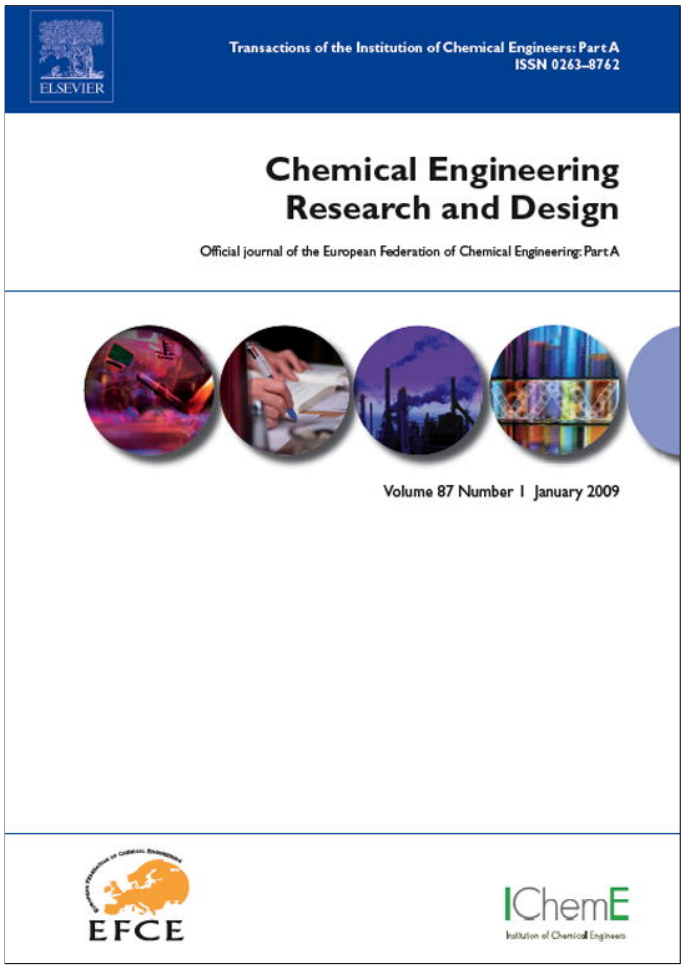

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Monitoring of liquid flow through microtubes using a micropressure sensor

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ABSTRACT

The pressure-driven liquid flow through microtubes was studied in a range of very low Reynolds numbers (<0.15) by monitoring the pressure change *in situ*. Cylindrical microtubes with diameters ranging from 50 μm to 500 μm were examined and two types of tube material, namely PEEK polymer and fused silica were compared. A good linear relation for the pressure drop *versus* flow rate was obtained. Apparent deviations between the measured slopes with those calculated using conventional theory were attributed to uncertainties in the calculated values which are dominated by the uncertainties in the microtube diameters. It was found that a period of stabilisation time was required for reaching a steady flow after the syringe pump was switched on/off or to a different flow rate. The stabilisation time was likely due to the compressibility of the fluid. Insignificant difference between PEEK polymer and fused silica microtubes in terms of flow resistance was observed. The *in-situ* measurement of pressure drops provides a convenient approach for monitoring fluid flow through microtubes and detecting dimensional changes within microchannels in Lab-on-a-Chip and microreactor systems.

Keywords: Microtube; Laminar flow; Pressure sensor; Liquid flow monitoring

1. Introduction

The increasing interest in the development of miniaturized micro chemical systems has led to the emergence of micro chemical engineering, a new field of research embracing microfabrication, microfluidics, microreaction technology, and their applications in chemical syntheses and analytical measurements (Viovy, 2007; Schütte et al., 2006; Ehrfeld et al., 2000; Jensen, 2001; Zhang et al., 2006, 2008). Such systems have feature sizes in a range of 1–1000 μm, and reaction channels are usually integrated with microsensors and microactuators. In these systems, understanding and controlling microfluidics is key to controlling reagent delivery, mixing, separation, and heat and mass transfer. In general, most microchemical systems studies to date have employed either electrokinetic mobilization or hydrodynamic (pressure driven) pumping of reagents. In previous studies we have demonstrated the successful modelling and control of microfluidics driven by electrokinetic (i.e. voltage driven electroosmosis and electrophoresis) forces for the control of the *spatial* and *temporal* evolution of chemical reactions (Fletcher et al., 2002). However, to create some complex flow patterns desired by certain chemical processes in the microreactor channel network, a pressure-driven flow is required.

There have been a number of studies on the microscale flow behaviour in the laminar flow regime under pressure-driven flow conditions. Most of the work has focused on comparing flows for a range of fluids measured in microchannels of different shapes with predictions based on conventional theory developed for macroscopic scale pipes (Tuckerman and Pease, 1981; Peiyi and Little, 1983; Wilding et al., 1994; Papautsky et al., 1999, 2001; Mala and Li, 1999; Brutin and Tadrist, 2003; Choi et al., 1991; Yu et al., 1995; Pfahler et al., 1990; Xu et al., 2000; Weilin et al., 2000; Sharp et al., 2000, 2002; Koo and Kleinstreuer, 2003; Jiang et al., 1995; Spence and Crouch, 1998). The initial work on microfluidics for an electronic chip cooling system with water through microchannels fabricated directly on silicon chips was conducted by Tuckerman and Pease (1981). Following that, a number of studies have been carried out with fluid flows in microchannels or microtubes and

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Table 1 – The specifications of the microtubes used

Inner diameter (i.d.) (μm)	Outer diameter (o.d.) (μm)	Material	Colour	Upchurch part number
50	360	PEEK	Natural	1570
75	360	PEEK	Black	1573
100	360	PEEK	Red	1571
150	360	PEEK	Yellow	1572
250	1/16″	PEEK	Blue	1531B
500	1/16″	PEEK	Orange	1532
75	360	Fused silica	Natural	FS-175

some significant disagreements have been observed between experiments and conventional theory used in macroscale fluidics. Peiyi and Little (1983) measured the friction factors for gas flow in microchannels and found that the measured values were larger than that predicted by conventional theory for macroscale pipes. They attributed these differences to the large relative roughness of the microchannel surface. Similar increases in friction factors have also been observed by other researchers (Wilding et al., 1994; Papautsky et al., 1999; Mala and Li, 1999; Brutin and Tadrist, 2003). Papautsky et al. (1999) developed a numerical model based on micropolar fluid theory which augmented the laws of classical continuum mechanics by incorporating the effects of fluid molecules on the continuum. Their model showed better predictions for water flows in microchannels than the classical theory. A roughness-viscosity model was proposed by Mala and Li (1999) to interpret the experimental results. Brutin and Tadrist (2003) suggested that a modification of local viscosity due to the fluid ionic coupling with the surface might be accountable for the increase in friction factors. In the meantime, other researchers have found that the friction factors were lower than those predicted by theory (Choi et al., 1991; Yu et al., 1995; Pfahler et al., 1990), and most of the deviation was attributed to the uncertainty of the microchannel dimensions. In addition to the effect from the microscale tubes and errors from channel dimension determinations, other factors including viscosity variations due to temperature changes or surface roughness, entrance effects, and possible geometric non-uniformities, e.g., a contraction and/or bend at the inlet to the microchannel, have been taken into account for the explanation of the deviation from theory (Papautsky et al., 2001; Xu et al., 2000; Weilin et al., 2000; Sharp et al., 2002; Koo and Kleinstreuer, 2003). On the other hand, some experiments have shown good agreements with the conventional theory (Tuckerman and Pease, 1981; Jiang et al., 1995; Spence and Crouch, 1998; Sharp et al., 2000).

The aim of the present study was to obtain further understanding of the behaviour of the liquid flow driven by a syringe pump under microfluidic conditions. Microtubes with inner diameters ranging from 50 μm to 500 μm were examined; a range which is similar to that of microreactor channels. Three main aspects of the liquid flow were examined. Firstly, the relationships between pressure drops and flow rates were examined for the different microtube diameters. Secondly, we measured the times required to achieve steady flows and pressure drops when the pump flow rate was altered. This aspect is particularly relevant to attempting fast switching of flows between different limbs of a microreactor channel network, and controlling integrated on-chip valving. Thirdly, we examined the viability and usefulness of continuous, *in-situ* monitoring of the pressure drop across the channel lengths.

2. Experimental

The experimental apparatus consisted of a syringe pump, a micropressure sensor, a series of lengths of microtubes with connectors, and a data acquisition system with PC. The syringe pump (Model 200, kdScientific Inc., USA) was controlled by the computer using a LabVIEW™ software program via RS232 serial ports, and can deliver liquid at flow rates ranging from 0.001 mL/h to 2.203 mL/min with a 1 mL luer-lock gas-tight glass syringe (i.d. 4.61 mm, SGE, Australia). The volumetric flow rate was set by the computer via the pump's control system and the average volumetric flow rate was confirmed by a weighing method.

A miniature threaded pressure sensor (Model EPX-V01-35B, Entran® Sensors & Electronics, Fairfield, NJ, USA), powered by a 10 VDC power supply, was used to measure the pressure in a range of 0–35 bar above atmosphere. The output signal of the sensor in millivolts (125 mV/FS) was collected by the computer using a LabVIEW™ software program via the data acquisition interface card (DAQ Card-6024E, National Instruments, USA). The data acquisition frequency was set at 20 scans/s, which were then averaged over every second. The pressure sensor was connected to the microtube inlet with a P775 MicroTee (Upchurch Scientific Inc., USA) connector where the outlet of the microtube was open to atmosphere. The pressure sensor was zeroed against atmosphere so the pressure measured was equal to the pressure difference between the microtube inlet and outlet, which is often referred to as the pressure drop.

The microtubes used in this study were supplied by Upchurch Scientific Inc., USA, and made of two types of material, namely PEEK™ (polyetheretherketone) polymer and fused silica. All the microtube sections examined were cut to a length of 25 cm for comparison. The specifications of the microtubes used are summarized in Table 1. MicroTight Unions (Upchurch P720) were used to directly connect two pieces of microtube with o.d. 360 μm. For a connection between o.d. 1/16″ and o.d. 360 μm tubes a MicroTight Adapter (Upchurch P770) was used.

Squalane was chosen as the test fluid in this study in view of its biomedical applications (Allison, 1999; Hilgers et al., 1999; Shahiwala and Amiji, 2008). Squalane is a linear hydrocarbon precursor of cholesterol found in many tissues, notably the livers of sharks (Squalus) and other fishes (Allison, 1999). It has been used in pharmaceuticals and as a skin lubricant, as an ingredient in suppositories (Allison, 1999; Hilgers et al., 1999). In recent years, its applications associated with lipophilic drug delivery and vaccine studies have increasingly attracted attention while studies have shown that (squalane) oil-in-water emulsions can elicit both humoral and cellular immune responses (Shahiwala and Amiji, 2008). Squalane is generally considered as a Newtonian fluid (Chaomleffel et al., 2007), and studies on its viscosity under different conditions have been

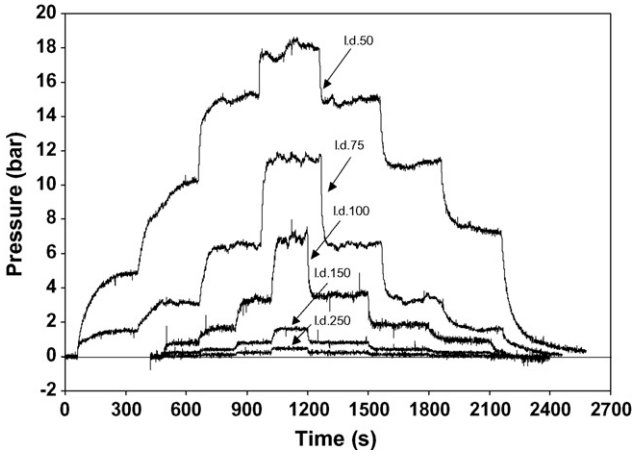

Fig. 1 – Pressure *versus* time when the flow rate was raised then lowered step by step for microtubes with different diameters (Flow rate cycles: PEEK tubes with i.d. 250, i.d. 150 and i.d. 100, 0-2-4-8-16-8-4-2-0 μL/min; PEEK tube with i.d. 75, 0-2-4-8-12-8-4-2-0 μL/min; PEEK tube with i.d. 50, 0-2-4-6-8-6-4-3-0 μL/min).

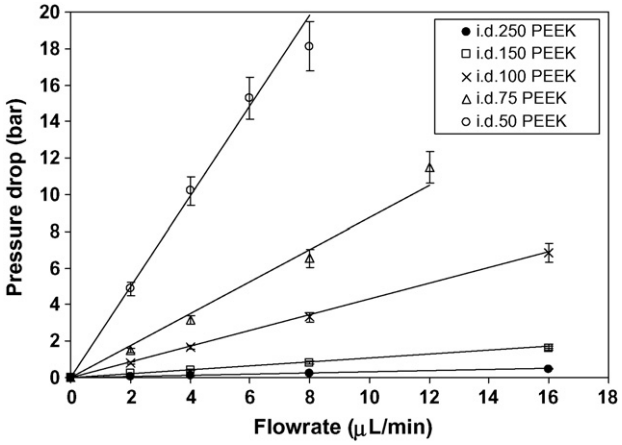

Fig. 2 – Pressure drop as a function of flow rate for microtubes with different diameters.

reported in a number of publications (de Ruijter et al., 1998; Kumagai et al., 2007; Ling and Shaw, 2008). The viscosity was found to be sensitive to temperature, e.g., 35.6 mPas at 20 °C and 23.01 mPas at 30 °C, and the relationship can be found in reference (de Ruijter et al., 1998). In this study squalane was supplied by Aldrich and used without further treatment (http, 2008a). All measurements were carried out at 25.0 °C.

3. Results and discussion

3.1. *Pressure drops at different flow rates*

Pressure drops across microtube sections with different diameters were monitored as the flow rate was raised step by step and then decreased in steps to investigate the relationship between pressure drops and flow rates. The results are depicted in Fig. 1.

As the flow rate was raised, in general, the pressure drop increased in response to a higher level and tended to be stable after a period of stabilisation time. When the flow rate was reduced step by step the pressure drop also decreased and tended to reach a lower stable level again after a period of time. The pressure drop at the stable level was found to be reproducible when the flow rate was cycled up and down. Fig. 2 shows the relation of the pressure drop at the stable level to the flow rate for microtubes with different inner diameters in a flow rate range of 0–16 μL/min. It can be seen from Fig. 2 that the pressure drop across a length of microtube increases linearly with flow rate.

Pressure-driven fluidics on macroscale has been extensively studied and the well-known Hagen–Poiseuille equation for laminar flow in a circular pipe can be represented by

$$\frac{P}{F} = \frac{128\mu L}{\pi D^4} \quad (1)$$

when the Reynolds number, *Re*, is in the laminar flow range,

$$Re = \frac{Du\rho}{\mu} < 2000 \quad (2)$$

where *P* is the pressure drop across a length *L* of pipe with an inner diameter *D*, *F* is the volumetric flow rate, *u* is the average linear velocity, μ is the fluid viscosity, and ρ, the fluid density. Under the experimental conditions in the present study, the Reynolds number is below 1 indicating that the flow is restrictively in the laminar flow range.

In agreement with Eq. (1), the measured pressure drop increases linearly with flow rate (Fig. 2) for all tube diameters tested. However, calculated values of the slopes of the plots of Fig. 2 (i.e. *P*/*F*) using Eq. (1) and the microtube manufacturers' values for the inner diameters deviate from the measured values of *P*/*F*. In previous studies similar deviations have been observed (Wilding et al., 1994; Papautsky et al., 1999, 2001; Mala and Li, 1999; Brutin and Tadrist, 2003; Choi et al., 1991; Yu et al., 1995; Pfahler et al., 1990; Xu et al., 2000; Weilin et al., 2000; Sharp et al., 2002; Koo and Kleinstreuer, 2003) and a range of models (mainly based on surface roughness and non-uniform fluid viscosities very close to channel walls) have been developed to account for the observations. Here we note that $(P/F) \propto D^{-4}$ and so a relatively small fractional uncertainty in *D* leads to a large uncertainty in the calculation of *P*/*F*. Using the tube inner diameter tolerances specified by the manufacturer (Table 1, http, 2008b) the uncertainties in *P*/*F* were estimated. Fig. 3 compares measured and calculated *P*/*F* val-

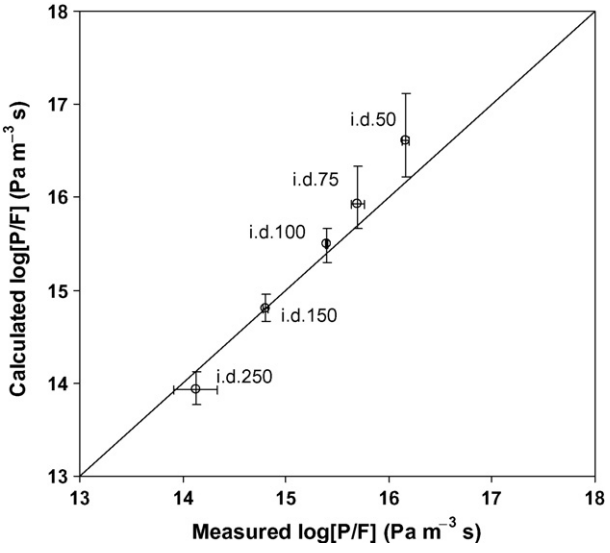

Fig. 3 – Comparison of calculated and measured log[P/F] for microtubes with different inner diameters.

ues with the estimated uncertainties and it can be seen that the apparent discrepancies are all within the estimated uncertainties. However, possible contributions to the deviation due to departures from non-circularity of the microtube cannot be excluded even it is unlikely to determine that along the entire tube length. Although the uncertainties are relatively large, particularly for the smaller tube diameters, there is no significant evidence for special microscale fluidic behaviour in this case.

3.2. *Effects of changing pumping conditions*

It has been seen from Fig. 1 that a stabilisation period prior to reaching a steady state flow always existed after the pump was switched on/off or to a different flow rate. This phenomenon was also observed by other researchers and generally believed to be the time for reaching a pressure equilibration in the whole flow system including the syringe used (Weilin et al., 2000; Spence and Crouch, 1998). Clearly, this introductory time is problematic for control and change of flow conditions in an instantaneous way, where special flow patterns such as slugs or pulses of reagents are usually required in microreactor systems or integrated on-chip valving is being used.

Fig. 4 shows the pressure changes at different flow rates when the pump was switched on for 5 min and then off where a PEEK tube with an inner diameter of 75 μm was used. It can be seen from the figure that the variation of the stabilisation time became more significant as the pump was switched on/off with different flow rate settings and, consequently, the pressure in the flow system was altered. It is found that the relation of the introductory time τ to the pressure can be represented by

$$P = P_0 + \Delta P\left[1 - \mathrm{Exp}\left(-\frac{t - t_0}{\tau}\right)\right] \quad (3)$$

where P_0 is the pressure at time t_0 when the pumping conditions are altered, i.e., on/off or changing flow rates. ΔP is the pressure difference between two adjacent stable pressure levels. By fitting the measured pressure profiles to this model,

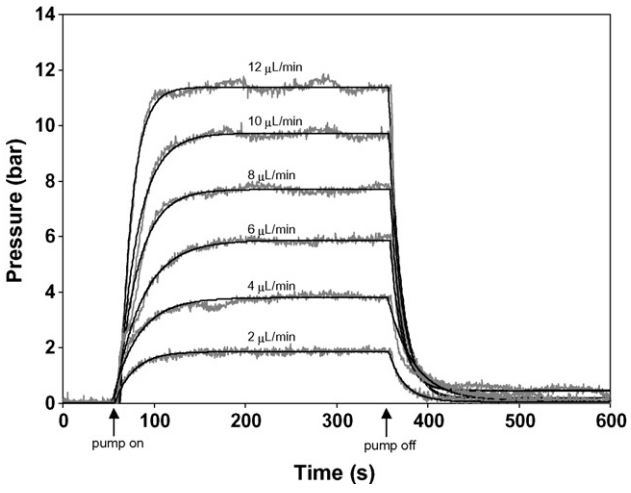

Fig. 4 – Pressure *versus* time at different flow rates for PEEK tubing with an inner diameter of 75 μm when the pump was switched on/off. The gray dash lines show the measured data and the black solid curves are the best-fits to the model described in the text.

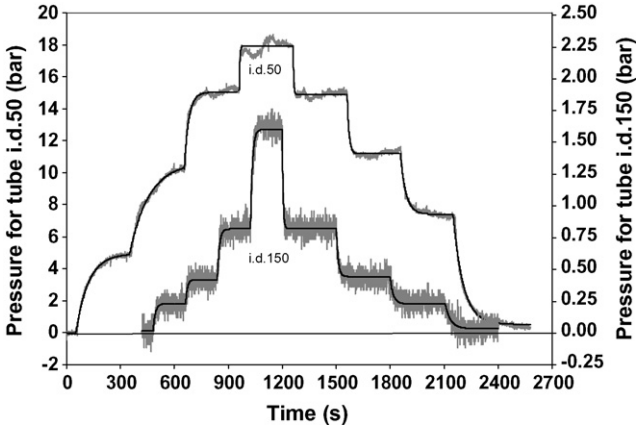

Fig. 5 – Pressure *versus* time when the flow rate was raised and then lowered step by step for the microtube with inner diameters of 50 μm and 150 μm (Flow rate cycles: i.d. 50 μm tube, 0-2-4-6-8-6-4-3-0; i.d. 150 μm tube, 0-2-4-8-16-8-4-2-0 μL/min). The gray dash lines show the measured data and the black solid curves are the best-fits to the model.

the introductory time τ for different flow rate was obtained. The best-fit results are shown in Fig. 4 as the solid curves. This model was also applied to the experimental data shown in Fig. 1 where the pressure corresponding to the flow rate was cycled up and down. The solid curves in Fig. 5 show two examples of the best-fit results for the microtubes with inner diameters of 50 μm and 150 μm.

In general, the volume of most fluids varies in response to the pressure change at a given temperature and this thermophysical property of fluids is referred to as its compressibility C_{comp}. The effect of compressibility on the flow stability is believed in most cases to be negligible in macroscale liquid flow systems where a relatively high volumetric flow rate is applied. In microscale flow systems, however, the volume variation due to pressure change could result in significant variation in the instant flow rate for the liquid flow. Thus, the stabilisation time for reaching a steady state flow is likely to be the relaxation time for building a pressure equilibration in the whole liquid flow system, and the relaxation time τ can be represented by

$$\tau = \frac{\Delta V}{F_{mean}} = \frac{\Delta P C_{comp} V}{F_{mean}} \quad (4)$$

where ΔV is the volumetric variation due to a pressure change ΔP. V is the volume of the whole liquid flow system and F_{mean}, the mean volumetric flow rate during the pressure change. Although the volume of the whole liquid system is varying during the liquid flow it is possible to determine the system volume in a short period of time with a known flow rate setting. Based on the results shown in Figs. 4 and 5 for the relaxation time, the best fitting of the liquid compressibility could be obtained according to Eq. (4). Fig. 6 shows the relation of the relaxation time τ *versus* $\Delta PV/F_{mean}$. The best-fit value for the liquid compressibility C_{comp} is found to be $2.3135 \times 10^{-4}\,\mathrm{bar}^{-1}$ under the experimental conditions. Although the deviation is relatively big, this result is in rough agreement with the compressibility of other hydrocarbons that is typically on the order of 10^{-4} to $10^{-5}\,\mathrm{bar}^{-1}$ at a temperature of 25 °C (Lide, 2003).

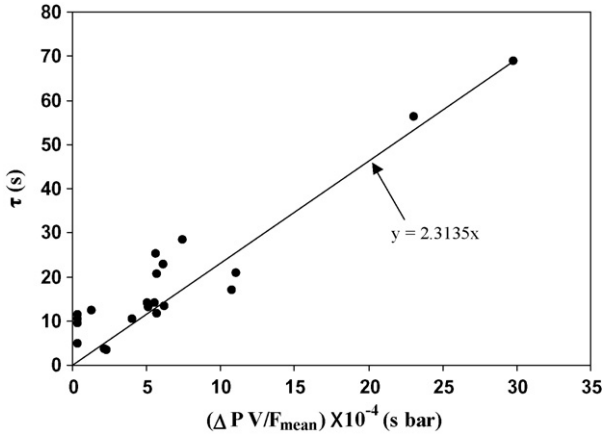

Fig. 6 – Relaxation time τ *versus* ($\Delta PV/F_{mean}$).

3.3. *Comparison of PEEK polymer and fused silica microtubes*

The effect of material properties in particular the surface roughness of tubes on pressure drops was found to be important under turbulent flow conditions but insignificant under laminar flow conditions in macroscale tubes. In the laminar flow regime on microscale, the assumption that the effect from the tube material is negligible in terms of flow resistance is still under discussion in the literature (Peiyi and Little, 1983; Wilding et al., 1994; Papautsky et al., 1999; Mala and Li, 1999; Brutin and Tadrist, 2003; Jiang et al., 1995; Spence and Crouch, 1998; Sharp et al., 2000). In this present study, two types of microtubes, which are commonly used in microreactor research laboratories, made of either PEEK polymer or fused silica were compared for different flow rates where the two microtubes were cut to a same length. The results are illustrated in Fig. 7. It can be seen from the figure that insignificant difference between the two types of material in terms of pressure drop was observed.

This insignificance was also observed by Brutin and Tadrist (2003), and they suggested that with small Reynolds number of less than 100 the effect from the surface roughness on the pressure drop was negligible although this effect was found notable on the transition from laminar to turbulent regime. On the other hand, Mala and Li (1999) observed the dependence of the flow behaviour on the material of the microtubes, where fused silica microtubes required higher pressure gradients compared to the stainless steel microtubes under the same conditions. The effect of the roughness on the surface of microchannels was also believed, by Peiyi and Little (1983) and Papautsky et al. (1999), to be the cause of deviations of the pressure drop from the conventional theory prediction.

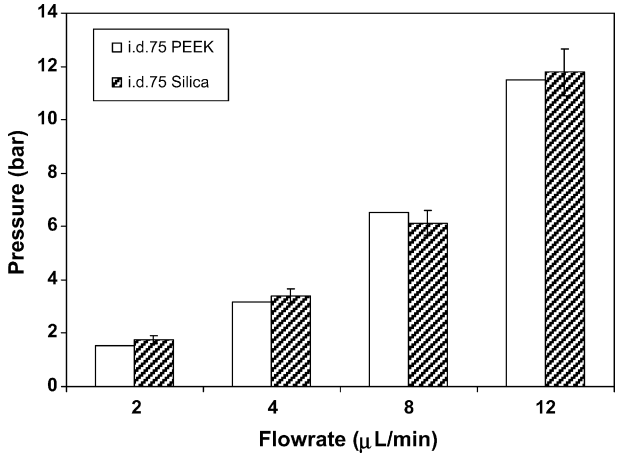

Fig. 7 – Comparison of pressure drops for a same length of microtubes made of PEEK polymer and fused silica.

3.4. *Monitoring of liquid flow through a series of microtubes*

As noted above, the measured pressure drop for liquid flow is very sensitive to the tube diameter and this can give rise to apparent discrepancies between microfluidics and macroscale theory. However, if there are no complications due to rough surfaces, measuring the pressure drop can provide a sensitive and non-destructive method of estimating the dimensions of channel sections. During the filling of an empty microtube, the measured pressure drop increases in proportion to the filled length and the pressure drop per unit of filled length depends on the channel cross section dimensions in the section of interest.

To investigate this aspect, we have monitored the pressure drop as a function of time as squalane is pumped at a constant volumetric flow rate though a series of three connected tube sections of different dimensions. The three sections were 26.5 cm of 250 μm i.d., 11 cm of 500 μm i.d. and 44 cm of 150 μm i.d. The time needed for the liquid to fill each section is given by

$$t = \frac{L}{u} = \frac{L\pi D^2}{4F} \quad (5)$$

For a fixed flow rate of 15 μL/min, the tube section filling times are 52 s, 86 s and 31 s respectively and 26 s, 45 s and 15.5 s for a flow rate of 30 μL/min. Fig. 8 shows the pressure drop as a function of time along the three pieces of microtubes with inner diameters of 250 μm, 500 μm and 150 μm, respectively. It can be seen that the plot clearly indicates the changes in tube dimensions experienced by the moving liquid front. It is also seen that the plot scales as expected with the set volumetric flow rate. Using Eqs. (1), (3) and (4), the curve of pressure *versus* time was calculated and is compared with the measured data in Fig. 8. The agreement is good indicating that the relaxation time considerations derived initially for changing pump flow rates also apply to considerations of time dependent changes in hydrodynamic resistance to flow. Thus, the measurement of pressure drop along a microtube could be used for *in-situ* monitoring of liquid passing through the microtube. Moreover, if

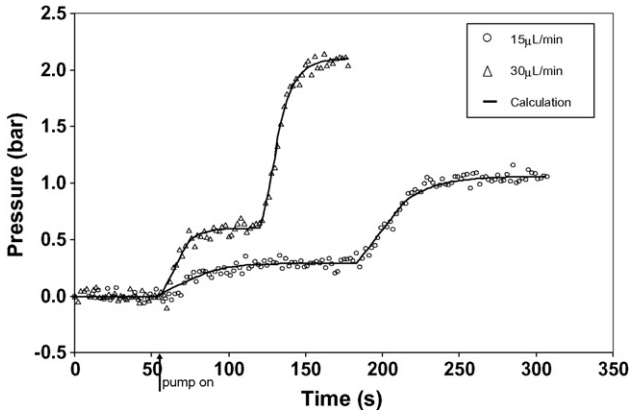

Fig. 8 – Pressure drop *versus* time for a series of three pieces of tubes with different diameters.

the sensitivity and accuracy of the sensor and data acquisition system are high enough, a change in the microchannel dimension could be detected with a sudden pressure variation.

4. Conclusions

The liquid flow driven by a syringe pump within microtubes in a range of very low Reynolds numbers (< 0.15) was investigated by monitoring the pressure change *in situ*. Cylindrical microtubes with diameters ranging from 50 μm to 500 μm were examined and two types of tube material, namely PEEK polymer and fused silica were compared. A good linear relation for the pressure drop *versus* flow rate was obtained. Apparent deviations between the measured slopes with those calculated using conventional theory were attributed to uncertainties in the calculated values which are dominated by the uncertainties in the microtube diameters. It was found that a period of stabilisation was required for reaching a steady flow after the syringe pump was switched on/off or to a different flow rate. The stabilisation time was likely due to the compressibility of the fluid. These relatively long stabilisation times (tens of seconds, contrasting sharply with ms flow switching times by electrokinetic pumping) have implications for pressure-driven flow control in Lab-on-a-chip microreactor applications where interconnecting tubing or on-chip pumping/valving is used. By comparing the two types of microtubes made of either PEEK polymer or fused silica, insignificant difference was found between the two types of material in terms of flow resistance. This approach of *in-situ* monitoring of pressure drop in microchannel liquid flow systems provides a simple and effective means of monitoring the liquid flow and can be used as a non-destructive method to characterize the local dimensions of the channel sections. Conversely, the method would also enable the detection of viscosity changes in specific channel sections. In addition to miniaturizing viscosity measurements of pure liquids, viscosity changes would enable *in-situ* detection of diverse processes such as protein denaturation and emulsion instability.

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