Polymer microfabrication technologies for microfluidic systems

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Abstract Polymers have assumed the leading role as substrate materials for microfluidic devices in recent years. They offer a broad range of material parameters as well as material and surface chemical properties which enable microscopic design features that cannot be realised by any other class of materials. A similar range of fabrication technologies exist to generate microfluidic devices from these materials. This review will introduce the currently relevant microfabrication technologies such as replication methods like hot embossing, injection molding, microthermoforming and casting as well as photodefining methods like lithography and laser ablation for microfluidic systems and discuss academic and industrial considerations for their use. A section on back-end processing completes the overview.

Keywords Microfluidics · Microfabrication · Polymers · Biochips · High throughput screening · Miniaturization

Abbreviations

CE	Capillary electrophoresis
COC/	Cycloolefin/copolymer
COP	
DT	Decomposition temperature
HDT	Heat distortion temperature
LIGA	*Lithographie* (lithography), *galvanoformung* (electroplating), *abformung* (molding)
MEMS	Micro electromechanical systems

μ-TAS	Miniaturized total analysis system
μ-EDM	Micro-electrode discharge machining
MST	Microsystem technology
TAS	Total analysis system
T_g	Glass transition temperature
PC	Polycarbonate
PDMS	Poly(dimethylsiloxane)
PE	Polyethylene
PEEK	Polyetheretherketone
PFPE	Perfluoropolyether
PI	Polyimide
PMMA	Poly(methyl methacrylate)
POC	Point-of-care
PP	Polypropylene
PS	Polystyrene
TPE	Thermoset polyester

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Introduction

Since the first conceptual suggestions to use microfabrication technologies (MEMS or MST) for the miniaturization of methods in analytical and bioanalytical chemistry in the late 1980s and early 1990s (for an overview of the early works see e.g. [1]), this field has grown into the mainstream of academic as well as commercial interest. While scientifically intriguing from the earliest days, it took several years for the first commercial systems to appear on the market and even now after almost 20 years since the first publications, a "killer application" which was hoped for early on has not emerged. Instead miniaturization has proven itself to be more of an enabling technology, diffusing into various application areas and affecting the way that novel

products are being developed. The true progress of micro-system technologies in the life sciences lies in the fact that nobody disputes anymore the advantages of miniaturization and no new diagnostic kit or analytical system is developed which does not contain miniaturized components, elements or strategies to a certain extent. In order to penetrate the targeted markets (e.g. diagnostics, food and environmental analysis, bioanalytical techniques etc.), microfabrication technologies had to be established which allow the manufacturing of such devices at a cost which is at least comparable to conventional devices. While in the first years of microfluidics the devices were predominantly made with methods borrowed from the microelectronics field and involved materials like glass, quartz or silicon [2], most applications demand devices which can be used as disposables in order to eliminate risks of sample contamination. Polymer materials and their fabrication methods proved to be the solution to this challenge. This trend towards the use of polymers as device material is furthermore supported by the fact that many standard laboratory items (e.g. Eppendorf tubes, pipette tips, polystyrene beads, tubing, cell culture plates etc.) have traditionally been made out of polymers so that not only the users are familiar with the material but also the necessary chemistries have been developed for their use. Furthermore, microfluidic applications have expanded from the "simple" analysis of biomolecules into a wide variety of scientific disciplines and in particular into the field of cell biology, where material properties like oxygen and carbon dioxide permeability favour polymeric materials. This expansion of applications in conjunction with the increased availability of polymer microfabrication technologies and resources has led to an exponential growth of activities in this area. This can be demonstrated by a simple search in the PubMed database [3] for publications involving one of the most widespread used materials in microfluidics, the elastomer poly(dimethylsiloxane) (PDMS; for details see Casting). The results of this search are shown in Fig. 1,

indicating a 30-fold increase in the number of publications within 10 years. Even if not all publications are solely for microfluidic devices (PDMS is also used in macroscopic medical devices), the trend is clear. Similar growth can also be seen in the commercial activity as documented in the number of issued patents [4]. One potentially critical aspect of the development of microfluidic systems in recent years, however, should be mentioned in this introduction: there is an increasing gap between methods and materials used in the academic environment for the fabrication of microfluidic devices (namely casting of PDMS and the use of the photoresist SU-8) in comparison to methods used in the manufacturing of commercial products (namely injection molding of thermoplastic materials). This development poses a threat for the future commercialization of methods and devices developed in academia, as their results cannot directly be transformed into commercial devices due to the different chemistries and physical parameters involved.

In this paper, we give an overview of the current state-of-the-art in polymer microfabrication for microfluidic applications, its recent trends and possible future developments. We have limited ourselves to the literature published since about the year 2000 and have cited only selective earlier works. Figure 2 gives a schematic overview of the process steps involved and which are covered in this article. Materials will introduce the materials involved with their physical and chemical characteristics. Photodefinable polymer technologies is devoted to microfabrication methods involving optical methods for the structuring of the polymer. In Replication methods, the polymer replication methods are discussed. In Further techniques, further methods for structuring are introduced. Back-end processing is devoted to the crucial methods of back-end-processing to make a fully functioning device out of a microstructured polymer part. Current trends and future developments will give a short outlook of actual trends in the field and Conclusions contains a summary of this review.
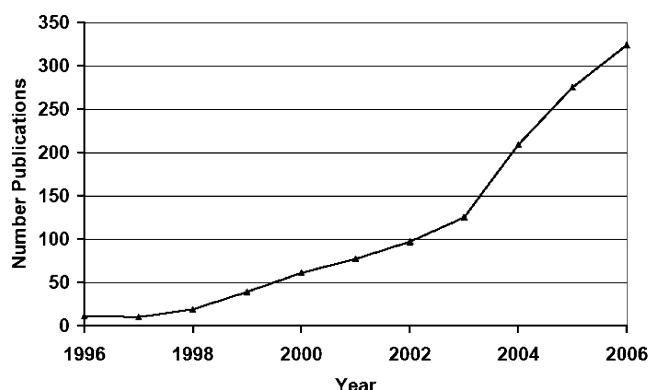

Fig. 1 Number of publications per year listed in PubMed with the search query "PDMS"

Materials

Polymer materials exhibit a "Jekyll and Hide" character in comparison with other material classes used for microfluidics, namely glass (including fused silica) and silicon. The huge amount of different materials available with a broad range of chemical, mechanical, electrical and optical properties as well as the multitude of different methods to manufacture microstructures in polymers allows on the one hand the selection of the optimal material for almost any given application but on the other hand this diversity often makes the correct choice of material a very difficult task, especially when one is not familiar with either the polymer chemistry or the available microstructuring techniques. This

Fig. 2 Process diagram of polymer microfabrication technologies
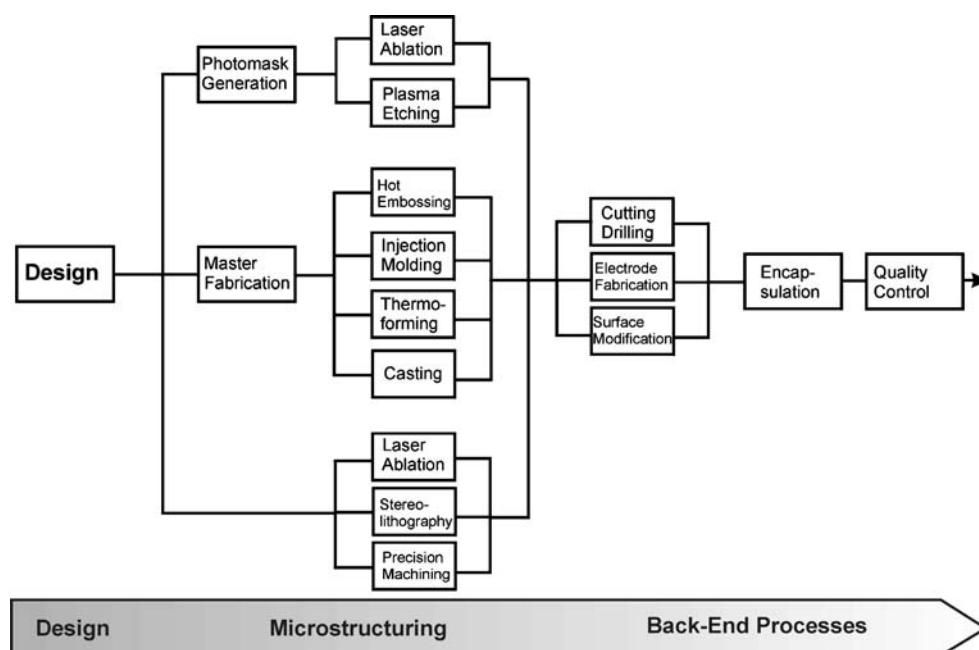
typically leads to a narrowing of the material choice in the scientific literature to only a few favourite, often-cited materials which in most cases will suffice for the desired application. It can however be debated that in many cases results could be improved by a more sophisticated selection of the polymer material.

In terms of physical parameters and thus technological pathways to fabrication, polymers can be divided into three main classes. The main parameter which has to be considered in this classification is the so-called glass transition temperature (T_g). This parameter, which can be measured as a more or less distinct bend in the curve of the specific heat capacity versus temperature (a first-order phase transition), has its origin in the molecular behaviour of the polymer material. If a polymer gets heated up at a certain temperature the energy of motion of parts of the polymer chain becomes large enough to overcome intramolecular friction. At this point in the temperature curve, larger segments of the polymer chain can suddenly start to move quite freely, leading to a significant softening of the material. Below T_g, a polymer behaves very much like a rigid, solid amorphous glass; beyond T_g, the material becomes flexible and soft. A second important parameter for the technical use is the so-called heat distortion temperature (HDT). It is a more empirically determined parameter and describes the maximum temperature for structural use of the material; beyond the HDT, the polymer cannot be exposed to any mechanical stress as it would simply give way. The third temperature relevant for polymers is the decomposition temperature (TD), at which the polymer decomposes and the polymer chains are broken, changing the basic nature of the polymer.

So according to the position of T_g and the behaviour of the polymer, the following material classes can be defined:

1. Thermosets (duroplastic materials): in these materials, which can be liquid or solid at room temperature (often called resins), the molecular polymer chains start to cross-link (a process called curing) if the polymer is heated up or is exposed to sufficiently high doses of light or other radiation, thereby generating a rather hard and inflexible three-dimensional molecular network. If the curing process has taken place once, the polymer remains stiff even if reheated, as the curing involves an irreversible chemical reaction. Thermosets can therefore not be reshaped once cured. If heated further, the polymer decomposes or burns instead of melting. T_g typically is rather high and close to the decomposition temperature (TD). Typical examples of thermoset polymers in microfabrication are the resist materials for lithography [5], for microfluidic applications especially the photoresist SU-8 (see Photolithography). Another important material in this class is polyimide, a very durable and high-temperature stable material frequently used in microelectronics. The photocurable resins for stereolithography also belong to this material class.

2. Thermoplastic materials: this class contains the technical polymers which can be structured using replication methods like injection molding or hot embossing. Thermoplastic materials show a distinct softening at T_g which makes them processable around this temperature and a rather large temperature difference between T_g and TD, allowing for a large process window. In

thermoplastic materials, no curing takes place at elevated temperatures so the molded parts can be reshaped many times by reheating. In practice, a certain degree of thermal degradation takes place so reprocessed material often does not have the same quality as virgin material. Most polymer components in the macroworld consist of thermoplastic materials, so it is not surprising that a large variety of microfabrication methods have also been developed for this material class. Typical examples are poly(methyl methacrylate) (PMMA) and polycarbonate (PC), which were among the first materials used for polymer microfabrication. For microfluidics, the cycloolefin polymers and copolymers (COP, COC) have attracted much attention in recent years owing to their favourable optical properties, moldability and low water uptake [6–8].

3. Elastomers: in elastomers, the molecular chains are longer than in the other cases and typically do not show a chemical interaction but are physically entangled. If an external force is acting on the polymer, the polymer chains disentangle and allow the polymer to stretch elastically (as a technical definition, an elastomer exhibits at least 200% elastic elongation), returning to its original shape immediately if the external force is withdrawn. Owing to their low cost and easy handling, elastomeric materials, namely poly(dimethylsiloxane) (PDMS), have become a primary material for the low-volume manufacturing of microfluidic devices. In addition their permeability for oxygen and carbon dioxide make them well suited for cell-based systems. Novel materials are being developed to overcome some of the limitations of PDMS, namely the swelling in the presence of some organic solvents [9].

As a further definition "polymer" denominates the pure material, while the word "plastic" describes a polymer with additives like fillers (for improved mechanical stability, e.g. carbon fibres), plasticizers (for easier mold fill) or stabilizers (e.g. against UV radiation). A compilation of physical and chemical properties of the most widely used polymers for microfluidic applications is shown in Table 1. A good introduction and a broad technical overview of (macroscopic) polymer technology and materials can be found elsewhere [10].

To obtain a quick overview, Table 2 summarizes the principle properties of polymeric materials in comparison with glass and silicon, historically the first materials used for microfluidics [1]. It is clear from the complexity of the task that this table can only give rough guidelines. One property which should be mentioned separately is the autofluorescence of polymers which is mostly higher than in glass. As many optical detection schemes involve fluorescence signals from biomolecules, care should be taken in the selection of materials [22–24]. Increasingly, data is also available on the zeta-potential of polymers [25] which determines the electroosmotic behaviour of the material.

Photodefinable polymer technologies

One of the technologies frequently used for the fabrication of microfluidic devices involves the reaction of a polymer material with light. This can take place constructively in the form of a polymerization reaction (photolithography, stereolithography; see Photolithography and Stereolithography), building a solid structure out of a liquid resist or destructively in the form of ablating the material with a laser beam (see Laser ablation). In terms of manufacturability, both methods have a limited device throughput, as the cycle time for the preparation of the resin and the other process steps involved are typically of the order of many minutes per step so they are currently limited mainly to academic use. In particular, the availability of SU-8 as a photoresist for high aspect ratio polymeric structures has led to a large number of academic activities with this material.

Photolithography

Close to the technological origins of microsystem technologies, conventional photoresists (i.e. thermoset polymer resins which cross-link under exposure to light) from microelectronic processes have been used to manufacture fluidic manifolds [26–28]. Due to their physical parameters (i.e. viscosity), only comparatively low structural heights (between 0.5 and 3 μm) can be realized with these materials. In the mid-1990s, however, a novel resist material was developed for the manufacturing of high microstructures in an attempt to simplify the very complex LIGA microfabrication process which involves synchrotron radiation for the resist exposure. This material is called SU-8 as its monomer contains eight epoxy groups. Very strong cross-linking takes place during exposure to UV light in a process of cationic polymerization. This leads to the main advantages of SU-8: high mechanical, thermal and chemical stability. As a side effect of this strength, however, SU-8 can be difficult to process, as it generates large internal stresses in the film, leading to structural deformation upon release from the carrier substrate with increasing film thickness. Furthermore, due to its strong adhesion, cured SU-8 can be difficult to remove from a substrate, particularly from a three-dimensional structure with large surface areas. The availability of photolithography process equipment in academic institutions, however, has also led to the widespread application of this material in the microfluidic/BioMEMS field [29–35]. Figure 3 gives an overview of some of the existing process technologies for the fabrication of microchannels using

**Table 1** Overview of polymer material properties

Name	Trade name (examples)	Density (g cm⁻³)	T_g (°C)	Heat distortion temperature (°C)	Resistivity (Ω cm⁻¹)	Water absorption (%)	Refractive index	Young's (tensile) modulus (MPa)	Thermal expansion coeff. (10^{-6}/K)	Resistant against	Not resistant against	Organic solvent stability
PMMA [11]	Perspex, Plexiglas	1.19	110	90	1×10^{15}	2	1.492	3,200	80	Acids, bases (medium conc.), oil, petrol	Alcohols, acetone, benzole, UV radiation	Attacked by most solvents (e.g. acetone, benzene, dichloromethane)
PC [12]	Makrolon, Calibre, Lexan, Trirex	1.19–1.24	148	125	1×10^{14}	0.30	1.58–1.6	2,200–2,400	70	Alcohols, acids	Hydrocarbons, ketones, KOH	Attacked by most solvents (e.g. acetone, methylene chloride)
PP [13]	Ektar, Fortilene, Hostalene	0.9	0–10	100–110	$>1\times10^{14}$	0.01–0.1	1.49	1450	100–200	Acids, bases, Alcohol, organic solvents, fats	Petrol, benzole, hydrocarbons	Xylol, tetraline, decaline
PS [14]	Styron, Noryl	0.9–1.24	100	70	$>1\times10^{16}$	<0.4	1.59	2,300–4,100	30–210	Bases, alcohols	Conc. acids, ether, hydrocarbons	Attacked by most solvents (e.g. acetone, benzene, dichloromethane)
PE (LD/HD) [15]	Rexlon, Bapolene, Dowlex	0.91 (LD) 0.967 (HD)	110/140	80/100	10^{15}–10^{18}	<0.015	1.51 (LD)	200/1,000	170/200	Acids, bases, alcohols, oil	Hydrocarbons	Trichlorobenzole, xylole, hexane
COC [16]	Topas, Zeonor	1.02	78	170	$>1\times10^{14}$	0.01	1.53	2,600	70	Acids, bases		
COP [17]	Zeonex	1.01	138	140	$>1\times10^{17}$	0.01	1.525	2,400	70			
PEEK [18]	PEEK	1.3	143	250	$>1\times1{,}016$	0.5		3,700	17	Most organic and inorganic substances	Conc. nitric acid, sulfuric acid, UV light	
PDMS [19]	Sylgard	1.03	−120	200	1.2×10^{14}	0.1	1.43		960	Weak acids and bases	Strong acids, hydrocarbons	
SU-8 [20]		1.19	210		2.8×10^{16}		1.58	2,000	52	Acids, bases, most solvents		
PI [21]	Kapton	1.42	360–410	400	$>1\times10^{12}$	2.9–4	1.7	2,500	20	Acids, bases, solvents		No known solvents

Table 2 Comparison of materials for microstructuring

	Silicon	Glass	Technical thermoplastics (e.g. PMMA, PC, PEEK)	Thermoset polymers	Elastomers
Microfabrication	Easy–medium	Easy–medium	Easy	Medium	Easy
Structuring processes	Wet and dry etching	Wet etching, photostructuring	Injection molding, hot embossing, thermoforming, laser ablation	Casting, lithography, etching	Casting
Possible geometries	Limited, 2D	Limited, 2D	Many, 2D, 3D	Mostly 2D, 3D possible	Mostly 2D, 3 D possible
Assembly	Easy	Medium	Easy	Medium	Easy
Interconnections	Difficult	Difficult	Easy	Easy	Easy–medium
Mechanical stability	High	High	Low–medium	High	Very low
Temperature stability	High	High	Low–medium	Medium	Low
Acid stability	High	High	High	High	High
Alkaline stability	Limited	High	High	High	High
Organic solvent stability	High	Medium–high	Low–medium	Medium–high	Low
Optical transparency	No	High	Mostly high	Partly	High
Material price	Medium	Medium–high	Low–medium	Medium	Low

photoresists. First, a layer of resist is spin-coated onto a substrate, usually a silicon or glass wafer. It is then structured with a photomask to the target structure. This creates open microchannels which can be used for e.g. cell growth experiments [36]. In the so-called fill process (middle column in Fig. 3) [37–43], a second sacrificial material, e.g. Araldite or another photoresist, fills the structure and creates an even surface for the second layer of resist. In this second layer, access holes to the sacrificial layer must be present to expose the sacrificial layer to a solvent after processing the second resist layer. The main problem in this process is the slow dissolution of the sacrificial layer as diffusion is the only transport mechanism in the solvent. This method is therefore limited to comparatively short channels. A second method (right column in Fig. 3) uses a lamination process (application of heat and pressure through a thin film) to close the open SU-8 channels. The lamination can be carried out using a film of dry SU-8 or any other laminate film [44, 45], e.g. commercially available PE/PP films (see also Encapsulation). This method allows for a rather simple process; however,

Fig. 3 Lithography processes for the formation of microchannels
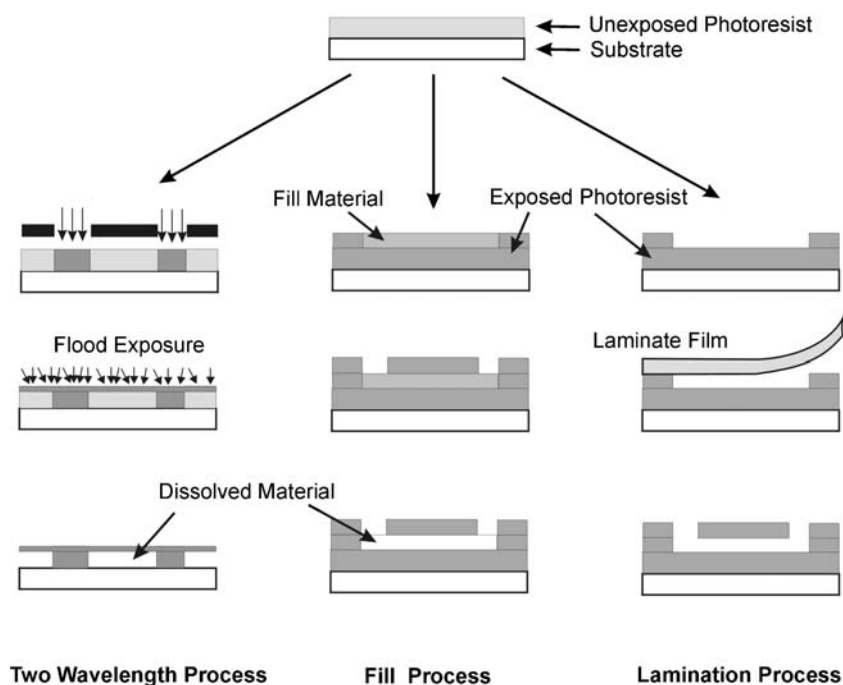
care has to be taken in the selection of lamination parameters to fully seal the structures. A third process concept (left column in Fig. 3) [46] makes use of the fact that SU-8 has a different optical density (= absorption depth) for different wavelengths. In a first exposure with 365-nm light through a mask, the desired channel structure is defined in the resist. This is followed by a flood-exposure (without mask) with light of 254 nm. This light has a much shorter absorption depth and exposes only the top of the SU-8 layer. After baking and developing the SU-8, closed microchannel structures can thus be created (Fig. 4). Similar results can be obtained by partial exposure with different exposure doses [47, 48]. Other processes use metal masks or other embedded masks after the first SU-8 layers to create the same effect; this complicates the process significantly [49]. A collection of processes and references on SU-8 can be found elsewhere [50].

Hydrogels are a special class of photostructurable polymers that show a significant volume change either in the presence of a suitable solvent or on change in pH value of the surrounding solution. This property allows for the fabrication of active components, especially valve structures, in a polymer device [51–54]. Figure 5 shows the fabrication sequence of such a valve structure [55]. A given microchannel structure is flushed with the photosensitive pre-polymer mixture, e.g. a mixture of isobornyl acrylate (IBA), 2,2-bis [p-(29-hydroxy-39-methacryloxypropoxy)phenylene]propane or tetraethyleneglycol dimethacrylate (TeEGDMA), and Irgacure 651 as photoinitiator. A mask defines the area where hydrogel polymerization should take place. The hydrogel pre-polymer is then exposed through this mask, cross-linking

and solidifying only in the exposed areas. After exposure, the unlinked remains of the pre-polymers are washed away, leaving a hydrogel structure in place. Other methods use gelatine as a sacrificial material to form hydrogel microfluidic networks [56].

Other photostructurable materials include elastomeric materials based on perfluoropolyethers (PFPEs) [6], dry resists [57–59], epoxy resins [60] and parylene [61]. A simple method to use laser printer polyester toner to define a structured layer was reported by Lago and the group of Xia [62–66]. Photolithographic contact liquid polymerization (CLiPP process) in a stainless steel box was described by Hutchison et al. [67].

Stereolithography

A well-established method for rapid prototyping in the macroworld is stereolithography. The structure is created by exposing liquid resin locally to two high intensity light beams, usually from one (with a split beam) or two laser sources. Using two beams allows the light of each single beam to penetrate the liquid without generating a photoinduced cross-linking. Only at the location where the two beams meet is the light intensity high enough to cross-polymerize the photoresist [68–71]. In practice, a vessel containing the liquid resin in placed on a stage which can be moved in the z direction. Movement in x and y is usually realized by scanning the laser beam. By computer-controlled motion, the desired structure is thus built up volume element by volume element (so-called voxel). The advantage of this method is the simplicity of the process and the fast time to produce the first device [72, 73]. Also, structures can be directly built around components made out of other materials, e.g. silicon [74] or SAW sensors [75]. Disadvantages are the comparatively long cycle time for each device due to the serial character of the method; it is therefore typically used for prototyping or low volumes. Also the surface roughness can be quite high, depending on the selected voxel size and the accuracy of the motion control in the three axes. Furthermore, the choice of material is rather limited. A variant of the process is the so-called frontal-photopolymerization (FFP) [76, 77], where a polymerization front is generated through an exposure of a mask with a collimated UV light source. The height of the structure is determined by the exposure length and dose.

Laser ablation

Another method for the rapid prototyping of microfluidic structures is laser ablation (for recent reviews see [78, 79]). In this case, a high-intensity laser beam is focussed onto the material and the concentrated energy of the beam evaporates the material at the focal point. The geometry can be realised either by using a mask and exposing the substrate
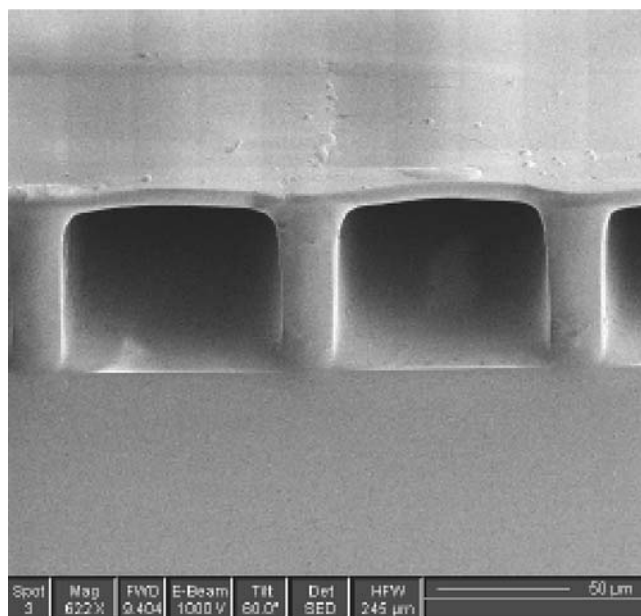
Fig. 4 SEM image of a microchannel in SU-8 formed with the two-wavelength process (courtesy of B. Gray, Simon Fraser University)

Fig. 5 Process for the formation of a valve in a microchannel using a photodefinable hydrogel (adapted from [55])
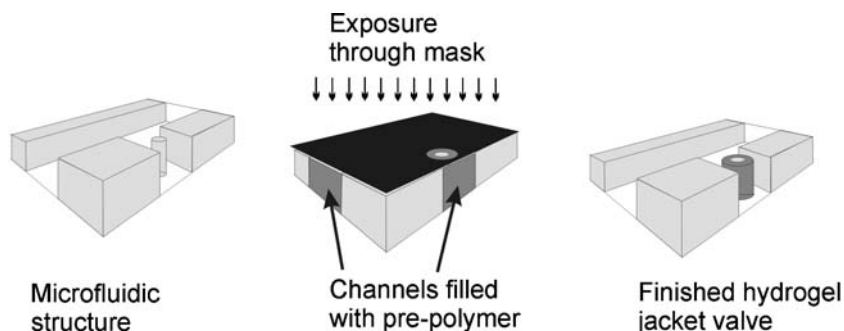

through the mask or by move either the laser beam or the substrate in x and y direction to generate the desired pattern. As the lasers used for this method are typically pulsed lasers (typically excimer lasers [80] with a wavelength of 193 nm [ArF], 248 nm [KrF] and 308 nm [XeCl], Nd:YAG lasers with wavelengths of 266, 352 or 532 nm or Ti:sapphire lasers), each laser shot will ablate a defined amount of material, depending on material type, laser wavelength and intensity. Typical values for the ablation depth per laser shot are of the order of 1 μm. Therefore, for deeper structures, several shots have to be fired for each location. This leads to a characteristic surface roughness of laser-ablated micro-channels. The ablated material (so-called debris) has to be removed from the device by suitable means. Figure 6a shows an example of a microwell structure fabricated using this technology. A commercial application can be found in a microfluidic electrospray nozzle for MS injection (Fig. 6b). Here the microchannel is laser-ablated in thin laminated polyimide sheets [81, 82]. In general, laser ablation is well suited for the structuring of thermoset polymers like PI [83, 84]. One of the critical features of laser ablation is the fact that the interaction of the material with the intense laser light changes the surface chemistry and surface charge of the material in comparison with the bulk property [85–88]. This effect is difficult to control and can lead to strong variations in the performance of the device in surface-sensitive application fields like electrokinetic transport systems. An alternative is the use of CO_2 lasers which have a continuous beam and cut the material [89, 90] or femto-second lasers [91–93] which also allows the machining of transparent materials.

Replication methods

The enormous economic success of polymers in the macroscopic world is largely owing to the fact that low-cost, high-volume fabrication methods exist. These methods are all based on the replication of a master structure (the geometrical inverse of the desired structure). Over the last 10 years, these replication methods have allowed large progress in the microfabrication field [94] and built the

foundation for the commercialization of microfluidic devices particularly in price-sensitive markets like the point-of-care (POC) diagnostic market. In terms of commercially applicable methods, hot embossing and injection molding play the major role, with microthermoforming being introduced recently. In the academic world, elastomer casting is the dominant method.
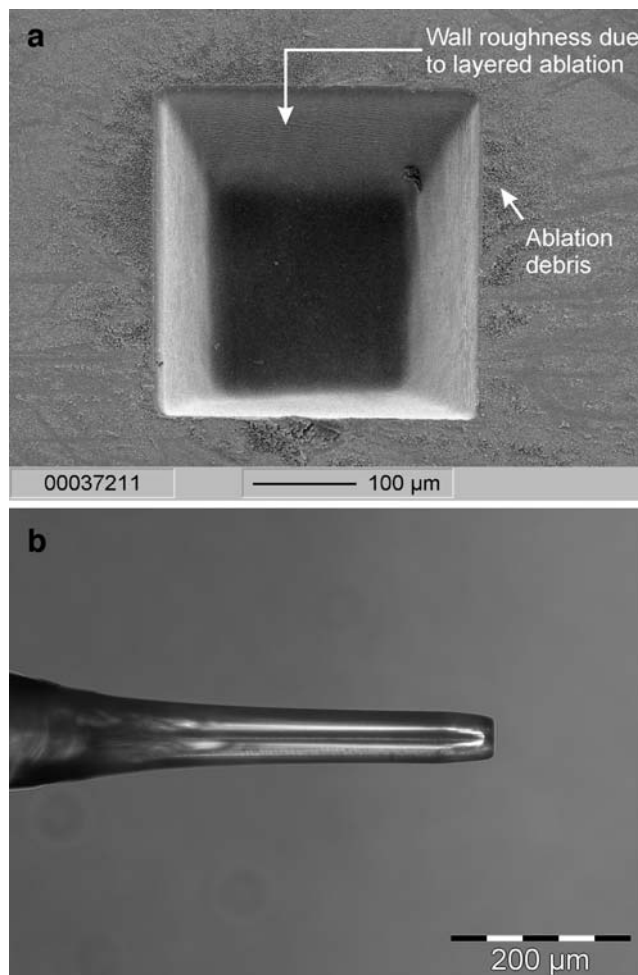
Fig. 6 a Laser-ablated microwell structure. The surface roughness and surrounding debris can be clearly seen. **b** Injection tip for MS electrospray injection laser-ablated in a polyimide sheet (courtesy of R. Brennen, Agilent Technologies)

Replication master fabrication

All replication methods have in common the need for a master structure (often also referred to as the replication tool, mold or mold insert). Although the requirements for such a master structure differ with respect to the physical parameters of the chosen replication method (e.g. force, temperature), four basic statements can be made: (a) the geometrical replication result can only be as good (or as bad) as the geometrical accuracy of the master, (b) for the ability to separate mold and molded part (demolding step), no undercuts in the structure itself can be allowed, (c) the surface roughness of the master should be as low as possible (ideally peak–valley values of below 100 nm), and (d) a suitable interface chemistry between master and substrate has to be chosen. In order to generate the master structure, principally all microfabrication methods are suited. The proper selection of the master fabrication technology [95–97] is one of the crucial steps in the product development of commercial microfluidic devices, especially as there is no generic recipe for this selection. Table 3 lists the most common master fabrication methods with their properties. For commercial applications the most suitable methods are nickel masters which are generated by electroplating of photoresist or silicon structures [98] and (ultra)precision machined stainless steel masters [99]. For larger structures, micro electrode discharge machining (μ-EDM), which is among the most common methods for stainless steel tooling in the macroworld, becomes possible. Both methods combine long master lifetimes with good geometrical definition at reasonable cost and availability. The LIGA process generates the masters with the highest precision and best surface roughness available; however, the manufacturing process is complex, expensive and time consuming. On the opposite side, masters consisting of silicon can be made quickly [95] at low cost; due to the brittleness of the material they can

mainly be used for casting and hot embossing. A recent development is the use of polymers (e.g. fully cured SU-8 [100], other epoxy resins or even PDMS [101, 102]) as a material for replication masters. The master lifetime in this case is limited typically to a few ten to hundred replications at moderately complex designs and low aspect ratios. For more complex geometries, namely when comparatively large structural dimensions (millimetre-sized features) have to be combined with small features, hybrid tooling such as the combination of precision machining for the larger features and lithography [100, 103] or laser ablation [104, 105] for the finer features can offer a solution. Figure 7 shows examples of a multilevel nickel, a silicon and a SU-8 master structure.

Hot embossing

Hot embossing has established itself in the last 10 years as a widely used method for the fabrication of polymeric microstructures both in academia and in industry [106–113]. The reasons for this development are the comparatively simple process which simplifies the selection of process parameters, the comparatively low requirements for master structures, the large range of suitable materials and the availability of commercial instrumentation.

The process itself consists of the following steps:

(a) The polymer substrate (wafer or sheet material) is placed in the system and heated in vacuum to a temperature just above the glass transition temperature;
(b) The master structure is also heated to the same (or slightly higher) temperature;
(c) The master structure is pressed into the polymer substrate with a force of typically 500 N cm^{-2} in the case of PMMA or PC, the force depending on design, material and master material;

Table 3 Overview on main master fabrication methods

Microfabrication technology	Choice of geometry	Minimum feature size	Height	Total surface area	Aspect ratio	Lifetime	Cost	Commercial availability
Wet silicon etching	−	+	0	++	−	+	+	++
Dry silicon etching	+	++	+	++	+	−	0	+
Photoresist	+	++	+	++	++	−	+	0
Polymer casting (elastomer)	+	++	0	++	−	−	++	−
Optical lithography & electroforming	+	++	+	++	0	+	0	0
Laser ablation & electroforming	++	+	+	−	+	+	−	−
LIGA	+	++	++	−	++	+	−	−
(Ultra) precision micromachining	+	0	+	+	0	++	−	−
μ-EDM	−	0	+	−	+	++	−	−

Fig. 7 Examples of replication masters: **a** electroplated nickel mold insert with multiple depth, **b** silicon tool manufactured with deep reactive ion etching (reprinted with permission from [100]), **c** master structure manufactured from SU-8 (reprinted with permission from [100])
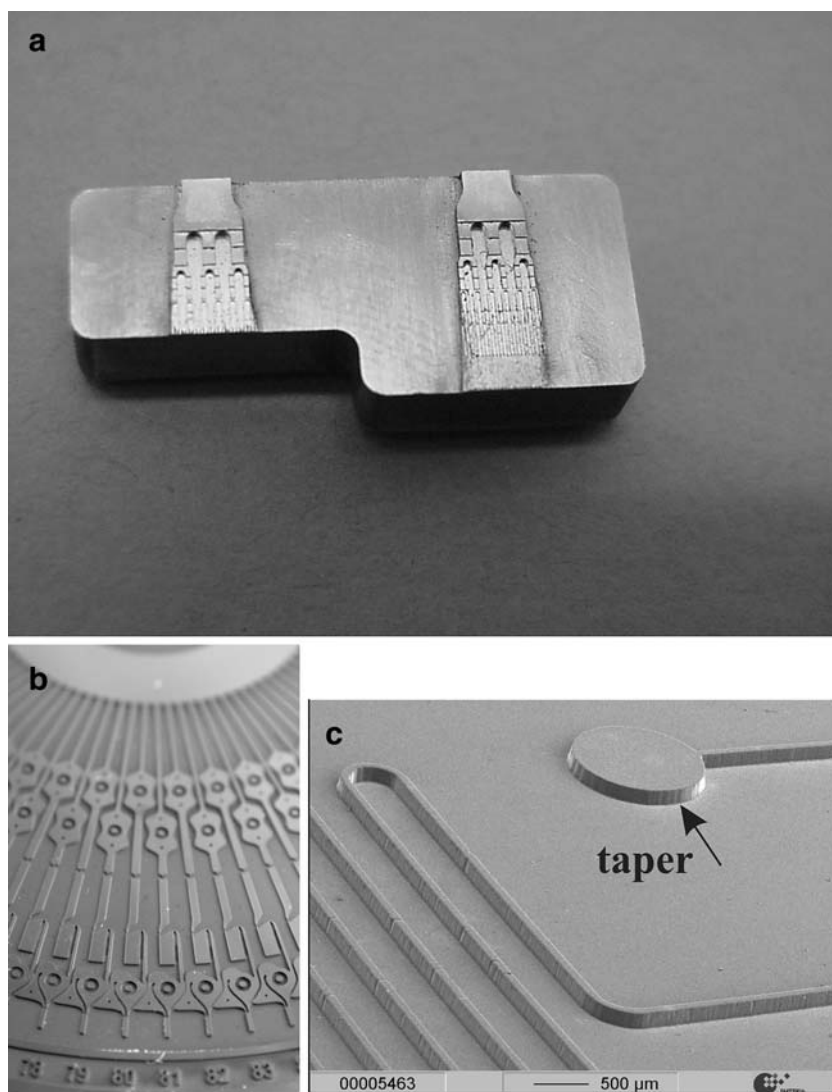
(d) Master and substrate are isothermally cooled to a temperature just below T_g and then separated (demolding).

Typical cycle times which can be achieved by hot embossing are of the order of 4–15 min for a 4″ wafer. This shows that the technology is rather suited for prototyping and low to medium volume productions which makes it an attractive process for academic activities [96, 114–132]. Industry developments move towards larger embossing areas ([133], up to 8″ or SBS titerplate format [134]) and shorter cycle times [135].

Critical for the success of the replication process is a uniform temperature distribution across the master structure, the vacuum to prevent trapped air forming bubbles, a good surface quality of the master and a chemical compatibility between master and polymer material to prevent sticking. Figure 8 shows a commercially available hot embossing system. An example for a typical embossing result can be seen in Fig. 9, where a two-level mechanically

precision machined master is replicated. A big advantage of the process is its very high replication accuracy which can be seen from the replication of the machining grooves of the master in Fig. 9. This accuracy enables the reliable fabrication of structures in the few tens of nanometres range. In this size range, the process has been named nanoimprint [126, 136–140] and is one of the potential methods for future lithography in the nanometer range. Figure 10 shows an example of such a nanoimprinted pattern. As no phase transition of the material takes place during the process, the internal stress of the material tends to be rather low, leading to low birefringence and little warpage, which are important features if optical detection technologies in the microfluidic application are employed.
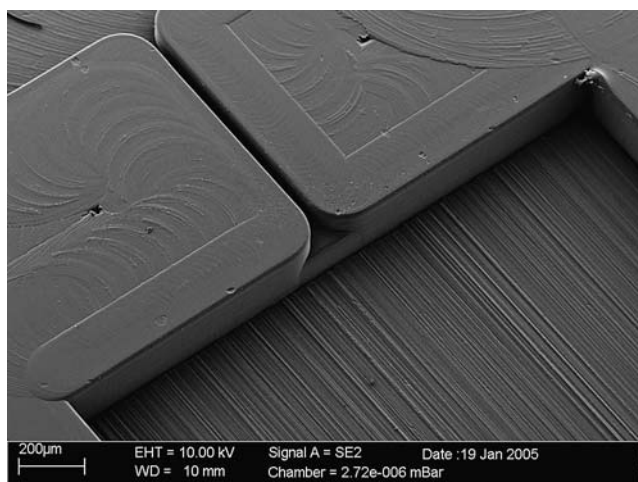
Microthermoforming

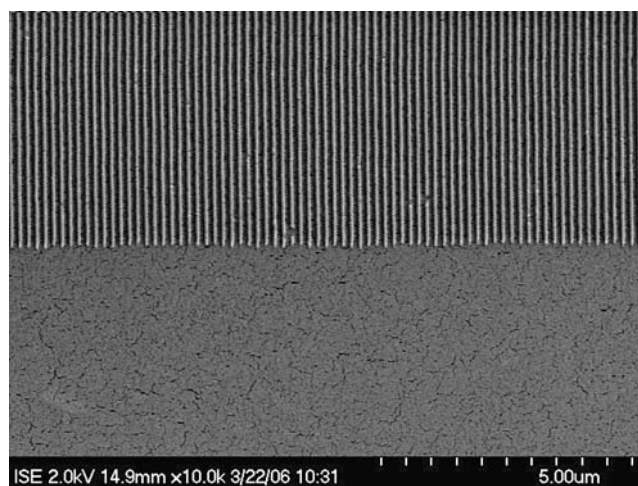Some applications have recently been published on microthermoforming [141, 142], a technology known in the
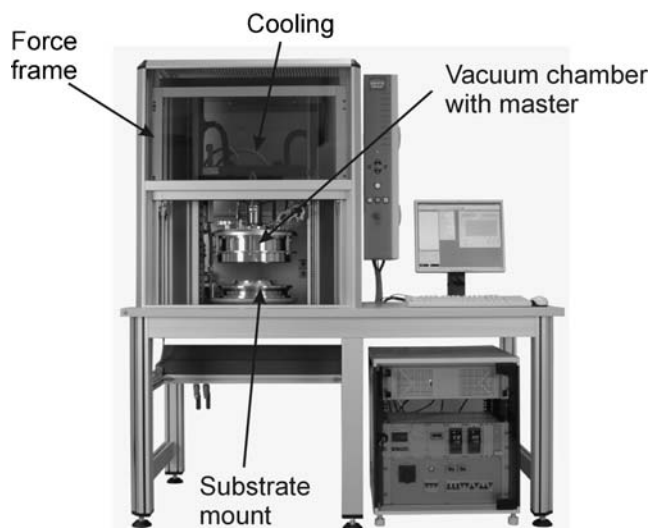
Fig. 8 Hot embossing system (courtesy of E. Piechtoka, Jenoptik Laser Optik Systeme GmbH)

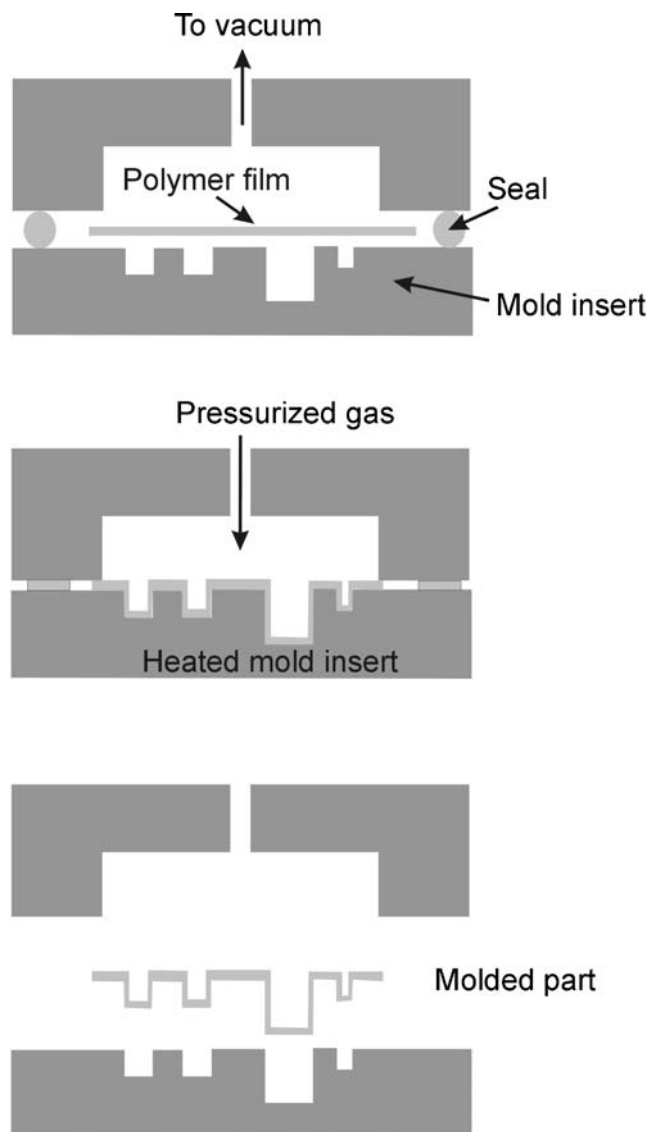Fig. 10 Example of a nanoimprinted structure (courtesy of E. Piechotka, Jenoptik Laser Optik Systeme GmbH)

macroworld for the low-cost production of thin-walled plastic devices like yoghurt cups. The process is shown in Fig. 11. A thin polymer foil (typically ≤50 μm) is clamped in a mold tool which on one side contains the microstructure. The foil is heated up to approximately 10 °C above T_g and pressed into the microstructured master by compressed gas at 40–60 bar. The polymer then is cooled down to 20 °C below T_g and the part is ejected. Advantages of the process are its simplicity and speed. The replication accuracy is limited compared with hot embossing, as well as the ability to form high aspect ratio structures and sharp angles. Thus the process is suited for rounded structures where the geometrical accuracy is of less importance. A first commercial application, a multichannel capillary electrophoresis system, is scheduled for launch this year [143].

Fig. 9 Example of a fluidic structure hot embossed with a mechanically machined master structure. Note the machining traces on the embossed surface (courtesy of E. Piechtoka, Jenoptik Laser Optik Systeme GmbH)

Fig. 11 Diagram of the microthermoforming process

Injection molding

By far the most widespread fabrication process for polymers in the macroworld is injection molding. Therefore it is not surprising that the first application of this production technology for microfluidic components was published over 10 years ago [144]. However the distribution of this process (for a recent review see e.g. [145]) in the academic world remains rather limited [146–156] due to the comparatively high demands in terms of equipment and process. For the commercial success of microfluidics, it will nevertheless play a crucial role.

In Fig. 12, an injection molding machine is shown in cross section. The polymer material is fed as pre-dried granules into the hopper. In the heated barrel, a screw transports the material towards the injection port of the molding tool. During this transport, the polymer melts and reaches the tool in liquid form with a melt temperature of the order of 200–350 °C depending on the polymer. It is now injected under high pressure (typically between 600 and 1,000 bar) into the mold which contains the microstructured mold insert. For microstructure replication, it has to be evacuated to achieve a good filling of the mold and to prevent the formation of air pockets. Depending on the surface-to-volume ratio of the structure, the mold can be kept at temperatures below the solidification temperature of the polymer (typically between 60 and 120 °C, so-called cold-cavity process) or, in the case of small injection volumes and high aspect ratio structures, has to be kept at temperatures above T_g and cooled together with the melt. The need for this so-called variotherm process drastically increases the cycle time; therefore, in commercial applications one goal of the development of the microstructure is the moldability with a cold cavity process. Typical cycle times for a cold-cavity process are of the order of 30 s– 2 min; a variotherm process can take up to 5 min. After opening the mold, the molded part will be ejected. Normally, remains of the material from the injection port

(so-called sprue) will still be connected to the part which has to be removed, either mechanically by cutting, sawing or breaking, or with a laser.

Figure 13 shows an example of a multi-level structure injection molded from the mold insert shown in Fig. 7a. The big advantages of injection molding are the ability to form three-dimensional objects, which, in the case of microfluidic devices, means e.g. the integration of fluidic interconnects [155] (see Fig. 14) or through-holes. Furthermore, the ejected part does not normally need additional mechanical process steps, thus reducing the production time further. Owing to the highly industrialized development of the process, a large variety of equipment suppliers are available as well as automation solutions for large-volume manufacturing. The disadvantages are the complexity of the process and the need for an often mechanically complicated molding tool which is capable withstanding high temperatures and forces while retaining the highest mechanical precision. Furthermore, as the material undergoes a phase change in the process, internal stresses, shrinkage and birefringence are usually higher than in the other replication processes and have to be taken into account.
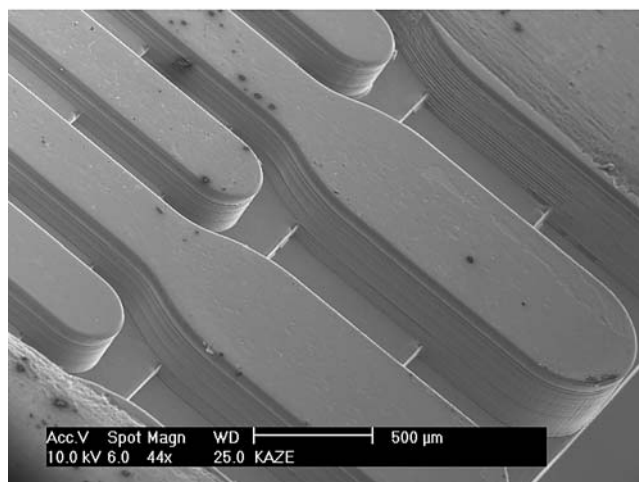
Injection compression molding (CD process)

A combination of basic principles of injection molding and hot embossing can be found in the injection compression molding process. Originally developed for the optical data storage industry (CDs and DVDs), several attempts have been made to apply this process for microfluidic applications, with significant success in the field of centrifugal microfluidics (for recent reviews see [157, 158–177]). It combines the advantage of an even quicker cycle time than injection molding (down to about 5–10 s) with the replication accuracy of hot embossing basically by compressing the liquid melt in the cavity with a piston to achieve complete mold filling. The disadvantage is the fixed format, as most of the equipment is designed for CD

Fig. 12 Cross-sectional diagram of an injection molding machine
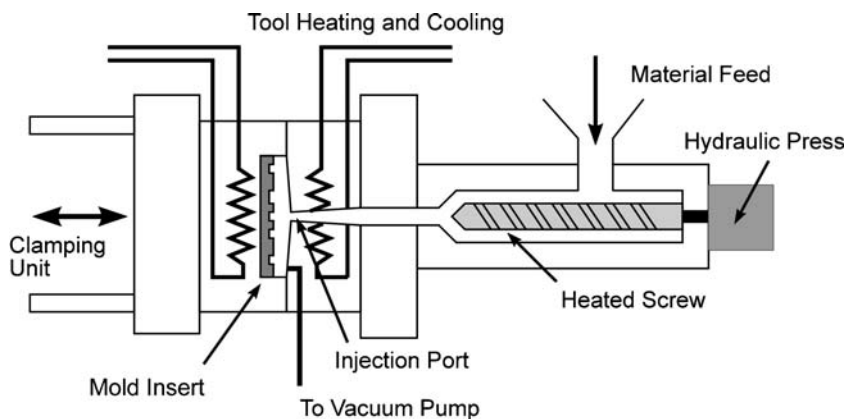
Fig. 13 SEM of an injection-molded fluidic structure replicated from the tool shown in Fig. 7a

or DVD production. However, many injection molding machines can nowadays be updated with a compression unit, alas adding complexity to machine and process.

Casting

By far the most widely published polymer fabrication process is the casting of elastomeric material [178], also often referred to as soft lithography (for recent reviews see [179–181]). Over recent years, the basic casting process has been modified into a large variety of different variants (e.g. microcontact printing μCP [182], replica molding, micro-transfer molding μTM [183], micromolding in capillaries MIMIC [184], solvent-assisted micromolding SAMIM [185]). The success of this process family is mainly owing to the following properties: (a) process simplicity, (b) material properties, (c) cost, (d) advantageous surface chemistries and (e) replication accuracy. The underlying process is shown in Fig. 15. The starting point is the preparation of the elastomer. The most often used materials, Sylgard 184® by Dow Corning, General Electric RTV 615 and Elastosil® by Wacker are two-component systems, where typically ten parts of the base elastomer are mixed with one part of the curing agent. The curing itself is an organo-metallic cross-linking reaction, where three-dimensional bonds are formed. The resulting elastomer is optically transparent (down to about 300 nm), electrically insulating and chemically inert. To prevent the formation of air bubbles during mixing and casting, it is advisable to thoroughly degas the mixture, e.g. in an exsiccator or a simple low vacuum system. Typical degassing times are of the order of 20 min. The mixture is then simply poured over the master (e.g. an etched silicon wafer in a glass beaker) and cured. The curing can take place at room temperature in about 48 h or at elevated temperatures, e.g. 30 min at 115 °C, with a typical process window in the range between 40 and

80 °C. Curing temperature and ratio of the curing agent determine the stiffness of the elastomer sheet which can thus be adjusted depending on the application. After curing, the elastomer sheet is simply peeled away from the master. For a better release, it is advisable to make the surface of the mold hydrophobic, e.g. by silanization. Reservoir holes can simply be punched into the cured material. Structured PDMS sheets can easily be bonded to a glass plate or another sheet of polymer owing to its excellent adhesion properties. For a non-permanent bond for low-pressure applications, the PDMS sheet can simply be pressed against the closing sheet (cleanliness of both contact surfaces is very important!). The bonding strength is increased by a hydrophilic surface treatment either of the PDMS, the cover lid or both. PDMS is particularly suited for a plasma treatment, e.g. in an oxygen plasma at 0.1 mbar for 10–30 s at 100 W. This can lead to a permanent bond between two PDMS layers, if the assembly takes place immediately after the surface treatment. Theoretically, a PDMS structure can be reused after being peeled off the cover lid again; in practice, however, the surfaces are likely to be contaminated and a second sealing does not hold tight. With this method, three-dimensional structures can be built up layer by layer, e.g. fluidic channels and mixers [186, 187], valves [188, 189] and pumps [190–194], or structures holding biological samples [195]. Highly complex structures with a high number of pneumatically or hydraulically activated valves and pumps connected to an active microfluidic matrix to perform programmable tasks have also been fabricated with this material [196–202]. The replication accuracy is extremely high; the replication of structures below 10-nm feature size have been reported [203]. Two application field has proven to be especially suited for elastomer use: chips for the examination of cells (for reviews see [204–209]) [210–219] and bacteria [220, 221], as the elastomers are permeable for oxygen and carbon dioxide which facilitates cell culturing in microchannels and protein crystallization due to the precise reaction
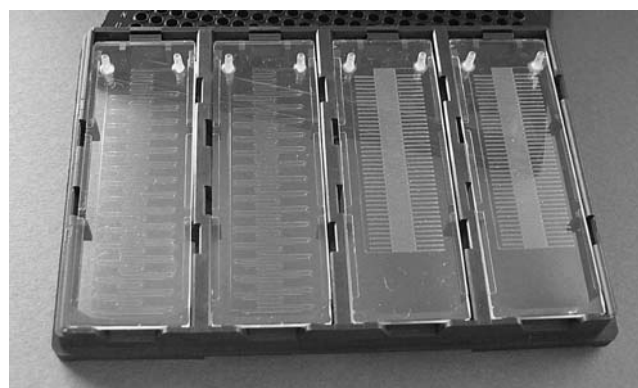
Fig. 14 Injection-molded chips for continuous PCR with integrated fluidic interconnects

Fig. 15 PDMS casting processes
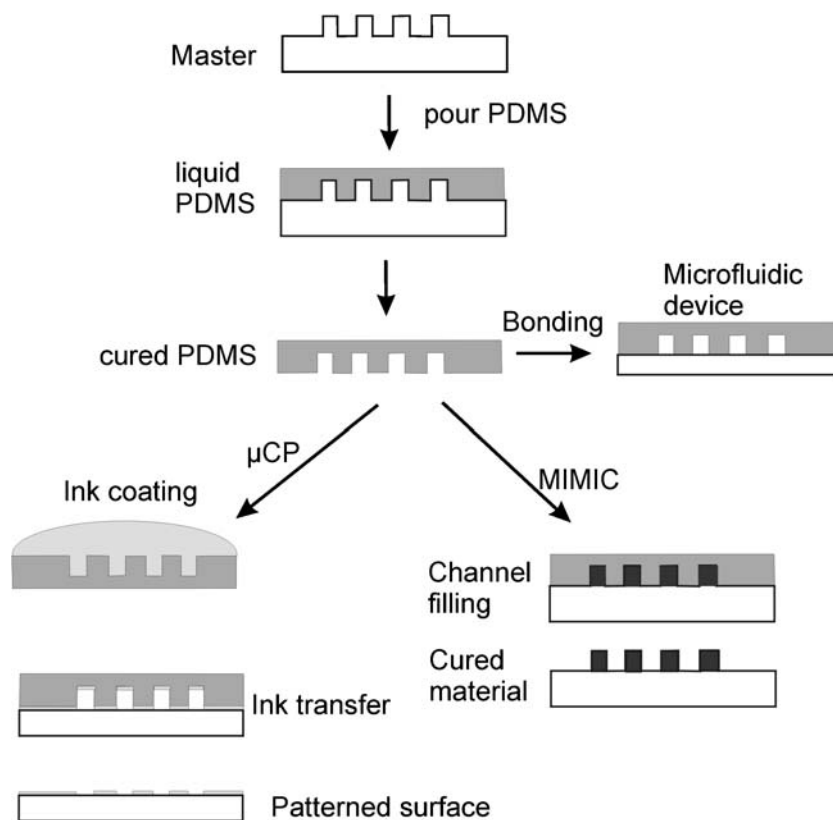
control [222, 223]. This has supported a general trend in microfluidics, from biomolecular analysis to more complex biological systems [224, 225]. Elastomer structures have also been reported as masters for replication processes [100, 101] as well as a mold for the in situ polymerization of liquid pre-polymers (e.g. for PMMA [226–228]).

In addition to elastomers, liquid resins (thermosets) have been used in casting microfluidic structures since they can then be cured using either temperature or UV light. This allows the use of materials like thermoset polyester (TPE) [229–231] or resins containing metal powder for increased stability for the use as replication masters [100]. Also active electronic components can be embedded in a microfluidic structure built this way.

Industrial considerations on replication technologies

In terms of commercial viability, each of the different replication technologies displays a distinct behaviour as summarized in Table 4. The resulting economy of scale in the production of microfluidic devices is shown in Fig. 16, where the approximate cost per device is plotted versus the production volume. Injection molding shows by far the highest initial cost, with high capital investment cost in equipment as well as the mold itself and the mold insert (master). For higher volumes, however, the short cycle time significantly contributes to the strong decrease in cost per

device. In comparison, hot embossing equipment has a similar cost while only requiring a mold insert for the replication, thereby lowering the initial cost. For higher volumes, the longer cycle time reduces the economy of scale so that for a certain production volume hot embossing eventually becomes more expensive than injection molding. Casting has only very little initial equipment cost, mainly the replication master. The dominant cost factor here is process time (e.g. labour and lab costs), which does not generate a significant economy of scale, i.e. the cost per device remains almost constant. This figure explains why casting and hot embossing are currently seen mainly as prototyping or low- to medium-volume production technologies and are therefore preferred in the academic environment, while for large-volume manufacturing in an industrial environment which e.g. is required in the field of point-of-care diagnostics, injection molding, despite all the technological challenges, is the dominating process.

Further techniques

Two further structuring techniques for polymer microfluidic systems should be mentioned: (a) precision machining and (b) plasma etching.

The availability of highly precise and very small (diameter down to about 30 μm) machine tools have made

Table 4 Comparison of the different replication processes

| Process	Process and equipment setup	Equipment/ infrastructure requirements	Tooling requirements	Cycle time	Geometrical flexibility	Equipment availability	Production automation	Process availability
Casting	Simple (hours)	Very low	Very low(<2 k$)	Long (min– hours)	High	No special needs	Not existing	Yes
Hot embossing	Medium (hours–days)	Low (some water & 10 kW elec.)	Low (mold insert, 2–15 k$)	Medium (min)	Medium (2D)	Various suppliers	Medium	Limited
Injection molding	Difficult (days)	High (water & 20 kW elec., material drying & feed)	High (closed cavity mold, 20–150 k$)	Short (sec– min)	High (3D)	Various suppliers	High	Partly yes
CD process	Difficult (days)	High (water & 20 kW elec., material drying & feed)	High (closed cavity mold, 10–100 k$)	Very short (sec)	Limited	Medium	Very high	Yes

the fabrication of polymer microfluidic structures by direct machining possible [232, 233]. The advantage of this method is the rapid turnaround from CAD data to the finished device. As polymers are soft materials, the lifetime of such very fine machine tools is acceptable. The disadvantages are the comparatively long processing time per device, which can be of the order of hours or even days for a more complex device (making this method a prototyping method instead of an industrial fabrication method) and the comparatively rough surface (peak-to-peak roughness R_z up to 10 μm, median roughness R_a around 1 μm, see also Fig. 9), which might not be smooth enough for given application, e.g. in the case of the need for optical quality channels. Figure 17 shows an example of a micromachined PMMA substrate.

The second method is the plasma treatment (plasma etching) of thermoset polymers, namely polyimide (for a review, see [234]) [235–239]. Although this method requires a further masking step (e.g. with a metal layer) to define the areas to be structured, the availability of large plasma systems allows for an acceptable process time per device. It furthermore is a technology that is at least theoretically compatible with most semiconductor processes and can therefore bridge the gap between the normally distinct worlds of silicon and polymer microfabrication.

Back-end processing

As indicated in Fig. 2, the microfabrication step usually does not yield yet a functioning microfluidic device. Instead, one or more processing steps, called back-end processing, have to be carried out to generate the targeted functionality. In economic terms, the back-end processing steps can make up to 80% of the device manufacturing cost, a figure comparable with experiences in microelectronics or sensor technology, where packaging has roughly the same share of cost.
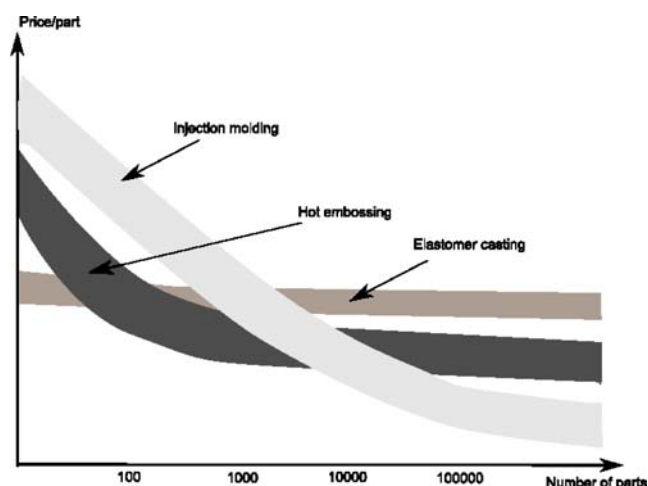
Fig. 16 Economy of scale considerations for the polymer replication processes (adapted from lecture notes of Prof. R. Zengerle, IMTEK, University of Freiburg)
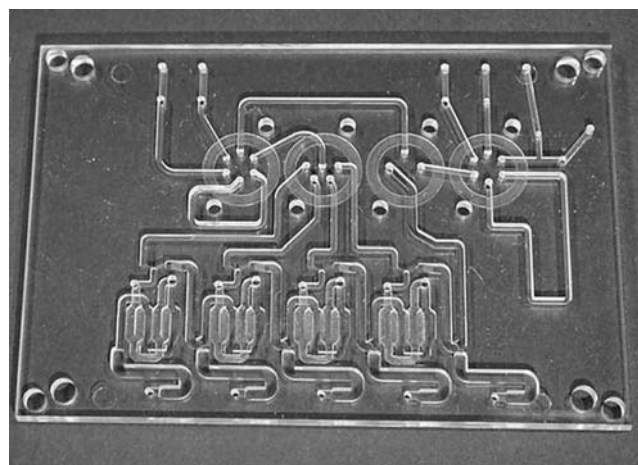
Fig. 17 Microfluidic device fabricated using mechanical precision machining. Typical channel dimensions are 800 by 800 μm (courtesy of S. Drese, IMM, Mainz)

Cutting and dicing

If the microfluidic device is manufactured from wafer or sheet material by hot embossing, laser ablated or fabricated by lithography on a wafer, the individual device often has to be diced out of the polymer substrate. This can be realized using a mechanical saw (typically a wafer saw), by water jet or by a laser (typically a CO_2 laser). It is advisable to include features which facilitate the separation of the device from the substrate in the initial design, e.g. outlines or trenches which reduce the material thickness.

Electrode fabrication

An increasing number of devices employ conducting elements, either as electrodes for electrochemical detection [240–244], as electrodes for the manipulation of liquids or biological material in the case of dielectrophoresis [245, 246], as base layers for chemical or physical sensing in e.g. surface plasmon resonance [247] and hybridization sites or as simple pads or wires to connect the chip to electronic circuitry. The fabrication of these conducting areas can be realized by a variety of methods. Closest to the microelectronic fabrication technologies are the so-called thin-film technologies of sputtering and evaporation. In both cases, a thin (typical thickness between 50 and 250 nm) metal film (typically aluminium, gold, chromium or platinum) is deposited in vacuum onto the polymer substrate. The critical process parameter in these cases is the substrate temperature. It should be kept as close to room temperature as possible, as polymers have typically a thermal expansion coefficient (see Table 1) which is about one order of magnitude higher than that of metals. High thermal gradients therefore lead to a cracking of the electrodes. For most material, the metal deposition takes place through a metal shadow mask which projects the pattern onto the substrate. This method has a geometrical resolution of the order of a few tens of micrometres. For smaller electrodes, the lift-off lithographic technique has to be used which involves photoresist and a development step. As these steps are often chemically incompatible with most thermoplastic polymers, this method is limited mainly to thermoset polymers (polyimide, SU-8 etc.). Another aspect which has to be addressed is the adhesion of the metal film on the polymer. This can be enhanced either by using an adhesion promoter, typically a second metal, e.g. chromium underneath a gold layer, or by a pre-treatment of the polymer e.g. by oxygen plasma or commercially available adhesion promoters.

A second group of technologies for electrode fabrication are the so-called thick-film methods. In the case of screen-printing [58, 243, 248, 249], a paste containing metal particles (e.g. Ag/AgCl or graphite) is doctor-bladed over a screen containing the geometrical pattern of the electrode.

Afterwards, the screen is removed and the paste dried to evaporate the solvent. This technique generates electrodes with a height of typically some tens of micrometres (thus thick-film) and has a worse resolution than a shadow-mask process. It has the advantage that no vacuum is required and that the paste can contain organic particles e.g. enzymes for enzymatic electrodes e.g. for glucose testing. A process variant is the use of conducting ink, e.g. carbon ink [250] which can be either screen-printed or molded [251] by the MIMIC process. Figure 18 shows an injection-molded CE chip with a screen-printed electrode for electrophoresis with contactless conductivity detection.

Encapsulation

Most microfluidic systems require closed microchannels. With the exception of the two-wavelength SU-8 process described in Photolithography, all other fabrication technologies require an additional process step to achieve this enclosure. In the early days of polymer microfluidic devices this often proved to be the technologically most challenging step and in large-scale production it still is critical factor. A variety of methods have been developed:

Adhesion

If processed under very clean conditions, the surface adhesion of most polymers, especially elastomers (e.g. PDMS) can be sufficient to create a tight seal, at least as long as no high pressures or mechanical forces are involved. The adhesion can be improved by priming the surfaces in plasma [178, 252–256]. The effects however are not normally stable long-term, but allow a resealing of a microchannel if cleanliness is maintained.


Fig. 18 Injection-molded chip for CE with screen printed carbon (*top*) and silver (*bottom*) electrodes

Adhesives

The most widely used method for joining polymer parts together is the use of adhesives [60, 257–260]. A large variety of adhesive materials are commercially available; PDMS has also been used to join PMMA together [261]. The activation can take place either by simple solvent evaporation (normal glue), by irradiation with UV light, by heat or pressure (typical for lamination processes [45, 62, 83, 262, 263]) or a combination of these factors. In all cases, it is important to use an adhesive with a high viscosity to prevent blocking of the channel by adhesive overflow. This risk can be reduced by the introduction of support structures which direct the flow of the adhesive. The adhesive can be either spin-coated over a large area (e.g on an unstructured cover plate) or locally deposited by a liquid dispenser. Figure 19 shows an example of an adhesively covered microchannel.

Thermal pressure bonding

Thermoplastic polymers can be bonded together by heating them up above the glass transition temperature and pressing them together [6, 24, 130, 264–271]. This works especially well, if the bottom and top plate are made out of materials with slightly different T_g, for example the same base material (e.g. PMMA) with slightly different polymer chain lengths (molecular weight) [272]. In this case, only one of the materials softens. This allows a good control of the process. Care has to be taken not to damage the
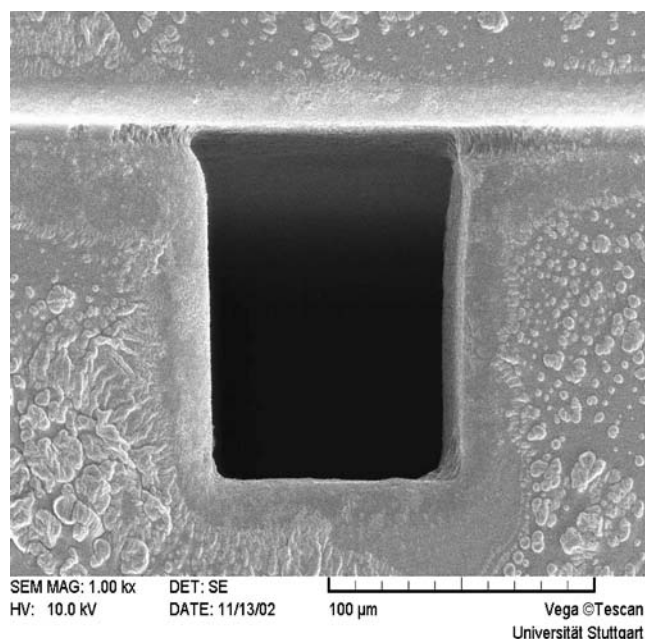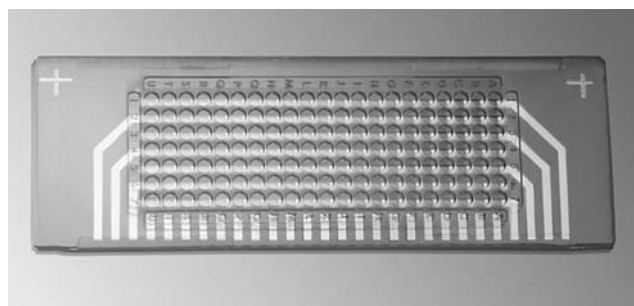
Fig. 20 Microwell plate with integrated photodiodes made out of organic semiconductors (courtesy of M. Sonnleitner, Nanoident Technologies AG)

microstructure, as often the process window (range of temperatures and pressures) is comparatively narrow. For this process, use can be made of the same equipment used for the hot embossing of polymers, as long as temperature and pressure can be controlled with the required precision. Additional surface treatment, e.g. with plasma or UV light, can improve the bonding quality [273, 274].

Solvent bonding

A variation of the gluing process is the use of a suitable solvent [89, 121, 275–279]. In this case the interface between two polymer parts is covered by a thin layer of solvent which is typically sprayed on one of the substrates. The material at the interface dissolves and, after subsequent evaporation of the solvent, solidifies again, combining the two parts by forming chemical bonds between the two parts. The critical aspect in solvent bonding is the prevention of structural damage by "melting" the micro-structures due to solvent excess. This can be prevented by a geometrically restricted application of the solvent. Critical for this process is cleanliness and suitable equipment, as most solvents involved (e.g. methylene chloride, trichloro-ethane for PC, dichloroethane for PMMA, or toluene and xylene for PS) can present a health risk if not properly handled.

Ultrasonic welding

In this process [280, 281], thermal energy is deposited at the interface of two polymer parts by ultrasonically actuated relative mechanical movement of this interface. The method is valuable in cases where certain chemistries are not allowed (e.g. solvents) at the interface because of the presence of biological materials. The critical point in ultrasonic welding is currently the limited depth resolution of this method, which limits the size of the channels that can be created without damage. It is therefore a method for larger structures.

| SEM MAG: 1.00 kx | DET: SE | | |
| HV: 10.0 kV | DATE: 11/13/02 | 100 µm | Vega ©Tescan Universität Stuttgart |

Fig. 19 Microchannel enclosed by using adhesives (courtesy of H. Kück, HSG-IMAT)

Laser welding

Another method of depositing energy at the interface between two polymer sheets uses lasers [282–287]. In this case, laser radiation, typically a diode laser with IR-wavelength emission, is transmitted through one polymer layer and absorbed close to the interface in the second layer. This requires polymers with two different absorption coefficients for the radiation. An advantage of this method is the comparatively short process time necessary. As an example, polymer micropumps have been sealed with this method [288].

Surface modification

A field which would command a review paper on its own is the chemical modification of the polymer surface [289–291]. One of the great advantages of the use of polymers as materials for microfluidic systems is the fact that polymers make available a wide range of highly tunable surface chemistries owing to the fact that a large variety of material parameters are already provided by the various polymers themselves. In addition, the surface parameters, e.g. like hydrophilicity [292], can be modified either with treatment methods like plasma exposure or by surface coating, e.g. with hydrophobic ink. This allows e.g. the formation of hydrophobic valves or flow stops. Other applications which make use of attached surface chemistries are DNA arrays [150, 293–295], biosensors where biomolecules are attached to the polymer surface [296], the suppression of unspecific molecular binding [297] or the control of electroosmotic flow [298]. Also for controlled cell adhesion [299, 300] and growth, polymer surfaces can be structured chemically in addition to a geometrical patterning (micro-contact printing μCP [182]).

Current trends and future developments

Two developments in the field of polymer-based microfluidic devices should be mentioned here as they highlight the scientific and commercial evolution of the discipline:

(a) Increasing integration and system complexity: a clear trend towards the increased integration of functions on the chip instead of just performing single steps on each microfluidic device. Examples can be found in the field of genetic analysis [301], cell handling [199] or POC diagnostics [302, 303], combining sample preparation, diverse reactions, and analytical separations/sensing on-chip.

(b) Hybrid systems: for the integration of additional functions, often the polymer substrate material might not be suitable. Therefore, additional materials might have to be added, improving on the one hand the functionality of the device while on the other hand adding complexity to the fabrication process [247]. Good examples are organic semiconductor materials or dye doping of polymeric materials, which allow the integration of light source and detector on a chip [304] or the integration of optical waveguides [305, 306]. Another example is the integration of silicon-based sensors with signal pre-processing capability on-chip. Figure 20 shows an example of a microwell plate which is a polymer-glass-ITO-organic semiconductor sandwich for the detection of reaction products in the microwells. Instead of expensive optical microplate readers for conventional titerplates, such a microwell plate, generates a simple electronic output signal which can be recorded by a small handheld device.

Conclusions

In this paper we have presented the current state of the rapidly evolving field of polymer-based microfabrication technologies for microfluidic systems. The breadth of technologies available and the generated critical mass of application know-how as well as the commercial interest in polymer-based microfluidics has led to an exponential growth in this field. One important factor for a successful pervasion of these technologies in the academic world is the existence of rapid and low-cost processes for the structuring of polymers like the casting or lithography. For the commercial success on the other hand, scalable production technologies like injection molding are of utmost importance. The availability of technologies and fabrication infrastructure [4] for both academic and industrial projects has played an important role in the rapid growth of the field. A state of maturity has now been reached which can be identified by the fact that almost no development of an analytical instrument or a diagnostic kit takes place without including one or more microfluidic components, typically made out of a polymer.

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