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Frequency-Induced Stratification in Viscoelastic Microfluidics

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We present a mechanism in the field of microfluidics by which the stratification of a viscoelastic fluid can be induced in a channel on the microscale by applying a dynamic pressure gradient at frequencies within the range of sound. Stratification is obtained with identical layers, parallel to the channel walls, whose number can be tailored. These layers are separated by 2D zero-velocity planes. This would allow different tracer particles with small diffusion coefficients to be confined in different fluid layers within the same microchannel. We obtain analytical results that allow us to make theoretical predictions regarding the possible experimental realization of stratification in a microchannel using a biofluid. We find a relation among the diffusion coefficient, fluid properties, and microchannel thickness that establishes a condition for the confinement of tracer particles to a layer. This mechanism has potential use in micrototal analysis systems and MEMS-containing viscoelastic fluids.

In the past decade, the development of microfluidics has led to the fabrication of microfluidic devices that are useful in chemical and biochemical analysis, biomolecular separation, and micromixing to mention a few.[1−7] Microfluidics aims to integrate many functions on a single device (lab-on-a-chip) for technological applications in physics, materials science, biology, and medicine.[8−12] It does this by the integration of microscale pumps, filters, sieves, valves, and sensors within the microfluidic channels. Whereas from an engineering point of view the development has been explosive, from a theoretical point of view there is the need for a better understanding of the underlying physics.[13] Theory in this area could lead to the control and optimization of existing processes and also to the conception of new techniques for manipulation, separation, mixing, and analysis.

In general, convective terms on the microscale are negligible because fluid viscosity rather than inertia dominates the fluid behavior;[14,15] therefore, the fluid flow in microsystems is not turbulent. In laminar flow, it is possible to create devices in which streams of the same fluid run in stripes parallel to each other. Mixing between parallel stripes occurs only during the long times necessary for diffusion to take place. By playing with system sizes, one can have small devices in which miscible fluids in parallel stripes do not mix (because diffusion has not had time to mix them). This in turn allows for having microchannels that are effectively much narrower than the actual device width. Such devices have been used primarily with the hydrodynamic focusing technique,[16] which allows for cell sorting and counting cytometers on the microscale[17,18] or having a stripe of the size of a single tracer particle in such a way that the detection and counting of particles is done with high precision.[19] The technique has also been used to study the release of ATP from erythrocytes,[20] selective protein deposition,[21] and the delivery of small molecules into mammalian cells,[22] among others. Recently, the boosted migration of large particles has been achived by slaving their dynamics to solute gradients. Applications to microfluidics include filtering and concentrating operations.[23] The coexistence of parallel stripes has been achieved for constant fluid flux, leading to steady flow.

Microfluidic devices often manage fluids with properties that are viscoelastic. The study of viscoelastic fluids is particularly important in dynamic situations such as oscillatory and pulsatile flows. This has been widely analyzed in macroscopic systems in order to understand fluid complexity and optimal flow conditions.[24−28] Theory pertaining to microscopic situations is important

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(1) Whitesides, G. *Nature* **2006**, *442*, 368.
(2) Reyes, D.; Iossifidis, D.; Auroux, P.-A.; Manz, A. *Anal. Chem.* **2002**, *74*, 2623.
(3) Auroux, P.-A.; Iossifidis, D.; Reyes, D.; Manz, A. *Anal. Chem.* **2002**, *74*, 2637.
(4) Weibel, D.; Whitesides, G. *Curr. Opin. Chem. Biol.* **2006**, *10*, 584.
(5) Atencia, J.; Beebe, D. *Nature* **2005**, *437*, 648.
(6) Leslie, D.; Easley, C.; Seker, E.; Karlinsey, J.; Utz, M.; Begley, M.; Landers, J. *Nat. Phys.* **2009**, *5*, 231.
(7) Meldrum, D.; Holl, M. *Science* **2002**, *297*, 1197.
(8) Inglis, D.; Morton, K.; Davis, J. A.; Zieziulewicz, T.; Lawrence, D.; Austin, R.; Sturm, J. *Lab Chip* **2008**, *8*, 925.
(9) Boedicker, J.; Li, L.; Kline, T.; Ismagilov, F. *Lab Chip* **2008**, *8*, 1265.
(10) Kim, D.; S.H., L.; Ahn, C. H.; Lee, J.; Kwon, T. *Lab Chip* **2006**, *6*, 794.
(11) Yang, A.; Under, S.; Zahn, J. *Lab Chip* **2006**, *6*, 871.
(12) Stone, H.; Stroock, A.; Ajdari, A. *Ann. Rev. Fluid Mech.* **2004**, *36*, 381.
(13) Squires, T.; Quake, S. *Rev. Mod. Phys.* **2005**, *77*, 977.
(14) Tabeling, P. *Introduction to Microfluidics*; Oxford University Press: Oxford, U.K., 2005.
(15) Bruus, H. *Theoretical Microfluidics*; Oxford University Press: Oxford, U.K., 2008.
(16) Knight, J.; Vishwanath, A.; Brody, J.; Austin, R. *Phys. Rev. Lett.* **1998**, *80*, 3863.
(17) Chung, S.; Park, S.; Kim, C.; Chung, J. K.; Han, D.; Chang, J. *Microsyst. Technol.* **2003**, *9*, 525.
(18) Lin, C.-H.; Lee, G.-B. *J. Micromech. Microeng.* **2003**, *13*, 447.
(19) Rodriguez-Trujillo, R.; Mills, C.; Samitier, J.; Gomila, G. *Microfluid Nanofluid* **2007**, *3*, 171.
(20) Price, A.; Martin, R. *Biotechnol. Bioeng.* **2006**, *100*, 930.
(21) Bransky, A.; Korin, N.; S., L. *Biomed. Microdev.* **2008**, *10*, 421.
(22) F., W. *Biotechnol. Bioeng.* **2008**, *100*, 150.
(23) Abécassis, B.; Cottin-Bizonne, C.; Ybert, C.; Ajdari, A.; Bocquet, L. *Nat. Mater.* **2008**, *7*, 785.
(24) Castrejón Pita, J. R.; del Río, J. A.; Castrejón Pita, A. A.; Huelsz, G *Phys. Rev. E* **2003**, *68*, 046301.
(25) Hale, J. F.; McDonald, D. A.; Womersley, J. R. *J. Physiol.* **1955**, *128*, 629.
(26) Rahaman, K. D.; Ramkissoon, H. *J. Non-Newton Fluid Mech.* **1995**, *57*, 27.
(27) Torralba, M.; Castrejón-Pita, J. R.; Castrejón-Pita, A. A.; Huelsz, G.; del Río, J. A.; Ortín, J. *Phys. Rev. E* **2005**, *72*, 016308.
(28) Collepardo Guevara, R. R.; Corvera Poiré, E. *Phys. Rev. E* **2007**, *76*, 026301.

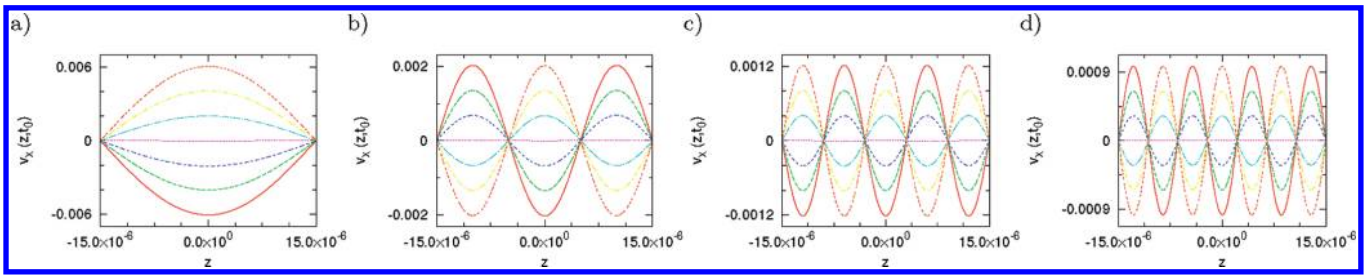

Figure 1. Flow stratification induced by frequency. Velocity profiles (in m/s) are shown for a fluid in a 30 μm microchannel with fluid parameters of $\eta = 4 \times 10^{-3}$ kg/ms, $\rho = 1050$ kg/m^3, and $t_r = 1 \times 10^{-3}$ s driven by an oscillatory pressure gradient with a maximum amplitude of 5 kPa/m at the first four resonance frequencies: (a) 1029, (b) 3086, (c) 5143, and (d) 7201 Hz.

for the analysis of biofluids, for instance, regarding possible implementations on lab-on-a-chip devices in clinical analysis, which often contain plasma or whole blood and are viscoelastic.[8,10,11]

Here, we present a mechanism by which a viscoelastic fluid inside a rectangular microchannel can be stratified in layers parallel to each other and parallel to the plates that conform the microchannel. We find that stratification can be induced by driving the fluid with a dynamic pressure gradient at frequencies in the range of sound. These are determined by the channel thickness and the fluid properties. Figure 1 illustrates the velocity profiles v(z) for a fluid driven at four different resonance frequencies. Velocities in adjacent layers are always of the opposite direction with signs that alternate in time according to the driving pressure gradient. Different tracer particles could be confined within the different layers as long as diffusion does not mix them.

We take a simple equation of motion for a homogeneous viscoelastic fluid in a microchannel for which convective terms are negligible.[29]

$$t_r \rho \frac{\partial^2 \mathbf{v}}{\partial t^2} + \rho \frac{\partial \mathbf{v}}{\partial t} = -t_r \frac{\partial \nabla p}{\partial t} - \nabla p + \eta \nabla^2 \mathbf{v} \qquad (1)$$

The equation contains a relaxation time t_r, defined as the viscosity divided by the elastic modulus of the fluid. In the limit $t_r \to 0$, the equation reduces to the Navier−Stokes equation for a Newtonian fluid. In the limit $t_r \to \infty$, it reduces to the response equation of an elastic solid. The parameter t_r is called the Maxwell relaxation time. In the equation, ∇p is the pressure gradient, $\mathbf{v}$ is the velocity, and η and ρ are respectively the viscosity and density of the fluid.

We consider the flow in the x direction of a fluid in a rectangular microchannel whose velocity at the confining plates ($z = \pm \ell$) vanishes. The separation between these plates, 2ℓ, which gives the microchannel thickness, is considered to be much smaller than any other dimension in the system so that the effect of the lateral walls (in the y direction) can be neglected. We consider the effect of a time-dependent pressure gradient in the flow direction and solve eq 1.

For a sinusoidal pressure gradient $\nabla p = (\mathrm{d}p_0/\mathrm{d}x)\cos(\omega_0 t)\hat{\imath}$ with frequency ω_0, the velocity profiles are given by

$$v_x(z,t) = -\frac{1}{\eta}\left[Re\,K(z,\omega_0)\cos(\omega_0 t) + Im\,K(z,\omega_0)\mathrm{sen}(\omega_0 t)\right]\frac{\mathrm{d}p_0}{\mathrm{d}x} \qquad (2)$$

where the complex response function $K(z, \omega)$ is given by

$$K(z,\omega) = -\frac{\eta}{i\omega\rho}\left[1 - \frac{\cos(\sqrt{A}z)}{\cos(\sqrt{A}\ell)}\right] \qquad (3)$$

with $A \equiv (i\omega\rho/\eta)(1 - i\omega t_r)$. The real part of this response function presents maxima and minima at certain resonance frequencies that can be analytically obtained when $\omega t_r \gg 1$ and are given by

$$\omega_{res}(n,l) = \frac{(2n-1)^2\pi^2\eta}{2\ell\sqrt{(2n-1)^2\pi^2\eta\rho t_r + \rho^2\ell^2}} \qquad (4)$$

where the index n corresponds to the different maxima or minima of the real part of the response function and takes integer values of $n = 1, 2, 3,...$ Clearly, the resonance frequencies of the system depend on fluid properties ρ, η, and t_r and channel thickness 2ℓ. For microchannels containing viscoelastic fluids, the second term inside the square root of the denominator is negligible and a simple expression for the resonance frequencies can be written as

$$\omega_{res}(n,l) = (2n-1)\pi\left[\frac{\eta}{\rho t_r}\right]^{1/2}\frac{1}{2\ell} \qquad (5)$$

In this approximation, the real and imaginary parts of the response function at resonance, at z = 0, are given by

$$Re\,K(z=0,\omega_{res}) = \frac{4(-1)^{n+1}}{(2n-1)\pi}\frac{\eta t_r}{\rho} \qquad (6)$$

$$Im\,K(z=0,\omega_{res}) = \frac{2\ell}{(2n-1)\pi}\left[\frac{\eta t_r}{\rho}\right]^{1/2} \qquad (7)$$

Note that in this approximation $Re\,K$ ($z = 0$, ω_{res}) does not depend on the channel thickness 2ℓ but $Im\,K$ ($z = 0, \omega_{res}$) depends on it linearly. For typical viscoelastic parameters and microchannels from 10 to 100 μm, $Im\,K$ ($z = 0, \omega_{res}$) is 2 or 3 orders of magnitude less than $Re\,K$ ($z = 0, \omega_{res}$). This implies that the velocity at resonance is practically proportional to the pressure gradient.

The fluid can be stratified in identical layers parallel to the microchannel plates by driving the fluid with a sinusoidal pressure gradient at the resonance frequencies. Figure 1 shows the velocity profiles v(z) for the first four resonance frequencies. Each of the pictures contains several curves indicating velocity profiles at different times within a period. For the first resonance frequency, the system has only one layer whose instantaneous velocity has the same direction at any point. The sign of the velocity alternates in time according to the driving pressure gradient. For the second resonance frequency, the system is stratified in three layers parallel to each other that are separated by zero-velocity planes. Velocities in adjacent layers are always in opposite directions. For the third resonance frequency, five layers are formed and so on in such a way that for the nth resonance frequency the number of layers is $2n - 1$. It is important to see that as the number of layers

(29) Phan-Thien, N. *Understanding Viscoelasticity*; Springer-Verlag: Berlin, 2008.

increases the maximum amplitude of the velocity decreases. This is a direct consequence of the value of the real part of the response function for the different resonances (eq 6). This way of stratifying the fluid results in virtual microchannels with smaller thicknesses than the actual distance between plates. For instance, when comparing the second resonance frequency of a microchannel of thickness 2ℓ with the first resonance frequency of a microchannel of thickness $2\ell/3$, we can see that the result is identical. In general, the nth resonance frequency of a microchannel with plate separation 2ℓ is equal to the first resonance frequency of a microchannel with plate separation $2\ell/(2n-1)$. That is, $\omega_{res}(n, \ell) = \omega_{res}(1, \ell/2n-1)$. This can be analytically obtained from eq 4 or 5.

The present mechanism to induce stratification would allow for the use of the different layers to confine tracer particles for diverse purposes in micrototal analysis systems. Confinement to a layer is effective as long as diffusion does not mix tracer particles of different layers. Tracer particles will spread in a distribution whose mean moves with the mean fluid velocity and whose mean square distance grows in time as $\langle s^2 \rangle = Dt$, where D is the diffusion coefficient of the tracer particles. Tracer particles will remain in different layers as long as the standard deviation is less than the layer thickness. For instance, for the second resonance frequency, three layers are formed, each of which has a thickness $2\ell/3$; therefore, the necessary time for a tracer particle to stay within a layer has to be such that $t < 4\ell^2/9D$. However, the second resonance frequency, which depends on fluid parameters and microchannel thickness, has to be such that many periods have to be possible while the experiment takes place. That is, the time of the experiment should be $t \gg 2\pi/\omega_{res}(2, \ell)$, where $\omega_{res}(2, \ell)$ is given by eq 4 or 5 with $n = 2$. The two conditions that time has to satisfy imply a relation among fluid parameters, channel thickness, and the diffusion coefficient of tracer particles. For microchannels, this relation implies that

$$D \ll \frac{\ell}{3}\left[\frac{\eta}{\rho t_r}\right]^{1/2} \tag{8}$$

For an 30-μm-thick microchannel with fluid parameters as in Figure 1, the necessary frequency to obtain three layers is on the order of 3086 Hz. The condition for the diffusion coefficient indicates that $D \ll 3 \times 10^{-3}$ cm^2/s, which is easily satisfied for common tracer particles even in water. For an 100-μm-thick microchannel with fluid parameters as in Figure 1, the necessary frequency to obtain three layers is on the order of 926 Hz, and the condition for the diffusion coefficient is $D \ll 1 \times 10^{-2}$ cm^2/s. The thicker the microchannel, the thicker the layers formed in the stratification process and the easier it is for tracer particles to stay within the layers. For tracer particles with a relatively large Péclet number, applying higher resonance frequencies and large pressure gradient amplitudes to stratify the fluid might result in layers with the thickness of a single tracer particle.

Our results might be particularly relevant in the analysis of biological and biomimetic fluids. For example, Thurston[30] finds that blood in a microtube bundle with microtubes of 50 μm diameter does not exhibit shear thinning for shear rates of 100−800 s^{-1}.[31] (See Figure 4a in ref 30.) In the same shear rate range, he finds a practically constant Maxwell relaxation time. (See Figure 4a in ref 30.) Our Figure 1 has been obtained by using our results for the Maxwell model, with the parameters measured by Thurston[30] in the above-mentioned range of shear rates, for a 30 μm microchannel. From eq 5, we obtain a second resonance frequency of 3 kHz (necessary for stratification in three layers). Maximum shear rates at resonances can be estimated from eqs 2, 6, and 7. Pressure gradients on the microscale range from zero to a few MPa/m,[32] so they can be chosen to fall in the desired range of shear rates. Using a pressure gradient with an amplitude of 5 kPa/m would give a maximum shear rate at the second resonance on the order of 630 s^{-1} (from eqs 2, 6, and 7). The Thurston curve[30] is obtained at 2 Hz, and a curve at 3 kHz would require new experiments. Measurements on the kilohertz scale are within the actual technological capabilities of micro-PIV and cameras.[33−35] Most experiments in biofluids are done at biological natural frequencies. Our results provide a framework in which to design new experiments that would give rise to stratification at frequencies that have nothing to do with biological natural frequencies but that might be useful in clinical analysis.

In conclusion, we present a mechanism by which stratification of a homogeneous viscoelastic fluid can be induced in a microchannel by applying a periodic pressure gradient in the range of sound. Appropriate frequencies to induce stratification depend on fluid properties and the microchannel thickness. Stratification is obtained with identical layers, parallel to the channel walls, whose number can be tailored. These layers are separated by 2D zero-velocity planes. This would allow different tracer particles with small diffusion coefficients confined in different fluid layers within the same microchannel. We have obtained analytical results that allow us to make theoretical predictions regarding the possible experimental realization of stratification in a microchannel using a biofluid. In particular, we have made calculations for blood and have found a condition among the diffusion coefficient, fluid properties, and microchannel thickness that should be satisfied in order to have tracer particles confined to a layer. The present work opens experimental possibilities that can lead to the development of techniques involving the analysis of biofluids in microdevices.

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(30) Thurston, G. B.; Henderson, N. M. *Biorheology* **2006**, *43*, 729–746.
(31) It is important to note that our theory is particularly relevant to biofluids that present no shear thinning, such as blood in this particular range of shear rates. For other biofluids consisting of semidilute or concentrated solutions of entangled polymers, periodic shearing would produce shear thinning effects for which our theory would have to be reworked.
(32) Westin, K. J. A.; Choi, C.-H.; Breuer, K. S. *Exp. Fluids* **2003**, *34*, 635.
(33) Meinhart, C.; Wereley, S.; Santiago, J. *Exp. Fluids* **1999**, *27*, 414.
(34) Devasenathipathy, S.; Santiago, J.; Wereley, S.; Meinhart, C.; Takehara, K. *Exp. Fluids* **2003**, *34*, 504.
(35) Oddy, M.; Santiago, J. *J. Colloid Interface Sci.* **2004**, *269*, 192.