

Some basic problems of microfluidics

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Abstract

I present here several phenomena, which (I believe) are worth being discussed, because of their practical importance, the scientific challenge they convey, or both. The phenomena I discuss here are : slip of simple liquids over smooth surfaces, gas flows in microchannels, chaotic micromixing, two phase flows in microchannels, microelectrohydrodynamics, and bottleneck effect. The descriptions are made in a pedagogical rather than technical style. The few topics presented here represent a number of microfluidics situations of importance, which raise interesting fundamental and practical issues.

Introduction

Microsystems have generated a considerable activity, at economic and scientific levels, and their importance, in our everyday life, is expected to considerably increase over the next few years. Microfluidics, which is part of the domain of microsystems, follows similar trends. Microfluidics is about flows of liquids and gases, single or multiphase, through microdevices fabricated by MEMS (i.e. Micro ElectroMechanical Systems) technology. This statement provides an engineering type definition of microfluidics. Nonetheless, the domain uncovers a number of scientific challenges researchers are just beginning to tackle. Examples of scientific challenges are the inclusion of unconventional boundary conditions at micrometric scale, the identification of novel patterns in multiphase microflows, the control of physico-chemical phenomena, such as adsorption, desorption in unconventional contexts, the driving of single molecules through nanochannels, or the use of small turn-over times for chemical measurements. Microfluidics has grown recently, fostered by the development of lab-on a chip devices, i.e. systems able to perform an impressive number of tasks on a small chip, such as mixing, separating, driving fluids, and, analysing, detecting molecules. In the next few years, a variety of such systems, designed to identify a particular odor or analyse the DNA from a drop of blood, or a piece of cheese, will likely be made available. In almost all these systems, molecules must be conveyed in liquids ; this constraint requires one must be able to handle flows at the microscale, in possibly complex configurations. In this context, microfluidics arose as a new discipline. Indeed, microfluidics is also involved in other contexts, such as propulsion of miniaturized rockets, for space applications. It would thus be inaccurate to link microfluidics to the sole development of lab on a chip devices. However, the growth of microfluidics, at the moment, is certainly fostered by the considerable technological demand coming from the biomedical and chemical areas.

To the best of my knowledge, there does not exist textbooks on microfluidics. There exist chapters and courses one may find on the web. The domain is recent, and probably needs to expand to

reach a situation where it might be considered as a fully established branch of physico-chemical fluid dynamics. Several groups obviously work at this expansion at the moment.

I will focus here on a few hydrodynamical phenomena, associated to interesting and rather well defined issues which fluid mechanics community may be interested in. One should however be aware that physico-chemical phenomena (I do not discuss here) are also extremely important to consider. The style of the paper is pedagogical rather than technical.

Simple liquids slipping over solid surfaces

It is appropriate, in the context of this conference, to refer to Batchelor's textbook on Fluid Mechanics[2], in particular the first chapters establishing the hypotheses under which the classical fluid flow equations can be derived. Batchelor states that, in order to determine these equations, one needs to introduce a mesoscale, large enough to contain a huge number of molecules, and small enough to be viewed as pointwise in comparison with the system size. On such a mesoscale, one currently defines an elementary volume, called the "fluid particle". This concept is useful for a straightforward application of Newton's laws, from which the flow momentum equations can be obtained. G Batchelor, attempting to substantiate the concept of "fluid particle", proposed to illustrate it as a cube, 10 μm side, which would enclose about $3 \cdot 10^{10}$ molecules if filled with gas at normal pressure, i.e. a number large enough so as the microscopic fluctuations be negligible. It is true that 10 μm is small compared to the current sizes of ordinary fluid mechanical devices, but this scale lies well within the range of sizes of microfluidic devices. Following Batchelor's presentation, one would think that microfluidic systems might not be governed by the classical laws of fluid mechanics, and therefore, some unconventional fluid mechanics should perhaps be developed to tackle this novel situation.

This view is certainly too conservative. At the moment, one has several pieces of information which indicate that, as far as the bulk properties are concerned, 10 μm is still a scale governed by classical laws, for simple liquids, and ideal gases under normal pressure. On physical grounds, one may notice that a more appropriate order of magnitude for the size of the fluid particle would be several correlation lengths for the liquid, which would lead to nanometers for ordinary liquids, and several mean free path for a gas, which would lead to a few hundreds of nanometers under normal conditions. Concerning liquids, experimental studies, performed on extremely thin liquid layers, has confirmed this estimate in the last decade [9]. All this indicates that for liquids, the fluid particle needs not be as large as 10 μm , but rather be on the order of 10 nm to be considered as macroscopic, and, therefore, one may anticipate that for

ordinary liquids, the current microfluidic devices are subjected to the rules of classical fluid mechanics. I will come to the gas in the next section. These considerations apply for the bulk properties.

The boundary conditions are another matter, and I will concentrate here on liquids. In classical textbooks, it is considered that liquids do not slip on solid surfaces ; the so called "no-slip" boundary condition on the tangential velocity u , for ordinary liquids, has the form :

$$u=0$$

on fixed solid surfaces. This provides a fundamental condition in fluid mechanics, allowing for detailed calculations of velocity profiles and flow structures. The physical justification bears on the assumption that attractive Van der Waals forces tend to link fluid atomic layers to the solid, preventing slip to occur. As pointed out by Feynman [7], an unpleasant consequence of this condition is that one hardly removes small liquid drops from glass surfaces by solely blowing on them. More generally speaking, this condition has been confirmed by an overwhelming abundance of experimental measurements, performed in ordinary fluid systems. In contrast with this picture, we now have experimental evidence that simple liquids significantly slip on atomically smooth solid surfaces and, consequently, the no-slip condition should be replaced by a more general relation. One usually adopts the following form :

$$u = L_s \left(\frac{\partial u}{\partial n} \right)$$

in which L_s is the extrapolation or slip length, n is the normal (inwards to the fluid). This relation is at the moment not fully established ; it must be taken as a useful equation, which allows to determine the amplitude of the effect, by measuring L_s . The larger L_s , the larger the slip. Measurements of L_s have been performed in various situations, for a variety of solid surfaces, and several fluids (mostly alkanes) [17],[23]. Results indicate the slip length is on the order of micrometers, or fractions of micrometers, i.e much larger than typical liquid correlation lengths. A possibility suggested by De Gennes [23], is that a gaseous layer nucleates at the interface between the fluid and the solid, favouring slippage. This elegant proposal, which provides orders of magnitude consistent with the experiment, certainly remains to be investigated experimentally in depth.

A hydrodynamical consequence of this effect is that the relation flow-rate - pressure drop of laminar Poiseuille flows between parallel planes must be replaced by a more generalized law, where L_s comes into play as an additional parameter. By using the boundary condition displayed above (assuming the system is symmetric), one gets :

$$\Delta P = \frac{2\mu L Q}{wb^2 \left(L_s + \frac{b}{6} \right)}$$

in which w is the channel width, b its height or depth, L its length, and Q the flow-rate. The change in the pressure-flow rate law has been confirmed in our laboratory, using a microchannel flow etched in glass, and covered by a Silicium wafer, offering an atomically flat surface to the fluid (see Figure 1)

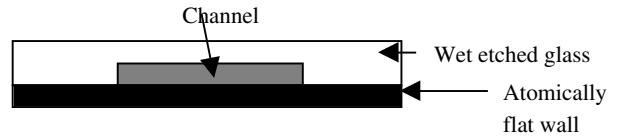


Figure 1 : Cross-section of the microchannel used to confirm a slip effect. The channel is $1.40 \pm 0.02 \mu\text{m}$ high (or deep), and 100 or 200 μm wide. It is etched in glass, and covered by an atomically flat Silicium wafer. The working fluid is hexadecane.

In these experiments, hexadecane is used as the working fluid. The pressure drop measurements, shown as a function of the flow-rate Q , are presented in Figure 2. The data is shown partially in a dimensionless form, using the quantity (called apparent viscosity factor) :

$$\frac{\mu_{app}}{\mu} = \frac{\Delta P w b^3}{12 \mu Q L}$$

in which μ is the fluid viscosity.

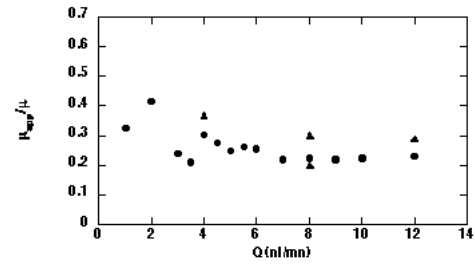


Figure 2: Apparent viscosity factor, as a function of the flow-rate, for the $1.4 \mu\text{m}$ high channel (disks are for a 100 μm width and triangles for a 200 μm width)

Should standard Poiseuille law applies, one would get an apparent viscosity factor equal to unity. We actually observe viscosity factors close to 0.3, at all flow-rates (see Fig 2). This implies that in the present case, the pressure drop required to drive the fluid is roughly one third of the one given by Poiseuille law. The slip lengths L_s one may boldly extract from the data, lie on the micrometer range, consistently with References [17] and [23].

Flowing a liquid through a small channel, and tracking deviations from Poiseuille law, has been done in the past, in a number of experimental conditions [16][3]. In all cases however, the surface was rough, favouring no slip at the wall. In this context, observed deviations from Poiseuille law were found small, not necessarily significant. The present experiment is the first, to the best of our knowledge, offering a smooth surface to the flow, and in which sizeable deviations are observed.

From the microsystem viewpoint, the pressure drop reduction we observe may facilitate the extreme miniaturization of the fluidic systems. For a 100 nm deep channel, the pressure drop one may infer from our data is one order of magnitude below Poiseuille expectation. This indicates that by using atomically flat walls rather than rough walls, one may appreciably facilitate the flow of ordinary liquids in nanodevices. However, much remains to be done to investigate and understand the slip effect,

which seems now well established for smooth surfaces, albeit at a qualitative level.

Gas flows through microsystems

We now consider the flows of gas through microsystems. This topics has been reviewed by Gad El Hak [8]. As mentionned above - again following Batchelor's presentation - the channel dimension should be larger than the mean free path to expect the classical laws of fluid mechanics to apply. A typical size of the cross-section of a micro channel lies between 1 and 300 μm , while it typically extends several millimeters in length. On the other hand, the mean free path of ideal gases has the following expression :

$$\lambda = \frac{1}{\sqrt{2}n\pi a^2} = \frac{kT}{\sqrt{2}\pi p a^2}$$

in which n is the density, a is the molecular size, k the Boltzmann constant and T the absolute temperature. At 270 K, λ is on the order of 70 nm. The flow regime is described by the Knudsen number, whose expression is :

$$Kn = \frac{\lambda}{L}$$

in which L is the system size. One has several regimes according to the value of this number. At large Kn , one has rarefied gas regimes, where most of the time, the molecules undergo collisions with the wall rather than with other molecules. These regimes have been studied in the past in various contexts (such as cryogenics), long before microfluidics emerged. At small Knudsen numbers, one recovers classical flow regimes. In practice, the cross-over between the two regimes is not $Kn=1$. The actual condition for which the gas behaves as an ordinary fluid is :

$$Kn < 0.1$$

This implies that microfluidic devices conveying gases under normal conditions are on the border of being affected by rarefied gas effects, and are certainly perturbed by such effects as soon as the pressure is decreased. These effects are currently discussed and analysed in the litterature [4][19] ; at the moment, a number of questions are under investigation, concerning the boundary conditions and the effective equations one may wish to write to describe the flow from a global viewpoint. We refer the reader to the corresponding references for a description of these aspects.

Chaotic mixing of liquids in microsystems

In ordinary systems, molecular diffusion leads to mixing, but is a slow process ; the time τ required to spread a dye over a distance L in a fluid at rest is classically estimated by :

$$\tau = \frac{L^2}{D}$$

in which D is the molecular diffusivity. For ink into water, D is on the order of $10^{-5} \text{ cm}^2/\text{s}$; the above formula shows that it takes days to spread ink over areas few centimeters large. This is why one stirs the fluids to rapidly get homogenous mixtures. By doing so, one generates instabilities and turbulence, which are favourable to mixing. The way how turbulence mixes is not straightforward. If one follows the evolution of a tracer blob, initially released in a turbulent flow, one sees it undergoes a sequence of stretching and folding, adopting, after a few turn-

over times, a finely striated structure, prone to be rapidly smoothed out by the action of molecular diffusion. This is the way turbulence efficiently mixes fluids and tracers.

In microsystems, owing to size reduction, turbulence is suppressed, but, on the other hand, diffusion processes are must faster. This fact is well exploited by chemical engineering at the moment. For small molecules (ink in water) in systems on the micron size, diffusive times, estimated by using the previous estimate, are on the order of seconds ; this is the time we would accept to wait for achieving a chemical reaction in a μTAS (microTotal Analysis systems). However, in practice, μTAS rather use 100 μm wide channels ; then the diffusive times are on the order of minutes, which may be unpleasant to handle in practical situations. This delay is orders of magnitude larger as soon as large proteins are involved as one of the reactants. The issue is thus how one can speed up the mixing process so as chemical reaction may be completed within a reasonable laps of time.

At the moment, several micromixers, chaotic and non chaotic, have been devised. A number of devices consist into dividing the flow into several part so as to enhance the effect of molecular diffusion. This is a conceptually simple idea, which offers a first pathway to obtain mixing.

Other devices bear on the the generation of chaotic trajectories. This idea traces back to studies performed in the eighties, in which it was recognized that chaos may considerably enhance mixing in laminar flows [15]. Microsystems offers, in this respect, a new field of application for these ideas, and an opportunity to make further theoretical progress, by considering novel configurations, difficult or simply too exotic to achieve in conventionnal systems. An early study [6], exploiting chaos to enhance mixing attempted to miniaturize a well documented source sink systems, initially proposed by Jones et al [11]. Lee et al [12] recently found a simple way to produce chaotic efficient mixing. The device consists in generating folding and stretching along a channel, using an external perturbation localized at the intersection between the main channel and an adjacent one. This is shown in Fig 3.

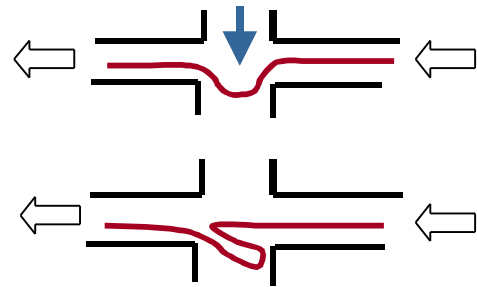


Figure 3: Schematic diagram showing how chaos is induced in a cross-flow. For the upper drawing, a cross-flow is superimposed to the mean flow (schematized by the arrows), and for the lower one, the cross-flow is switched off. The process is repeated indefinitely.

To see how the system operates, one may consider a material line, initially released in the main channel, along the symmetry axis. Without perturbation, the line is advected along the main stream, and remains straight. We caricature the temporal dependence of the perturbation by replacing the

sinusoidal wave-form by a square wave-form, with two positions - on and off. As the transverse flow is switched on, the material line is bent as it crosses the intersection. After the transverse flow is switched off, a folding takes place, since the flow is faster at the center of the main channel than on the sides. This elementary process is a step towards a chaotic regime, favorable to mixing. To get a complete chaotic regime (i.e. involving an infinite number of stretchings and foldings), one should replicate the structure *ad infinitum*, which is almost achievable by using MEMS technology.

For realizing chaotic mixing in microscale, Lee et al [12] fabricated a mechanical micromixer, by using standard MEMS technology. The channels, etched into Silicon wafer using DRIE technique, are anodically bonded to Pyrex plates. The scales on Fig 5 and 6 indicate the channel sizes. There is possibility to inject two distinct fluids in the main channel, in the upstream region. For the first fluid sucrose solutions, or glycerol were used, and for the second one the same solution, was used, but labeled with a fluorescent tracer. Both fluids are injected with the same flow-rate, so that the interface between them lies right in the middle of the channel, in the upstream section. The adjacent channels are connected to pressure sources and mechanical valves operating periodically in time

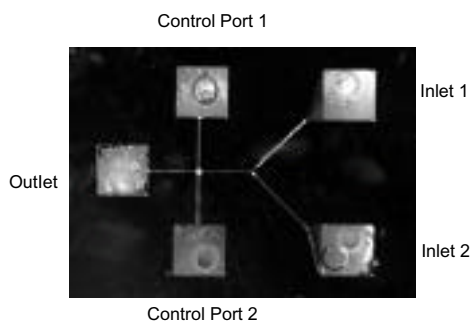


Figure 4 : Top view of the mechanical micromixer.

The interface is visualized by fluorescence microscopy.

Lee et al [12] could obtain several distinct regimes. In the chaotic regimes, the morphology of the interface can be extremely complicated. An example is given in Fig 5. The fact that in the experiment, the velocity profile is not uniform across the channels, but parabolic, reinforces the tendency to develop intricate interface patterns, in comparison to a plug flow. Here, contrarily to confined systems, the interface is folded only a finite number of times as it travels across the intersection.

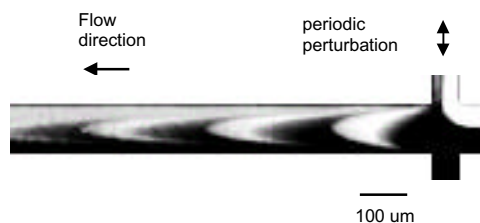


Figure 5 : Snapshot showing a highly convoluted interface

In the present experiment, and with the dye and fluids used, mixing can be obtained with only one basic unit if the parameters

are appropriately chosen. This is shown on Fig 6, which represents the interface before, and after it passes the intersection, for particular values of the amplitude and frequency of the perturbation. One sees mixing is reasonably achieved, as confirmed by further concentration measurements, which clearly show the profiles flatten out downstream

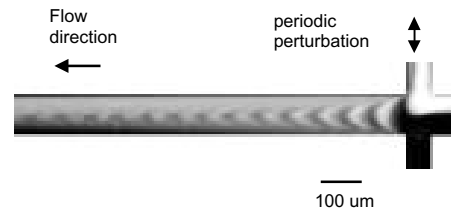


Figure 6: Chaotic mixing by the mechanical micro-mixer

These mixers may thus be efficient and well controlled, at the expense of requiring an external source (fortunately of low energy) to operate.

Recently, chaotic-like systems fully utilizing the third dimension to induce chaotic trajectories, have been realised. One of them consists in driving the flow along a three dimensional helicoidal system of microfabricated channels [13] ; another one generates spiraling flows, sustaining chaotic trajectories, by etching alternated grooves at the bottom of a rectangular microchannel [18]. These mixers have the advantage of being passive, i.e. they do not require external sources to operate.

We are in a stage where novel micromixers are devised, and one probably needs some time to assess the situation regarding the mixing problem. Apart from theoretical issues pertaining to the field of chaotic phenomena, mixing is also viewed as a first step towards the definition of efficient chemical micro-reactors ; this is a subject of interest for the development of lab-on a chip devices, or the progress of miniaturization in chemical engineering.

Multiphase flows in microsystems

The ability to control drop size in microfluidic systems has led to the exceptional success of ink jets techniques based on MEMS technology (Micro Electro Mechanical Systems). One is tempted to control in a similar way drops of liquids in liquids, so as to be able, for instance, to encapsulate particles or molecules in liquid structures of accurately controlled sizes and morphologies. In this approach, one faces the problem of driving immiscible fluids through microsystems. This situation raises new issues in the field and at the moment we are still at the beginning of the exploration of the fundamental regimes prevailing in these situations.

A recent study performed in a system using tetradecane and water (plus some surfactant), as the two working immiscible phases showed the existence of complex patterns [20]. The recent experiments that H Willaime [22] performed in our laboratory also used a mixture of tetradecane and water, driven

through micro-channels etched in Silicium. Similarly as in Ref [20] experiment, this study revealed the existence of a rich variety of patterns, depending on the flow-rates, and the injection configuration. The experiment was performed in a microchannel, etched in Silicium and anodically bonded to a pyrex plate. The flow configuration is schematized in Fig 7.

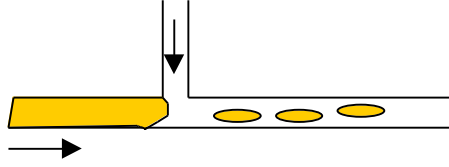
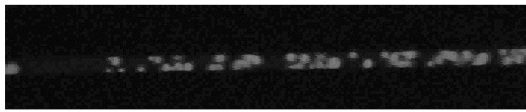
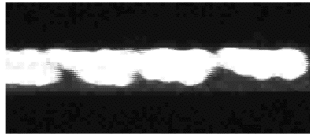


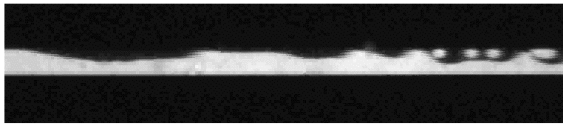
Figure 7 : Schematic view of the flow. Yellow represents tetradecane, although the opposite configuration has also been investigated



(a)



(b)



(c)

Figure 8 : Three regimes observed in the experiment, for different flow conditions. (a) bubbly (water drops), (b) pearl necklace (c) slug flow. Water is marked by fluorescein and therefore appear as white on the figure. The channel width is 100 mm in each case, and the height 20 μm .

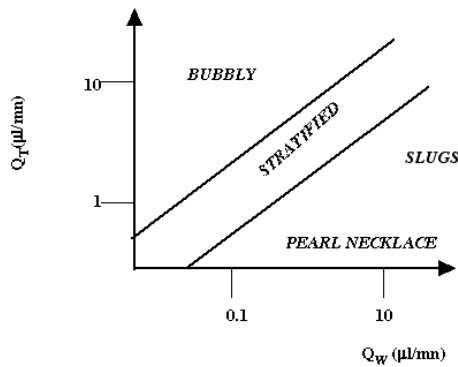


Figure 9 : Tentative phase diagram, showing various regimes, as observed in the experiment, for different flow conditions

The corresponding (tentative) phase diagram is shown in Fig 9. Q_T and Q_W represent, respectively the tetradecane and water flow-rates. Bubbly regimes, involving water drops in a tetradecane continuous phase, logically arise at large tetradecane flow-rates, and small water flow-rates. It turns out that water drops are more easily formed than tetradecane drops in this particular experiment. On the lower right part of the diagram, slug flows and pearl necklace type regimes seem to prevail. In between, stratified regimes, involving a flat or wavy interface between the two phases, is observed.

One certainly needs to investigate all these regimes, and determine robust phase diagrams in generic situations. The underlying physics involves the preeminence of wetting and capillary effects against inertia, which, in the present situation as in most microdevices is essentially irrelevant. The absence of inertia nonetheless does not mean instabilities are suppressed, and all is prescribed by the initial conditions. The present experiment shows interface instabilities survive, opening the possibility to reaching intrinsic states, weakly affected by the initial conditions. However, much is to be done on these systems, which at the moment, are largely unexplored.

Before closing this section, one may mention, concerning the multiphase microflow area, the work done in Berkeley, using water- air systems. The motivation of this study is the important problem of cooling of integrated circuits. One also has several regimes involved, and their analysis is in progress.

Electrohydrodynamics in microsystems (or MEHD - MicroElectroHydroDynamics)

Microsystems offer a context where large electric fields can be easily generated. The reason is that in a system of size l , the electric field has the following order of magnitude :

$$E \sim \frac{V}{l}$$

in which V is the voltage drop applied across scale l . With one volt applied across a micrometric cell, one gets an electric field on the order of 10kV/cm. Thus, one can produce substantial electrical forces to affect a flow.

At the moment, several electrohydrodynamical effects are currently used in microdevices. Dielectrophoretic forces have been used to drive particles, so as to mix or sort them [10][5]. Electrophoresis is currently used to separate DNA in biological devices. Another application is electroosmosis, which allows (in principle) to pump neutral fluids in a controlled way. The charges involved in this process are located close to the walls, in a Debye layer, whose role is to screen the electric field induced by permanent surface charges binded to the solid.

In general, electroosmosis is conceived in uniform geometries. Non uniform geometries have recently been analysed by Ajdari [1]. Using non uniform configurations gives rise to a rich variety of effects ; at the moment, only a couple of them have been demonstrated experimentally. Much remains to be done on the subject in my opinion. This is a situation where microsystems offer a new context for developing novel situations which would

have been extremely difficult to explore using ordinary configurations.

A counter-intuitive effect in microfluidics : the bottleneck effect

Bottleneck effect is a counter-intuitive effect which shows up when one drives liquids (and gases as well) through channels of micrometric size, using a device such as a syringe pump. This effect (previously known in the domain of chromatography [14]), is counterintuitive because it relies on the fluid compressibility, in conditions where the Mach number is extremely small. It illustrates some peculiar behavior one may encounter in microfluidic systems.

The basic geometry in which the bottleneck effect takes place is shown in Fig 10.

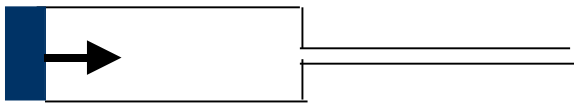


Figure 10 : Schematic representation of a geometry giving rise to an effect called "bottleneck effect".

One has a "large" chamber, of diameter D , length L , along which a piston is moved at velocity U . The liquid is driven outside the chamber, through a small capillary of length l , diameter d . The piston is moved at time $t = 0$, and the question which is raised is how long does it take to reach a steady state. It is not a complicated matter to solve this problem, and the result is the obtention of the following time constant :

$$\tau = \frac{32\mu D^2 L}{Ed^4}$$

in which μ is the fluid viscosity, and E the Young modulus of the fluid. τ is thus the time required to reach a steady state in this problem. Neglecting the compressibility amounts to consider the Young modulus is infinite, which would lead, consistently, to a zero time constant. The relevance of the above estimate has been shown by U Ulmane et al, who carried out a detail investigation of the problem, in carefully controlled experiments [21].

The difficulty raised by the above formula is the strong dependence of the τ with the capillary diameter, d . In practice, using water, and $1\ \mu\text{m}$ diameter capillaries, one needs several minutes to reach a steady state. For $100\ \text{nm}$ capillaries, the time constant would be on the order of months, which is considerable. The physical picture is that, for a piston moving at constant velocity, it takes time to pressurize the chamber at a steady state value. There is a sort of "bottleneck" to get through before stationary conditions can be achieved. Since the situation depicted in Fig 10 is typical of a laboratory experiment in microfluidics, it is worth being aware of this effect, especially if one works with extremely small channels. In this respect, working with pressure sources rather than mechanical pumps is appropriate, since this theoretically allows to reduce the time constant to zero. In practice however, the bottleneck effect is overweighted by the compliance of the tubes, especially when one uses plastic tubings.

Conclusion

Microfluidics is a domain growing at a fast rate at the moment. No doubt this domain will expand over the next few years, fostered by a considerable demand in the biological and chemical areas. The few situations presented here are important in the microfluidic context ; they raise interesting issues, both at practical and fundamental levels. Nonetheless, I would like to warn the reader that the paper does not intend to be fully representative of the domain : in particular, I did not discuss physico-chemical aspects which are exceedingly important in most of the applications of microfluidics, and which are indeed also worth being considered from a more fundamental viewpoint.

Acknowledgments

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