On the influence of non-Newtonian fluids on microsystems for biotechnology

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ABSTRACT

In biotechnology, it is generally the use to calculate and design prototypes of microsystems by considering aqueous or organic liquids that have a spatially uniform viscosity. However, many liquids used in biological applications are at least slightly or moderately viscoelastic; their viscosity decreases with the shear rate exerted by the flow field. This is the case for whole blood, sweat and tears, and polymeric liquids—like alginate or polysaccharide solutions. At first sight, it is tempting to neglect the viscoelastic effect assuming it is of second order; however, we show here that this is not always the case. In this work, we analyze the rheology of polymeric solutions and we show the implications of their viscoelastic behavior on the flow field in capillary ducts, microfluidic networks and flow focusing devices.

Keywords: viscoelasticity, shear thinning, non-Newtonian viscosity, polymeric liquids.

1 INTRODUCTION

Before the beginning of the 2000s, not much attention has been given to the rheological behavior of the liquids used in most in vitro microfluidic systems. The non-Newtonian behavior of some of the fluids used in biological applications has been pointed out in 2001 [1]. However, if the rheology of polymeric solutions of biological liquids has been investigated since [2], visco-elastic effects in microsystems for biotechnology are still not very well known and they are most of the time overlooked in the design of such systems.

Microsystems for biotechnology are usually designed by considering aqueous or organic Newtonian liquids. However, many liquids used in biological applications are at least slightly or moderately viscoelastic; their viscosity is a function of the shear rate exerted by the flow field. It decreases with the shear rate. This is the case of physiological fluids—blood, sweat and tears—and polymeric liquids—like alginate and polysaccharide solutions. It is tempting to neglect the viscoelastic effect assuming its effect is of second order. We show in this work that this is not always the case, especially for medium Reynolds number. We first analyze the rheology of polymeric solutions and we show the implications of their viscoelastic behavior on the flow field in capillary tubes, microfluidic networks, recirculation chambers and flow focusing devices.

2 NON-NEWTONIAN VISCOSITY

Polymeric liquids used in microfluidic systems are more or less visco-elastic depending on their concentration. Basically, the viscosity of visco-elastic polymeric liquids depends on the concentration in polymers, temperature and flow characteristics.

$$\eta = \eta\left(c, T, \dot{\gamma}\right) \tag{1}$$

In rheology of polymers, the very general Martin relation [3] usually applies for polymeric solutions

$$\eta_{sp} = \left(c[\eta]\right)\, e^{k'[\eta]c} \tag{2}$$

where η_{sp} is the specific viscosity, $[\eta]$ the intrinsic viscosity, and k' the Huggins coefficient. For dilute polymeric solutions, a Taylor expansion yields the Huggins law

$$\eta_{sp} = c[\eta] + k'\left(c[\eta]\right)^2 \tag{3}$$

For semi-dilute solutions, more terms in the expansion of (2) should be kept. However, it has been shown that the specific viscosity can generally be approached by the power law

$$\eta_{sp} = a\left(c[\eta]\right)^n \tag{4}$$

Taking alginate solutions as an example, it can be shown that relation (4) fits well the experimental results with a=0.1, $[\eta]$ of the order of 300-800 mL/g and n of the order of 3-4 depending on the type of alginate [3]. Finally, the viscosity of the polymeric solution is given by

$$\eta = \eta_s\left[1 + a\left(c[\eta]\right)^n\right] \tag{5}$$

As a general rule, the viscosity of a polymeric liquid decreases with temperature. The Vogel-Fulcher-Tamman (VFT) hyperbolic relation is often used to describe the thermal dependency of the viscosity [4] and writes

$$\log\eta = A + \frac{B}{T - T_0} \tag{6}$$

where A and B are experimentally determined coefficients.

Besides its dependency on concentration and temperature, the viscosity of polymeric solutions decreases with the shear rate of the flow, because, in high shear regions, the long polymer chains align with the flow; such a behavior is called shear thinning. Many different laws have been proposed for the non-Newtonian viscosity, depending on the carrier liquid and polymers. In the domain of medium shear rates, for shear thinning liquids, it is common to use the Carreau-Yasuda relation [5]

$$\eta = \eta_0[(1+(\tau\dot{\gamma})^{\alpha}]^{\frac{m-1}{\alpha}} \tag{7}$$

where η_0 is the viscosity at zero shear rate, $\dot{\gamma}$ is the shear rate, τ a relaxation time, α is a constant and m depends on the concentration of the solution. Again, taking alginates as an example, the Carreau-Yasuda relation fit well the experimental measurements as shown in figure 1. The relaxation times are deduced from a fit of (7) on the different experimental curves.

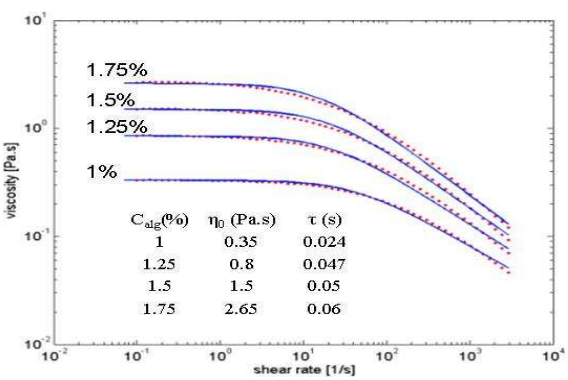

Fig.1. Viscosity of HV Keltone alginate solutions versus shear rate: the dots correspond to the experimental results, the continuous line to the Carreau-Yasuda model. The four curves correspond to four alginate concentrations: 1, 1.25, 1.5, 1.75 wt%. τ is the relaxation time.

3 MODEL

For shear dominated flows, the non-Newtonian viscosity can be taken into account by introducing a viscosity depending on the shear rate in the Navier-Stokes equation. Note that if the linear Stokes approximation is used when the inertial effects are negligible (small velocities) the equations regain their non-linear character with the introduction of the shear thinning viscosity. The expression of the shear rate depends on the spatial dimension of the problem. The general expression for the shear rate is

$$\dot{\gamma} = \sqrt{2D:D} \tag{8}$$

where D the deformation tensor given by

$$D = \frac{1}{2}\left(\nabla V + \nabla V^T\right) \tag{9}$$

where V is the velocity vector. For a 2D Cartesian coordinate system (x,y), the expression of the shear rate is

$$\dot{\gamma} = \sqrt{\frac{1}{2}\left[4\left(\frac{\partial u}{\partial x}\right)^2 + 2\left(\frac{\partial u}{\partial y}+\frac{\partial v}{\partial x}\right)^2 + 4\left(\frac{\partial v}{\partial y}\right)^2\right]} \tag{10}$$

The viscosity of the liquid is obtained by plugging (10) in (7).

4 CAPILLARY TUBE

In a cylindrical tube, a laminar flow field is determined by the Poiseuille-Hagen relation, and the velocity profile is parabolic. It has been shown at the macroscale that the viscoelastic profile differs from the parabolic profile. This is evidently also the case for microflows (fig.2). As a result the pressure drop is not given by the Newtonian expression. At low shear, or for dilute solutions, the Carreau law reduces to the Ostwald expression $\tau = \eta\dot{\gamma}^n$ and the Fanning friction factor can be expressed as $16/Re_{NN}$, where Re_{NN}, is a non-Newtonian Reynolds number [6]. However, to our knowledge, there is no closed-form expression for a Carreau fluid for rectangular channels (fig.3), and one must rely on numerical modeling. In the following section, we show some consequences of this change of frictional pressure drop.

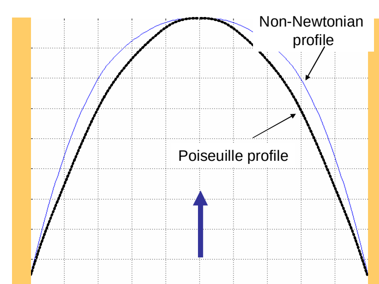

Fig.2. Newtonian and non-Newtonian velocity profiles in a cylindrical tube.

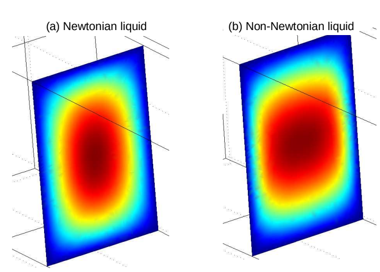

Fig.3. Contour plot of the velocity in a rectangular channel showing a different flow pattern: (a) Newtonian fluid, (b) non-Newtonian fluid (COMSOL)

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5 MICROFLUIDIC NETWORKS

An assembly of capillary tubes or microchannels is called a microfluidic network. Networks are now currently used in biotechnology: they are used to perform blood separation [7], concentration gradients [8], flow separation, and microporous needles [9]. Most of the time, the flow rate in each branch depends on the flow resistances of all the branches of the system. The system is then very difficult to design. If the flow is Newtonian, and only one fluid is used, it can be shown that the viscosity of the fluid does not affect the flow distribution [9]. However if the liquid is non-Newtonian, the design of the system must be adjusted specifically. Besides, the flow rate distribution will change with any change in the inlet conditions. In the Newtonian case, the hydraulic resistance R of a branch of rectangular cross section (a,b) is

$$R = R(\eta, L, a, b) = \Delta P / Q$$

where P is the pressure and Q the flow rate. In a non-Newtonian case, we can write symbolically the implicit expression

$$R = R(\eta(Q), L, a, b) = \Delta P / Q$$

A simple numerical calculation shows that after one bifurcation, the distribution of flow rates changes between a Newtonian and non-Newtonian fluid (fig.4). This is even more the case after two bifurcations: the flow rate inside the smaller channels is dramatically reduced. The reason for this behavior is obvious: when the flow rate is small in a channel, the shear rate is small and the viscosity high. The flow redirects into the larger channels.

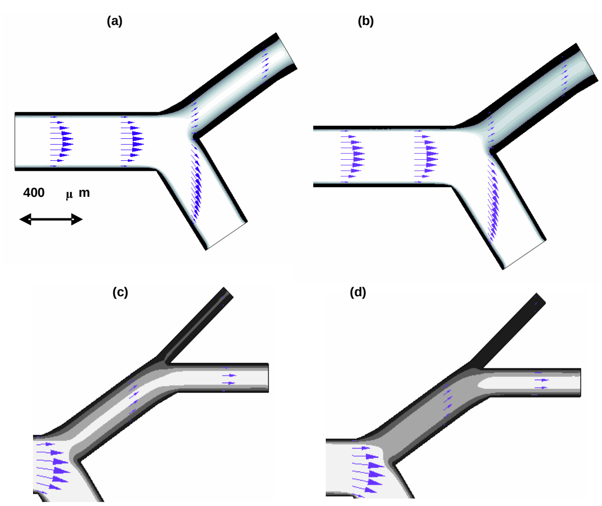

Fig.4. Flow in microfluidic networks: (a) and (c) Newtonian fluid, (b) and (d) non-Newtonian fluid (alginate) (COMSOL).

6 CONVECTIVE TRANSPORT

Convective transport of biochemical species is linked to the viscosity of the carrier phase, according to the Einstein relation $D = k_B T / 6\pi\eta R_H$. Hence, in viscoelastic fluids, the diffusion coefficient is not spatially uniform and depends on the viscosity distribution. Diffusion is slower in the channel centerline and more efficient near the walls where the viscosity is small. Figure 5 shows the ballistic random walk of species in a channel [10] showing larger diffusion near the wall.

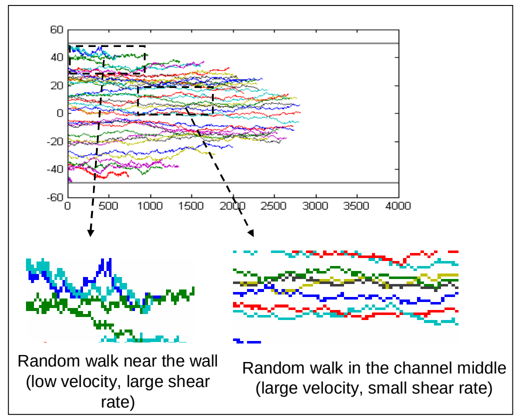

Fig.5. Convective transport of species in a microchannel.

7 RECIRCULATION REGION

Recirculation regions are commonly used to trap cells or biological objects [11]. Such systems work at medium Reynolds number (Re > 10) where recirculation can occur. The efficiency of trapping in the recirculation chamber is a function of the time (τ) a target takes to travel past the chamber aperture. With the same imposed flow rate in the channel, a numerical calculation shows that this time τ is increased by more than 15% from the Newtonian to the non-Newtonian case (fig.6). Hence the capture changes in the non-Newtonian case. To be complete a diffusion model should be added to the present reasoning in order to take into account the change of diffusion speed linked to viscosity. Moreover, the recirculation pattern is affected by the large viscosity change between the chamber entrance and its middle. A complete assessment of such trapping chambers for non-Newtonian fluids is yet to be done.

8 FLOW FOCUSING DEVICES

Encapsulation of biological objects is a fast developing technique. Flow focusing devices (FFD) such as the one shown in figure 7 are used to encapsulate biological objects.

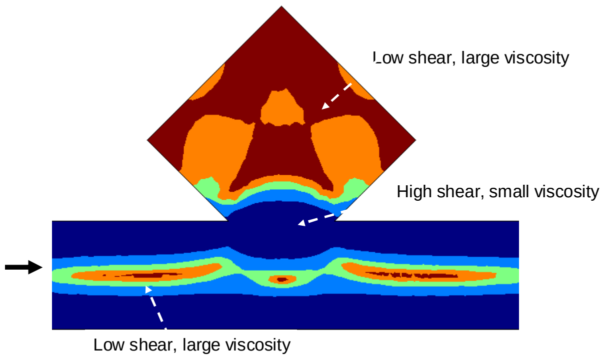

Fig.6. Viscosity contour plot of a non-Newtonian flow past a recirculation chamber (COMSOL).

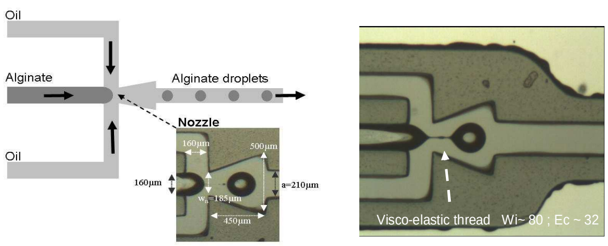

Fig.7. Flow focusing device and droplet formation [12].

The physics of droplet emission of Newtonian liquids (water, oil) has been thoroughly studied, but not yet that of viscoelastic alginate solutions. The first investigations show that the droplet formation is different, especially droplet detaches at the end of a much longer thread [12]. This thread is highly viscoelastic with Weissenberg or Deborah numbers of the order of 50 to 80, and Elastocapillary numbers of the order of 30. Besides, larger satellite droplets form during droplet detachment due to the retraction of an elastic filament. The dimensions of FFDs for cell encapsulation in alginates should take into account these remarks.

CONCLUSION

Non-Newtonian fluids are more and more used in microsystems for biotechnology (blood, alginates, and polymeric liquids). Their behavior differs from that of usual Newtonian liquids: in microsystems, even at low Reynolds number the shear rate can be important due to the small cross dimensions of the microfluidic channels, and the viscosity changes considerably spatially. Hence, microsystem design has to take into account the particular behavior of viscoelastic liquids.

REFERENCES

[1] George M. Whitesides and Abraham D. Stroock, "Flexible Methods for Microfluidics," Physics Today, Vol. 54, n°6, p. 42, 2001

[2] M.T. Nickerson, A.T. Paulson, "Rheological properties of gellan, k-carrageenan and alginate polysaccharides: effect of potassium and calcium ions on macrostructure assemblages," Carbohydrate Polymers, Vol. 58, pp. 15–24, 2004

[3] I. Donati, I.J. Haug, T. Scarpa, M. Borgogna, K.I. Draget, G. Skjak-Braek, and S. Paoletti, "Synergistic effects in semidilute mixed solutions of alginate and lactose-modified chitosan (chitlac)," Biomacromolecules, Vol. 8, pp. 957-962, 2007

[4] S. Girardo, R. Cingolani, and D. Pisignano, "Microfluidic Rheology of Non-Newtonian Liquids," Anal. Chem., Vol. 79 (15), pp 5856–5861, 2007

[5] R. B. Bird, R.C. Armstrong, O. Hassager. Dynamics of Polymeric Liquids. Wiley, New York, 1976

[6] A.B. Metzner, J.C. Reed, "Flow of non-Newtonian fluids-Correlation of the laminar, transition and turbulent-flow regions," AIChE, p.434, 1955.

[7] M. Kersaudy-Kerhoas, R. Dhariwal, M.P.Y. Desmulliez, L. Jouvet, "Blood Flow Separation in Microfluidic Channels," Proceedings of the 1st European Conference on Microfluidics - Microfluidics 2008 - Bologna, December 10-12, 2008

[8] S.K.W Dertinger, D.T. Chiu, N.L. Jeon, G.M. Whitesides, "Generation of gradients having complex shapes using microfluidic networks," Analytical Chemistry 73 1240 - 1246, 2001.

[9] J. Berthier, F. Rivera, P. Caillat, F. Berger, "Dimensioning of a new micro-needle for the dispense of drugs in tumors and cell clusters," Proceedings of the 2005 Nanotech conference, 8-12 May 2005, Anaheim, USA, 2005.

[10] J. Berthier, "Interfacing continuum and discrete methods: convective diffusion of microparticles and chemical species in Microsystems," Proceedings of the 2008 COMSOL Conference, Hannover, Germany, 4-6 November, 2008

[11] J.P. Shelby, D. S.W. Lim, J. S. Kuo, D. T. Chiu, "High radial acceleration in microvortices," Nature, Vol. 425, p.38, 2003

[12] S. Le Vot, J. Berthier, P. Tiquet, N. David, R. Blanc, P-Y Benhamou, F. Rivera, "Non-Newtonian fluids in Flow Focusing Devices: encapsulation with alginates," Proceedings of the 1st European Conference on Microfluidics - Microfluidics 2008 - Bologna, December 10-12, 2008