Microfluidics—a review

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Abstract. An overview is given of research activities in the field of fluid components or systems built with microfabrication technologies. This review focuses on the fluidic behaviour of the various devices, such as valves, pumps and flow sensors, as well as the possibilities and pitfalls related to the modelling of these devices using simple flow theory. Finally, a number of microfluidic systems are described and comments on future trends are given.

1. Introduction

Research on microfluidic devices, fabricated with micromechanics technology, has its origin about 20 years ago. At Stanford University [1–3] the research involved a gas chromatograph, and at IBM [4–6] ink jet printer nozzles were developed. The follow-up on these early and now legendary devices has been modest for a long time, but within the last six years a dramatic increase in research activities has taken place, and microfluidics is developing into a ‘hot’ research topic [7].

Many different devices are under development, ranging from single components such as flow sensors and valves for gas pressure regulation, to complex microfluid handling systems for chemical analyses, consisting of pumps, valves, flow sensors, separation capillaries, chemical detectors etc., all integrated on a single substrate or as sandwiched modules.

Micromechanics is a multidisciplinary research field. As new areas of application are still being investigated and the systems under development are becoming more complex, there is an increasing demand both for theoretical and experimental work on fundamental physical and chemical phenomena, and also for better modelling tools. Fluid mechanics is one of the many disciplines to be further addressed in the near future.

The aim of this paper is to give a review of the status of microfluidic devices and systems with focus on fluidic characteristics. In addition, the simplest models describing fluid flow are summarized, and special effects related to fluid flow on a micrometre scale are highlighted.

2. Fluid mechanics modelling

Most of the published work on microfluidic components includes fluid mechanic modelling as a design tool, or as a way to correlate and explain experimental results. In many cases, the flow–pressure characteristics of a device are dominated by one single restriction, and it is sufficient to use a simple analytical model well known from macroscopic fluid mechanics. This approach has been used successfully for valves [8–11], channels [12–14] and a flow sensor [15].

Numerical simulations are used in the case of more complex structures or systems. The most common method of numerical simulation is based on a subdivision of the complete structure into lumped elements, which can be described individually by simple analytical models, and for which simple relations between individually lumped elements can be formulated. These models and relations of interaction can then be fed into a dedicated or generally available computer program. In this way, micropumps have been simulated using a so-called Bond graph simulation tool [16]. Flow sensors have been simulated through the construction of an equivalent electronic circuit, and subsequently analysed using SPICE or a similar tool [17–19]. Various devices such as valves [20, 21], a micropump [22] and a fluid dispenser [23] have been simulated using dedicated computer programs.

The precondition for successful fluid mechanic modelling using direct analytical models or lumped elements models relies on correct assumptions as to type of flow.

In order to determine whether a given flow pattern is laminar or tubular, it is common practice to evaluate the Reynolds number and compare it to the transitional number 2000 or 2300. As we shall see, many microfluidic devices cannot be described by either a simple laminar or a turbulent model, because the length of the element in the direction of flow is shorter than the entrance length for fully developed laminar or turbulent flow. In practice, alternative assumptions are made for these elements in order to model the pressure drop for a given flow. For the sake of simplicity, we have assumed that all fluidic elements under consideration terminate as a sudden expansion, implying that the kinetic energy of the fluid is not transferred from one element to the next.

The line plotted in figure 1 represents the transitional Reynolds number defined in the following manner: for small $L/D_1$ ratios, the value for a slit type orifice is used [9]. For larger values the transitional Reynolds number is defined by setting the length $L$ of
the element equal to the entrance length $X_e$ for fully developed flow:

$$L = X_e = 0.03D_h Re_t, \quad Re_t \approx 30 \frac{L}{D_h}$$ (1)

which is consistent with the alternative definition, given by the balance between pressure drop due to inertial losses, and pressure drop due to viscous losses:

$$\Delta P_{\text{tot}} = \Delta P_{\text{visc}} = \frac{\rho U^2}{2} = U \frac{C L}{2 D_h^2}$$

$$Re_t = \frac{U D_h}{\nu} = \frac{C L}{\xi D_h}.$$ (2)

Definitions and values of parameters are given in table 1.

With large values of $L/D_h (>70)$, the well known and often cited value $Re_e = 2300$ is valid.

In this way, three different flow regimes are defined:

- at the bottom for $Re < Re_{\text{e}}$, the pressure drop is dominated by viscous losses and the flow is laminar.
- In the upper right corner the flow is fully developed turbulent, and in the upper left corner the flow is not fully developed, and the pressure drop is dominated by inertial losses.

Now, looking at the 32 microfluidic devices or components scattered on the graph it is striking that none of them was operated in the region of fully developed turbulent flow, and that the transitional Reynolds number 2300 seem to have little relevance to microfluidics.

Analytical formulas relating to flow and pressure drop do exist for each region. These have been gathered from various sources and are listed in tables 2 and 3.

### 2.1. Deviations from simple theory and break-down of customary assumptions

The simple formulas listed in tables 2 and 3 are only valid under a number of assumptions, which are often, but not always, fulfilled. One precondition, already mentioned above, is that kinetic energy is not transferred from one element to the next. This is true for most microfluidic elements such as valves and...
channels that are terminated with a sudden expansion in the flow path cross section. However, microfluidic amplifiers \[3, 24\], which we will describe later, are examples of fluidic devices that take advantage of the transfer of kinetic energy and the tendency of fluid jets to attach to nearby surfaces.

For laminar gas flows, at least two assumptions exist, which are normally fulfilled in macroscopic flow, but often violated in microfluidics. The first assumption is that the gas velocity is much lower than the velocity of sound. In macroscopic flow channels having a hydraulic diameter larger than about 0.1 mm the flow will develop into turbulent flow at subsonic velocity. In microfluidic devices, it is possible to have low Reynolds numbers along with flow velocity close to sound velocity. This has indeed been observed by Jerman \[10\] in conjunction with gas flow in a 5 μm valve seat gap. Neither Jerman nor we have found a model describing sonic gas flow in the laminar flow range. Considering the adiabatic precondition for the macroscopic value of sound, one could even question whether the macroscopic velocity of sound is valid in microfluidics.

The second assumption is that of no slip at the solid interface. For macroscopic fluid elements this is a safe assumption at atmospheric pressure; only at vacuum pressure is the no slip condition substituted by molecular flow models. As the dimensions of channels and gaps enter the micrometre or submicrometre range, one can no longer neglect the mean free path for gas molecules (60 nm at 1 atm). The no slip condition is no longer valid, and a higher flow than predicted by simple theory must be expected. Experiments on flow resistance in 0.5 μm channels by Pfahler et al \[25\] show a higher flow rate, and these results have been explained by theoretical work done by Arkillic and Breuer \[26\]. This phenomenon is important for gas damping of accelerometer \[27\], oscillating microstructures \[28\] and for ‘zipper’ effect actuators \[29\].

For liquids, there are two major phenomena to consider in conjunction with microfluidics. The assumption is normally that viscosity is independent of the dimension of the flow channel for liquids such as water, silicon oil and alcohol. There are, however, a number of observations indicating that this is not a valid assumption. Pfahler et al \[25\] have measured

\[
\Delta P = \frac{2\gamma_l \cos \theta}{r} \quad P_t = \frac{2\gamma_l}{r} \quad (3)
\]

where \(r\) is the channel radius, \(\gamma_l\) is the gas–liquid surface tension, \(\gamma_s\) is a frictional surface tension parameter and \(\theta\) is the contact angle. It is evident that both pressure differences increase with decreasing channel dimension. As long as a gas bubble completely covers the cross sectional area of the capillary, there will be no net reaction force from the first term of (3), since the pressure difference across the two identical gas–liquid surfaces of the gas bubble will outbalance one another. On the other hand, if the capillary radius suddenly changes or terminates in a cavity, the reaction force (or pressure) from the first term will dominate, because of the different radius of curvature of the two gas–liquid interfaces. The resulting blocking pressure
Table 3. Flow models for diatomic gases at isothermal conditions [10, 25, 129].

<table>
<thead>
<tr>
<th>Type of restriction</th>
<th>Definition</th>
<th>Viscous losses dominate laminar flow ((Re &lt; Re_0))</th>
<th>Inertial losses dominate ((Re &gt; Re_0))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orifice</td>
<td>(L/D_h &lt; 0.5)</td>
<td>(Q_v \approx \frac{A_0^2}{4} \frac{R_P}{\mu} \frac{p_{out} - p_{in}}{\sqrt{\epsilon}})</td>
<td>(Q_v = \frac{A_0}{\sqrt{\epsilon}} \frac{R_P}{\mu} \sqrt{\frac{2(\rho_{out} - \rho_{in})}{\rho_{in}}} \frac{p_{out}}{P_{out}} &gt; 2)</td>
</tr>
<tr>
<td>Short channel</td>
<td>(2 &lt; L/D_h &lt; 50)</td>
<td>(Q_v = \frac{A_0}{\sqrt{\epsilon}} \frac{R_P}{\mu} \sqrt{\frac{2(\rho_{out} - \rho_{in})}{\rho_{in}}} \frac{p_{out}}{P_{out}} &gt; 2)</td>
<td>(Q_v = \frac{A_0}{\sqrt{\epsilon}} \frac{R_P}{\mu} \sqrt{\frac{2(\rho_{out} - \rho_{in})}{\rho_{in}}} \frac{p_{out}}{P_{out}} &lt; 2)</td>
</tr>
<tr>
<td>Long channel</td>
<td>(L/D_h &gt; 100)</td>
<td>(U &lt; 0.3 , c_s)</td>
<td>(Q_v = A_0 \sqrt{\frac{2(\rho_{out} - \rho_{in})}{\rho_{in}}} \frac{p_{out}}{P_{out}} &lt; 2)</td>
</tr>
</tbody>
</table>

needed to discharge a gas bubble from the exit of a 1 μm water filled capillary is of the order of \((\kappa H/r)\), which amounts to about 1.4 bar!

The surface tension affects may explain observations by Pfahler et al. [31] reporting that 0.5 μm channels blocked for water flow \((\kappa H = 24 \text{ mN m}^{-1})\), and similar observations by Stemme et al. [32] reporting three times higher velocity of alcohol than water through a 0.2 μm filter.

Even if gas bubbles can be totally avoided in operational microfluidic handling devices, the surface tension effects still have practical relevance to the initial filling of these devices, i.e. micropumps [35, 36]. Further theoretical and experimental work on surface tension effects is needed.

2.2. Numerical modelling

Several tools, such as finite element analyses (FEA), finite difference and boundary element modelling, are suitable for microfluidic simulation. Only a few applications of FEA for microfluidics have been reported. Mettner et al report on a two-dimensional simulation of flow through a valve seat [37], and combined flow and heat transfer simulation on a fluid deflection beam [38]. Schmidt reports on flow in forward and backward direction in a micromechanical nozzle [39], and Miyake et al report on flow in a microshear flow channel [40] and on micronozzles for a fluid mixer [41]. Finally, Vollmer et al report on flow profile simulation in a bistable fluidic element [24].

3. Micromechanical valves

Fluid control will almost inevitably involve valves, and the design of valves has consequently attracted much attention, also within the micromechanical realm.

Micromachined valves have a number of advantages over traditional valves. They benefit from small size in terms of response time, power consumption, small dead volume and improved fatigue properties. However, in some applications, the small size can turn out to be an Achilles’ heel, where flow demands cannot be met. Additional advantages are the ability to be batch fabricated with high reproducibility, and the ability to be integrated with other functions, such as micromechanical sensors.

The valve designs for microfluidic applications can be categorized in numerous ways. The majority of micromechanical valves have been designed for gas flow control [8, 42–46]. Only a limited number are intended for liquid applications, as check valves integrated in pumps [47–49], or as valves in connection with chemical analysis systems [50, 51]. The flow rate requirements in these applications can be satisfied by micromechanical valves, despite the reduced dimensions and flow conductance. In other areas, such as small hydraulic pilot valves, it seems difficult for micromachined technology to compete on performance and cost with existing technology.

Due to the planar nature of the fabrication process, design of micromechanical valves is restricted. This constraint, and the matured process for silicon diaphragm fabrication, have favoured designs incorporating diaphragms as the moving elements [9, 21, 44, 52]. However, valves with cantilevers as moving parts [8, 20, 43, 46, 48, 53] and various types with perforated diaphragms [45, 54, 55] have also been constructed. Very small cantilever types can be fabricated, making them suitable for passive check valves in micropumps [48, 53]. These valves are surrounded entirely by liquid, which can contribute to failures through clogging or sedimentation of the narrow gaps encountered in these designs. This is normally overcome in the diaphragm valves, where the diaphragm separates the fluid side from the actuation side, and where the demands on cleanliness are frequently profound [29].

Figure 2 shows a diaphragm valve with integrated electric actuation presented by Jerman [44]. The valve is intended as a gas control valve and is one of the first commercialized microfluidic components. The valve seat design is illustrative of the majority of the diaphragm valves presented.

Tirén et al. [8] reported on a non-reverse cantilever valve manufactured in silicon as illustrated in figure 3. Tirén et al. have realized 800 of these cantilever valves on a single 2" wafer, illustrating the small size of a single valve and batch fabrication possibilities.

Actuators available for integration with micromachined valves are limited as regards both on force and motion. The valves with integrated actuation use a number of actuation mechanisms, for example piezoelectric [56], thermopneumatic [21], electrostatic [29, 37, 46], electromagnetic [57, 58] and bimetallic [10].
Huff et al [59, 52] have improved the performance of electrostatic actuation by designing a unique pressure balance in the hydraulic part of the valve so that electrostatic actuation can be used to control larger pressure differences than commonly expected. The outline of the valve structure is shown in figure 4.

Döring et al [38] have combined the Coanda effect with forced convection, to realize a cantilever structure for fluid control with thermoelectric actuation. The flow element is capable of controlling flow rates of up to 150 ml min⁻¹ at pressure levels of up to 4 bar, without the poor dynamic behaviour normally encountered in thermoelectric actuation. This principle is illustrated in figure 5.

The present stage of microvalve developments is represented in figure 6, where the numbers refer to the reference list. The points in figure 6 represent the highest Reynolds numbers reported in the papers, or calculated on the basis of measured data reported. \( L/D_b \) lies in the vicinity of unity for several of the microvalves, indicating that the valve seat length is comparable to the lift height. The transitional Reynolds number in this region is reduced, indicating that the valve restriction at this flow is dominated by inertial losses, while the flow at partly opened positions can be dominated by viscous losses.

The future trend in microvalve development is expected to divide into three branches: pilot valves for macroscopic valves, pressure or flow regulation and integrated system applications.

The pilot and regulation valves require in general large flow conductance, exemplified by their placement in the upper left corner of figure 6, while the system valves will typically be found in the laminar region of figure 6.

Analyses at Danfoss show that even high-volume production of individually packaged microvalves is not profitable as long as packaging expenses do not decrease. Probably, microvalves will never be a replacement technology for the majority of the valve market, but they can compete in specialized niches where their unique features are required.
Application of separate microvalves is justified predominantly in areas where performance enhancements, or cost reductions without performance loss, can be obtained. This is illustrated by the Novasensor design [64] of a pneumatic pilot valve. The valve is intended as a replacement for a cumbersome assembled valve, fabricated in a volume of about 200,000 per year worldwide. The microvalve benefits from the ability of micromechanics technology to obtain tight mechanical tolerances and reproducibility, along with the benefits of batch processing for high volumes, without performance reduction.

An attractive microvalve application is the microsystem domain, where valves can be integrated with other elements in one fabrication sequence. Compared to alternative hybrid solutions, microsystem technology offers cost reduction especially on assembly, and possible performance enhancements by the close spacing of the parts. This can launch completely new applications of microvalves. Examples of the system opportunities will be given in a subsequent section.

4. Micropumps

Research on micropumps based on microvalves was initiated at Stanford University in 1980. This work was later published by Smits [36]. Based on these ideas, membrane pumps were further developed at the University of Twente by Van Lintel et al [35, 65], and at the University of Neuchâtel by Van der Schoot et al [66]. A similar pump was later developed by Zengerle et al [48].
Recent developments on two of these pumps [68, 69] involve flow regulation through the integration of a flow sensor with the pump. This is described in more detail in the following section on microfluid systems.

Different directions for further development have been demonstrated: fabrication of an electrostatic actuated micropump using surface micromachining technology [70], and fabrication of a membrane pump using the LIGA technology [71].

One common problem with the membrane pumps is the input and output check valves. The leak rate of these check valves must be small compared to the pump flow rate, implying leak rates in the nl min$^{-1}$ range. This is achieved in prototype testing [35, 60], but long-term problems related to sedimentation or wear must be foreseen.

A membrane pump without check valves was recently presented by Stemme and Stemme [72]. The pump, shown in figure 9, is similar to other membrane pumps, having a pump chamber in which a certain pressure modulation and volume stroke can be generated. The check valves, however, are replaced by diffuser/nozzle elements having no movable parts, but yet showing fluid rectification.

The principle action of a diffuser/nozzle element is related to pressure recovery or the transformation of kinetic energy (flow velocity) into potential energy (pressure). Pressure recovery has a high efficiency in the diffuser direction, but not in the nozzle direction, and for a given pressure difference the element conducts more fluid in the diffuser direction than in the nozzle direction.

If the rectification of fluid is exclusively related to pressure recovery the pump should only be expected to work properly at Reynolds numbers higher than the transitional number. Stemme and Stemme [73] report on rectification at Reynolds numbers in the range 200–5000, and concludes that rectification takes place under laminar flow conditions. According to the definition given in this work, the transitional Reynolds number is about 200 for the diffuser/nozzle elements, and flow rectification should not take place at much lower Reynolds numbers.

The suggested existence of a fundamental lower limit on Reynolds number for the diffuser/nozzle pump has strong implications on the feasibility of scaling down the pump. The prototype has a pump chamber of 19 mm diameter, diffuser/nozzle elements 4 mm long, and demonstrates pump rates of 16 ml min$^{-1}$ and pump pressure of 0.2 bar! This is more than an order of magnitude higher than the membrane pumps mentioned above. It shall be interesting to see whether this ingenious valveless 'minipump' can be scaled down to a batch fabricated micropump.

Another interesting pump principle involving no movable parts is the electrohydrodynamic (EHD) pump. The motive force in EHD pumping is either the Coulomb force acting on ions injected from an emitter electrode into the fluid by electrochemical reactions [74–77], or the result of the interaction between a conductivity gradient and a travelling wave of potential [78]. The EHD pumps rely critically on the electric properties of the fluid. For example water pumping has only recently been demonstrated [102]. The simplest configuration of an EHD pump is two closely spaced, electrically isolated grids within a tube, making the principle suitable for micromechanical fabrication (see figure 10).

Pump rates of 14 ml min$^{-1}$ and static pressure built up of 2.5 kPa with organic solvents as liquid have been demonstrated [79]. This pump rate required 700 V operating voltage.

In the electrostatic pump [80, 81], a fluid is moved in a capillary tube due to the force acting on ionic species in an electric field. The electric field is obtained through
5. Flow sensors

Microfluidic flow sensors cover a wide range of devices and applications from macroscopic air flow measurements to the measurement of minute liquid flow.

Thermal detection principles are widely used for air and gas flow sensors [84–95]. These devices and several others have been reviewed recently by van Oudheusden [96], and there is no need to repeat this comprehensive work on air flow sensors and gas flow sensors.

An interesting alternative to thermal flow sensors is the shear force sensors, which have been realized for turbulent boundary measurements [97, 98], and high-viscosity fluid measurements [99].

This section will focus on micro flow sensors for liquids. At least four different measurement principles have been described: thermal dilution in a flow stream, transit time measurement of a tracer injected into the flow, pressure difference measurement across a flow restriction and force measurement on an element placed in the flow stream.

One of the first micro mechanical flow sensors for liquids was presented by Branebjerg et al [100]. The flow sensor shown in figure 11 demonstrates excellent accuracy and long-term stability in the 0.05–0.5 ml min⁻¹ range when operated in the thermal transit time mode. In this mode, the flow is measured as a phase shift between a 5 Hz heat pulse signal supplied to the heater, and the temperature signal picked up by the down-stream sensor. In thermal dilution mode, the heater is supplied with constant power and the temperature difference between down-stream and up-stream sensors is monitored. High sensitivity is obtained in the 0.0–0.2 ml min⁻¹ range.

This sensor has been tested with special reference to FIA (flow injection analysis) systems, and proper signal processing schemes have been developed for transit time measurements [101].

The same measurement scheme, including one heater and two temperature sensors, has also been realized in an elegant way using suspended microbridges for thermal decoupling [18]. This sensor has been designed to be integrated with a micropump [68] and is further described in the following section.

As an alternative to the injection of a heat pulse into the flow stream, Fuhr et al suggest the injection and subsequent detection of a charge pulse carried along in the fluid as ionic species [102]. The structure of a so-called electrohydrodynamic (EHD) flow sensor is identical to the EHD pump shown in figure 10. Using an injection voltage of 300 V and a grid spacing of 10 μm, flow rates down to 8 μl min⁻¹ could be detected.

An inherent problem with heat pulse injection as well as charge injection is changes of the chemical properties of the fluid under measurement. Measurement of the pressure drop across a flow restriction is one solution widely used in macroscopic flow measurement. An all integrated micro mechanical device including both flow channel and pressure sensor has only been realized for gas sensing [103], not for liquid flow sensing. However, the drag force measuring device presented by Gass et al [15] is quite similar to pressure difference measurement (see figure 12).

The flow sensor consists of a cantilever beam, with integrated piezoresistive strain gauges, situated in the flow stream. As a liquid flow is passed through the sensor a drag force will act on the beam. The drag force has two components: the skin friction due to the flow in the narrow slit at the tip of the beam, and the
resulting pressure difference across the beam. For small deflections of the beam, and assuming laminar flow in the slit, one would expect a linear response. This is indeed reported [15, 67] in the flow range 0–1 ml min⁻¹. The flow sensor has been tested in conjunction with a micropump, demonstrating regulated flow rates in the range 10–100 µl min⁻¹ [67, 69].

6. Microfluidic systems

The history of microfluidics is short; the number of fluidic components is limited and the number of microfluidic systems is even smaller. Three clear fields utilizing the advantages of micromechanics and system design materialize. The application fields are ink jet printer heads with nozzle arrays, micro dosing systems and micro chemical analysis systems.

The synergy of combining micromechanics and system design is illustrated by the following examples:

(i) A system containing many identical fluidic components. This could be an array of ink jet printing nozzles working in parallel [4], or an array of valves in a pneumatic or hydraulic system.

(ii) A system containing actuators with sensors that monitor the performance of the actuators on site. The sensor signal is used in a feedback loop to regulate the action of the actuator. A valve or a pump with an on site pressure sensor or flow sensor is an example [21].

(iii) A system containing sensors with improved performance due to on site self-test or calibration. An example of a simple self-test was presented in a micro flowmeter based on capacitive readout of a pressure drop over a flow channel. The self-test was performed by the electrostatic generation of a dynamic pressure drop over the flow channel [103].

(iv) A system generating a new function by the combination of different fluidic components. Chemical analysis systems in micromechanics may consist of valves, pumps, flow sensors, mixing units, channels and chemical detectors built together to perform the explicit function of the chemical analysis.

(v) Improved reliability by stiffly integrated channels and internal filters. In fluidic systems of small size the tubing between the fluidic components is often the least reliable, and stiff fluidic connections fabricated as an integrated part of the system will improve the systems' overall reliability. The sealing of the systems' internal channels in the clean microfabrication environment as well as integration of filters in the inlets will also improve performance.

The ink jet printer heads with arrays of nozzles in micromechanics was first presented in 1977 [4] and utilized nozzles obtained by anisotropic etching of holes in a (100) silicon wafer. Later, different shapes of nozzles were fabricated [5]. The challenge in the design of ink jet printer heads was to place the nozzles with minimal spacing, shaping them to deliver reproducible droplets, and to integrate actuators with sufficient force and speed to spray droplets with a frequency in the kHz range. The demands are tough, especially if the actuators have to be fabricated in micromechanics, and a complete micromechanic system is, to the knowledge of the authors, not in production.

Constant flow rate dosing systems are realised by integrating a flow sensor with either a valve or a pump. Several individual flow sensors, valves and pumps have been developed but only a few have been integrated into dosing systems. In 1987 Zdehlick [21] presented the idea of integrating a thermopneumatic actuated micromechanical valve and a flow sensor. The components could be fabricated on the same chip with internal fluidic channels. Another dosing system, also based on an integrated flow sensor and a valve, was presented by the group at Tohoku University [54]. The application of the 'integrated micro flow control system' was intended to improve the controllability of process gases in MOCVD and MOMB equipment.

A micromechanical pump with an integrated flow sensor was fabricated by the group at the MESA Institute [68], as illustrated in figure 13. A comparable structure has been presented by the group at Neuchâtel [67].

The dosing systems can be part of a transport system in a chemical analysis system or can be used in a drug delivering system. The demands of drug delivery systems correspond to the properties of micromechanical systems with small size, chemically durable materials, robust construction and the delivery of small precise doses of drugs. In the future, the medical application could imply disposable systems, which sets strong limitations on the cost of the total system.

The third and largest identified field of application is micromechanical chemical analysis systems. Today there are very few chemical sensors that can be
used for process control and monitoring in industrial environments [104]. Furthermore, the concentrations of most chemical species cannot be measured by simple sensors, but must be measured in an analyser, where the sample is pretreated, and the system frequently calibrated. Micromechanical chemical analysis systems have the potential of combining advanced analyses and robustness for industrial applications.

The systems can be divided into simple chemical systems, chromatographic analysers, liquid analysis systems with low-pressure pumps, such as systems for flow injection analysis (FIA), and analysers based on capillary electrophoresis and electro-osmotic pumps.

The simple analysis systems consist of a flow chip in which the sample is pumped in by use of external pumps, and measured by integrated chemical sensors. After measurement, the sample is pumped out and the system is calibrated with a calibration solution. Systems such as these are fabricated for in vivo blood gas analyses [50, 105, 106]. Other analysers were built as titration systems based on the integration of an ISFET sensor, and an electrochemical actuator in a flow channel [107, 108]. The titration is performed by a titrant, either of hydroxyl or hydroxide ions, generated in the electrochemical actuator, and the titration point is detected by the ISFET.

The gas chromatograph fabricated at Stanford University was the first chemical analyser in micromechanics, and showed the potential of these systems nearly twenty years ago [1]. Another gas chromatograph based on the same idea was later presented in Japan [109]. A liquid chromatograph has also been fabricated in micromechanics and has the remarkable small detection volume of 1.2 pl [12]. Common to the presented chromatographs is the integration of the chromatographic column and the detector, while the high-pressure pump needed is not integrated, and as long as high-pressure pumps are not available in micromechanics an all micromechanical liquid chromatograph analyser cannot be fabricated.

The group at Tohoku University was the first to build an FIA system in micromechanics [51, 110]. The system was built from a sandwich of two silicon wafers and two glass plates and consisted of two three-way valves, two pumps, a reaction channel and an optical detector, as illustrated in figure 14.

The group at Neuchâtel University has concurrently developed an FIA system, and designed it in a modular fashion so that reconfiguration is easy [111–115]. Pump and sensor modules are stacked, and the liquid is transported between modules in channels scaled by polymer layers in the interface between the modules, as illustrated in figure 15.

Analysers built in micromechanics, and based on capillary electrophoresis and electro-osmotic pumps have been developed by the group at Ciba-Geigy Ltd in Basel [116–121]. In these systems, high electric fields are used for the separation of the species in the sample and in the valveless liquid transport systems of the analysers. The systems are generally fabricated in isolating glass plates in order to allow for the high voltages involved, but integration on silicon is also possible [122, 123]. The use of electro-osmotic pumps is elegant and the performance scales well with miniaturization. Furthermore the electro-osmotic pumps have an intrinsic high reliability, since they are without moving parts.

All micromechanical chemical analysis systems need much smaller sample volumes than analysers in traditional technology. This results in the ability to make many measurements and still only consume small volumes of samples, which can be of importance in medical applications. Furthermore the consumption of chemicals is reduced, decreasing the operating costs of the system, and enabling storage of analysis fluids in the equipment for longer operation periods, important in process monitoring.

The small overall size of the analysers makes installation of these systems in process lines easier, and portable equipment possible. If the systems can be placed in line for process control fast response times and practically continuous monitoring can be performed.

The applications of the presented analysers are different and it is impossible to point one type that is suitable for all applications. They will probably all find suitable applications. The choice of detector principle will depend on the actual detection volume [116]. One class of detectors, including absorbance and photoluminescence, exhibits a resolution inherently dependent on the sample volume. Another class, represented by potentiometric detectors, is almost insensitive to the sample volume. The first class of detectors is favourable with sample volumes larger than 10 pl, which is typical in FIA-like systems, unlike the case of chromatography or electrophoresis, where a typical sample volume of less than 1 pl favours potentiometric detection [116].

Microfluidic systems seem to have obvious medical applications in drug delivery systems, because of the potential of precise dosing of small volumes, the small
overall size of the system, and its potential low cost. However, pump reliability is a crucial issue for successful use in medical applications.

The demand is strong for small reliable chemical analysis systems which can withstand typical industrial environments and have a low service frequency. Micromechanical analysers seem to have the potential of fulfilling these needs. However, the development of these systems is in its infancy, and many problems have to be overcome before the systems are ready for commercialization.

Only a few different chemical analysers have been developed, and none of them include the pretreatment of the sample before injection into the analysing part of the systems. This pretreatment step, as well as the acquisition of a representative sample, has to be included in the concept of the micromechanical chemical analysis system before the system is complete.

The characteristic dimensions in future systems are expected to shrink, putting new issues such as the nature of bubbles, sedimentation, erosion and corrosion on the research agenda. These phenomena relate to microfluidics and have to be studied more thoroughly.

7. Other fluidic elements

A few interesting microfluidic devices do not belong to any of the formerly described categories (valves, pumps and flow sensors).

Among these are the microfluidic amplifiers first presented by Zdeblück et al [3]. Many different applications of these devices were suggested [124], ranging from a linear angular sensor to complicated ‘electrofluidics’ systems incorporating micromechanical sensors as well. No progress seems to have been made in this direction. Recently, a fluid amplifier based on the LIGA technique was presented by Vollmer et al [24], and an optopneumatic converter was presented by Hu et al [125]. In these papers, the need for electrical or optical control is emphasized.

Another medical application of microfluidics is a pressure–time recorder [14] operating without any electrical connections.

Measurements of material properties of liquids is a major research field in itself, including chemical sensors, optical detectors etc. These sensors are not covered by this review, but a small exception will be made for sensors measuring the fundamental flow properties of liquids. Martin et al report on a viscosity and density measuring device based on ultrasonic plate waves [126], and Liu et al [127] report on a microchannel with integrated pressure sensor array for the study of flow in microchannels. Microsensors capable of measuring fundamental properties on a micrometre scale are needed for further basic research on microfluidics.

The issue of sedimentation has been addressed by Stenberg et al [128] demonstrating a sensor for measuring the thickness of fouling biofilms.

8. Conclusion

Microfluidics is a multidisciplinary research field, and researchers in this field are compelled to seek knowledge in a wide range of diverse disciplines. Fluid mechanics is one of them.
We believe that most of what we need to know about fundamental microfluidics has yet to be learned. Strong interaction with researchers from the fluid mechanics and other research fields is essential for progress in this direction, in order to establish fundamental material properties and valid models that take into account all the important phenomena related to microfluidics. These special phenomena include rarefaction due to the mean free path of gas molecules, sound velocity in laminar flows, change of liquid viscosity with channel dimension and surface tension effects encountered with gas bubbles in liquids.

In parallel with basic research there is a need for better design tools making modelling of a complete microfluidic system feasible. Such a system should include design and process modelling, simulation for fluid mechanics, thermal distribution, structural deformation and electromagnetic field distribution.

Commercialization of microfluidic devices is at its very start, with only a few silicon valves for gas flow or pressure control available on the market. Prediction of future commercialization is difficult, but some similarities with micromechanical sensors may be exercised. The development of pressure sensor and accelerometer chips, and the related encapsulation technologies, has been boosted by high-volume needs from the automotive industry. Future needs of fuel injection control and monitoring, and hydraulic valves for smart suspension systems, may, in the course of time, create a similar boost for microfluidics. However, competition from alternative technologies seems to be even harder, one of the reasons being unsolved problems related to encapsulation and interfacing with macroscopic fluid systems.

Encapsulation costs seem to hamper the maturation of microfluidics as a replacement technology for a wide range of existing applications. The most promising future is seen in applications that benefit from special material properties or integration of two or more elements (for example valve and flow sensor, or valve and pressure sensor).

Microsystem technology (MST) seems to be the most attractive future application of microfluidics. One example from the medical field is implantable microsystems capable of sensing biological parameters and delivering minute and precise amounts of drugs. Such microsystems are under development, and a micropump suitable for this purpose will probably be the first micro liquid handling device to be commercialized by Van Lintel et al at Debiotec. A second example is an integrated chemical analysing system, consisting of several functional elements. Such a system is highly favoured compared to alternative technology in terms of assembly costs, consumption of chemical and reliability. In addition, the small size of a microsystem may even imply performance improvements not possible with any other known technology.

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