UPPSALA
UNIVERSITET

Digital Comprehensive Summaries of Uppsala Dissertations from the Faculty of Science and Technology 1085

High-Pressure Microfluidics

SAM OGDEN

ACTA
UNIVERSITATIS
UPSALIENSIS
UPPSALA
2013

ISSN 1651-6214
ISBN 978-91-554-8773-7
urn:nbn:se:uu:diva-208915

Dissertation presented at Uppsala University to be publicly examined in Polhemsalen, Ångströmlaboratoriet, Lägerhyddsvägen 1, 751 21, Uppsala, Friday, November 29, 2013 at 09:30 for the degree of Doctor of Philosophy. The examination will be conducted in English.

Abstract
Ogden, S. 2013. High-Pressure Microfluidics. Acta Universitatis Upsaliensis. *Digital Comprehensive Summaries of Uppsala Dissertations from the Faculty of Science and Technology* 1085. 53 pp. Uppsala. ISBN 978-91-554-8773-7.

In this thesis, some fundamentals and possible applications of high-pressure microfluidics have been explored. Furthermore, handling fluids at high pressures has been addressed, specifically by creating and characterizing strong microvalves and pumps.

A variety of microstructuring techniques was used to realize these microfluidic devices, e.g., etching, lithography, and bonding. To be able to handle high pressures, the valves and pumps need to be strong. This necessitates a strong actuator material. In this thesis, the material of choice is paraffin wax.

A new way of latching paraffin-actuated microvalves into either closed or open position has been developed, using the low thermal conductivity of paraffin to create large thermal gradients within a microactuator. This allows for long open and closed times without power consumption.

In addition, three types of paraffin-actuated pumps are presented: A peristaltic high-pressure pump with integrated temperature control, a microdispensing pump with high repeatability, and a pump system with two pumps working with an offset to reduce flow irregularities. Furthermore, the fundamental behavior of paraffin as a microactuator material has been explored by finite element modeling.

One possibility that arises with high-pressure microfluidics, is the utilization of supercritical fluids for different applications. The unique combination of material properties found in supercritical fluids yields them interesting applications in, e.g., extraction and cleaning. In an attempt to understand the microfluidic behavior of supercritical carbon dioxide, the two-phase flow, with liquid water as the second phase, in a microchannel has been studied and mapped with respect to both flow regime and droplet behavior at a bi-furcating outlet.

Keywords: phase change, actuator, valve, pump, supercritical fluid

Sam Ogden, Uppsala University, Department of Engineering Sciences, Microsystems Technology, 516, SE-751 20 Uppsala, Sweden.

ISSN 1651-6214
ISBN 978-91-554-8773-7
urn:nbn:se:uu:diva-208915 (http://urn.kb.se/resolve?urn=urn:nbn:se:uu:diva-208915)

To my Family

List of Papers

This thesis is based on the following papers, which are referred to in the text by their Roman numerals.

I **Ogden, S**., Bodén, R., Hjort, K. (2010) A latchable valve for high-pressure microfluidics. *Journal of Microelectromechanical Systems,* 19(2):396-401

II Sharma, G., Svensson, S., **Ogden, S**., Hjort, K., Klintberg, L. (2011) High-pressure stainless steel active membrane microvalves. *Journal of Micromechanics and Microengineering,* 21(7):075010

III **Ogden, S**., Jonsson, J., Thornell, G., Hjort, K. (2012) A latchable high-pressure thermohydraulic valve actuator. *Sensors and Actuators A: Physical,* 188:292-297

IV Jonsson, J., **Ogden, S**., Johansson, L., Hjort, K., Thornell, G. (2012) Acoustically enriching, large-depth aquatic sampler. *Lab on a Chip*, 12 (9):1619 - 1628

V Malik, A., **Ogden, S**., Amberg, G., Hjort, K. (2013) Modeling and analysis of a phase change material thermohydraulic membrane microactuator. *Journal of Microelectromechanical Systems,* 22(1):186-194

VI Svensson, S., Sharma, G., **Ogden, S**., Klintberg, L., Hjort, K. (2010) High pressure peristaltic membrane micropump with temperature control. *Journal of Microelectromechanical Systems,* 21(6):1462-1469

VII Bodén, R., **Ogden, S**., Hjort, K. (2013) Microdispenser with continuous flow and selectable target volume for microfluidic high-pressure applications. *Journal of Microelectromechanical Systems,* In Press, digitally published*,* DOI:10.1109/JMEMS.2013.2279976

VIII **Ogden, S**., Knaust, S., Dahlin, AP., Hjort, K., Bodén, R. (2013) On-chip pump system for high-pressure microfluidic applications. *Proceedings of μTAS 2013*, Accepted

IX **Ogden, S**., Bodén, R., Do-Quang, M., Wu, ZG., Amberg, G., Hjort, K. (2013) Fluid mechanics of supercritical carbon dioxide with water in a double-Y-channel microfluidic chip. *Microfluidics and nanofluidics,* Submitted

In addition, the following paper is included to give an overview of paraffin microactuation and its applications.

A **Ogden, S**., Klintberg, L., Thornell, G., Hjort, K., Bodén R. (2013) Review on miniaturised paraffin phase change actuators, valves, and pumps. *Microfluidics and nanofluidics*, Submitted

Reprints were made with permission from the respective publishers.

Author's contributions to the publications

I Most of concept, planning, and evaluation, all experimental.
II Part of concept, planning, and experimental, major part of evaluation.
III Most of concept, planning, and evaluation, all experimental.
IV Major part of concept, planning, experimental and evaluation.
V Major part of concept, planning, experimental, and evaluation.
VI Part of concept and planning, major part of experimental and evaluation.
VII Major part of concept, planning, experimental, and evaluation.
VIII Major part of concept and planning, most of experimental and evaluation.
IX Most of concept, planning, and evaluation, all experimental.

Contents

Abbreviations

CVD	Chemical vapor deposition
FEM	Finite element method
EOF	Electroosmotic flow
GC	Gas chromatography
HPLC	High-performance liquid chromatography
IC	Integrated circuit
LC	Liquid chromatography
LMA	Low-melting-point alloy
LPME	Liquid phase microextraction
MEMS	Microelectromechanical systems
MST	Micro systems technology
NC	Normally closed
NO	Normally open
PCM	Phase change material
PCR	Polymerase chain reaction
PDMS	Poly(dimethylsiloxane)
RIE	Reactive ion etch
$scCO_2$	Supercritical carbon dioxide
SFC	Supercritical fluid chromatography
SFE	Supercritical fluid extraction
SMA	Shape memory alloy
SPME	Solid phase microextraction
TP	Thermopneumatic
VLE	Vapor-liquid equilibrium

Introduction

Microfluidics is an interdisciplinary part of micro systems technology (MST, a.k.a. microelectromechanical systems, MEMS), combining engineering, physics, chemistry, and biology (Squires and Quake 2005; Whitesides 2006). Microfluidic systems are usually composed of sub-mm-sized fluidic channels, and consequently handle sub-microliter volumes. However, microfluidic chips are often found in the millimeter to centimeter size range. These chips are usually fabricated using processes inherited from the integrated circuit (IC) industry, enabling complex channel geometries and integration of active components within systems.

By decreasing the size, the fluidic behavior changes drastically from what we are used to, introducing new possibilities but also challenges. This can be used to increase speed, reduce costs, or even find new functions unavailable outside microfluidic applications.

This thesis covers the handling of high-pressure fluidics at the microscale through the development and evaluation of strong paraffin-actuated microvalves and micropumps for use in various applications. Furthermore, the fundamentals of paraffin-based microactuation are explored by using finite element method (FEM) modeling of a paraffin actuator. Additionally, the use of supercritical carbon dioxide ($scCO_2$) in high-pressure microfluidic systems is evaluated, primarily with respect to fluid mechanics. For better understanding of how the work done in the different papers presented in this thesis correlate to each other, a map is shown in figure 1.

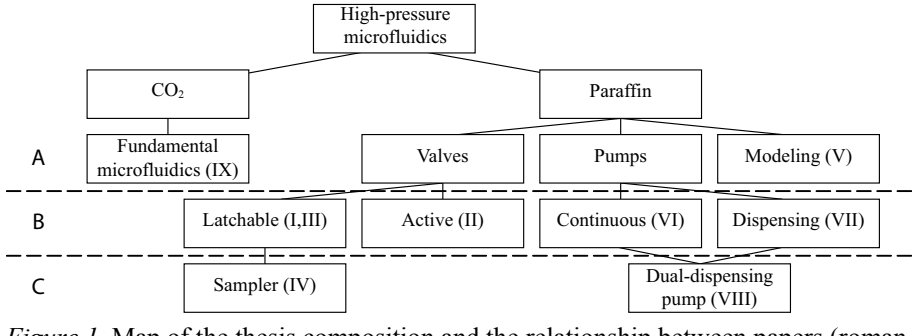

Figure 1. Map of the thesis composition and the relationship between papers (roman numerals). The levels A, B, and C correspond to Fundamental understanding, Devices, and Applications, respectively.

This comprehensive summary will first cover potential applications of high-pressure microfluidics. As the balance of different forces is changed when scaling down to the microscale, high-pressure fluid handling of minute volumes as well as pure scaling effects will be discussed briefly. A short introduction to the microfabrication techniques used is followed by a presentation of the actuator materials used. The actuator materials section also covers modeling of paraffin for microactuator purposes, coupled to one of the papers included. After an introduction to microfluidics, the summary is concluded by presenting and discussing the results of the remaining papers.

Applications at high pressures

Since the birth of microfluidics in the early 90's, it has found extensive use in biological applications such as single cell sorting and analysis, and cell microculturing for *e.g.* drug analysis (Holmes and Gawad 2010). Another important application field for microfluidics is chemistry, especially analytical chemistry, where the development of microfluidic separation techniques has played a major role in shortening analysis times and increasing performance. Furthermore, the use of microreactors, either by fabricating designated reaction vessels (Jensen 2001; Verboom 2009), or by utilizing discrete droplets (Nightingale and deMello 2013) has also been a major application area.

Although most microfluidic chips are designed to function at moderate pressures, there are a few application areas where the handling of high microfluidic pressures is necessary, or even imperative. Examples of such applications can be found in chromatography, microreactors, and sampling.

Chromatography

Part of analyzing a sample is to define its constituents, and subsequently take the parts you want and discard the rest. To achieve this, the different parts of the samples need to be separated. One way to do this is chromatography, which utilizes different compounds' affinity to bind to specific surfaces (Skoog *et al.* 1996). Essential components of a typical chromatographic system are: One or more pumps to drive fluids, an injector to load the sample, an agent for the actual separation, usually a column, and a detector to analyze the separation.

Basically, the pumps drive a solvent, the mobile phase, through a column (*i.e.* the stationary phase). The separation starts when a sample plug is injected into the system. This plug is driven through the column, which is either a packed-bed, *i.e.*, particle-filled, column (most common for liquid chromatography, LC) or an open tubular column (most common for gas chromatography, GC), where the different constituents will interact with the surface of the column, giving different retention times. The variation in retention time between different compounds will make them exit the column at different times, enabling detection of one compound at a time, and, if needed, extract a specific compound for further analysis.

Besides LC and GC, there is also supercritical fluid chromatography (SFC) (Lee and Markides 1990). This technique utilizes the fast mass transport and high density of a supercritical fluid to speed up analyses. It can be run both in a packed-bed LC-like configuration as well as in an open tubular GC-like configuration. The separation in a packed-bed column is shown schematically in figure 2.

High-performance liquid chromatography

High-performance liquid chromatography (HPLC) is a chromatographic technique where the efficiency is improved by increasing the active surface area of the column through the use of smaller particles (Skoog *et al.* 1996). Like the name implies, HPLC utilizes a liquid mobile phase, and, as previously mentioned, usually packed-bed columns. These are essentially steel tubes packed with small (1-5 µm diameter) porous silica particles. This gives the packed-bed columns an enormous effective surface area per unit volume, enabling much shorter columns. The surface area is increased with decreasing particle size. However, the increased surface area and thus efficiency, of the column comes at a cost. The pressure needed to maintain the same flow

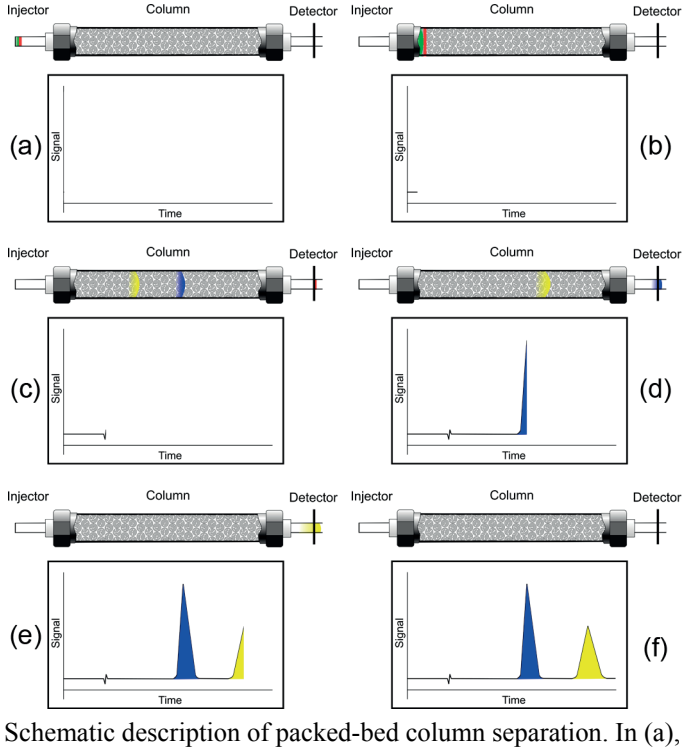

Figure 2. Schematic description of packed-bed column separation. In (a), the sample is injected. In (b), the constituents start to separate, which becomes more pronounced in (c). In (d) and (e), the two separated constituents arrive at the detector, and in (f), the separation is completed.

through the column is increased with smaller particles, putting high demands on the pumps, valves, and seals of the system. Furthermore, smaller columns need smaller injected sample volumes (which is usually about a percent of the column volume). Thus, miniaturized chromatography lowers sample consumption, which is especially important with expensive samples, but also puts high demands on the sample injection volumes and reproducibility. **Papers I-IV** address valving at high pressure, **Papers VI** and **VIII** focus on pumping at high pressures, and **Paper VII** focus on the dispensing of small volumes in a reproducible manner.

Microreactors

A microreactor is by definition a device housing chemical or physical reactions. Furthermore, at least one dimension of the device is on the micrometer scale. As mentioned previously, microfabricated reaction chambers, flow-through channels, as well as droplets within a microfluidic channel system can be utilized. Microreactors can be used for a wide variety of applications such as nanocrystal synthesis (Marre *et al.* 2009a; Nightingale and deMello 2013), catalytic reactions (Kiwi-Minsker and Renken 2005), organic synthesis (Mason *et al.* 2007), fluorination reactions (Navarrini *et al.* 2012), etc.

Due to the small dimensions, microreactors offer shorter reaction times and pathways compared with their larger counterparts. Furthermore, more aggressive conditions, *e.g.*, higher temperature and pressure, can be used, and temperature control is easier due to the large relative area and short transport paths through the device. This is especially valuable when highly exothermic reactions are studied. Hazardous reactions, due to toxic or highly reactive compounds, can even be performed, as the amount released at a potential failure can be easily contained. The integration of sensors and actuators into the reactor, as well as their close proximity to the reaction site, enables better control, or even real-time monitoring, of the reaction kinetics.

Microextraction

When dealing with complex samples, most constituents of the sample are usually of little or no interest. Extraction is a collection of techniques, where one or a few specific compounds are selectively removed from the sample, either for further examination or simply to be discarded.

Extraction can either be accomplished chemically or physically. Chemical extraction is commonly done by introducing a medium that can dissolve the desired compound(s), whereas physical extraction is usually done by introducing filters or by other means selectively hindering specific compounds from passing through the system.

Chemical microextraction is usually divided into solid phase microextraction (SPME) and liquid phase microextraction (LPME) (Rios *et al.* 2009). In SPME, the analyte molecule is either absorbed into the solid, or adsorbed to the surface of the solid. In the latter case, porous solids are commonly used to increase the extracting surface area. The selectivity towards specific compounds can be, and usually is, tailored by surface coatings. In LPME, a medium with higher or equal affinity to the compound to be extracted is introduced. Since this process is diffusion-controlled, short transport paths are preferred as this shortens the equilibration times. The microfluidic mapping done in **Paper IX**, where three flow regimes were characterized with respect to flow parameters, can be used for chemical extraction purposes. Most compounds have a limited solubility in a given solute, *i.e.*, a specific amount that can be extracted per unit volume solute.

A classic example of physical microextraction is a filter, which will let any molecule or particle below a given size pass through the filter, whereas larger particles will stick to it. If filters are undesired, the use of ultrasonic standing waves can be utilized to trap particles (Hill and Harris 2007). In **Paper IV**, this technique is used to extract microscopic particles, such as cells, from water flowing through a microfluidic channel.

Sampling in extreme environments

Extreme environments are usually defined as environments with very elevated levels of, *e.g.*, temperature, pressure or corrosiveness. Conversely, very low temperatures or pressures (*i.e.* vacuum) can also be included in the definition. In the work included in this thesis, the main focus has been on handling large pressure differences, realized by applying a high pressure, although the devices could easily be adapted for applications in vacuum.

On earth, the highest naturally occurring pressures, available to man, are located at great water depths, with the highest pressure being found in the Challenger Deep, almost 11,000 m deep. This depth corresponds to a pressure of almost 110 MPa, or 1,100 bar. However, depth is not the only limitation to accessibility. For example, the largest subglacial lake on Antarctica, Lake Vostok, has a maximum depth of only 900 m, but is covered by a glacier over 3,400 m thick (Siegert *et al.* 2005). Just recently, on Jan 10 2013, the glacier was bored through, accessing water that had possibly been sealed for millions of years. This is of course an amazing possibility for new discoveries. However, the narrow diameter of the bore hole limits exploration to remotely operated underwater vehicles.

Recently, such a device, denoted DADU (Deeper Access Deeper Understanding), was presented (Jonsson *et al.* 2012a). It is smaller than two soda cans put together end-to-end, but still contains a side-scanning sonar (Jonsson *et al.* 2010), a topography measurement device (Jonsson *et al.* 2012b),

flow velocity sensors (Palmer *et al.* 2013), and a salinity measurement device (Jonsson *et al.* 2013). The microfluidic sampler developed in **Paper IV**, was designed for this submersible. A rendering of it with the sampler mounted is shown in figure 3.

The sampling device addresses the need for high-pressure valves to reliably seal samples once taken, as well as keep the device from being contaminated prior to sampling. Furthermore, how to sample a large amount of particles in a small confined space is also evaluated. By using ultrasonic standing waves within the device, particles can be captured from water flowing through the system. Thus, cells, sediments, and in other ways interesting particles can be extracted from a large volume to enrich the small volume within the device.

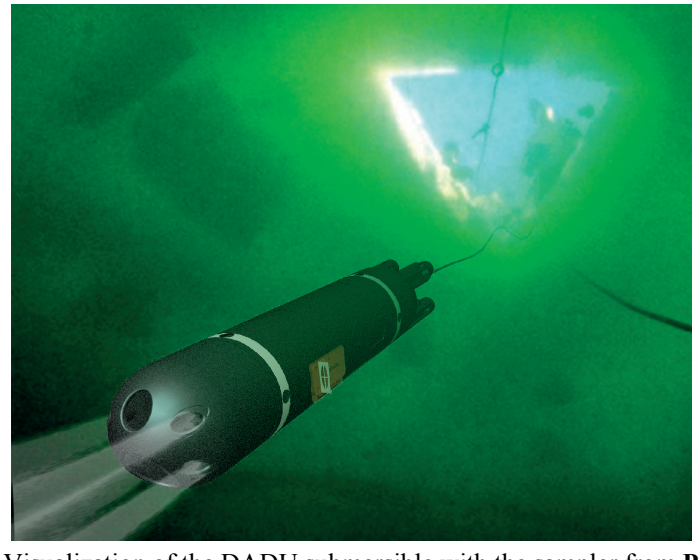

Figure 3. Visualization of the DADU submersible with the sampler from **Paper IV** mounted on the side. Reproduced from **Paper IV** with permission from RSC.

Handling fluids at high pressures

Handling fluids at high pressures is quite demanding. Firstly, the forces present must be considered, and measures be taken to ensure that the structural strength of the device and material is sufficient. At macroscale, this can result in quite bulky structures. Secondly, interfacing and sealing need to be accounted for, usually solved at macroscale by welding and the use of o-rings. Finally, all components that are supposed to manipulate the fluid, *e.g.*, valves and pumps, need to have a sufficient actuation strength to overcome the forces present.

The structural strength needed to handle and generate high pressures makes high-stiffness materials such as glass (Verboom 2009), silicon (Marre *et al.* 2010), metals (Schubert at al. 2001), and high-strength polymers (Sollier *et al.* 2011) popular for these applications. However, even if the material itself is strong enough, the microfluidic structures have to be sealed to be of any use in high-pressure applications. If the bonding or interface strength is much lower than the structural strength of the material, leakage will ultimately occur, even at moderate pressures.

Although many microdevices handling high pressures have been presented, the actual generation and control of both flow and pressure are usually done off-chip. This adds both dead volume and size to the system. For instance, in **Paper IX**, the flow inside a 15x10 mm^2 microfluidic chip is studied within its 200 μm diameter channels. To achieve this, two macroscale pumps are connected to the chip with tubing containing several times the channel volume on the chip. To achieve truly advanced microfluidic systems, the pressure and flow generation and control must also be addressed.

In order to make fluid-handling components in a system strong enough to cope with high pressures, the actuator itself needs to be strong. Several factors affect the strength of an actuator, *e.g.*, actuator material and size. Paraffin and shape memory alloys are the strongest actuator materials used in microsystems at the moment (Krulevich *et al.* 1996; Gilbertson and Busch 1996; Srinivasan and Spearing 2009). Actuator materials in general, and paraffin in particular, are treated in greater detail in the actuator materials section.

Scaling

One purely geometrical scaling effect from miniaturization is the relative increase in surface area. If a regular cube is considered, its volume is a^3, and its surface area $6a^2$, where a is the side length of the cube. The surface-to-volume ratio, A/V is thus $6/a$, showing that the relative magnitude of surface over volume increases at smaller dimensions. Due to this, surface-based effects such as heat transfer are more efficient at a smaller scale.

In microfluidics, the lack of turbulent flow at most conditions makes the dominant flow type the perfectly predictable laminar flow regime. In this regime, most of the transport of species or heat etc. is due to diffusive effects (Squires and Quake 2005). Furthermore, separation of immiscible fluids into well-defined droplets or plugs is much easier to accomplish in microfluidic flows than at the macroscale. All these effects are due to the higher surface-to-volume ratio, as surface-acting forces, such as surface tension, become increasingly important at smaller scale. The limitation in mass transfer to diffusion is also the enabling factor of chromatographic separations, as there is only one transport parameter to study.

The dominant behavior of surface-based effects at the microscale can also be seen in wetting, which is a fluid's ability to passively maintain contact with a solid surface. The wetting depends on several factors such as surface tension of the fluid, free surface energy of the solid, and chemical composition, *i.e.*, polarity of both fluid and solid. A specific example of wetting effects can be found in the capillary rise phenomenon, shown schematically in figure 4, where the competing forces are gravity, trying to keep the liquid down, and surface tension, pulling it upward.

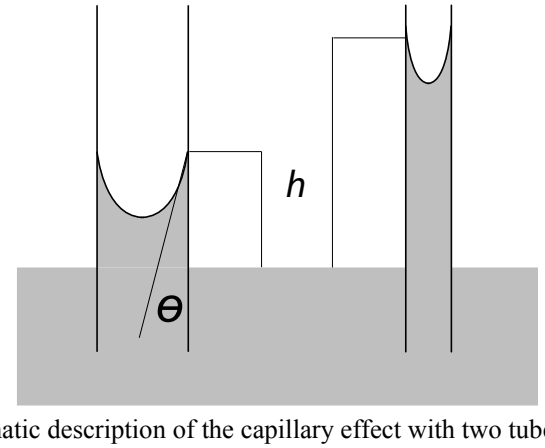

Figure 4. Schematic description of the capillary effect with two tubes, one narrower than the other. The liquid (gray) climbs higher in the narrow tube than in the wider one.

If an upright cylindrical tube is considered, the gravitational force is $F=\rho gh\pi r^2$, and the force from surface tension is $F=2\gamma\cos\theta\pi r$, where ρ is the density of the fluid, g is the gravitational constant, h is the liquid pillar height, r is the radius of the tube, γ is the surface tension of the liquid, and θ is the contact angle between the liquid and the tube wall. By balancing these forces, the height at equilibrium can be calculated, according to

$$\rho gh\pi r^2 = 2\pi r\gamma\cos\theta \Rightarrow h = \frac{2\gamma\cos\theta}{\rho gr}. \quad (1)$$

As seen in the equation, the height of the capillary rise increases linearly with a decreasing radius. This is due to the increased relative magnitude of the surface-acting surface tension over the volume-acting gravity.

One of the gains from miniaturizing high-pressure equipment is that the forces present decrease with the surface area, although pressure is maintained. Thus, the risk with handling high-pressure equipment is significantly reduced by miniaturization. Furthermore, as distances decrease, so do equilibrium times, *e.g.*, thermal equilibrium.

As a result from handling much smaller volumes, the consumption of expensive chemicals will also be greatly reduced. When handling hazardous chemicals, a small volume lessens the danger at device failure.

Fabrication methods

When fabricating details at the microscale, many of the processes used are significantly different from those used at the macroscale. Mechanical removal of material, like in milling, is difficult to adapt to sizes smaller than a few hundred micrometers. Instead, the microsystem fabrication schemes generally turn to chemical removal processes. In order to achieve the selected geometries, a pattern transfer onto the substrate is done, usually by using lithography. Since the microfabrication toolbox is very diverse, and the focus of this thesis is applications rather than fabrication processes, only a brief description of the processes used is included in this summary.

Etching

Wet etching is a collective name for material removal through chemical reactions between a liquid etchant and a solid substrate (Madou 2002). To achieve selectivity in the etching process, the substrate is masked with a compound that exhibits a lower etch rate than the substrate or, in the ideal case, is completely inert. Wet etching can be either isotropic or anisotropic. Isotropic etching has the same etch rate in all directions, whereas anisotropic etching is orientation dependent, figure 5.

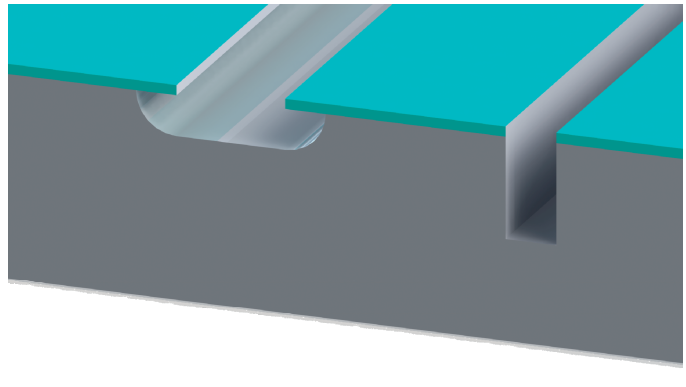

Figure 5. Schematic representation of isotropic (left) and anisotropic (right) etching. As the isotropic etching has the same etch rate in all directions, it undercuts the mask at a lateral distance equal to the depth.

Examples of etch processes are isotropic HF etching of glass, and anisotropic KOH etching of silicon. The use of HF etching of glass has been used in **Paper IV** to thin a glass cover lid to the desired thickness.

Photo chemical machining is a mature technique, used extensively in the industry, mainly to produce IC leadframes, and previously shadow aperture masks for pre-flatscreen TVs (Allen 2004). Basically, it is a wet etching process of different metals, with stainless steel as the most commonly used. Through the use of thick photo masks and delivery of the etchant through spray nozzles, a resolution down to 100 μm over several square decimeter large sheets is achieved. This manufacturing technique has been utilized to create structures in the stainless steel stencils used in **Papers I-VIII**. Two examples of devices fabricated by laminating such stencils are shown in figure 6.

Dry etching denotes a collection of techniques where a solid surface is etched by a gas phase compound or plasma, either physically by ion bombardment, chemically through a chemical reaction, or, most commonly, a combination of the two (Madou 2002). As with wet etching, a dry etching technique can be either isotropic or anisotropic. A reactive ion etch (RIE) consisting of O_2 and CHF_3 is used to etch polyimide substrates in **Papers I-VIII**.

Joining

In most non-monolithic microfluidic systems, there is a need for joining, or bonding, to make sure the fluid remains where it is wanted. In high-pressure microfluidic systems, this becomes a crucial fabrication parameter, due to the high demands on the system. Furthermore, solid-to-liquid phase change actuators, like paraffin, need to be properly sealed to avoid leakage and corresponding stroke degradation. Many different techniques exist, and the choice can depend on the materials involved, allowed process conditions, surface parameters, etc.

Parylene interlayers

Parylene, or poly(para-xylylene), is a thermoplastic polymer widely used in the electronics industry as an insulation layer due to its high dielectric strength. It is also used to coat medical implants, sealing them from the body. Parylene is chemically inert and very resistant to corrosion, and also has a very high resistance to most organic solvents.

The technique to use parylene layers to join laminates of different types was first presented by Noh *et al.* (2004), and have since then been the subject of several studies (Kim and Najafi 2005; Ciftlik and Gijs 2011). The main advantage with using parylene interlayers as a bonding agent is the low

process temperature, in general below 250°C, which allows for integration of heat-sensitive materials such as polymers. When comparing parylene interlayer bonding with other low-temperature bonding techniques, *e.g.*, adhesive bonding, there are several advantages to using the technique. Firstly, the deposition of parylene is made with a chemical vapor deposition (CVD) process. As such, the material is polymerized from a gas phase, allowing for uniform and well-controlled coatings. This is especially important when coating already patterned structures, where application of liquid glue would likely fill most channels and grooves present on the substrates. Secondly, bonding of materials with different coefficients of thermal expansion is possible, due to the flexibility of the parylene, but also due to the low, process temperature. Finally, for use in high-pressure applications, the parylene interlayers offer an otherwise stiff laminated structure, some flexibility. In the work presented in this thesis, this bonding technique has been used in **Papers I-VIII**, allowing for integration of polyimide membranes and heater layers with stainless steel stencils.

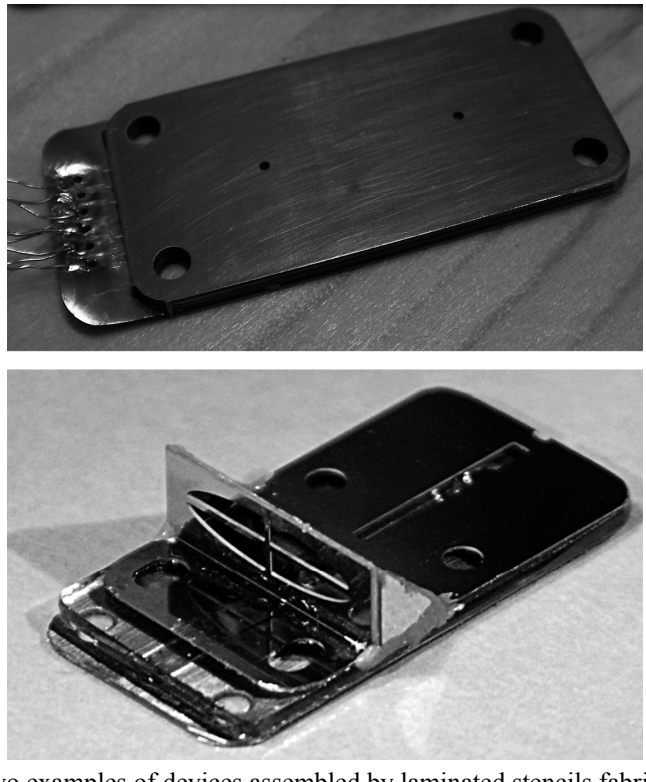

*Figure 6.*Two examples of devices assembled by laminated stencils fabricated using photo chemical machining and subsequently joined through parylene interlayer bonding. Top: The microdispenser presented in **Paper VII**. Bottom: The microfluidic sampler presented in **Paper IV**.

Actuator materials

There are numerous actuator materials and principles adapted to the microscale (Madou 2002; Bell *et al.* 2005). Some, like solenoids, are very common at macroscale as well, whereas, *e.g.*, piezoelectric actuation is virtually unheard of at a larger scale. When comparing different actuator materials, the strain energy density, E_d, defined as the available energy per unit volume, is often used according to

$$E_d = \sigma\varepsilon, \tag{2}$$

where σ is the material stress, and ε is the material strain.

Figure 7 shows the energy density for several commonly used microactuation materials and principles. As seen, paraffin phase change materials (PCM) have the highest available energy density, closely followed by shape memory alloys (SMA).

A high energy density is a great asset when handling high pressures or large forces. However, other factors usually have to be considered when

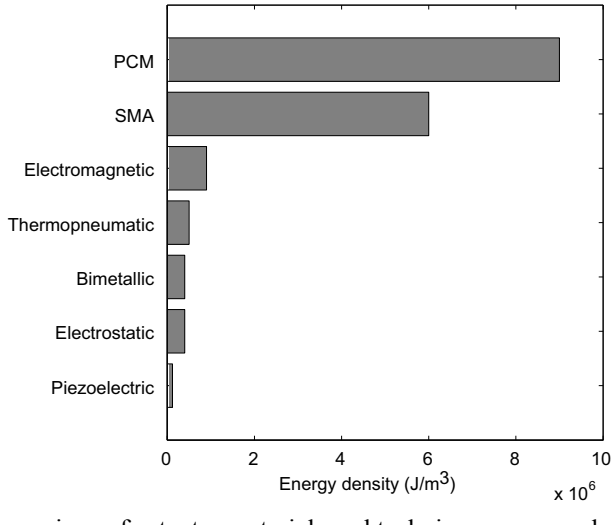

Figure 7. Comparison of actuator materials and techniques commonly used in microactuation, with respect to their energy density available for repeatable actuation. Data from Krulevich *et al.* (1996), Gilbertson and Busch (1996) and Srinivasan and Spearing (2009).

selecting the actuator material. The actuation speed varies significantly between different techniques, from the few tens of Hz for the thermally actuated techniques (PCM, SMA, bimetallic) to the MHz actuation frequencies available for piezoelectric actuation. Furthermore, it must be considered if a rigid force transmission (SMA, electromagnetic, piezoelectric) is desired, or if a compliant hydraulic (PCM) or pneumatic (thermopneumatic) force transmission is preferred. A detailed description is only included for the two actuation principles used in the papers included in this thesis, *i.e.*, piezoelectric and PCM.

Piezoelectric materials

Piezoelectric materials is the collective name of all materials that exhibit the direct and the converse piezoelectric effect. The direct piezoelectric effect is the ability to respond to mechanical stress by releasing electrical charges, whereas the converse piezoelectric effect is the property to respond to an applied electric field with mechanical stress and strain.

For actuator purposes, the converse effect is the one used. Piezoelectric actuators typically exhibit small strains and can be driven at high frequencies, making them well-suited for ultrasound applications, where they are widely used. Another large application field is the quartz oscillators, either used for mass detection through a mass-dependent resonance frequency shift, or as the time base in clocks. In microsystems, numerous publications on piezoelectric actuation have been presented in a wide variety of fields (Maeda et al. 2004). In microfluidics, the most common usage is in micropumps (Laser and Santiago 2004) and microvalves (Oh and Ahn 2006). In **Paper IV**, piezoelectric actuators driven at ultrasound frequencies are used to create a standing wave to trap particles from water flowing through a microfluidic channel.

Phase change materials

Phase change materials are defined, in actuation applications, by their ability to deliver force and/or movement from a phase change, most commonly solid to liquid. In addition to actuators, PCMs have found extensive use in energy storage applications. Commonly used phase change materials include hydrated salts (Sharma *et al.* 2009), poly(ethylene glycol) (Sethu and Mastrangelo 2003), and paraffins.

Paraffin is a collective name for all mixtures of n-alkanes, which are long hydrocarbon chains of the composition C_nH_{2n+2}. Paraffins that are liquid at room temperature are referred to as oils, whereas paraffins that are solid at

room temperature are denoted waxes. In **Papers I-VIII**, paraffin with a melting range of 44-48°C was used.

When used as an actuator material, the phase change expansion of paraffin is utilized. The expansion at the solid-to-liquid phase change comes from the crystalline nature of solid paraffin. As such, the hydrocarbon chains are densely packed. As the paraffin is melted, it needs to expand in order to facilitate the increased movement of the hydrocarbon chains. Since paraffin also exhibits a low compressibility in the liquid phase, it is ideal for use in thermohydraulic actuation. In fact, paraffin retains about 50% of its expansion even at pressures as high as 200 MPa (Zoller and Walsh 1995).

However, there are some drawbacks in using paraffin as an actuator material: It requires heating for actuation, which is generally a slow process, especially if the actuation is cyclic, where cooling is also needed. This issue is further complicated through the large latent heat of paraffin, slowing the actuation down even more, as well as increasing the energy needed for actuation. However, this issue is somewhat remedied by miniaturization. As thermal transport paths become much shorter, actuation time constants decrease. This, combined with the fact that the energy density is normalized by volume, and thus is unaffected by scaling, makes paraffin a very suitable material for miniaturization. For use in latchable valves (**Papers I** and **III-IV**), the mechanical stability also plays an important role, as the solid paraffin needs to carry a load in its latched state. As paraffin is a viscoelastic material, it yields over time, even at loads substantially lower than the yield stress. For more information on paraffin properties as well as a comprehensive overview of paraffin-actuated systems the reader is referred to **Paper A**.

Paraffin modeling

Lately, with the growing number of available software and rapidly increasing computing power, modeling has been increasingly used as an aid in designing and evaluating components and systems. Modeling of paraffin-actuated devices is no exception. There are, however, a few complicating factors related to modeling of paraffin. Firstly, the latent heat of paraffin must be accounted for. Secondly, paraffin is usually melted during actuation. This significantly changes the material properties. Furthermore, most paraffins have one or more solid-solid phase transitions, which must also be accounted for. This results in a need for experimental data to build a truthful model of paraffin actuators. The most common way to model paraffin is to approximate the paraffin as a thermally expanding solid (Lee and Lucyszyn 2007; Bodén *et al.* 2008). However, in doing so, the model will not take the liquid behavior of paraffin into account, especially the ability to conform to localized loads and, the convective heat transfer occurring inside the actuator. For a full description and comparison of the modeling efforts made to this date, the reader is referred to **Paper A**.

Paper V attempts to alleviate the issues connected to the thermally expanding solid approach by modeling the paraffin as a liquid in all phases, varying its viscosity and density to simulate the phase change. The actuator modeled in the paper is of the same geometry as the ones used in **Papers II** and **VI**. As seen in figure 8, the modeled and experimental deflection values correspond well, with only slight deviations.

Furthermore, time constant variation due to width-to-height ratio as well as the dependence on power input, figure 9, was analyzed. The time constant was defined as the time needed to reach 70% of the maximum deflection

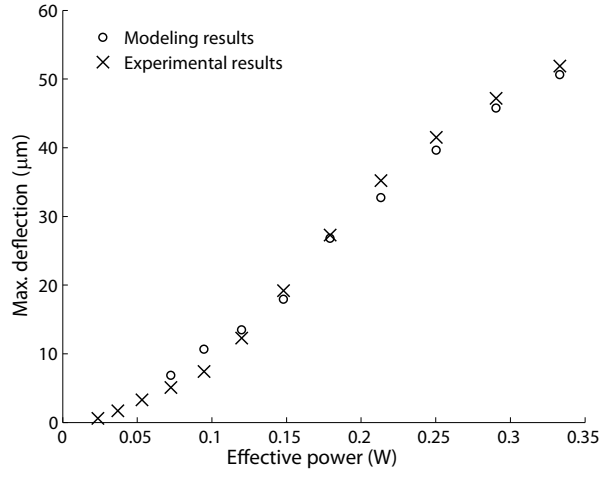

Figure 8. Maximum deflection at different powers for both modeling and experimental results from **Paper V**. © 2013 IEEE

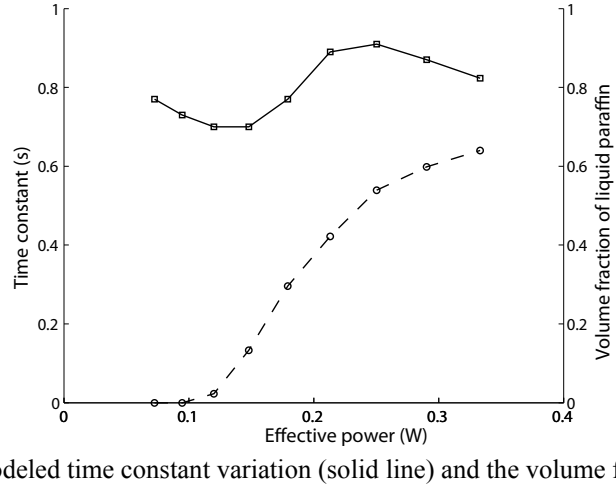

Figure 9. Modeled time constant variation (solid line) and the volume fraction of liquid paraffin (dashed line) at different input powers from **Paper V.** © 2013 IEEE.

for the given power input. In these parameter sweeps, heat was always supplied through virtually the entire width of the actuator. As seen in figure 9, the time constant initially decreases with an increased input power, but then starts to increase. This is due to the onset of the energy-consuming solid-liquid phase transition in paraffin. When comparing the change rate of the volume fraction of liquid paraffin to the time constant variation, it is seen that, when the increase of liquid paraffin is high, the time constant increases. When the increase slows down at approximately 0.25 W, the time constant starts to decrease again. In the width-to-height ratio parameterization, with the paraffin volume kept constant, it was found that, for the same heating power, the time constant decreased exponentially with an increasing width-to-height ratio. This means that if short actuation times are needed, a flat and wide actuator is preferred over a narrow and high one.

The all-liquid modeling approach presented, not only takes convection within the actuator and the ability to conform to localized loads into account. It also addresses the viscoelastic behavior of solid paraffin. With this, the modeling approach becomes more truthful as solid paraffin behaves more like a highly viscous fluid. However, the viscosity used in the model was a rough approximation with one value for solid paraffin, and one for liquid. Furthermore, in the material properties section of **Paper A**, the change in mechanical and rheological properties of paraffin is reviewed. From the literature data, it can be concluded that the properties of paraffin change substantially during solid-solid phase transitions. For further improvement of the model, the viscosity at different temperatures should be mapped and integrated in the model.

Microfluidics

Through the evolution of MST and micro engineering, a new interdisciplinary field, microfluidics, emerged in the late 20th century (Manz *et al.* 1990a). Since then, several reviews have been dedicated to this field (Gravesen *et al.* 1993; Squires and Quake 2005; Whitesides 2006), or specific parts as micromixers (Nguyen and Wu 2005), hydrodynamic separations (Wu and Hjort 2009), microvalves (Oh and Ahn 2005), and micropumps (Laser and Santiago 2005; Iverson and Garimella 2008). The field of microfluidics usually combines physics and engineering with chemistry and biology to miniaturize components for, *e.g.*, polymerase chain reaction (PCR) (Kricka and Wilding 2003) or chromatography (Terry *et al.* 1979; Manz *et al.* 1990b; Kutter 2012).

The general equation for fluid dynamics is the Navier-Stokes equation

$$\rho\left(\frac{\partial\vec{v}}{\partial t}+(\vec{v}\cdot\nabla)\vec{v}\right)=-\nabla p+\eta\nabla^2 v+\vec{f}, \tag{3}$$

where ρ is the fluid density, v is the fluid velocity, p is the pressure, η is the fluid viscosity, and f is the body forces acting on the fluid. When the inertial term is small enough to be neglected, the remaining expression is referred to as the Stokes equation:

$$\rho\frac{\partial\vec{v}}{\partial t}=-\nabla p+\eta\nabla^2\vec{v}+\vec{f}. \tag{4}$$

Furthermore, when the body force is negligible and velocity is constant, which is often the case in microfluidic devices, the equation is further simplified to:

$$\nabla p=\eta\nabla^2\vec{v}. \tag{5}$$

When equation 5 is applied to a 1-dimensional case, which most microfluidic systems can be simplified to, the flow can be expressed according to

$$Q = \pi \frac{\Delta p}{8\eta l}\left(\frac{D_h}{2}\right)^4, \tag{6}$$

where Q is the volumetric flow rate, Δp is the pressure drop over the channel, and D_h is the hydraulic diameter of the channel. Thus, the governing equation in static microfluidic flows has become quite manageable, at least compared to the Navier-Stokes equation. As seen in the equation, if the flow rate is to be maintained, the required pressure increases rapidly with a decreasing hydraulic diameter. This indicates that microfluidics will suffer from large pressure build-ups within a system to a much larger extent than macroscale flows.

Dimensionless numbers

In fluid dynamics, several dimensionless numbers exist. Their main purpose is to give an indication of the characteristics of a flow under various conditions. The most widely used is the Reynolds number,

$$\mathrm{Re} = \frac{\rho v L}{\eta}, \tag{7}$$

where L is the characteristic length, *e.g.*, the diameter of a cylindrical flow channel. The Reynolds number compares inertial effects with viscous effects and is used to predict if the flow regime is turbulent or laminar, with a low Re indicating laminar flow. In microsystems, the laminar flow is usually completely dominating, due to the inherently small characteristic lengths. As both the density and viscosity are material parameters, the only two parameters that can be changed for a given fluid are the velocity and characteristic length. When decreasing the length, the flow velocity must increase with the same factor to maintain the same Reynolds number.

In two-phase flows of immiscible fluids, the dimensionless number with the most relevant information is the capillary number,

$$\mathrm{Ca} = \frac{\eta v}{\gamma}, \tag{8}$$

where γ is the interfacial tension between the two fluids. The capillary number compares viscous forces with interfacial tension, and thus reveals whether the flow will be an annular or parallel flow with the two fluids flowing alongside each other or break up in droplets and a sheath flow.

When evaluating two-phase flows with constant viscosities, an additional dimensionless number can be used, the Weber number. It combines the Reynolds and capillary numbers to compare inertial to interfacial effects according to:

$$\mathrm{We} = \mathrm{Re}\cdot \mathrm{Ca} = \frac{\rho v^2 L}{\gamma}. \tag{9}$$

There are numerous other dimensionless numbers that describe different phenomena in fluid dynamics. However, the three presented here will suffice to describe the fundamental effects studied, primarily in **Paper IX**.

Supercritical microfluidics

Besides the three well-known aggregation states, solid, liquid, and gas, there exists three more: Bose-Einstein condensate, plasma and supercritical state. Since no material is in its supercritical state at room temperature and atmospheric pressure, it is less known than the first three mentioned. The supercritical state is only present when the critical temperature, T_c and the critical pressure, p_c are both exceeded, figure 10. The material properties change drastically in the transition to the supercritical state, resulting in a fluid with both liquid-like and gas-like qualities. At some distance from the transition region, where the properties have somewhat stabilized, a supercritical fluid exhibits liquid-like density, gas-like viscosity (Fenghour *et al.* 1998), and a diffusivity intermediate that of gas and liquid.

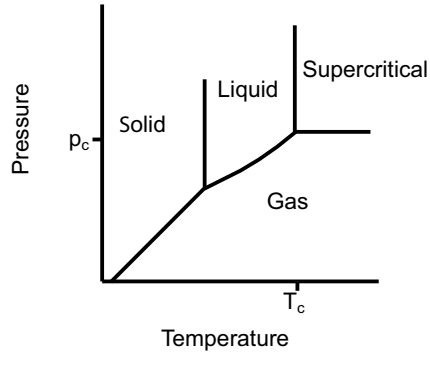

Figure 10. Pressure-temperature phase diagram of an arbitrary substance.

The existence of this state was first noted by Caignard de la Tour (1822). However, the first systematic study of the supercritical region was not published until almost 50 years later (Andrews 1869).

Supercritical fluids in microsystems have only recently begun to be utilized in, *e.g.*, extraction and chemical synthesis (Marre *et al.* 2012). As this field grows, there is a need to characterize the microfluidic behavior of supercritical fluids. Until now, only a few dedicated studies have been conducted, including dripping to jetting transitions in an annular flow configuration of $scCO_2$ and water (Marre *et al.* 2009b; Guillaument *et al.* 2013), flow behavior of ethanol-$scCO_2$ and methanol-$scCO_2$ in a T-junction (Blanch-Ojea *et al.* 2012), and the development of a microfluidic device for water-$scCO_2$ parallel flow (Ohashi *et al.* 2011).

Supercritical fluid extraction (SFE)

The first mentioning of supercritical fluids' enhanced solvating properties is found in the works of Hannay and Hogarth (Hannay and Hogarth 1879, 1880; Hannay 1880). As a side note, it is worth mentioning that they actually used supercritical short-chain paraffin as a solvent in the latter study. In supercritical fluid extraction, the most commonly used fluid is supercritical carbon dioxide. It is used partly because of its fairly low critical temperature, 31°C, and pressure, 7.38 MPa. Another contributing factor is that $scCO_2$ is an efficient solvent for non-polar compounds due to its apolar molecular configuration.

The use of supercritical carbon dioxide as a solvent offers a greener alternative to, *e.g.*, chloroform or toluene. Although extraction of essential oils and antioxidants from food is the most common application, extraction of, *e.g.*, petrochemicals, pharmaceuticals, and pesticides can also be conducted (Herrero *et al.* 2010). Besides being used for extraction of specific compounds, $scCO_2$ has found use in semiconductor cleaning (Cansell *et al.* 2003), primarily due to its ability to dissolve, and thus remove, apolar or low-polarity compounds while leaving the substrate surface unaffected. High-density liquid CO_2 has also been used for extraction purposes, primarily dry cleaning (Bannerjee *et al.* 2012). In many applications, such as SFC, where an increase in solvent polarity is needed, a co-solvent can be added (Lee and Markides 1990). Common additions to increase the solvent power are ethanol, methanol, or acetone, all having a higher polarity than CO_2.

Due to the inherently high surface-to-volume ratio at the microscale, a very efficient extraction can be achieved. This is because of the large amount of extracting interface compared with the bulk volume to be extracted from. Despite the potential high efficiency, very few devices have been presented for supercritical microfluidic extraction (Ohashi *et al.* 2011; Assmann *et al.* 2012).

Before conducting an actual extraction, a few things should be known. Firstly, the compound of interest must be soluble. Secondly, the flow behavior in the microfluidic device needs to have been characterized, as in the work presented in **Paper IX**, in order to select extraction parameters.

If a co-solvent is added, the phase behavior of the mixture also needs to be known. This is usually done by time-consuming experiments such as vapor-liquid equilibrium (VLE) (Dohrn *et al.* 2012).

An alternative approach for VLE to be explored is to use the high fluidic resistance in narrow microfluidic channels. By using equation 6, the design parameters (length and hydraulic diameter of the channel) can be tuned to obtain the desired flow rate at given process conditions (pressure and temperature). Figure 11 shows measured and reference VLE points of a CO_2-acetone mixture when a glass microfluidic channel over 500 mm long is used. Besides concurrent screening of the entire pressure region studied, such a microfluidic approach would also enable rapid temperature changes due to the low thermal mass and short transport paths of the system.

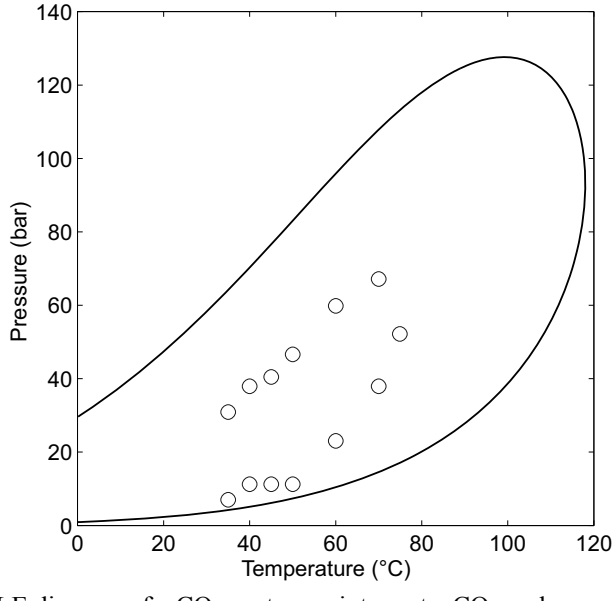

Figure 11. VLE diagram of a CO_2-acetone mixture at a CO_2 molar concentration of 88%. The line denotes reference data and the points denote data acquired with a microfluidic device. The area enveloped by the data is where two phases (liquid and gas) coexist, whereas the outer areas only have one phase present (liquid, gas or supercritical fluid).

Supercritical two-phase flows

There are basically three different flow regimes in two-phase microfluidic flows: Segmented flow, where each phase forms discrete droplets or plugs,

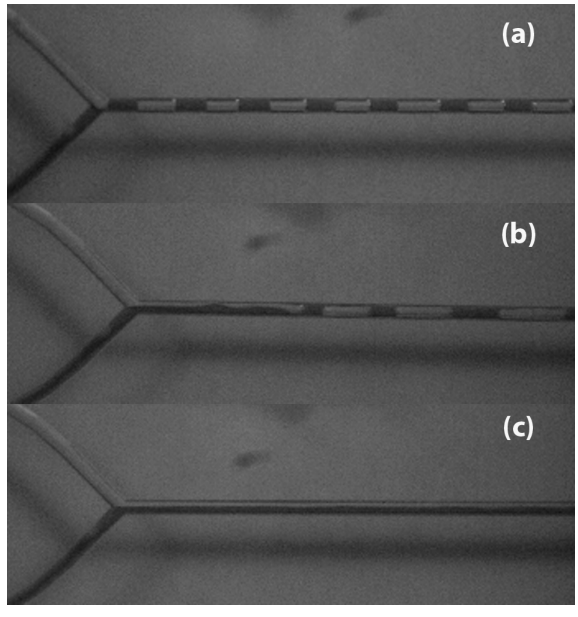

Figure 12. Three two-phase microfluidic flow regimes, (a) segmented, (b) wavy, and (c) parallel. The flow direction is from left to right.

parallel flow, where the two immiscible fluids flow alongside, and a transition state, the wavy flow, where an initial unstable parallel flow breaks up into segmented flow downstream. These flow regimes are exemplified in figure 12. In two-phase segmented flows, the flow that wets the chip surface is denoted continuous phase, whereas the phase forming droplets is denoted dispersed phase. In the setup used in **Paper IX**, the continuous phase is water and the dispersed phase is $scCO_2$.

In **Paper IX**, the microfluidic two-phase flow of water and scCO2 was explored by varying the flow parameters and mapping the resulting flow regime. Figure 13 shows the obtained flow regime map. At lower Ca, and consequently lower We numbers, the segmented flow dominates completely. However, at higher We numbers, parallel flow was observed, with a higher relative dispersed phase flow rate shifting this transition to lower We. At a combination of high We and a high relative continuous phase flow rate, the parallel flow transitions into wavy flow.

As previously mentioned, droplets can themselves function as microreactors. Knowing the droplet dynamics for such reactors is interesting for mixing within droplets, merging or splitting droplets. In **Paper IX**, the droplet dynamics at a bifurcating outlet was observed at different conditions. Primarily, the splitting/non-splitting behavior was characterized. Due to the wetting nature of water and the glass surface, water plugs always split at the exit, regardless of the conditions. Supercritical CO_2, however, proved to be

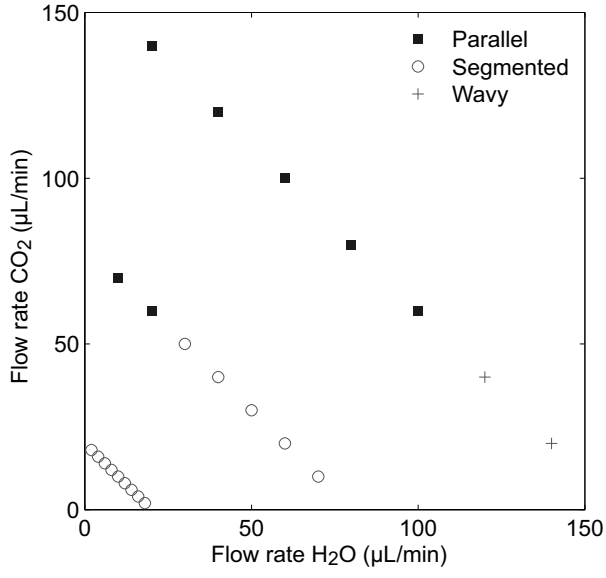

Figure 13. Flow regime map of water-scCO2 two-phase flow. Each diagonal corresponds to a specific Ca and We number.

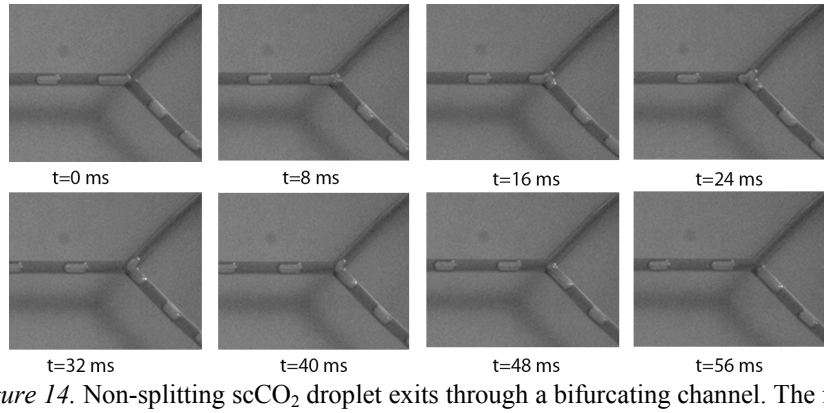

Figure 14. Non-splitting $scCO_2$ droplet exits through a bifurcating channel. The flow direction is from left to right.

affected by both the We number and the length of the droplet. Droplets exhibited a non-splitting behavior at shorter droplet lengths, and a splitting behavior at longer. Furthermore, the maximum non-splitting droplet length increased with lower We. Figure 14 shows a non-splitting behavior of a $scCO_2$ droplet.

Fluid control

In any macro or microfluidic system, there are some key parameters that need to be controlled for a fully functioning system: Flow rate, pressure, and timing. The flow rate is mainly controlled by a pump, but can be accompanied by a regulation valve for increased sensitivity. Pressure is also controlled by the pump, as it governs the flow rate, which, as seen in equation 6, is closely correlated with the pressure. The valve also plays a major role in pressure control. Finally, the timing is usually controlled by a valve, especially in sampling where timing can be crucial.

Valves

In most microfluidic systems, valves are crucial components needed to control flow rates, fluid supply, correct timing. Generally, valves are classified according to their equilibrium state, normally open (NO) or normally closed (NC) (Oh and Ahn 2006). An extension of the classification also includes bistable and latchable valves. Bistable valves are valves with two equilibrium states that only consume energy when switched between these two states, whereas a latchable valve is either NO or NC. A NO latchable valve then, by definition, has the open state as its equilibrium state, but can latch itself into a closed state. Valves can be further divided into active and passive valves. Active valves need external power supply to hold or change to their non-equilibrium state, whereas passive valves use the internal energy of the system, usually from the flow itself (Oh and Ahn 2006).

At macroscale, needle valves and ball valves are, besides check-valves, by far the most commonly used valve types. However, due their inherent three-dimensionality, reports on miniaturized examples of these are hard to come by. Instead, the membrane type and plug type valve have been the most prevailing in microsystems. Membrane type microvalves function through the pressurization of a thin membrane or diaphragm, acting as the valve head, causing it to deflect and subsequently close against a valve seat (in the NO configuration) to restrict the flow path. Plug valves function by introducing a plug of solid material into the flow stream to close the flow path. For proper function, the valve plug needs to be either moveable or dissolvable/meltable to ensure that the valve can be reopened. Paraffin-actuated microvalves follow the same trends as microvalves in general, with the plug

type and membrane type being the most common. A wide variety of paraffin-actuated microvalves, fabricated using both micromachining techniques and simpler back-end processes has been presented. Since paraffin microvalves have been treated at length in **Paper A**, only a brief description is included here.

Active

As previously stated, active valves need external power input to switch to their non-equilibrium state, as well as a continuous power input to hold it. This puts a high demand on the power supply, especially if long timeframes in the non-equilibrium state are desired. However, the versatility of active microvalves are usually superior to that of their passive counterparts, as an active valve can be switched at any time desired, whereas a passive valve will switch when a given stimulus reaches a threshold level. The switching parameter in passive valves is therefore, to a larger extent than in active valves, a design parameter, which cannot be changed after manufacturing. In **Paper II**, an active paraffin-actuated high-pressure valve is presented. This valve could handle a 20 MPa back-pressure, applied either through water or air.

Latchable

A latchable or bistable valve is defined by its ability to hold more than one position without any continuous energy consumption. This is especially advantageous in cordless and mobile applications, where the energy is usually supplied by a finite energy battery source. The latchable valves and actuators presented in this thesis (**Papers I**, **III**, and **IV**) all rely on lateral control of temperatures of either paraffin (**Papers I** and **IV**) or paraffin and a low-melting-point alloy (LMA) (**Paper III**). This is achieved by integrating separately addressable heaters into the actuation cavity, dividing it into three heating areas, denoted reservoir, channel, and actuator. A schematic latching process is shown in figure 15.

Although working according to the same principle, there are some differences between the systems presented in the different papers. Compared to **Paper I**, some improvements have been done in the later papers to remedy performance issues such as lack of long-term stability, henceforth referred to as endurance, or increasing the leak pressure. In addition to better performance, the development described in these later papers has yielded valuable knowledge regarding potential intermixing of LMA and paraffin as well as the interaction between the valve head (membrane) and valve seat.

In **Paper III**, the material in the actuator heater area was changed from paraffin to LMA to improve the endurance. The reason for this is that

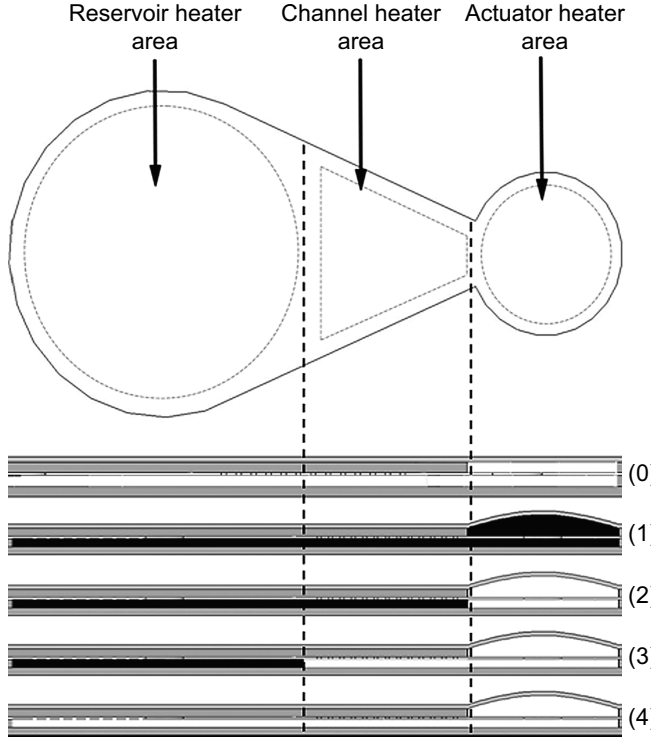

Figure 15. Latching process investigated in papers I, III, and IV. The upper image shows the top view of the actuator, and the bottom image shows the side view. At (0), all heaters are off and all material is in solid state. At (1), all three heaters are turned on, melting all of the material. At (2), the actuator heater is turned off and the material is solidified in an only slightly decreased deflected state due to the still-liquid paraffin in the reservoir and channel areas. At (3) and (4), the channel and reservoir heaters are turned off and the paraffin is solidified. As the material in the actuator area is already in its solid state, this will not induce any further change in deflection. Black color denotes liquid material, whereas white denotes solid. Reproduced from **Paper I.** © 2010 IEEE.

paraffin acts as a highly viscous liquid, when in its solid state, and will consequently yield over time, even at loads significantly lower than the leak pressure.

In **Paper I**, the leak pressure was 2.5 MPa, but already after 110 minutes, the valve started leaking at an applied pressure of 0.3-0.4 MPa. The change of material from paraffin to LMA ensures that the load-bearing material is more rigid, with a much smaller influence from the viscoelastic behavior. This actuator managed to hold its deflection losses below 2.5 μm during a 50-hour period at an applied pressure of 1.8 MPa. This performance

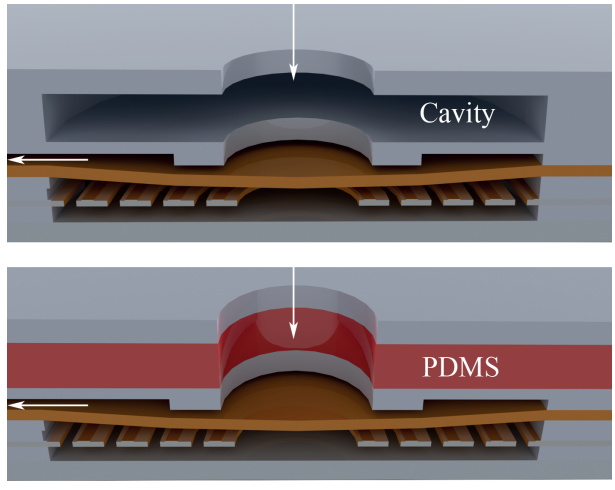

Figure 16. Valve seat design from paper IV (top) and paper I (bottom). The PDMS is colored red for better contrast. The white arrows indicate flow direction.

increase further confirms paraffin's viscoelastic behavior. However, a sufficient amount of paraffin must still be retained in the actuator to ensure a proper stroke. In **Paper IV**, the aim was to improve the leak-pressure capability, to be able to seal a deep-sea microsampler. To achieve this, the valve seat was redesigned.

The original and redesigned valve seat designs are both shown in figure 16. In the original one, a layer of PDMS was sandwiched between steel stencils to accommodate the deflection loss occurring when the actuator heater was turned off. This layer was replaced with a cavity in its place in the updated design. This cavity still allows for a deflection loss without the valve seat losing contact with the membrane. The major difference is that when the system is pressurized, the cavity is also pressurized, forcing the valve seat downwards, which aids the sealing. In the original design, all the downward force was directed at the membrane, ultimately causing it to yield. The valve seat redesign improved the leak pressure from 2.5 to 12.5 MPa.

Pumping

In pumping, an actuator is used to displace fluid in a pump chamber. The actuator is usually accompanied by passive or active valves to create a directional flow, although valveless solutions have occurred (Andersson *et al.* 2001).

The main pump classification is usually done by distinguishing displacement (mechanical) from dynamic (non-mechanical) ones. Displacement

pumps use various kinds of moving parts to displace the fluid, whereas dynamic pumps typically rely on magnetic or electric fields to manipulate the fluid (Laser and Santiago 2004).

Macroscale displacement pump principles, relying on, *e.g.*, rotating parts or moving pistons, generally become decreasingly efficient with decreasing pump size. The primary reason for this is a pure scaling phenomenon: With a decrease in size, the relative importance of surface-acting forces, such as friction between sliding parts, increases as the surface-to-volume ratio increases. Another issue in translating macroscale techniques to microscale is fitting tolerances, as a micropump is typically smaller than a cubic centimeter. To overcome these issues, micropumps often use membranes to displace the fluid (Laser and Santiago 2004).

There are many actuation principles available for micropumps, as evident from previous reviews (Laser and Santiago 2004; Iverson and Garimella 2008), among which paraffin-actuated pumping has its niche in high-pressure low-throughput pumping, figure 17. For a full summary on paraffin micropumps and a comparison with other actuation principles, the reader is referred to **Paper A**.

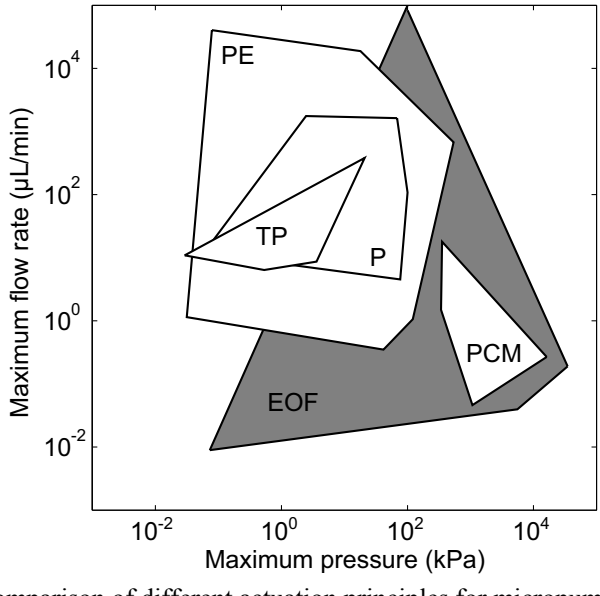

Figure 17. Comparison of different actuation principles for micropumping. PE – Piezoelectric, TP – Thermopneumatic, P – Pneumatic, EOF - Electroosmotic flow, and PCM – Phase change material (paraffin).

Continuous pumping

Continuous pumping is defined by the lack of a maximum deliverable volume without refilling the pump. Especially at the microscale, this is usually

achieved by utilizing a repetitive motion within the pump, pushing a fluid in one direction to create a net flow. In **Paper VI**, a paraffin-actuated displacement pump is designed, manufactured, and evaluated. This pump comprises temperature readout, enabling closed-loop control of the pumping in order to compensate for temperature fluctuations in the surroundings. Compared to previous work on paraffin-actuated pumps (Bodén *et al.* 2006, 2008), this pump can handle substantially higher pressures (12.5 MPa compared with 0.9 and 5 MPa in the previous work) without loss of flow rate. However, this maximum pressure proved to be dependent on the pumping frequency. As seen in figure 18, a higher pumping frequency is more sensitive to an increase in pressure than a lower one is. Furthermore, two different driving schemes were evaluated, a 4-phase and a 6-phase. The main differentiating factor is that the 6-phase scheme has an overlap between the inlet and outlet valve activation, which the 4-phase scheme lacks. When comparing the two driving schemes, the 4-phase scheme sustained higher flow rates at low pressure, especially at higher pumping frequencies. However, this scheme proved to be much more affected by an increase in back pressure, and could not sustain any flow at all at 7.5 MPa at pumping frequencies exceeding 0.5 Hz. This was most likely due to insufficient sealing at the inlet and outlet valves, as these did not have time to seal with the 4-phase scheme. The choice of driving scheme thus depends on the driving conditions, and if a high pressure capability or a higher flow rate is preferred.

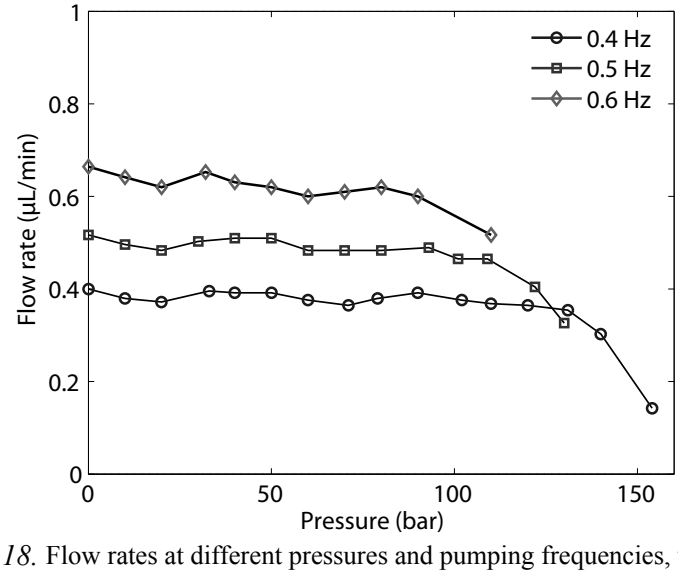

Figure 18. Flow rates at different pressures and pumping frequencies, using the 6-phase driving scheme, from the pump presented in **Paper VI**. © 2011 IEEE.

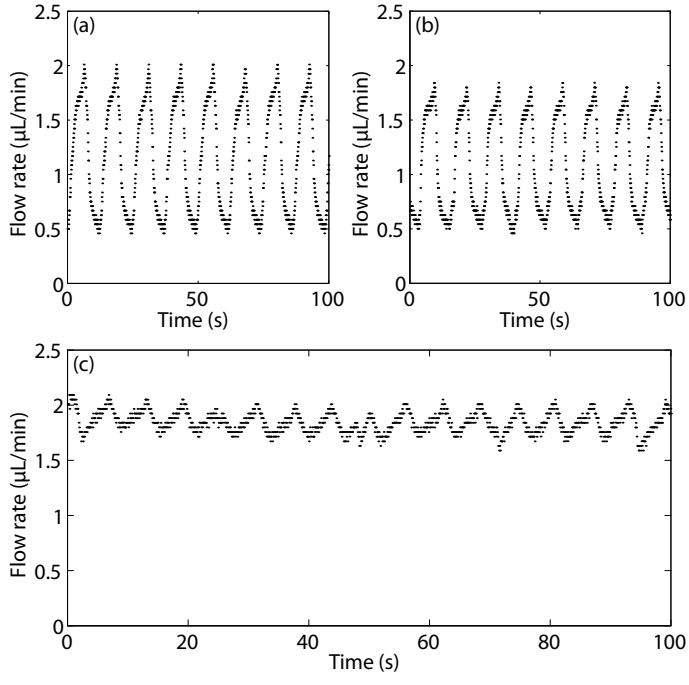

Figure 19. Flow rates performance of the pump system presented in **Paper VIII**. (a) and (b), pump 1 and 2 operated individually, and (c) both pumps in a combined operation.

Although the pump presented in **Paper VI** can handle pressures in a useful range for HPLC applications, cyclic micropumps generally suffer from pulsating flows, this pump being no exception. Variations in flow rates can cause band broadening in HPLC, limiting the resolution. **Paper VIII** addresses this pulsating flow by combining two pumps on the same chip driving them with an offset. Furthermore, the pump chambers are larger (6 mm diameter compared to 2 mm diameter) than the ones used in **Paper VI**. Figure 19 illustrates the reduction in flow variations.

Dispensing

Pumping of discrete amounts of fluid, or dispensing, is defined by a finite volume to be delivered. Usually this is achieved by utilizing a pre-filled reservoir that is discharged in a controlled manner. In **Paper VII**, a reusable paraffin-actuated dispenser is designed, manufactured, and evaluated. Although the design allows for continuous pumping, the main objective of the device was to deliver specific volumes with high control. Figure 20 shows the delivered volume for two target volumes, dispensed by two separate devices. As seen, both a high repeatability of dispensing and a high reproducibility between devices were accomplished. The different target volumes can be achieved within the same device by controlling the amount

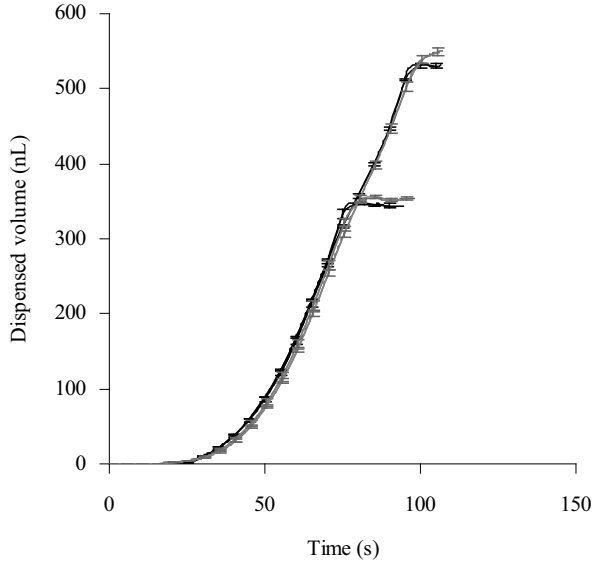

Figure 20. Dispensed volumes for two target volumes by two separate devices presented in **Paper VII**. The black line denotes device 1, and the gray line denotes device 2. © 2013 IEEE.

of expansion of the paraffin, which is done by controlling the input power to the dispensing actuator. Since paraffin has a low compressibility, the dispensed volume was independent of the back-pressure of the system within the evaluated pressure region 0.6-2.0 MPa. This is a major advantage compared with other dispensers, since the dispensing parameters do not have to be tuned to accommodate a change in back pressure. To achieve this functionality, the pump chamber is larger (8 mm diameter) than in both **Paper VI** and **VIII.** Besides the dispensing functionality gained, the flow behavior at different activation schemes can be used qualitatively to increase the understanding of the phase change behavior of paraffin. Furthermore, the model from **Paper V** was adjusted to the larger actuator and used to predict the flow characteristics.

Sampling

When a fluidic sample is to be taken for further analysis, a few important factors must be addressed. Firstly, the timing and amount of sample need to be controlled. After the sample is acquired, it needs to be sealed to avoid contamination before analysis can be conducted. Contamination also needs to be avoided prior to sampling. This is usually controlled by valves connected to the sampler. Secondly, it has to be ensured that a sufficient amount

of the compound of interest is present within the sample. With microsystems, this is usually an issue. As the sampled volumes in microfluidics commonly are in the range of microliters, or even nanoliters, this small volume may not contain enough cells, or in other ways interesting compounds, to be studied. In **Paper IV**, both the sample control, and enrichment is addressed. As mentioned previously in the valve section, the latchable valve was improved to be able to handle deep-sea sampling missions of long durations. The enrichment was addressed by integrating piezoelectric transducers in the channel floor, and sealing the device with a Pyrex cover. When the transducers are operated at ultrasound frequency, a standing wave is created within the channel.

The standing wave has pressure nodes in which particles are trapped. Using this technique, water can be flushed through the system, enriching the sample to ensure a sufficient amount of particles is present to be studied. Figure 21 shows particles trapped on the transducer surface, and subsequently released, and figure 22 shows the amount of particles trapped at varying flow rates and trapping times. Since the force acting on the particles is dependent on both particle size and frequency (Evander *et al.* 2007), these types of systems can be tailored to trap particles of a specific size range. Furthermore, several transducers with different characteristics could be combined to trap different particle types.

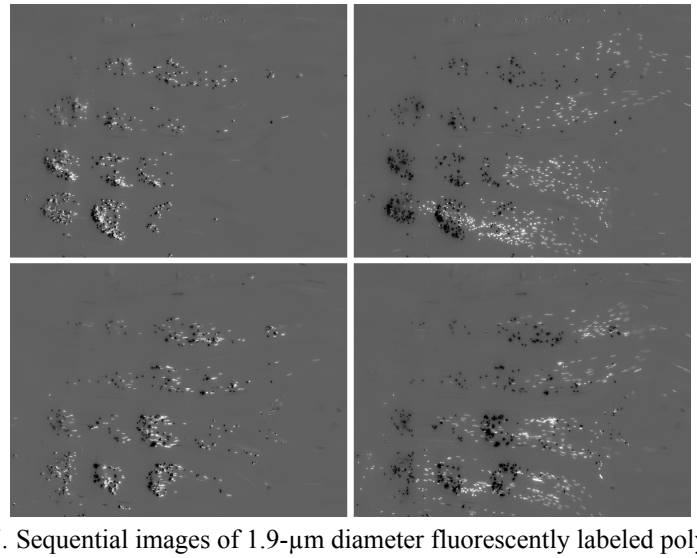

Figure 21. Sequential images of 1.9-µm diameter fluorescently labeled polystyrene particles captured at the surface of the piezoelectric transducer after 6 minutes of activation at a flow rate of 10 µL/min (top half) and 15 µL/min (bottom half). The left images were taken when the particles had just been released, and the right images a few seconds later. White dots represent the particles' location after the release, and black dots their initial position. Reproduced from **Paper IV** with permission from RSC.

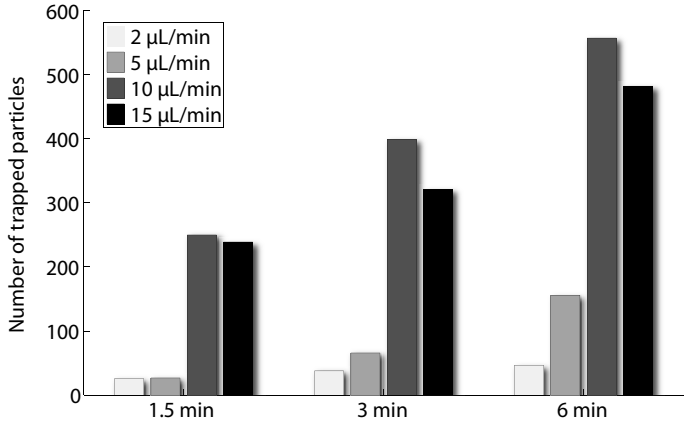

Figure 22. Number of particles trapped at different flow rates and trapping times. Reproduced from **Paper IV** with permission from RSC

Conclusions

As proven through several studies in recent years, paraffin is a very powerful actuator material, well suited for high-pressure microfluidic manipulation.

The low thermal conductivity of paraffin is usually perceived as a disadvantage. However, this property, in combination with the material's large specific heat, can be used to create large thermal gradients within an actuator. In this thesis, the thermal gradient has been used to latch valve actuators to save energy. The endurance measurements on these latchable valves brought an important material property to attention: The viscoelastic behavior of solid paraffin. This behavior is seen from the valves' yielding with time at constant load, and ultimately led to the modeling approach used, where all phases were modeled as a liquid. Furthermore, the understanding of this viscoelastic behavior was used to improve the long-term stability of a latchable microvalve.

The low viscosity of $scCO_2$ heavily affects its microfluidic behavior. As the viscosity affects both the Reynolds number and the capillary number, it also affects both the onset of turbulence and the affinity to segmented flow rather than parallel. Therefore, the fluidic behavior of supercritical fluids at the microscale needs to be further studied to be fully understood

Utilizing the strength of paraffin in micropumping applications definitely has its merits, especially concerning the ability to handle high back pressures. The low flow rate accompanied by the thermal actuation of paraffin becomes less of an issue at the microscale. As volumes get smaller, precise control of delivered volumes and flow rates becomes more important than high flow rates in, *e.g.*, HPLC applications. Furthermore, with smaller fluidic channels come higher fluidic resistances and consequently higher back pressures, wherefore strong pumps become increasingly important at the microscale. The pumps presented in this thesis take a first step towards fully integrated on-chip HPLC.

Outlook

Paraffin-actuated microdevices have since the first published articles in the late 90's proven to be a competitive way of controlling high-pressure microfluidic systems. However, most have been stand-alone devices, and manufactured and characterized as such. The next natural step is to integrate more actuators and fully couple these systems to additional functionalities such as, *e.g.*, detection sources. This would finally enable such applications as fully integrated μHPLC chips.

As proven in the work covered by this thesis, paraffin-actuated valves can both withstand very high pressures and be made latchable in a self-contained manner. This opens up for possibilities in a wide range of exploratory applications, with deep-sea sampling used as an example in this thesis.

Furthermore, the thermal actuation of paraffin can be utilized to create passive safety valves coupled to microreactors conducting exothermal reactions. As the reaction starts, the valve would close from the supplied heat, and would not open until the reaction has been finalized.

With the current evolution of nanofluidics, strong micropumps seem to become increasingly important due to the high back-pressures created in the systems. Furthermore, with decreasing sample volumes, the importance of the dead volume increases. Integrating micropumps on chips containing nanofluidic components would be a significant contribution towards minimizing dead volume.

Regarding supercritical microfluidics, functionalized surfaces, where, *e.g.*, the wetting can be tailored to suit either polar fluids like water or apolar fluids like $scCO_2$, can be used for phase separations in extraction applications. Finally, the introduction of active on-chip control of, *e.g.*, supercritical microfluidic chips would enable much more complex functionalities and enable systems to be evolved rather than single-purpose devices.

Summary in Swedish

Mikrosystemteknik definieras av system där en eller flera komponenter har en storlek i mikrometerområdet. Ofta handlar det om komponenter som givare, små motorer eller en kanal för transport av vätska. För att tillverka komponenter och delar i denna storleksordning, är det oftast nödvändigt att frångå traditionella tillverkningstekniker. Istället används ofta kemisk avverkning av material, så kallad etsning. För att etsningen ska kunna utföras endast på utvalda delar av materialet, används en mönstrad mask som inte angrips av kemikalierna och på så sätt skyddar valda delar.

Varför gör man då saker mindre om man måste utveckla och använda helt nya tekniker för att tillverka komponenter och system? Det vanligaste svaret är att man kan tillverka många fler komponenter samtidigt på en liten yta, vilket gör att dessa komponenter blir mycket billigare. Det finns dock ytterligare skäl att krympa saker. När man krymper saker tillräckligt mycket ändras kraftbalansen från att domineras av volymsverkande krafter, som gravitation, till ytverkande krafter som exempelvis friktion. Denna förändring i kraftbalans ger upphov till en mängd spännande effekter som kan studeras och användas.

Mikrofluidik är den del av mikrosystemteknik som behandlar hanteringen av fluider i mikroskala. Det är en tvärvetenskaplig disciplin med inslag av fysik, kemi och biologi. Även här förändras beteendet när man går mot mikroskala. Exempelvis beter sig vatten som sirap när det flödar i kanaler som är ca 100 µm stora. Ytterligare en effekt av ytkrafternas dominans är att det är mycket enklare att skapa stabila droppar mellan två vätskor som inte blandas.

Vid sidan av de tre, vid atmosfäriskt tryck och rumstemperatur, naturligt förekommande aggregationstillstånden för materia: Fast, flytande och gas, finns ytterligare tre faser: Bose-Einstein kondensat, plasma och superkritisk fluid. Den superkritiska fasen kräver att både trycket och temperaturen är högre än den så kallade kritiska punkten. Superkritiska fluider har flera spännande egenskaper: Densiteten (vikt/volym) är som hos en vätska, diffusionshastigheten (transporthastighet av molekyler) befinner sig mellan den hos en vätska och en gas och viskositeten (hur trögflytande en fluid är) är som hos en gas. Studier av denna fas är dock inte särskilt vanliga inom mikrofluidik på grund av de förhöjda tryck och temperaturer som krävs.

Arbetet bakom denna avhandling gäller främst vätskehantering under höga tryck. Särskilt undersöks ventiler och pumpar. Vidare studeras mikrofluidik för superkritisk koldioxid.

För att en ventil eller pump ska kunna hantera höga tryck, måste det som driver ventilen eller pumpen, det vill säga aktuatorn, vara stark. För att aktuatorn ska vara stark behövs ofta ett starkt aktuatormaterial. I alla ventiler och pumpar som ingår i avhandlingen har därför paraffin använts som aktuatormaterial. Paraffin, för många känt som något man använder vid syltkonservering eller det som värmeljus består av, expanderar ca 10 % när det smälter. Denna expansion, kombinerad med att paraffin är i det närmaste inkompressibelt, gör att det kan hantera mycket stora krafter. Vidare gör det faktum att större delen av expansionen inträffar i samband med smältningen att det blir enklare att hålla en lägre temperatur, vilket framför allt är viktigt vid biologiska tillämpningar.

Fasändringar är ofta relativt komplicerade förlopp med ett flertal materialegenskaper som förändras. I **Artikel V** görs en ansats för att öka förståelsen för hur miniatyriserade paraffinaktuatorer beter sig. För att kunna utforska vad som sker inuti en av dessa aktuatorer används modellering med finita elementmetoden. Resultaten jämförs sedan med de från mätningar på en tillverkad aktuator för att bekräfta modellen. Därefter kan modellen användas för skalningsanalys och för att bättre förstå vad som händer inuti en av dessa paraffinaktuatorer.

Ventiler kan vara normalt öppna eller normalt stängda. Denna beteckning anger i vilket läge ventilen kommer att vara när den inte är kraftförsörjd. Följaktligen kommer en aktiv normalt öppen ventil, som i **Artikel II**, att förbruka energi i sitt stängda läge, och tvärtom. Om det finns ett behov av att använda en ventil under långa tider i både öppet och stängt läge, kan det finnas en stor energivinst i att använda sig av en så kallad låsningsbar eller bistabil ventil. Sådana använder bara energi när man byter läge från öppen till stängd eller tvärtom. Den här typen av ventiler presenteras i varierande utföranden i **Artikel I** och **III-IV**.

En pump kan arbeta antingen kontinuerligt eller dispenserande. Skillnaden består i att en dispenserande pump har en maximal volym som den kan leverera innan den måste fyllas på, medan en kontinuerlig pump kan drivas utan övre begränsning i volym. I **Artikel VI** utvecklas och karakteriseras en mikropump som klarar mycket höga tryck, upp till 125 bar, utan att pumphastigheten påverkas. Pumpen fungerar genom att en cyklisk rörelse kramar vätskan framför sig.

Ett vanligt förekommande problem med den här typen av pumpar är att den cykliska rörelsen medför fluktuationer i pumphastigheten. För att komma tillrätta med det undersöks det i **Artikel VIII** hur man kan parallellkoppla två integrerade pumpar och driva dem ur fas och på så sätt låta de två pumparnas variationer i pumphastighet ta ut varandra. För dispenserande pumpar ställs ofta inte lika höga krav på jämnhet i pumphastighet. Däremot

är det desto viktigare att de kan leverera en bestämd volym med mycket stor noggrannhet. I **Artikel VII** utvärderas en dispenserande paraffindriven pump med avseende på dess förmåga att leverera bestämda volymer vid olika mottryck.

Som tidigare nämnts, har superkritiska fluider en spännande kombination av materialegenskaper. Dessa blev än mer påtagliga i **Artikel IX** då de mikrofluidala egenskaperna utvärderades genom att under olika betingelser flöda vatten och superkritisk koldioxid tillsammans. De speciella materialegenskaperna hos superkritiska fluider gör också att flera av dem, bland annat superkritisk koldioxid, är mycket bra lösningsmedel. Resultaten från **Artikel IX** skulle kunna användas för att bestämma processparametrar för extraktion av vissa intressanta komponenter från vattnet till koldioxiden.

Arbetet som presenteras i denna avhandling har ökat förståelsen för hur miniatyriserade paraffinaktuatorer beter sig under olika betingelser. Vidare har viskoelasticiteten hos paraffin visats ha långtgående effekt på prestandan hos en låsningsbar ventil. Slutligen har ett första steg tagits mot att förstå hur superkritisk koldioxid beter sig i mikrofluidala system genom att de fluidmekaniska egenskaperna har utvärderats.

Acknowledgements

First of all, I would like to thank my supervisors for supporting and guiding me through these years.

Klas, for taking me in and letting me embark on this journey. Also, for all inspiring discussions and your endless source of new ideas. It's fantastic that a quick question can turn into an hour-long discussion about the future.

Greger, for your endless patience and constructive comments with my manuscripts, and for helping me finish projects as well as start new ones.

Roger, for helping me off to a good start, and for returning to help me finish the job.

Lena, for always having time to discuss my projects, although seldom officially involved.

Stefan, for nice collaborations and good companionship in the lab.

Andreas, for answering all my questions about analytical chemistry as well as good travelling company.

Mikael, for all the interesting discussions about important things. Football is a Sirius game.

Zhigang, for introducing me to the world of microfluidics.

Jonas, for the nice collaboration as well as good travelling company.

Anders, Atena, Johan, Kristofer, Martin, Mingzhi, Peter, Pontus, Seung-Hee, Tao, and Ville for nice kick-offs, conferences, MST-dinners and football games.

Irene and Charlotta, for teaching me all I know about supercritical fluids.

Amer, Minh, and Gustav for a nice collaboration.

The old-timers, Erik, Gunjana, Hanna, Linda, Marcus, Niklas, and Sara, for making me feel welcome when I started at the department.

The materials in medicine and tribology groups for making the coffee-table at the department such a nice place to be at.

Bagge, for keeping my computer running all these years.

The administration, Anja, Per-Richard, and Sara, for always helping out.

My family, for your support and interest in what I've been doing.

Molly and Jim, for making a lousy day disappear as soon as I see you.

Last, but not at all least, Jessica, for always believing in me, even when I didn't. And for your patience and support throughout these years. Most of all though, just for being the one you are. I love you.

References

Allen DM (2004) Photochemical machining: from'manufacturing's best kept secret' to a $6 billion per annum, rapid manufacturing process. CIRP Ann. Manuf. Technol., 53(2):559-572

Andersson H, van der Wijngart W, Nilsson P, Enoksson P, Stemme G (2001) A valve-less diffuser micropump for microfluidic analytical systems. Sens. Actuators B: Chem., 72(3):259-265

Andrews T (1869) On the Continuity of the Gaseous and Liquid States of Matter. Phil. Trans. Roy. Soc., 159:575-590

Assmann N, Kaiser S, von Rohr PR (2012) Supercritical extraction of vanillin in a microfluidic device. J. Supercrit. Fluids, 67:149-154

Bannerjee S, Sutanto S, Klein JM, van Roosmalen MJE, Witkamp G-J, Stuart MAC (2012) Colloidal interactions in liquid CO2 – A dry-cleaning perspective. Adv. Colloid Interface Sci., 175:11-24

Bell DJ, Lu TJ, Fleck NA, Spearing SM (2005) MEMS actuators and sensors: observations an their performance and selection for purpose. J. Micormech. Microeng., 15:S153-S164

Blanch-Ojea R, Tiggelaar RM, Pallares J, Grau FX, Gardeniers JGE (2012) Flow of CO_2-ethanol and of CO_2-methanol in a non-adiabatic microfluidic T-junction at high pressures. Microfluid. Nanofluid., 12:927-940

Bodén R, Lehto M, Simu U, Thornell G, Hjort K, Schweitz J -Å. (2006) A polymeric paraffin actuated high pressure micropump. Sens. Actuators A: Phys., 127(1):88-93

Bodén R, Hjort K, Schweitz J-Å, Simu U (2008) A metallic micropump for high-pressure microfluidics. J. Micromech. Microeng., 18(11):115009 (7pp)

Cansell F, Aymonier C, Loppinet-Serani A (2003) Review on materials science and supercritical fluids. Curr. Opin. Solid State Mater. Sci., 7:331-340

Ciftlik AT, Gijs MAM (2011) A low-temperature parylene-to-silicon dioxide bonding technique for high-pressure microfluidics. J. Micromech. Microeng., 21(3):168-182

Dohrn R, Fonseca JMS, Peper S (2012) Experimental methods for phase equilibria at high pressures. Annu. Rev. Chem. Biomol., Eng. 3:343-367

Evander M, Johansson L, Lilliehorn T, Piskur J, Lindvall M, Johansson S, Almqvist M, Laurell T, Nilsson J (2007) Noninvasive acoustic cell trapping in a microfluidic perfusion system for online bioassays. Anal. Chem., 79:2984-2991

Fenghour A, Wakeham WA , Vesovic V (1998) The viscosity of carbon dioxide. J. Phys. Chem. Ref. data., 27(1):31-44

Gilbertson RG, Busch JD (1996) A survey of micro-actuator technologies for future spacecraft missions. JBIS-J. Brit. Interpla., 49:129-138

Guillaument R, Erriguible A, Aymonier C, Marre S, Subra-Paternault S (2013) Numerical simulation of dripping to jetting in supercritical fluids/liquid micro coflows J. Supercrit. Fluids, 81:15-22

Gravesen P, Branebjerg J, Jensen OS (1993) Microfluidics-a review. J. Micromech. Microeng., 3(4):035011 (12pp)
Holmes D, Gawad S (2010) The application of microfluidics in biology. Methods Mol. Biol., 583:55-80
Hannay JB, Hogarth J (1879) On the solubility of solids in gases. Proc. Roy. Soc., (London), 29:324-326
Hannay JB, Hogarth J (1880) On the solubility of solids in gases. Proc. Roy. Soc., (London), 30:178-188
Hannay JB (1880) On the solubility of solids in gases. II. Proc. Roy. Soc., (London), 30:484-489
Herrero M, Mendiola JA, Cifuentes A, Ibáñez E (2010) Supercritical fluid extraction: Recent advances and applications. J. Chromatogr. A, 1217(16):2495-2511
Hill M, Harris NR (2007) Microfluidic technologies for miniaturized analysis systems, Chapter 9 Ultrasonic particle manipulation, Springer US, ISBN 978-0-387-68424-6
Iverson BD, Garimella SV (2008) Recent advances in microscale pumping technologies: A review and evaluation. Microfluid. Nanofluid., 5(2):145–74
Jensen KF (2001) Microreaction engineering – is small better? Chem. Eng. Sci., 56:293-303
Jonsson J, Edqvist E, Kratz H, Almqvist M, Thornell G (2010) Simulation, manufacturing, and evaluation of a sonar for a miniaturized submersible explorer. IEEE T. Ultrason. Ferr., 57(2):490-495
Jonsson J, Sundqvist J, Nguyen H, Berglund M, Ogden S, Palmer K, Smedfors K, Johansson L, Hjort K, Thornell G (2012) Instrumentation and vehicle platform of a miniaturized submersible for exploration of terrestrial and extraterrestrial aqeous environments. Acta astronaut., 79:203-211
Jonsson J, Berglund M, Kratz H, Nguyen H, Thornell G (2012) A compact system to extract topography information from scenes viewed by a submersible explorer. Sens. Actuators A:Phys., 188:401-410
Jonsson J, Smedfors K, Nyholm L, Thornell G (2013) Towards chip-based salinity measurements for small submersibles and bio-loggers. International Journal of Oceanography, In press, published online.
Kim H, Najafi K (2005) Characterization of low-temperature wafer bonding using thin-film parylene. J. Microelectromech. Syst., 14(6):1347-1355
Kiwi-Minsker L, Renken A (2005) Microstructured reactors for catalytic reactions. Catal. Today, 110(1-2):2-14
Kricka LJ, Wilding P (2003) Microchip PCR. Anal. Bioanal. Chem., 377:820-825
Krulevitch P, Lee AP, Ramsey PB, Trevino JC, Hamilton J, Northrup MA (1996)Thin film shape memory alloy microactuators. J. Microelectromech. Syst., 5(4):270-282
Kutter JP (2012) Liquid phase chromatography on microchips. J. Chromatogr. A, 1221:72-82
Laser DJ, Santiago JG (2004) A review of micropumps. J. Micromech. Microeng., 14(6):R35–64
Lee JS, Lucyszyn S (2007) Design and pressure analysis for bulk micromachined electrothermal hydraulic microactuators using a PCM. Sens. Actuators A: Phys., 133(2):294–300
Lee ML Markides KE (1990) Analytical supercritical fluid chromatography and extraction. Chromatography Conferences Inc., ISBN 0-8425-2394-4.
Madou MJ (2002) Fundamentals of microfabrication 2nd edition. CRC Press, ISBN 0-8493-0826-7

Maeda R, Tsaur J, Lee S, Ichiki M (2004) Piezoelectric microactuator devices. J. Electroceramics, 12(1/2):89-100
Marre S, Baek J, Park J, Bawendi MG, Jensen KF (2009) High-pressure/high-temperature microreactors for nanostructure synthesis. J. Lab. Autom., 14:367-373
Marre S, Aymonier C, Subra P, Mignard E (2009) Dripping to jetting transitions observed from supercritical fluid in liquid microcoflows. Appl. Phys. Lett., 95:134105 (3pp)
Marre S, Adamo A, Basak S, Aymonier C, Jensen KF (2010) Design and packaging of microreactors for high pressure and high temperature applications. Ind. Eng. Chem. Res., 49:11310-11320
Marre S, Roig Y, Aymonier C (2012) Supercritical microfluidics: Opportunities in flow-through chemistry and materials science. J. Supercrit. Fluids, 66:251-264
Mason BP, Price KE, Steinbacher JL, Bogdan AR, McQuade DT (2007) Greener approaches to organic synthesis using microreactor technology. Chem. Rev., 107:2300-2318
Manz A, Graber N, Widmer H M (1990) Miniaturized total analysis systems: a novel concept for chemical sensing. Sens. Actuators B:Chem., 1(1-6):244–248
Manz A, Miyahara Y, Miura J, Watanabe Y, Miyagi H, Sato K (1990) Design of an open-tubular column liquid chromatograph using silicon chip technology. Sens. Actuators B Chem., 1(1-6):249-255
Navarrini W, Venturini F, Tortelli V, Basak S, Pimparkar KP, Adamo A, Jensen KF (2012) Direct fluorination of carbon monoxide in microreactors. J. Fluorine Chem., 142:19-23
Nguyen NT, Wu Z (2005) Micromixers-a review. J. Micromech. Microeng., 15(2):R1-R16
Nightingale AM, deMello JC (2013) Segmented flow reactors for nanocrystal synthesis. Adv. Mater., 25:1813-1821
Noh H-S, Moon K-S, Cannon A, Hesketh PJ, Wong CP (2004) Wafer bonding using microwave heating of parylene intermediate layers. J. Micromech. Microeng., 14(4):625-631
Oh KW, Ahn CH (2006) A review of microvalves. J Micromech. Microeng., 16(5):R13-R39
Ohashi A, Sugaya M, Kim H-B, (2011) Development of a microfluidic device for measurement of distribution behaviour between supercritical carbon dioxide and water. Anal. Sci., 27:567-569
Palmer K, Jonsson J, Nguyen H, Thornell G (2013) 2-D thermal velocity sensor for submersible navigation and minute flow measurements. IEEE Sensors J., 13(1):359-370
Rios A, Escarpa A, Simonet B (2009) Miniaturization of analytical systems. John Wiley and Sons Ltd., ISBN 978-0-470-06110-7
Schubert K, Brandner J, Fichtner M, Linder G, Schygulla U, Wenka A (2001) Microstructure devices for applications in thermal and chemical process engineering. Microscale Thermophys. Eng., 5:17-39
Sethu P, Mastrangelo CH (2003) Polyethylene glycol (PEG)-based actuator for nozzle-diffuser pumps in plastic microfluidic systems. Sens. Actuators A, Phys., 104(3):283-289
Sharma A, Tyagi VV, Chen CR, Buddhi D (2009) Review of thermal energy storage with phase change materials and applications. Renew. Sust. Energ. Rev., 13(2):318-345
Siegert MJ, Carter S, Tabacco I, Popov S, Blankenship DD (2005) A revised inventory of Antarctic subglacial lakes. Antarct. Sci., 17(3):453-460

Skoog DA, West DM, Holler FJ (1996) Fundamentals of analytical chemistry, 7th Edition. Saunders College Publishing, ISBN 0-03-005938-0
Sollier E, Murray C, Maoddi P, Di Carlo D (2011) Rapid prototyping polymers for microfluidic devices and high pressure injections. Lab. Chip, 11(22):3752-3765
Squires TM, Quake SR (2005) Microfluidics: Fluid physics at the nanoliter scale. Rev. Mod. phys., 77(3):977-1026
Srinivasan P, Spearing SM (2009) Material Selection for Optimal Design of Thermally Actuated Pneumatic and Phase Change Microactuators. J. Microelectromech. Syst., 18(2):239-249
Terry SC, Jerman JH, Angell JB (1979) A gas chromatograph air analyzer fabricated on a silicon wafer. IEEE Trans. Electron. Devices, ED-26:1880-1886
de la Tour C (1822) Exposé de quelques résultats obtenu par l'action combinée de la chaleur et de la compression sur certains liquides, tels que l'eau, l'alcool, l'éther sulfurique et l'essence de p´etrole rectifiée.,Ann. Chim. Phys., 21:127-132
Verboom W (2009) Selected Examples of High-Pressure Reactions in Glass Microreactors, Chem. Eng. Technol., 32:1695-1701
Whitesides GM (2006) The origins and future of microfluidics. Nature, 442(7101):368-373
Wu Z, Hjort K (2009) Microfluidic hydrodynamic cell separation: A review. Mater. Res. Soc. Symp., P., 1(3):181-192
Zoller P, Walsh DJ (1995) Standard pressure-volume-temperature data for polymers Lancaster, CA:, Technomic

Acta Universitatis Upsaliensis

Digital Comprehensive Summaries of Uppsala Dissertations from the Faculty of Science and Technology 1085

Editor: The Dean of the Faculty of Science and Technology

A doctoral dissertation from the Faculty of Science and Technology, Uppsala University, is usually a summary of a number of papers. A few copies of the complete dissertation are kept at major Swedish research libraries, while the summary alone is distributed internationally through the series Digital Comprehensive Summaries of Uppsala Dissertations from the Faculty of Science and Technology.

Distribution: publications.uu.se
urn:nbn:se:uu:diva-208915

ACTA
UNIVERSITATIS
UPSALIENSIS
UPPSALA
2013