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Front Microrheology of Biological Fluids

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Abstract. We present a study of front microrheology through the development of a microfluidic device and method that describes accurately the non-linear rheology of blood, by means of a simple optical detection method based on tracking the fluid-air interface moving inside a microchannel. We study the behavior of Newtonian fluids of different viscosities and densities, as well, we performed measures for blood at different red blood cells concentration and at different days from its extraction. We have developed a scaling method which allows us to determine a relation between the red blood cell properties at different days from its extraction, according to the aggregation properties of red blood cell. Our results have been compared with theoretical and bibliographical results, which shows reliable results with an error around 6%. In general, our device and method is usefull as a viscometer and rheometer, as well as, it enables to establish a relation between blood viscosity and its red blood cells characteristics.

1. Introduction

Since Poiseuille times, several techniques have been developed to measure the viscosity of blood. During the 60s and 70s, with the appearance of the first rheometers, the rheological properties of blood were accurately measured and it was observed that blood had shear thinning properties, meaning, that if the velocity of the blood flow increases, the viscosity of blood decreases. From a medical point of view, blood and its blood plasma are the most effective fluids to detect global pathologies in human and animals. These pathologies may be related to their viscosities, their plasma proteins, or the properties of its red blood cells, as their aggregation, deformability or the elastic properties of its cellular membrane. With the birth of microfluidics at the beginnings of the 90s, new techniques for the diagnostic of diseases have been developed. The advantages in the use of microfluidic devices for diagnostics are: the low amount of sample required to perform a measure, their portability, that they are easy to use and the low cost of its fabrication. We have



developed a microfluidic device and method that describes accurately the non-linear rheology of blood, by means of a simple optical detection method based on tracking the fluid-air interface moving inside a microchannel. We present the results for two Newtonian fluids water and blood plasma. As well, we presents viscosity results for blood at different red blood cells concentration and at different days from its extraction.

2. Experimental Setup

The microsystem is a rectangular channel, of heights $b = 150$ and $b = 300 \mu m$, width $w = 1 mm$ and length $l = 4 cm$, molded in a biocompatible hydrophobic silicone, PDM (polydimethylsiloxane), on a glass substrate according to Replica Moulding and Soft Lithography microfabrication methods [1, 2]. The bottom surface of the microchannel is made of glass and the top and lateral surfaces are made of PDMS. The inlet and the outlet are perpendicular holes set at each extremity of the channel. The observation of the flow inside de microchannel is made using and inverted microscope Optika XDS-3 with a $4\times$ objective and a high speed camera, Photrom Fastcam Viewer 3, recording between 1000 and 125 frames per second.

We perfomed measurements of the velocity of the fluid interface across the length of the channel at different injected pressures. Pressures range from $\Delta P = 4116$ to $490 Pa$. The mean velocity of the fluid, is obtained by tracking the fluid front mean position, h , as a function of time between several contiguous images and averaging its values thought the channel length. Pressure is controlled through a fluid column inside a reservoir set at heights from $H = 0.40$ to $0.050 m$ and conected to a biocompatible tube of uniform internal circular cross-section of diameter $d = 0.254 mm$ and length $L = 0.430 m$, see Figure 1.

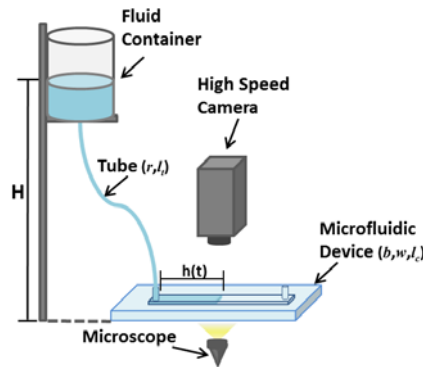


Figure 1. Schematic representation of the experimental setup [3].

3. Results

3.1. Viscosity of Newtonian Fluids

The viscosity of the newtonian fluids is calculated considering the coupled system, reservoir-tube-microchannel, by means of the relation between the shear rate, $\dot{\gamma} = \dot{h}/b$, and a rescaled stress defined as:

$$\sigma_{rs} = \frac{\pi r^4}{8wb^2l_t} (\rho gH - P_L), \quad (1)$$

where P_L is the Laplace pressure due to the curvature of the fluid front. The viscosity value is then obtained as a function of the velocity, \dot{h} , by means of:

$$\eta = \frac{\sigma_{rs}}{\dot{\gamma}} = \frac{\pi r^4}{8wbl_t} \frac{(\rho gH - P_L)}{\dot{h}} \quad (2)$$

The viscosity results for Newtonian fluids are shown in Figure 2, for two different channel heights.

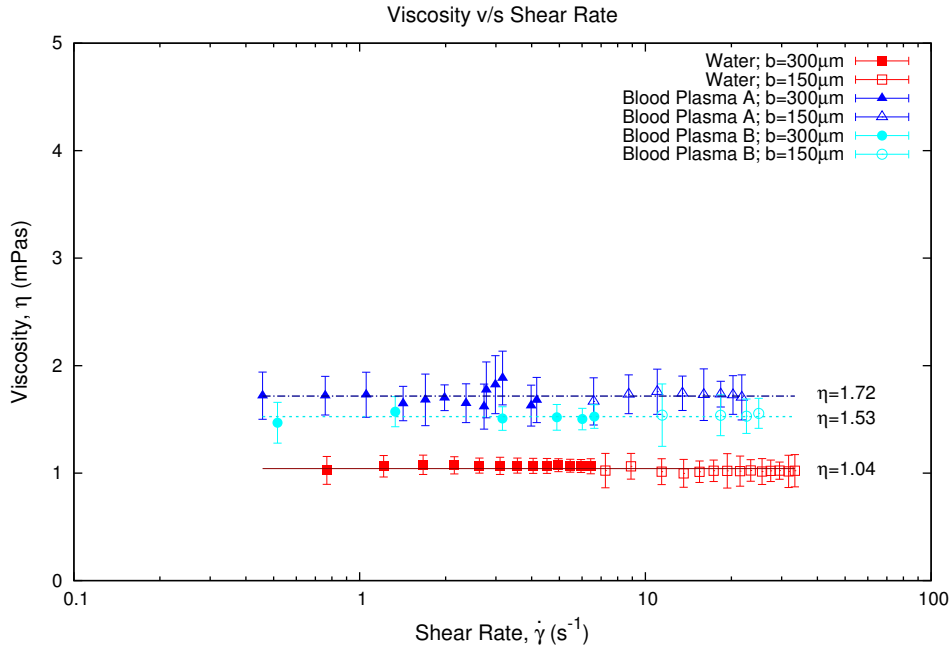


Figure 2. The figure shows the viscosity of two different blood plasma samples: sample A (blue) and sample B (cyan) compared with water (red). The viscosity values are obtained by mean of Eq. (2) as a function of the shear rate for two different channels heights. The viscosity values for each samples are $\eta_{pA} = 1.72 \pm 0.01 \text{ mPas}$ and $\eta_{pB} = 1.53 \pm 0.02 \text{ mPas}$.

We observe from Figure 2 that combining the results for different channel heights we are able to extend the viscosity estimation for almost 2 decades [4].

3.2. Viscosity of Blood

In the case of blood, which is non-Newtonian, we obtained the viscosity as a function of the shear rate using a Power Law Model [5]:

$$\eta = m\dot{\gamma}^{n-1}, \quad (3)$$

where n is the viscosity exponent, m is the base viscosity value and the shear rate is defined as:

$$\dot{\gamma}_F = \frac{b^2 w}{\pi r^3} \left(3 + \frac{1}{n} \right) \frac{\dot{\gamma}}{b} \quad (4)$$

according to the Weissenberg-Rabinovich-Mooney correction for non-Newtonian rheometry.

Studying a 48% hematocrit blood sample, measured at different days from extraction, we observe a shear thinning behavior for blood viscosity, see Figure 3. Furthermore, the viscosity values of the fifth day sample are higher than the viscosity values of the fresh sample.

3.3. Aggregation of Red blood cells

Comparing images of the sample at diferents days from its extraction we observed an increased aggregation of the red blood cells, see figures 4 and 5.

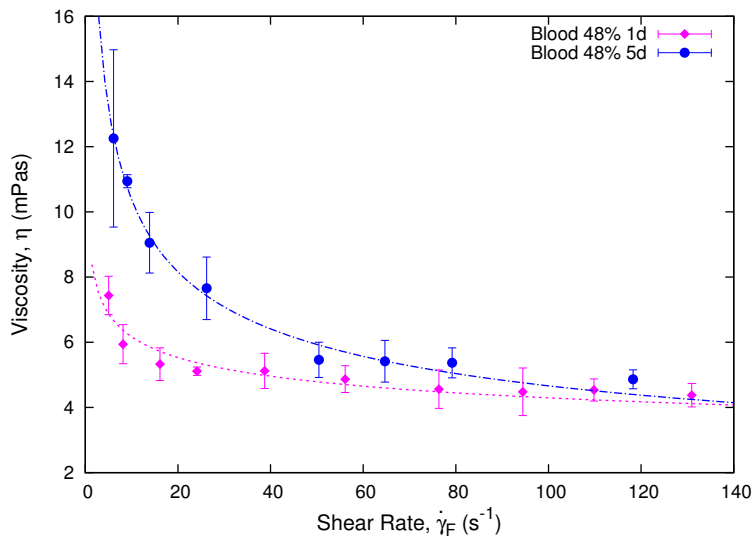


Figure 3. The figure shows the viscosity of a blood sample at a 48% hematocrit, at different days from its extraction, in magenta for a fresh blood sample and in blue for a 5 days blood.

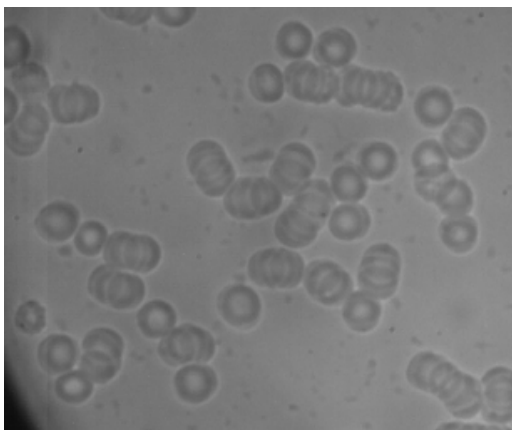


Figure 4. Image of the red blood cells at the first day from its extraction. The image was taken using a x100 objective.

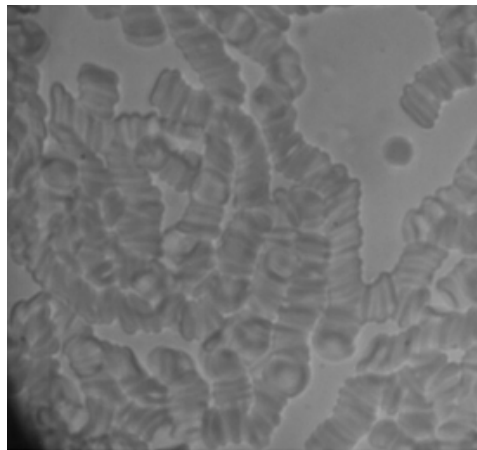


Figure 5. Image of the red blood cells at the fifth day from its extraction. The image was taken using a x100 objective.

To analyze the effects of aging, we fix the value of the hematocrit and study the behavior of the blood sample as it ages. We introduce a new, non-linear scaling parameter, the adhesion scaling number, A , which quantifies the effects of aging on RBC's aggregation [6]. This quantity is defined as:

$$A = \frac{\eta_0 \dot{\gamma}_F d^3}{E(\dot{\gamma}_F, a, E_0)} \quad (5)$$

where η_0 is the viscosity of plasma, $d \approx 7.8 \mu\text{m}$ is the average diameter of a red blood cell, E is the energy scale associated to the aggregation forces between RBCs, where $E = E(\dot{\gamma}_F, a, E_0) = k_a(\dot{\gamma}_F, a)E_0$. The scaling factor k_a is a function of the front shear rate $\dot{\gamma}$ and a the age of the sample and $E_0 \approx 500k_B T$ is a reference value of RBC's aggregation [7].

The scaling factor is obtained by collapsing the curves for the variation of the viscosity as the shear rate changes. In order to quantify how aggregation induces this viscosity increment we establish a relation between the sample viscosities by means of the aging factor, $k_a(\dot{\gamma}_F, a)$, defined as:

$$k_a(\dot{\gamma}_F, a) = \left(\frac{\eta_{n5d}}{\eta_{n1d}} \right)^2. \quad (6)$$

The last step of the scaling, consist of writing the normalized viscosity of blood as a function of the adhesion scaling number, A , which depends on the aggregation energy correspondent to each sample. For an unaggregated sample, $E_0 \approx 2 \times 10^{20} J$ which using Eq. 6, is increased by $k_a = 2.79$ for the non-Newtonian regime and $k_a = 1.22$ for the Newtonian regime, for the 5 days aggregated sample. In this case, the viscosity of both regimes show changes which are assumed a consequence of the aggregation of RBCs, due to the aging of the sample.

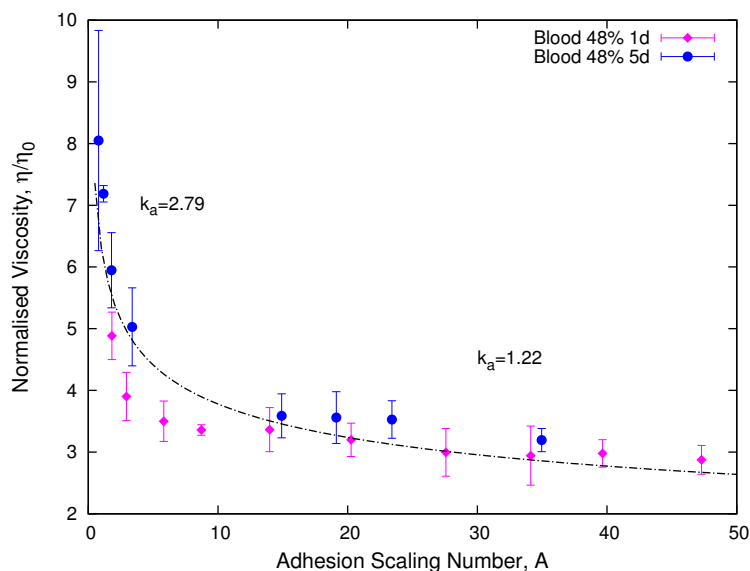


Figure 6. The figure shows the normalized viscosity of the blood samples against the Adhesion Number, A , correspondent to the non-Newtonian $k_a(\dot{\gamma}_F, a) = 2.79$ and $k_a(\dot{\gamma}_F, a) = 1.22$ for the Newtonian regime. We appreciate the collapse of the viscosity curves as a result of our scaling method.

4. Discussion

We have shown that variations in the non-linear viscosity of blood associated to aging can be explained by means of a scaling theory based on the introduction of an adhesion scaling number, A . This quantity is defined as the ratio between the viscous energy and the aggregation energy. Our scaling theory allows us to quantify the increase in aggregation energy by aging with respect to its reference characteristic scale, E_0 . The increase in the characteristic aggregation energy is given by the aging factor, $k_a(\dot{\gamma}_F, a)$, which is observed to increase as the sample ages. A strength of our approach comes from the introduction of a novel front microrheometer that allows to extract bulk non-linear viscosities from the simple observation of a moving fluid-air interface.

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