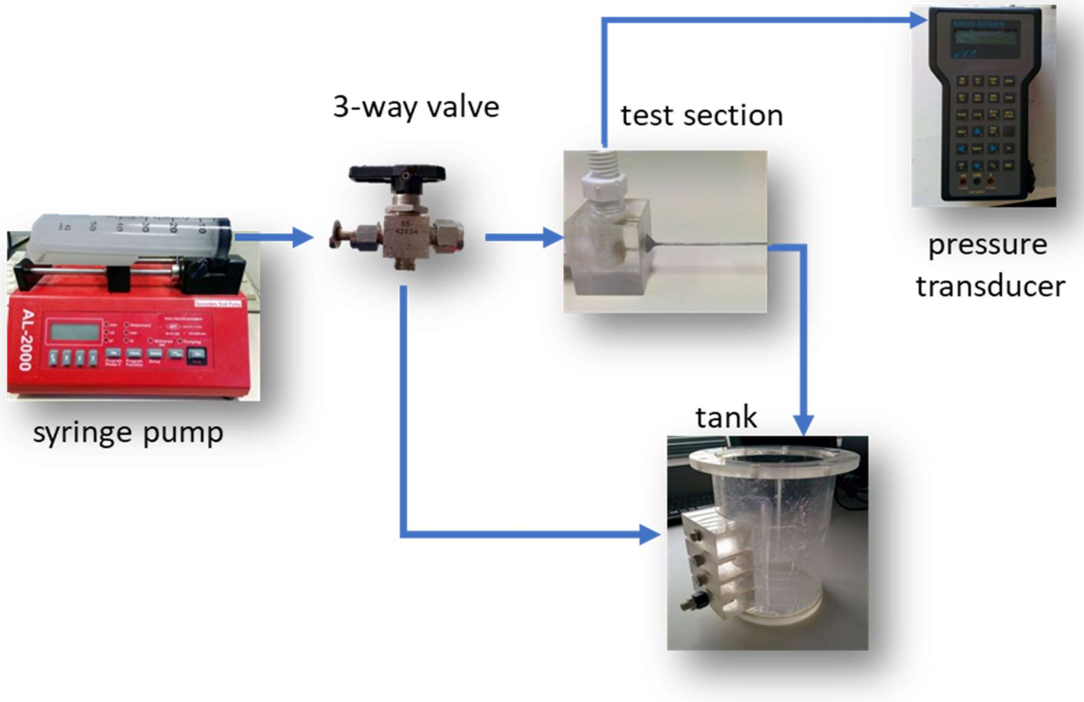

Figure 1. Experimental setup.

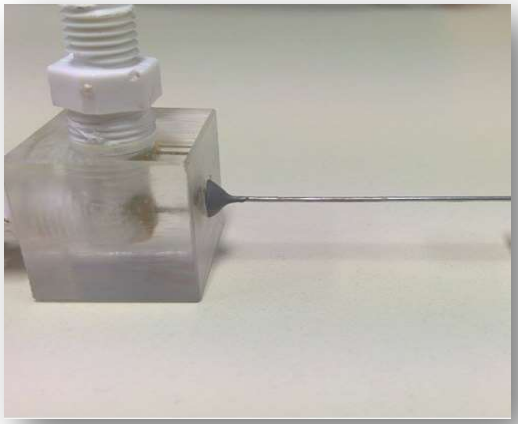

Figure 2. Test section.

The use of two pumps was necessary to cover the desired Reynolds number range. The three-way valve allows for refilling the syringes without exposing the system to the atmospheric air. The pressure was monitored by connecting one of the manometer tubes to the microtube inlet, while the second was left open to the atmosphere.

The test section (Figure 2) consists of a 50 mm microtube, i.e. a stainless steel (SS 304) chromatography needle (Gauge 33, Hamilton), whose internal diameter, measured via a microscope was

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400 μm. The microtube was adjusted on a PMMA cube and connected to the feed and the manometer. All experiments were conducted at a room temperature (i.e. 20±1 C).

The functionality of the setup was confirmed by performing experiments with a Newtonian fluid (i.e. water), while the CFD model was validated with data obtained by performing experiments with a non-Newtonian fluid, i.e. a blood analogue.

2.1. Blood analogue

As experiments with blood are difficult to perform due to coagulation, we used blood mimicking fluids, i.e. fluids whose rheological properties are similar to blood and whose viscosity follow the Casson model. As already mentioned the constants of Casson model depend on the value of hematocrit, whose normal range is between 30 and 55 % [8].

The viscosity of blood can be expressed by Equation (1) [3]:

$$\mu = \left(\sqrt{\frac{\tau_y}{\gamma}} + \sqrt{n_N}\right)^2 \tag{1}$$

where μ is the viscosity of blood, γ the shear rate, τ_y the yield stress and n_N the viscosity corresponding to high shear rates (asymptotic value). The yield stress is a measure of the energy required for breaking down the aggregates of red blood cells formed at very low shear rates. Merrill [8], who extensively investigated blood rheology, confirms the strong relation between viscosity and hematocrit, H_t, and suggests that the terms n_N and τ_y of Equation (1) can be expressed as functions of hematocrit, i.e.,

$$n_N = n_p[1 + 0.025H_t + 7.35 \cdot 10^{-4} H_t^2] \tag{2}$$

where n_p is the viscosity of the plasma,

$$\tau_y = A(H_t - H_{tc})^3 \tag{3}$$

and H_{tc} is the critical hematocrit, below which the yield stress, τ_y, can be considered negligible. For normal blood H_{tc} ranges between 4 and 8 and A is a constant ranging between 0.6x10^{-7} and 1.2x10^{-7} Pa. These expressions are employed hereafter for predicting blood viscosity as a function of hematocrit [8]. In this study, the values selected for A and H_{tc} are 0.9x10^{-7} Pa, and 6 respectively, i.e. the middle values of the corresponding range.

For the sake of simplicity, the variations in viscosity, which, as already mentioned, can be attributed to several factors, will be expressed in the simulations as a function of hematocrit alone. Blood density, ρ, is assumed to be constant, i.e., independent of the hematocrit value investigated, and equal to 1060 kg/m^3.

Thus, human blood with H_t~55% can be simulated by a 30% v/v aqueous glycerol solution that contains 0.035% w/v xanthan gum, i.e. a polysaccharide that acts as rheology modifier and renders the fluid non-Newtonian. The viscosity curve of the fluid was measured in our Laboratory via a magnetic rheometer (AR-G2, TA Instruments), for shear rates between 1-1000 s^{-1} (Figure 3) and it is excellent fitted by a Casson-type curve (Equation (1)).

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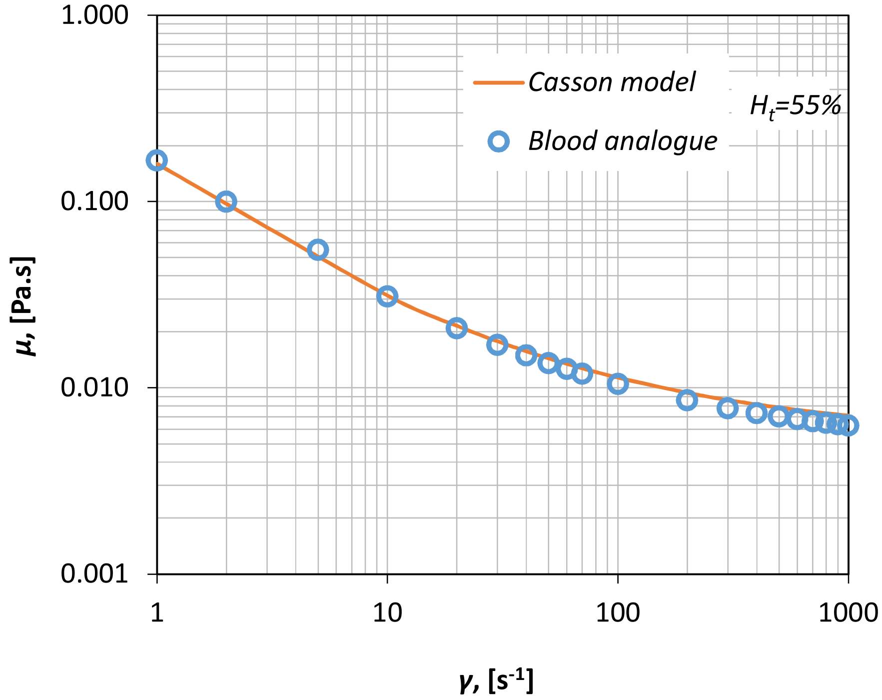

Figure 3. Viscosity measurements of the blood analogue (H_t= 55%).

3. Numerical Simulations

CFD modeling is considered a dependable tool for studying blood flow characteristics in small-caliber vessels [11]. In this study a CFD code (ANSYS CFX 18.1, ANSYS, Inc., Karnosboro, PA, USA), which comprises the usual parts of a standard CFD code, was employed for simulating the flow. The blood vessel was modeled as a 3D computational domain, while the geometry of the computational domain and the mesh were designed using the parametric features of ANSYS Workbench package. The length of the conduit is 5 cm, the fluid density is assumed constant (i.e. 1060 kg/m^3), while the diameter of the conduit is a parametric variable and is set to be between 0.3 -1.8 mm. Aiming to reduce memory consumption and CPU time and as the geometry has two symmetry planes, only one fourth of the domain is used (Figure 4).

Due to the small characteristic dimension of the conduit, the flow is laminar and hence the Direct Numerical Simulation (DNS) model was selected, while the high-resolution advection scheme was used for the discretization of the momentum equations. A high-performance unit for parallel computing was used (24 nodes, 64GB RAM). The simulations run in steady state, the vessel walls are considered smooth, the non-slip boundary condition is imposed at the walls, while for each run the flow rate is kept constant.

As the numerical diffusion in the CFD calculations can influence the accuracy of the calculations, an optimum grid density was chosen by performing a grid dependency study. Figure 5 presents typical results that illustrate the dependence of pressure drop on the number of cells and correspond to the maximum flow rate tested. Hence, the number of cells were chosen to be around 270,000 to ensure that the solution is independent of the grid density.

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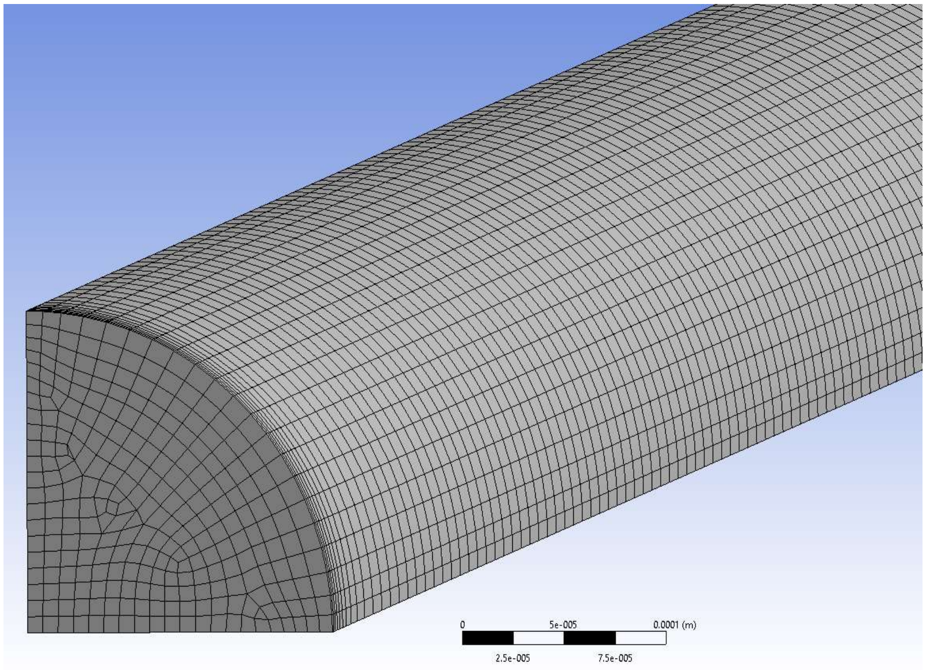

Figure 4. Typical computational domain of the simulations.

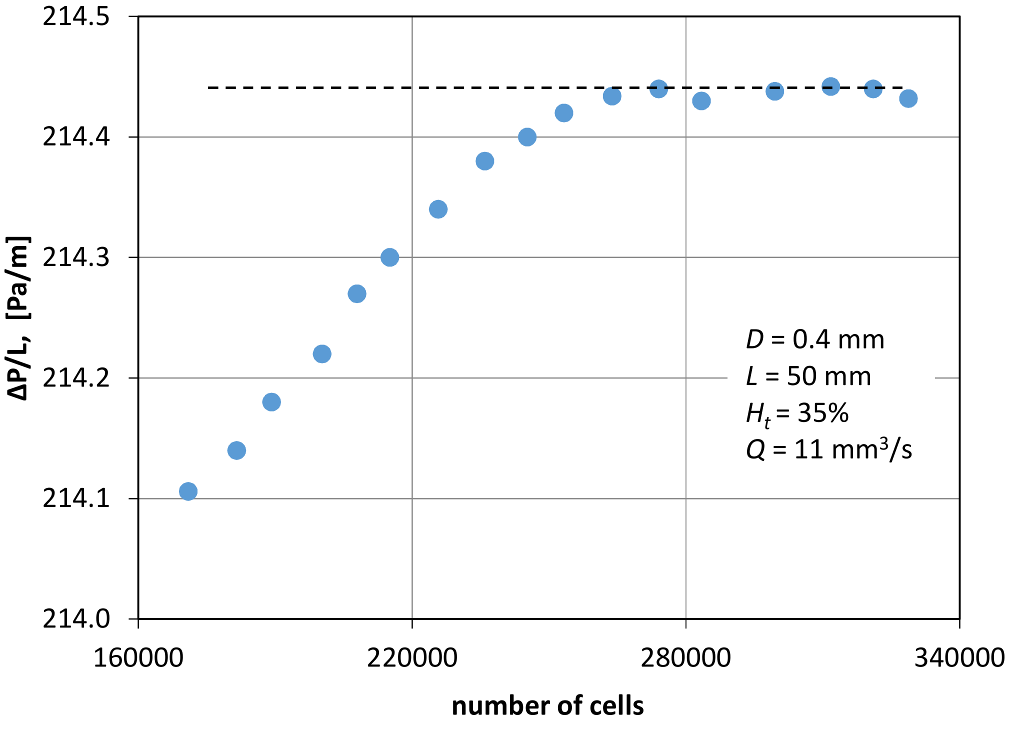

Figure 5. Grid dependency study (*D=0.4 mm, L=50 mm, Q=11 mm³/s, Hₜ=35%*).

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3.1. Code Validation

Usually the validity of a CFD code is checked by comparing the numerical results with relevant experimental data. In the present study appropriate experiments were performed using the experimental set-up described in Section 2. The experimental data acquired are presented in Figure 6 along with the computational results and proved to be in very good agreement (±10%). Since the viscosity of the non-Newtonian fluids is not constant, in Figure 6 the pressure drop is plotted versus a modified Reynolds number Re^*,

$$Re^* = \frac{UD\rho}{\mu^*} \quad (4)$$

which in place of the fluid viscosity uses an effective viscosity, μ^*, that corresponds to the pseudo-shear rate γ^* defined by Equation (5) [3]

$$\gamma^* = \frac{U}{D} = \frac{4Q}{\pi D^3} \quad (5)$$

where U is the average fluid velocity, Q the volumetric blood flow rate and D the inside vessel diameter.

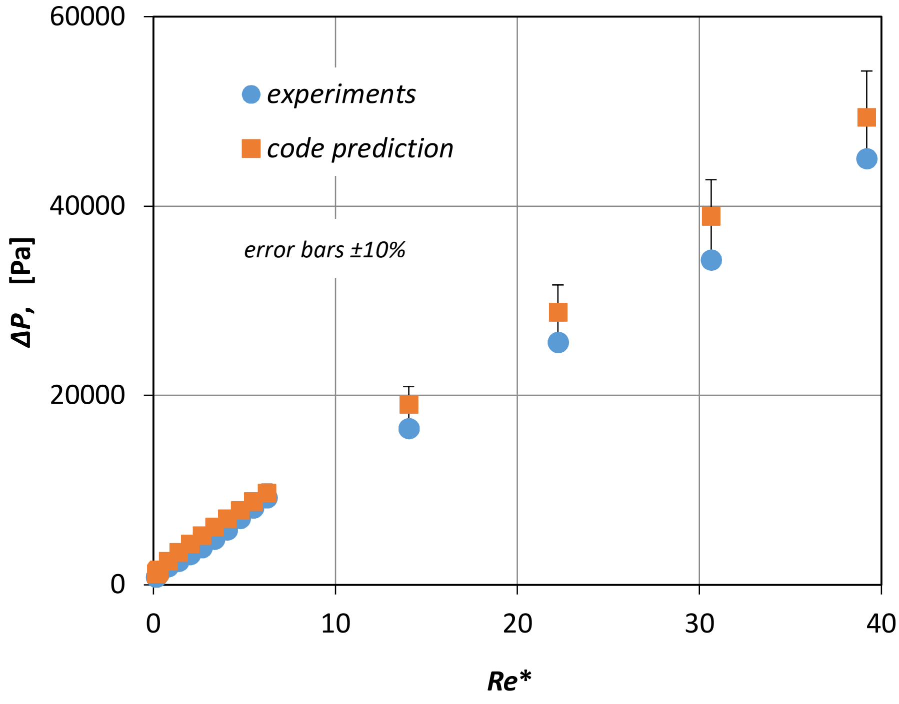

Figure 6. Validation of the CFD code (error bars ±10%).

Figure 7 presents typical CFD results of pressure distribution along the axis of the conduit. The type of the curve (i.e. straight line) denotes that the flow is fully develop.

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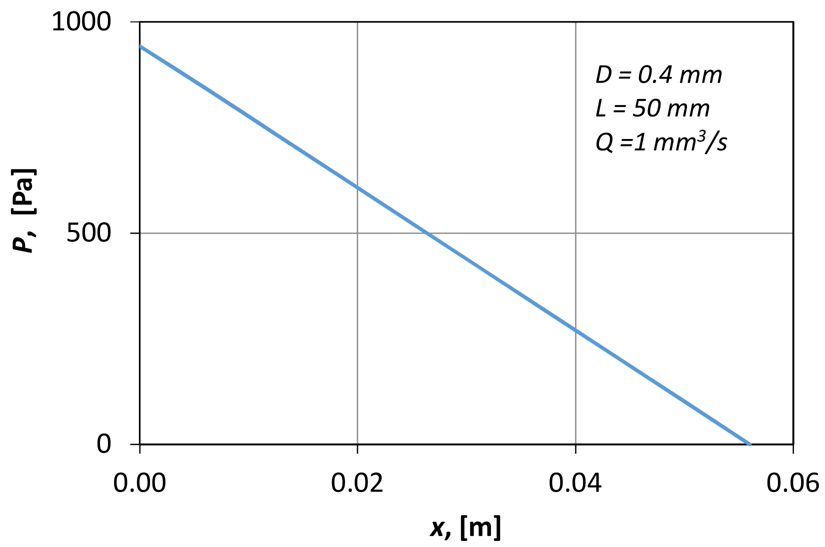

Figure 7. Typical simulation results of pressure distribution across the small vessel (L=50 mm, D=0.4 mm, Q=1 mm^3/s).

3.2. Numerical Procedure

The parametric study was performed by employing the Design Exploration features of the ANSYS Workbench® package. The design variables selected along with the imposed upper and lower bounds are presented in Table 1. The upper bound of the vessel inside diameter corresponds to the larger arterioles and venules of an adult male [12], while the corresponding lower bound was chosen to be 500 μm to avoid the consequences of the Fahraeus-Lindqvist effect. Due to this effect in small vessels (smaller than 300 μm) red blood cells tend to drift towards the central axis of the vessel and a cell-free layer, called a plasma layer, is formed along the vascular wall resulting to an apparent blood viscosity that declines substantially with decreasing diameter [13]. The hematocrit range chosen is typical for healthy adult humans [8] and the blood flow rate bounds imposed are typical for such μ-vessels.

To extract the necessary information from a limited number of test cases the Design of Experiments (DOE) methodology was followed. In the present study the effect of the design parameters is investigated by performing a series of "computational experiment" for certain values of the design parameters chosen by employing the Box–Behnken method [14], i.e., an established DOE technique.

Table 1. Constraints of the design variables.

Parameter	Lower Bound	Upper Bound
Vessel inside diameter, *mm*	0.50	1.80
Hematocrit, %	35	50
Blood flow rate, *mm*^{3}*/s*	7.0	88.0

Table 2 presents the various design points selected. The aim is, based on the computational results, to formulate appropriate design correlations that can be applied for predicting friction factor values during laminar blood flow in micro vessels. The first three columns of Table 2 include the

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design points dictated by the Box-Behnken method. The following three columns contain some additional points that extend the D range to 0.3 mm. The last part of Table 2 presents appropriate verification points that are used for testing the applicability of the design equation.

Table 2. Design and verification points.

Design points						*Verification points*		
Box-Benken			*Additional points*					
Q	*D*	H_t	*Q*	*D*	H_t	*Q*	*D*	H_t
mm^3/s	*mm*	%	mm^3/s	*mm*	%	mm^3/s	*mm*	%
72.0	1.15	35	6.0	0.40	35	6.7	0.40	55
72.0	1.15	50	8.5	0.40	35	7.0	0.50	40
72.0	1.80	43	11.0	0.40	35	10.0	0.40	55
72.0	0.50	43	13.0	0.40	35	11.7	0.40	55
80.0	0.50	35	16.0	0.40	35	15.0	0.40	55
80.0	0.50	50	18.0	0.40	35	20.0	0.30	45
80.0	1.15	43	21.0	0.40	35	33.4	0.40	55
80.0	1.80	35	23.0	0.40	35	40.0	0.90	50
80.0	1.80	50	25.0	0.40	35	66.8	0.40	55
88.0	1.15	35	45.0	0.40	35	68.0	1.20	35
88.0	1.15	50	50.0	0.60	37	83.0	0.60	37
88.0	1.80	43	7.0	0.30	43	83.5	0.40	55
88.0	0.50	43						

4. Results

In Figure 8 the measured pressure drop values for various blood flow rates, Q, are compared with pressure drop losses (Equation (6)):

$$\frac{\Delta P}{L} = f\,\frac{2}{D}\,\rho U^2 \tag{6}$$

where f is the Fanning friction factor given by

$$f = {}^{16}\!/_{Re_\infty} \tag{7}$$

where Re_∞ is a Reynolds number that uses the asymptotic value, μ_∞, of blood viscosity. From Figure 8 it is obvious that the correlation for Newtonian fluids can by no means be applied for non-Newtonian fluids because it underestimates ΔP by 30%.

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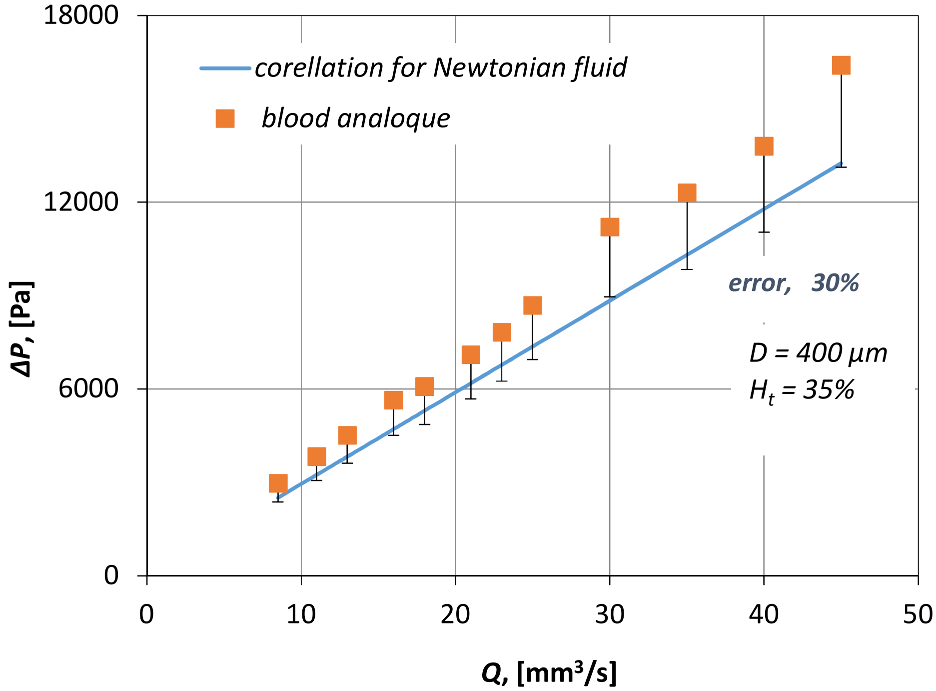

Figure 8. Comparison of experimental results for the blood analogue with theoretical prediction of ΔP using the correlation for Newtonian fluids (f=16/Re_∞).

Initially we used the numerically predicted pressure drop value to calculate, using Equation (6), the Fanning friction factor that corresponds to each "experiment". In Figure 9 the calculated friction factors are compared with the values predicted by Equation (8) that relates the Fanning friction factor with Re^* (defined by Equation (4)), i.e.

$$f = {}^{16}\!/_{Re^*} \tag{8}$$

The calculated friction factors deviate considerably from the ones predicted by Equation (8) especially for the lower Re^* values. It was obvious that a new correlation must be formulated.

As blood is a non-Newtonian fluid, we attempted to strengthen the contribution of its viscoplastic nature multiplying Re^* by the Bingham number, which for viscoplastic materials expresses the relative importance of yield stress to viscous stress and is defined as:

$$Bm = {}^{\tau_y D}\!/_{\mu^* U} \tag{9}$$

It is found that the friction factor can be well predicted by Equation (10):

$$f = 5.974\ Bm^{-0.266} Re^{*1.064} \tag{10}$$

whose coefficients are determined by fitting the numerical data that correspond to the design points (Figure 10). The validity of Equation (10) is further tested by comparing it with the data obtained using the verification points. Figure 10 shows that the proposed correlation is in excellent agreement with all the results.

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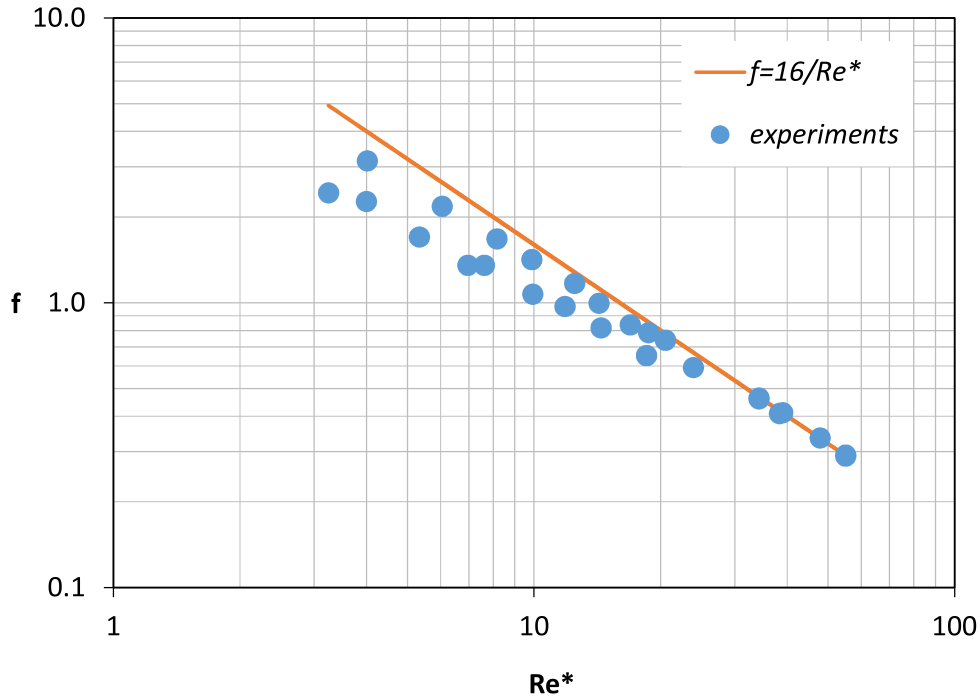

Figure 9. Friction factor vs. Re*.

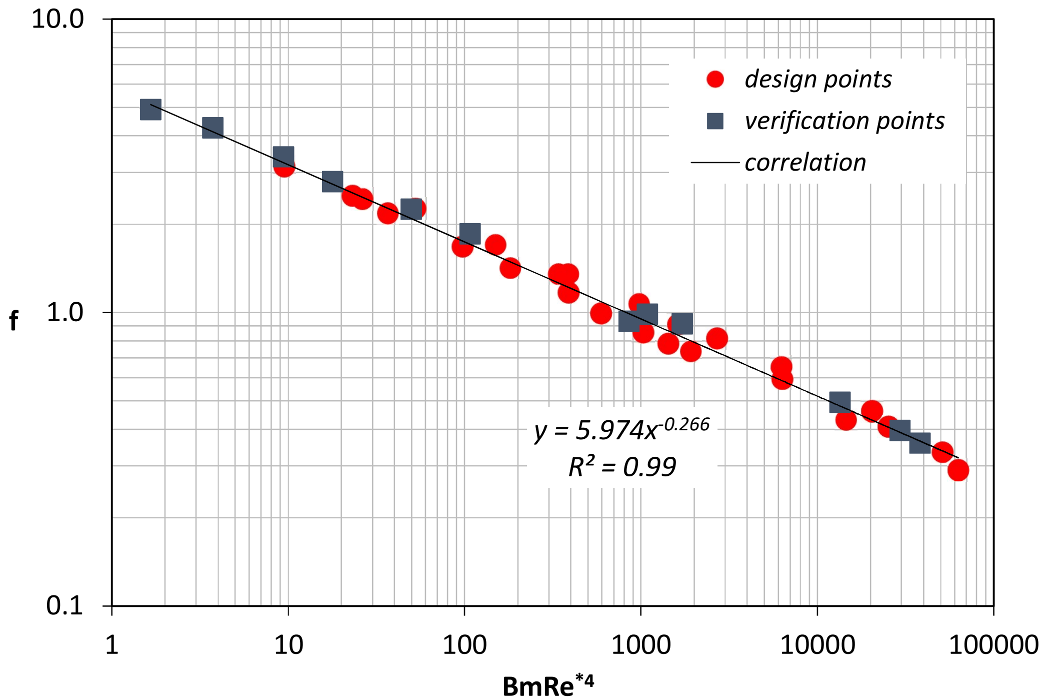

Figure 10. Friction factor versus the dimensionless group $BmRe^{*4}$.

Figure 11 compares the friction factor values, f_{calc}, calculated by Equation (10) with the ones resulted from the CFD simulations, f_{CFD}. It is proved that Equation (10) can predict the Fanning friction factor with 10% uncertainty.

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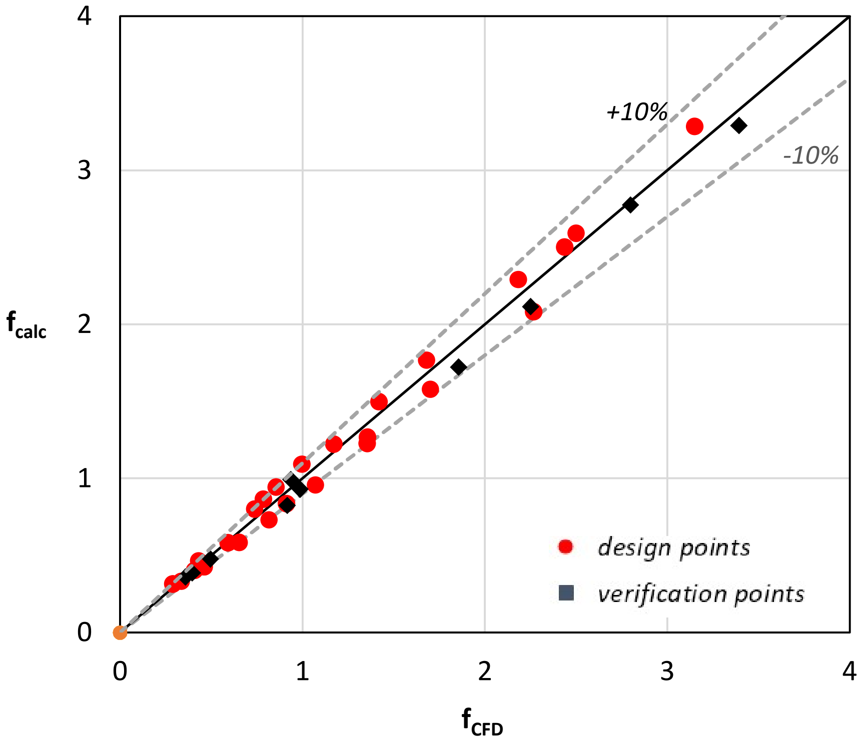

Figure 11. Comparison between calculated and predicted values.

5. Concluding Remarks

In this study a simplified model that can predict Fanning friction factors of laminar blood flow in small-caliber vessels is proposed. The study has been conducted using CFD simulations validated with relevant experimental data acquired by employing an appropriate experimental set-up. The effect of the flow rate, the hematocrit value and the vessel diameter on the pressure drop has been considered. The interpretation of the resulting data led to the proposal of a straightforward way for estimating with reasonable accuracy (i.e. better than ±10%) the Fanning friction factor and consequently the pressure drop, during flow of blood (for a hematocrit range 35-55%) in small diameter vessels (300-1800 μm).

The calculation procedure comprises the following steps:

1. For given volumetric flow rate, Q, and vessel inside diameter, D, the pseudo-shear rate γ^* is calculated by Equation (5).
2. For given hematocrit value, H_t, an effective viscosity, μ^*, that corresponds to the pseudo-shear rate is estimated using Equations (3, 2 & 1).
3. The corresponding Re^* and Bm numbers are calculated by Equations (4 & 9).
4. The Fanning friction factor, f, is then calculated by the proposed correlation (Equation (10)).
5. Finally, the pressure drop $\Delta P/L$ is calculated by Equation (6).

The proposed methodology (Figure 12) is an easy to use tool that can help scientist to quickly and accurately estimate the pressure drop exerted during blood flow in small caliber vessels. Obviously, this methodology is not exclusively applicable for blood flow, but, if step 2 is excluded, it can be applied for any shear thinning Casson fluid.

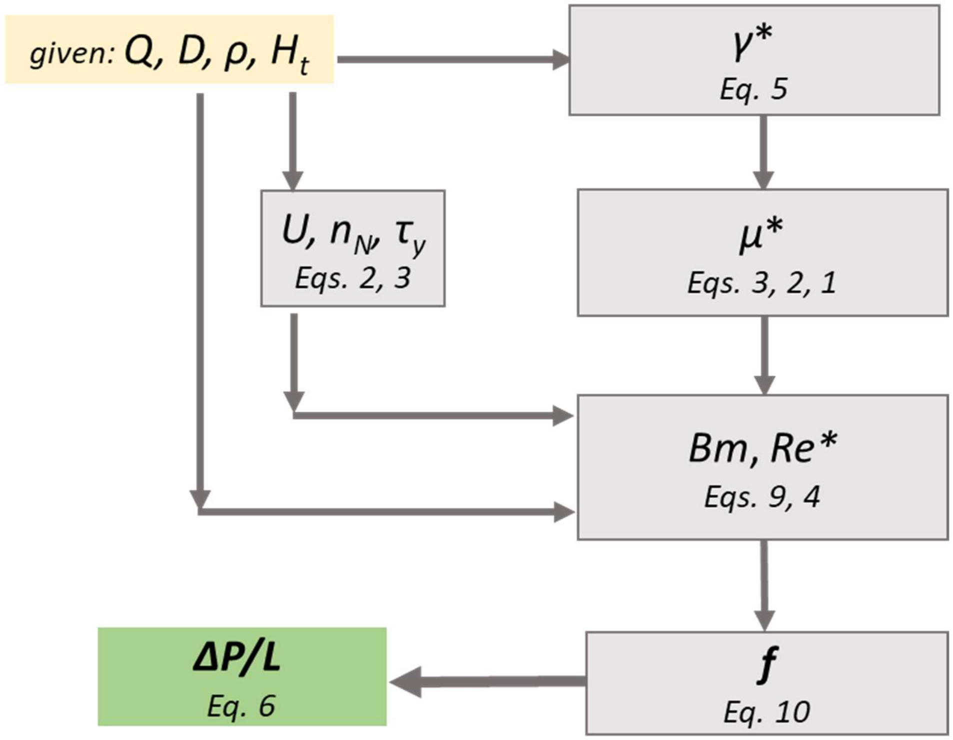

Figure12. Calculation procedure of the proposed methodology.

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Author Contributions: Spiros V. Paras had the initial conception of this work; Spiros V. Paras and Ioannis D. Tzouganatos designed the experiments; Ioannis D. Tzouganatos performed the experiments; Aikaterini A. Mouza designed the CFD simulations; Olga D. Skordia performed the simulations; Aikaterini A. Mouza and S.V. Paras interpreted the numerical results; Aikaterini A. Mouza wrote the manuscript.

Conflicts of Interest: The authors declare no conflict of interest.

Nomenclature

Bm	Bingham number, -
D	Inside vessel diameter, m
f	Fanning friction factor, -
f_{CFD}	Fanning friction factor from CFD simulations, -
f_{calc}	Fanning friction factor from Equation (7), -
H_t	Hematocrit, %
H_{tc}	Critical hematocrit, %
L	Length, m
n_p	Plasma viscosity, Pa·s
P	Pressure, Pa
Q	Volumetric flow rate, mm³/s
Re_∞	Reynolds number corresponding to μ_∞
*Re**	Effective Reynolds number (Equation (4)), -
U	Mean velocity, m/s
x	Axial coordinate, m

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Greek letters

γ^* Pseudo shear rate, s^{-1}
ΔP Pressure drop, Pa
μ Blood viscosity, Pa·s
μ^* Effective viscosity, Pa·s
μ_∞ Asymptotic viscosity value, Pa·s
ρ Blood density, kg/m^3
τ Shear stress, Pa
τ_y Yield stress, Pa

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