Capillary flow of whole blood in microsystems: non-Newtonian blood behavior and substrate reagent-coating effect

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ABSTRACT

The use of whole blood is a preferred solution for portable diagnostic and monitoring systems. We analyze here two particularities of microsystems for blood analysis: the blood non-Newtonian behavior, and the capillary flow in reagent-coated channels.

Most of the time, portable systems use capillary forces to move the samples. It is shown that the capillary flow of blood does not follow the Lucas-Washburn-Rideal law when the capillary flow velocity is small, due to its non-Newtonian rheology and to the formation of rouleaux of RBCs.

In a second step, we investigate the capillary flow of blood on reagent-coated surfaces; first experimentally by observing the spreading of a droplet of blood on different reagent-coated substrates (IgM, dye); second theoretically and numerically using the general law for spontaneous capillary flows and the Evolver numerical program.

Keywords: whole blood, point-of-care systems, non-Newtonian flow, reagent, RBC rouleaux, Hoffman-Voinov-Tanner (HVT) law, Lucas-Washburn-Rideal (LWR) law, sponatneous capillary flow (SCF).

1 INTRODUCTION

Portable diagnostic systems for the on-site monitoring of patient health directly use whole blood from finger's tip and capillary forces to move the blood inside the device [1-4].

The dynamics of whole blood flow is related to its viscosity. Whole blood rheology is complicated. It depends on many parameters, such as hematocrit and fibrinogen levels. A law for viscosity as a function of the shear rate is the Casson law (figure 1) [5], or the more general Herschel-Bulkley law [6]. When the shear rate is small, rouleaux of RBCs form, giving the blood its strong non-Newtonian, yield stress behavior (figures 2A and 2B) [7,8]. Hence the capillary flow of whole blood departs from the Lucas-Washburn-Rideal law for large penetration distances (figure 2C) [9,10].

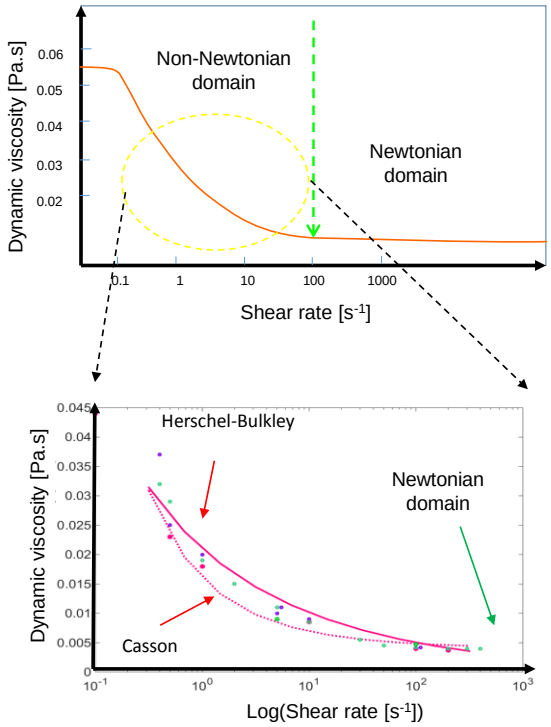

Fig.1. Dynamic viscosity of whole blood as a function of the shear rate (top), showing a shear-thinning behavior; blow-up on the shear-thinning of whole blood (bottom): the dots correspond to experimental data found in the literature, the two curves are the HB and Casson formulas.

Point-of-care or home-care systems need embedded reagents, coated on the walls or lyophilized [11,12]. Dry coatings modify both the geometry of the channel and their surface energy, resulting in a change of the capillary flow [13].

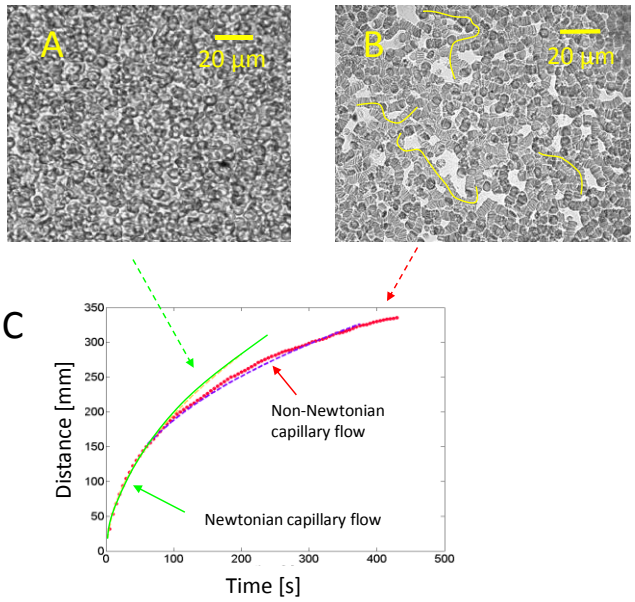

Fig.2. A: dispersed whole blood; B: whole blood forming "rouleaux" (the yellow lines point out some of the rouleaux); C: penetration distance as a function of time showing the Newtonian and non-Newtonian behavior: green line corresponds to the LWR law, red dots to the viscoelastic regime.

We have investigated the capillary flow of blood on reagent-coated surfaces: first experimentally by observing the spreading of a droplet of blood on different reagent-coated substrates such as IgM and dye (figure 3). It was checked that the Hoffman-Voinov-Tanner law is approximately verified for whole blood spreading on most reagent coated surfaces [14,15].

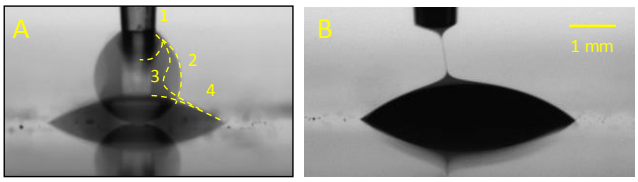

Fig.3. Spreading of whole blood on reagent coated surfaces: A, initial contours of the droplet detaching from the pipette (1,2,3,4 are the successive contours of the drop); B: spreading showing the formation of a thread.

Finally, the capillary flow on coated surfaces has been investigated theoretically and numerically using the general law for spontaneous capillary flows and the Evolver numerical program [13,16] (figure 4). We made the assumption that the spreading is fast compared to the redissolution of the coating.

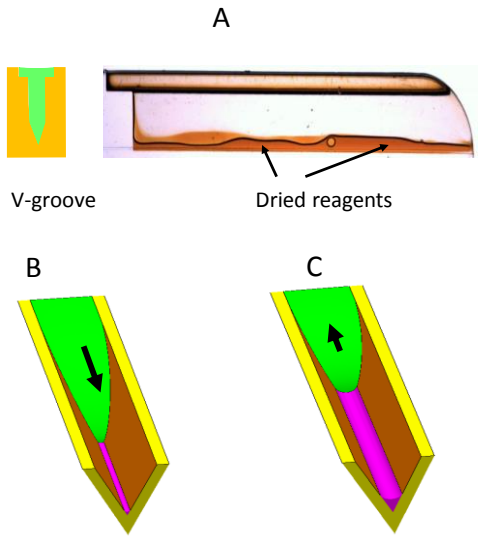

Fig.4. A: view of a V-groove with dried reagents coating the interior corners; B and C: Evolver calculation of the capillary flow in a V-groove coated with reagents.

2 WHOLE BLOOD CAPILLARY FLOW

Whole blood capillary flow has been studied using a simple capillary tube of 100 µm diameter plugged to an open inlet port (figure 5). The velocity and penetration of the flow are monitored by following the position of the advancing interface using a millimetric paper.

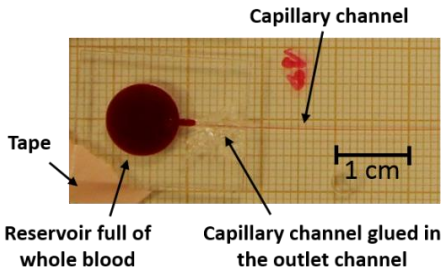

Fig.5. View of the cylindrical tube plugged to the reservoir.

At the beginning of the capillary flow, velocities are sufficiently high to produce shear rates larger than the threshold of approximately $\dot{\gamma}_{th} \sim 100\ s^{-1}$ characterizing the Newtonian-viscoelastic transition (figure 1). The penetration distance obeys the LWR law for a tube of radius R :

$$z = \sqrt{\frac{\gamma}{\mu}\frac{R}{2}\cos\theta}\ \sqrt{t}\ . \qquad (1)$$

After a distance z_t characterized by

$$z_t \approx \frac{\gamma}{\mu\,\dot{\gamma}_{th}}\cos\theta \qquad (2)$$

where γ is the surface tension, μ the viscosity (Newtonian) and θ the contact angle, the flow becomes non-Newtonian and LWR law is no more verified (figure 6). This viscoelastic behavior is associated to the formation of rouleaux[7,8].

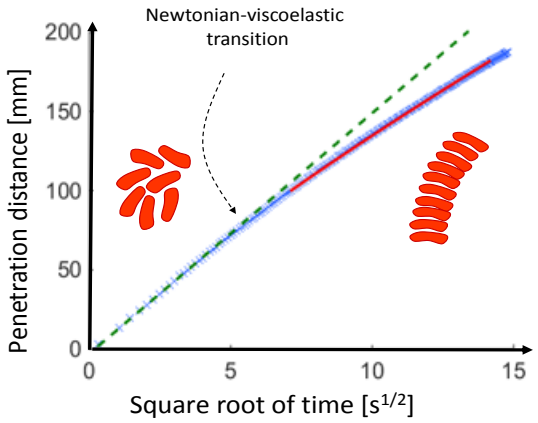

Fig.6. Penetration distance vs. elapsed time. The blue dots correspond to the experimental observations. Green dotted line the LWR law, the red line results from a model for the viscoelastic regime. LWR law is verified in the Newtonian regime while a Herschel-Bulkley regime fits the viscoelastic regime. In the Newtonian regime RBCs are dispersed, while they form rouleaux in the viscoelastic regime.

3 SPREADING OF WHOLE BLOOD ON REAGENT-COATED SUBSTRATES:

Experiments have been conducted to observe the spreading of whole blood on different substrates: non coated COP (cyclo-olefin polymer), COP coated with IgM and dyes containing various excipients (figure 7). The spreading was observed using a Drop Shape Analyzer (DSA100, Krüss, Germany). As shown in figure 3, the droplet first touches the flat substrate, then spreads. Often whole blood forms a thread before total release due to the strong viscoelastic behavior (figure 3B) [17].

The kinetics of the advancing contact angle $\theta_a(t)$ is monitored and a static contact angle θ_s is determined at the end of the spreading motion. The location of the advancing triple line $z(t)$ is recorded, which produces the spreading velocity $V(t)$. Eliminating the time, a plot of the dynamic contact angle as a function of the capillary number can be drawn (figure 7). It is checked that the Hoffmann-Voinov-Tanner law is satisfactorily respected, i.e.

$$\theta_a^3 - \theta_s^3 \cong c\,Ca\,. \qquad (3)$$

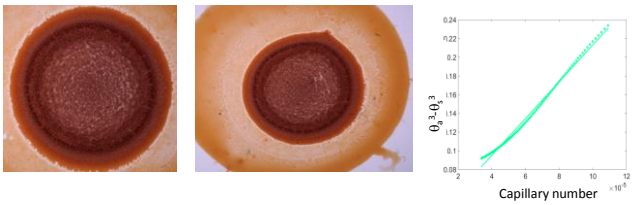

Fig.7. Left: spreading of whole blood on coated planar substrates; after drying blood leaves rings on the substrate. Right: HVT law is respected during the spreading.

Hence an advancing contact angle is determined as a function of the velocity: $\theta_a \cong \sqrt[3]{c\,Ca + \theta_s^3}$.

4 REAGENT COATED CHANNELS

It is observed that the reagent-coating of microchannels often concentrates in corners and wedges after drying (figure 4.A). Assuming different morphologies of these coatings, and using the contact angles determined in the preceding approach, the SCF conditions are determined for each different configuration (figures 4B and C). SCF condition in composite channels is given by the extended Cassie relation [13]

$$f_{air}\cos\pi + f_{not-coated}\cos\theta + f_{coated}\cos\theta_c > 0 \qquad (4)$$

where the coefficients f are the fractions of the cross section lengths of different wettabilities, and the contact angles θ et θ_c are respectively the wall and reagent-coated wall contact angles. We assume here that the capillary number is small and consequently that the advancing contact angles are equal to the static ones. For example, assuming the coating schematized in figure 8, the condition for SCF deduced from (4) is

$$\sin\alpha < \cos\theta - \frac{z}{h}\left(\cos\theta - \sin\alpha\cos\theta_c\right)\ , \qquad (5)$$

where α is the ½ dihedral angle.

Moreover, we can use the software Evolver to predict the SCF in channels which corners have been coated by the dried reagent, as shown in figure 9 in the case of a V-groove

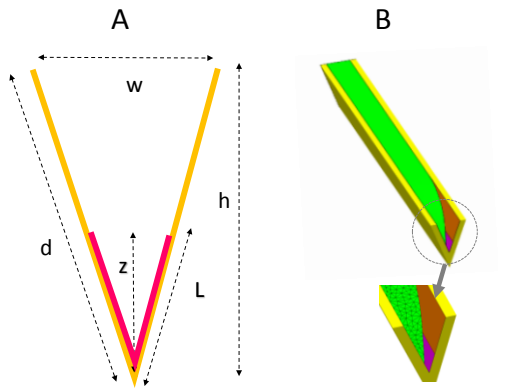

Fig.8. SCF in a V-groove uniformely coated in the corner (colors: red or magenta for coating, orange or brown for the naked wall).

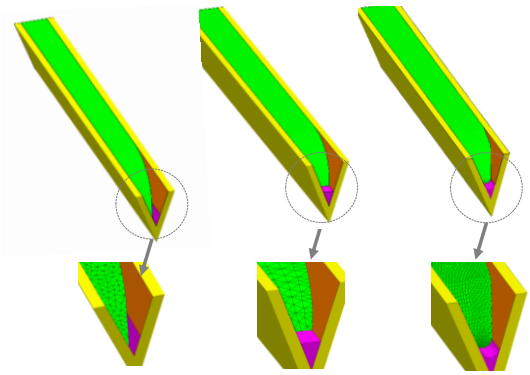

Fig.9. Evolver calculation of the SCF in V-grooves, depending on the shape of the coating (uniform, triangular or rounded coating/deposit in the wedge (colors: magenta for reagent, brown for naked walls)

5 CONCLUSION

The design of portable point-of-care and home-care systems for blood analysis relies on the rheology of whole blood, and on the wetting of walls coated with reagents.

In this work, an investigation of the viscoeleastic characteristics of whole blood has been done, showing that a Newtonian-viscoelastic transition may take place depending on the velocity of the flow.

The wetting of channels coated with reagent is analyzed by determining the contact angle of whole blood with different coatings. SCF conditions in channels which geometry and surface energy are modified by reagent-coatings has been investigated theoretically and numerically, under the assumption that the time scale for re-dissolution is larger than that of the flow. Work is still needed to investigate the re-dissolution of the reagents, and to predict the velocities of the capillary flow on inhomogeneous substrates.

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