

Micro-Injection Moulding of Polymer Microfluidic Devices

Usama M. Attia,* Silvia Marson^a and Jeffrey R. Alcock^b

** Building 56, Cranfield University, Wharley End, Cranfield, Bedfordshire, MK43 0AL, UK. Tel: +44 (0)1234 750111 ext: 2513; E-mail: u.attia@cranfield.ac.uk*

a Building 56, Cranfield University, Wharley End, Cranfield, Bedfordshire, MK43 0AL, UK. Fax: +44 (0)1234 751346; Tel: +44 (0)1234 750111 ext: 2379; E-mail: s.marson@cranfield.ac.uk

b Building 61, Cranfield University, Wharley End, Cranfield, Bedfordshire, MK43 0AL, UK. Fax: +44 (0)1234 752473; Tel: +44 (0)1234 754185; E-mail: j.r.alcock@cranfield.ac.uk

Microfluidic devices have several applications in different fields, such as chemistry, medicine and biotechnology. Many research activities are currently investigating the manufacturing of integrated microfluidic devices on a mass-production scale with relatively low costs. This is especially important for applications where disposable devices are used for medical analysis. Micromoulding of thermoplastic polymers is a developing process with great potential for producing low-cost microfluidic devices. Among different micromoulding techniques, micro-injection moulding is one of the most promising processes suitable for manufacturing polymeric disposable microfluidic devices. This review paper aims at presenting the main significant developments that have been achieved in different aspects of micro-injection moulding of microfluidic devices. Aspects covered include device design, machine capabilities, mould manufacturing, material selection and process parameters. Problems, challenges and potential areas for research are highlighted.

Keywords: Micro-injection moulding, microfluidics, polymers, polymer processing

I. Introduction

Microfluidics is a rapidly growing domain with many applications and a strong potential for development. The volume of microfluidic products was estimated to be approximately US\$600 million in 2006, and the market was forecast to grow to US\$1.9 billion by 2012 [1]. Microfluidic devices are already used in a number of domains, including chemistry, biotechnology and medicine. Prototype Lab-on-a-chip (LOC) systems are developing rapidly in several areas.

However, future mass-market usage of microfluidic devices is dependent on finding methods which will allow their manufacture in large volumes and at low costs [2]. This is especially important for medical applications where, for safety considerations, devices should be disposable to avoid cross contamination. In addition, from an economical viewpoint, a disposable device would not require maintenance or recalibration. Disposability is also useful in situations where there might not be access to human or technical resources to retest or recalibrate a microfluidic device for multiple usages, e.g. when devices are used in certain point-of-care situations or in developing countries.

For such mass-market applications, polymers possess several advantages over other materials, such as glass and silicon, which have previously been used in constructing microfluidic devices (advantages and limitations of polymers discussed later in section 1.3). They are obtainable at relatively low cost, require relatively simple processing techniques and can exhibit accurate repeatability in mass-production.

Several micromoulding techniques are available for the manufacturing of microfluidic devices from polymers. Of these, micro-injection moulding is one technique that offers mass-production capabilities with relatively low costs. Its other advantages include short-cycle times, the potential for full-automation, accurate replication and dimensional control as well as the existence of considerable know-how, transferable from conventional injection moulding.

The introductory section briefly summarises the relevant basic concepts of microfluidics, micromoulding and micro-injection moulding. Reviews of the micromoulding of thermoplastics [3,4], polymeric microfluidic devices [5] and fabrication of microfluidics and micro-Total Analysis Systems (μ TAS) [6-8] can also be found in the literature.

Section II discusses the design of microfluidic structures that are mouldable by micro-injection moulding.

Sections III through VI examine the challenges in mould and insert design, materials selection, moulding machine design and moulding process parameter optimisation for the micro-moulding of microfluidic components.

Section VII discusses modelling and simulation of micro-injection moulding, and Section VIII presents the state of the art in post-ejection processes, which is particularly important for integrated systems. The outlook for micro-injection moulding of micro-fluidic devices is discussed followed by a conclusion.

1.1 Micromoulding

Micromoulding is the process of transferring the micron or even submicron precision of microstructured metallic moulds to moulded polymeric products [9,10]. Several micromoulding techniques are currently available for fabricating microfluidic devices. They include micro-injection moulding, reaction injection moulding [11], hot embossing [12] and thermoforming [13].

A precise definition for a micro-moulded part is usually controversial. Several authors [14-16,16-19] mention a set of criteria for what is to be classified as a micro-moulded part. Such a part has one or more of the following specifications:

- It weighs less than 1 mg, or it is a fraction of a polymer pellet, where a pellet can be approximated to be spherical in shape with an average diameter of approximately 3 mm.
- It is a part with microstructured regions, or more specifically, with wall thicknesses less than 100 μ m. Microfluidic devices usually fall in this category.
- It is a micro-precision part, which is a part that can have any dimensions, but has tolerances in the micrometre range, or more specifically, between 2-5 μ m.

Due to the continuous developments, micro-moulded parts are soon expected to exceed the limits specified in these literature criteria. In fact, advances in micromoulding technology have already realized production of parts with masses of the order of micro-grammes [17].

1.2 Micro-injection moulding

Micro-injection moulding is the process of transferring a thermoplastic material in the form of granules from a hopper into a heated barrel so that it becomes molten and soft. The material is then forced under pressure inside a mould cavity where it is subjected to holding pressure for a specific time to compensate for material shrinkage. The material solidifies as the mould temperature is decreased below the glass-transition temperature of the polymer. After sufficient time, the material freezes into the mould shape and gets ejected, and the cycle is repeated. A typical cycle lasts between few seconds to few minutes. The process has a set of advantages that makes it commercially applicable with potential for further developments in the future. Advantages include the wide range of thermoplastics available and the potential for full-automation with short cycle times [10,20,21], cost-effectiveness for mass-production process, especially for disposable products [10,20,22-24], very accurate shape replication and good dimension control [20-22], low maintenance costs of capital equipment, when compared to lithographic methods, for example [21] and

applicability of the large amount of industrial information and ‘know-how’ available from conventional injection moulding. Within certain limitations, this may be scaled down to micro-injection moulding. A comparison between micro-injection moulding and other techniques for microfluidic device manufacturing, such as hot-embossing and PDMS casting, is available in the literature [25].

1.3 Applications for polymeric microfluidics

Due to the rapid development in micro-injection moulding, it has been used for producing parts suitable for a wide range of applications, which includes, for example:

- Micro-optical applications, such as gratings, waveguides and lenses [9,15,23,26-28].
- Micro-mechanical applications, such as micro-springs, gears and miniaturized switches [9,15,26,27].
- Sensors and actuators, such as sensors of flow-rates [23,27].

When it comes to microfluidics, micro-injection moulding is one of the main fabrication techniques to produce polymeric microfluidic devices for a number of applications, the majority of which are for medical diagnostics. Examples of polymeric microfluidics include components for micropumps, which are used for medical, chemical and environmental technology [9,10,15,26-28]. In industry, Bartels Microtechnik [29], for example, is specialized in micropumps for the delivery of small amount of fluids for different applications, such as point-of-care platforms or small fuel cells. The pumps are designed to be low in cost and disposable.

Reaction vessels and mixing structures are other commonly used microfluidic systems that are currently being produced by micro-injection moulding [26,30]. On a commercial basis, Thinxxs [31], for example, produces a lab-on-a-chip system for blood diagnostics. It includes functions such as sample absorption, separation, mixing with reagents, analysis and waste absorption. The “Snake” mixer slide is another commercially-available microfluidic system comprising of a plastic chip with meander-shaped mixers that can mix fluids possessing a range of viscosities and at different flow rates.

DNA analysis systems such as bio-MEMS, μ -TAS and Integrated LOC, which are typically manufactured of glass, are currently being manufactured in polymers [10,23]. Such integrated systems usually combine an entire process chain, such as storage and waste vessels, transport channels, filters, mixing and separating structures, reaction chambers and detection points on a plastic substrate [10,15,27,30,32,33]. Mass-producing such integrated systems in polymers rather than glass would decrease their cost. Micralyne [34], for example, which is a company specialized in MEMS-based products, has decided to expand its manufacturing capabilities to include polymers as a lower-price alternative to glass [34].

Other producers, such as Abbott [35] and Microfluidic ChipShop [36] produce polymeric microfluidic platforms for medical diagnostics and point-of-care applications.

Micro injection moulding was also reported in the literature to be used for microfluidic applications, such as capillary electrophoresis (CE) platforms [10,23,27,30,32], miniaturized heat-exchangers [26] and nanofilters [10].

Although several polymeric microfluidic systems have been made available commercially, it should be noted that due to process limitations, to be discussed in the following sections, the process is not fully implemented for relatively complex microfluidic systems. Integration of external elements, such as electrodes or micro-heaters, within a mass-production technique such as micro-injection moulding, still poses a major challenge for the technology. One of the major reasons for this limitation is the required price of the part compared with the costs of established techniques of insertion or encapsulation by injection moulding [2].

1.4 Using polymers for microfluidic applications

Several materials have been used for producing micro-featured parts, for example glass and silicon. Nevertheless, polymeric materials show superior properties over glass and silicon for a number of reasons.

Polymers are relatively low in cost, especially for high-production disposable devices [37,38]. In addition, costs are not greatly affected by the complexity of the design, as design complexity mostly impacts on mould design rather than on the moulding process itself [3,10,39-41]. More discussion about designing for micromoulding is detailed in section 2.

Polymers have a wide variety of characteristic material properties, such as mechanical strength, optical transparency, chemical stability and biocompatibility. They are therefore relatively easy to tailor to obtain required properties for processing and application [3,10,21,37,41-46].

Polymers have excellent replication fidelity, and if the optimum processing conditions are applied a typical polymer can completely fill and accurately replicate small features down to tens of nanometres. Due to the viscoelasticity of polymers, increasing the shear-rate and maintaining the polymer temperature above its T_g during the filling stage would usually ensure a low viscosity enough for the polymer to fill the smallest mould details. Therefore, the quality of the moulded surface features is almost completely dependent on the quality and precision of the mould [21]. Experiments have been reported on using injection moulding to successfully replicate, for example, sub-micron test features [47,48], sub-micron grating optical elements [22,49,50] and surfaces with nano-structured patterns [51,52] or nano-scale topography [53].

Polymers offer good electrical insulation compared to silicon. For example, the conductivity of silicon has proved problematic when applying high voltages necessary for the generation of electro-osmotic flow (EOF) [21,30].

On the other hand, polymers have some limitations related to their properties or processing techniques relative to glass. These include, for example, limited operation-temperature range, higher autofluorescence and limited well-established surface modification techniques. Table 1 presents a comparison between polymers and glass for manufacturing microfluidic devices, where information is compiled from the literature [5,21,30,34,43,54-57]. When it comes to processing, mass-production processing techniques impose limitations on the mouldable geometry of the microfluidic device (more details on these limitations are reported in section 2). These geometrical limitations restrict the flexibility of integrating external functional elements within a mass-manufacturing technique.

	Polymers	Glass
Manufacturing costs	Low in cost relative to glass, especially for mass-production.	Higher in cost, especially for relatively large-area substrates. Higher costs are also associated with clean-room facilities.
Fabrication complexity	Fabrication steps are simpler than glass, and no wet chemistry is needed.	Time consuming and expensive, and wet chemistry is used.
Clean room facilities	Clean-room facilities are necessary for applications where avoiding contamination with dust is critical. In certain cases, particles may become pressed into the polymer during processing without having an effect on device functionality.	Clean-room facilities are needed to avoid contamination.
Properties	Wide selection of polymers, hence mechanical, optical, chemical and biological properties can be tailored.	Less variability in available properties relative to polymers.
Operation temperature	Limited for polymers because of relatively low T_g compared to glass.	Wider range of operation temperature relative to polymers.
Optical properties and fluorescence detection	Optical transparency is lower than glass. Except for special grades, polymers also have higher autofluorescence relative to glass.	Excellent optical properties; autofluorescence levels do not affect detection capabilities.
Bonding	Different bonding options are available, for example: adhesives, thermal fusion, ultrasonic welding and mechanical clamping.	Time consuming relative to polymers. Bonding options include thermal, adhesive and anodic bonding.
Surface treatment	Surface treatment methods are available for polymers, but routine, well-established derivatization techniques are not available.	Established chemical modification procedures for glass are available using organosilanes
Compatibility with organic solvents or strong acids	Except for some special grades, polymers are generally not compatible with most organic solvents and in some cases, strong bases or acids.	Good resistance to organic solvents and acids.
Joule heating	Subject to significant Joule heating because of low thermal conductivity.	More resistant to Joule heating relative to polymers.
Electro osmotic flow (EOF)	Smaller EOF produced relative to glass, because of lack of ionisable functional groups.	Higher EOF relative to polymers.
Geometrical flexibility	Polymer processing techniques offer more flexibility for geometrical designs, including for example different cross-section (curved, vertical or V-groove), high aspect ratio square channels, channels with a defined but arbitrary wall angle, or channels with different heights.	Limited to 2½-D designs. Due to the isotropic nature of the etching process, only shallow, low aspect ratio, mainly semicircular channel cross-sections are possible in glass substrates.
Permeability to gasses	Higher gas permeability relative to glass.	Glass does not have the gas permeability required for some biological applications, such as living mammalian cells.

Table 1 A comparison between polymers and glass properties with respect to their use for microfluidic applications

II. Designing Mouldable Microfluidic Structures

Designing for conventional injection moulding takes into consideration a number of manufacturability aspects, such as the part dimensions, the position and shape of the parting line, the existence of undercuts, mould-cavity features in addition to tolerances and surface finishing [58]. A number of studies have suggested techniques to evaluate the complexity of injection-moulded shapes with respect to replication and demoulding [59,60].

It should be noted that very little is mentioned in the literature about rigorous criteria for designing microfluidic devices for manufacturability by microinjection moulding. Most of design considerations focus on specific geometrical aspects such as achievable aspect ratios. This section will therefore focus on design criteria associated with the geometry of the moulded part rather than designing for functionality. The following subsections will highlight some generic design considerations for injection-moulding, which are also important for micro-scale moulding (section 2.1). Design elements specific to micromoulding, such as aspect ratios and mouldable micro-features will also be reviewed (section 2.2).

2.1 Shrinkage and shape stability in precision injection moulding

Different forms of shape change takes place due to the thermal history of the injection moulded part. Volume changes due to part shrinkage, and shape distortions such as warpage, are common examples.

Shrinkage occurs with the decrease in part volume due to the temperature change between the demoulding temperature and the ambient temperature. The contraction in part volume affects the demoulding of the part due to the stresses induced upon contraction. One of the techniques to improve demoulding is by controlling the processing parameters and, hence, the shrinkage performance. Geometrical changes can also improve demoulding as will be shown in the following section. Considering the feature placement, the further the features from the shrinking centre, the harder demoulding becomes [3].

Another factor that affects demoulding is the orientation of the polymer being injected, because this affects the direction at which shrinkage is most observed. Therefore, a design consideration for microfluidic substrates, should consider the path of polymer injection inside the mould [3]. Examples of experiments investigating flow direction are presented in section 2.5.

In addition to demoulding and feature replication, shrinkage affects shape stability in the form of induced warpage. Warpage is produced due to the non-uniformity of the shrinkage because of the residual stresses induced by the complex thermal variation inside the mould [61]. Warpage, was investigated in parts incorporating micro features using a laser profilometer, and was reported to have an effect on micro-parts of the order of a few microns for a 3-mm length [26]. Warpage prediction is important for parts with relatively large area compared to its thickness, e.g. microfluidic chips. This is because the flatness of the chip is a demanding requirement for polymeric microfluidic chips, considering that optimum sealing of a polymer chip, with a quality level compared to glass, would not be achievable without a minimum flatness level. Otherwise, costly intermediate layers would be needed which compromises the economics of polymer mass-production. The flatness of the polymeric chip is affected by different factors including the flatness of the replicated mould [62], the processing parameters [61,63] and the ejection process. In comparison to its importance, flatness and its control have received little emphasis in the literature.

In injection moulding it is not always possible to design an ideal cooling system, because the position of the cooling channel is dependent on part geometry, cavity configuration and location of ejection mechanism. Thus, variation in temperature across the moulded part should be expected depending on the geometry [61]. Cooling the mould is not always required, especially when it is desired to keep the mould temperature above the T_g of the polymer to ensure complete filling of the mould cavity.

Different techniques have been suggested to decrease the effect of shrinkage. One method is to increase the amount of holding pressure, which, on the other hand, will also increase stresses inside the part [4]. Another technique is to have a long cooling time (i.e. to allow the part to thermally equilibrate inside the mould cavity). This allows the temperature to be approximately uniform. For precision moulding in particular, the part is likely to distort because of lack of homogeneity in shrinkage, which is likely to occur if the cycle is terminated before the thermal equilibrium is reached, i.e. the part is ejected before its temperature is reduced to the ambient temperature [61]. Again, a trade-off of this technique would be an increased cycle time.

It should be noted that shrinkage is not identical throughout long runs. Therefore, moulded parts that need to be assembled in subsequent stages should be placed on the same mould [3].

In addition to shape-changes, demouldability of injection-moulded components is also affected by the geometrical structure of the component. Similar to conventional moulding, micromoulded parts should be designed to allow for part ejection from a two-half mould. Most microfluidic applications possess an undercut-free 2½-D geometry that is relatively simple to demould. For more complex 3D shapes (or shapes with integrated functional elements) injection moulding would not be applicable unless significant changes are made to the mould structure or subsequent assembly steps are integrated in the production process.

Another geometrical consideration for successful demoulding is the existence of draft angles. Draft angles and side-wall roughness need to be considered to ensure that the moulded plastic can be demoulded (Fig. 1). A positive draft angle of greater than $\frac{1}{4}^\circ$ has been proposed for demoulding in plastic injection moulding [39].

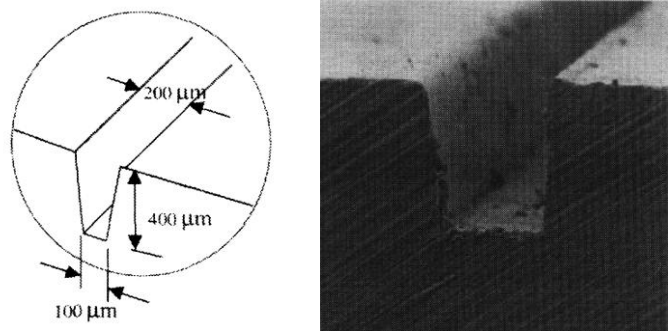


Fig. 1 A micro-channel with a positive draft angle (nominal dimensions and actual channel) [39]

2.2 Minimum channel dimensions and maximum aspect ratios (AR) for microfluidics

Section 2.1 presented design-for-manufacturability criteria common for injection-moulding processes. This section focuses on geometry-related design criteria specific for injection-moulding microfluidic devices. Careful considerations should be given to the channel dimensions to ensure the complete filling of the mould cavity. Polymeric melts can accurately fill microfeatures in the order of hundreds of nanometres. Therefore, the minimum mouldable dimensions will be determined by the tool-manufacturing capabilities. Because micromoulding is under continuous development, it is not possible to specify a size limit below which microfeatures can no longer be replicated successfully. Nevertheless, it has been reported in the literature that it is possible to replicate surfaces with a squares pattern having widths as small as 310 nm and heights of 220 nm [51]. In addition, optical grating elements of parallel walls having a thickness of 200 nm and depth of 1600 nm has also been fabricated [22].

The “hesitation effect” is a phenomenon that can occur during the filling of polymers, and is common when an injection-moulded part contains different thicknesses [20]. As shown in Fig. 2, this effect takes place when high-aspect-ratio microstructures (usually larger than 2) are placed on a relatively thick substrate, which is the case for microfluidic devices.

The polymeric melt tends to flow more easily into mould cavities with relatively lower resistance areas, i.e. areas of greater cross section. Thus, the melt tends to fill the substrate completely before entering the micro-structured features (i.e. the flow stagnates at the entrance of micro-structures). This results in premature freezing because the filling time of the substrate is usually greater than the freezing time of the micro-feature.

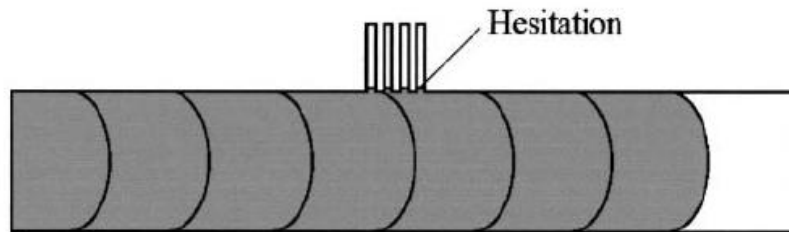


Fig. 2 Hesitation effect in high-aspect-ratio micro-cavities [20]

Taking the hesitation effect into consideration, replication depends on the size and aspect ratios of the structural features as well as the size of the area covered with such structures and their density. The filling of the structures has to compete with the filling of the underlying thicker substrate [40]. This could be the explanation for why it was recommended in the literature that injection moulded parts with high-aspect-ratio microstructures should have a thickness of at least 2 mm [62] so that a quick filling of the substrate can allow for filling the micro-cavities before solidification starts. It was recently reported, however, that micro-structures of aspect ratios of 5 carried on a 1.5-mm-thick disk substrate were successfully filled with poly lactic acid [64].

In addition, the effect of flow direction in either radial- and unidirectional injection was investigated in the literature [39], and it was shown that in unidirectional flow the depth of filling in microchannels is sensitive to the channel width, such that doubling the channel width from 200 μm to 400 μm causes the filling depth to increase from 150 μm to approximately 600 μm.

The concept of the so-called time to pressure (TTP) was introduced by researchers [65] to explain the fact that the degree of filling depends on the distance from the gate, which is the entrance of the polymer into the part cavity. Based on experimental measurements of the pressure drop vs. the injection speed at sections with different thicknesses, it was suggested that the shear stresses, and accordingly the pressure drop, required to fill the feature is in general much higher than that to fill the substrate.

Concerning achievable aspect ratios, it was suggested that there is a limitation regarding the achievable aspect ratio [3], which is a function of the geometry of the micro-features, its position on the sample, the polymer type and the process parameters. Thus, there is no simple rule to give the maximum aspect ratio which can be achieved in a particular case. Although it was not stated why these factors in particular affect the achievable aspect ratio, the experimental work presented throughout this section gives examples of how geometry and processing factors affect the aspect ratio.

With the recent developments in machine capabilities it has been reported that aspect ratios up to 20 can be filled [66,67]. Table 2 compares different experiments performed for different structural dimensions and materials. Information reported in this table is subject to change as more developments are continuously achieved in machining and processing. In the context of table 2, it should be noted that the issue of dimensional tolerances is rarely addressed in the literature.

Polymer	Abbr.	AR	Min. structural thickness [μm]	Example of application	Ref.
Polymethyl methacrylate	PMMA	20	20	Optical fibre connector	[66]
Polycarbonate	PC	7	350	Cell container	[66]
		4 - 8	0.2 - 0.5	Optical element	[22]
Polyamide	PA	10	50	Micro gear wheels	[66]
Polyoxymethylene	POM	5	50	Filter with defined pore diameters	[66]
		10	80	Micro-rods	[68]
Polysulfone	PSU	5	270	Housings for microfluidic devices	[66]
Polyetheretherketone	PEEK	5	270	Housing for micro-pumps	[66]
Liquid crystal polymers	LCP	5	270	Microelectronic devices	[66]
Polyethylene (High density)	HDPE	8	125	High aspect ratio squares	[69]
		10	225	Micro-wells	[20]
Cyclic Olefin Copolymer	COC	0.02 - 2	0.1 - 0.9	Microfluidic patterns	[47]
Conductively filled polyamide	PA 12-C	10	50	Housing for electrostatic micro valves	[66]

Table 2 Commonly used polymers for micro-injection moulding, maximum aspect ratios (AR), minimum structural thickness and applications

It has been suggested in the literature that the critical minimum dimensions which can be replicated successfully by injection moulding are mainly determined by the aspect ratio. Although this has not been presented in a rigorous numerical relation, experiments have shown that the sub-micrometer scale can be reached for aspect ratios less than 1, for example in CD and DVD fabrication. Polymeric materials with minimum wall thickness of 10 μm , structural details in the range of 0.2 μm , and surface roughness of about $R_z < 0.05 \mu\text{m}$ have been manufactured [66].

A few attempts have been made to find the relation between part geometry and filling behaviour on the micro-scale by introducing standard micro-sized features for testing. As suggested in the literature [70], standard testing shapes can be helpful in comparing filling of structures with different wall thicknesses but the same aspect ratio. This will help in investigating the relation between wall thickness and flow path length and their limits. They can also be used for a wider range of polymers, since material properties affect flow behaviour. In both cases, using a statistical method (e.g. Design of Experiments) will be useful in optimizing the experimental procedure.

In one attempt [70] circle-shaped and wedged structures were used as testing shapes (Fig. 3)

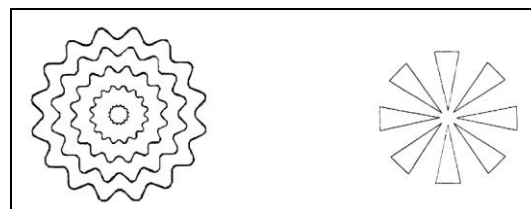


Fig. 3 Circular and wedged insert-shapes for testing [70]

For the circle shapes, the wall thickness was varied in steps from 2.5 μm (inner circle) to 20 μm (outer circle) at a constant height of 50 μm , whereas for wedges, the tip radii were varied from 0.5 μm to 5 μm . POM was the material used for filling. The authors chose these two shapes based on earlier studies [71] in which different designs were compared, and guidelines were deduced for designing standardized testing shapes.

For the circular shape, all the circles were filled completely, but the inner one (2.5 μm) was deformed during demoulding. For the wedged shapes, the shape with radius 0.5 μm was partially filled, whereas larger radii were completely filled.

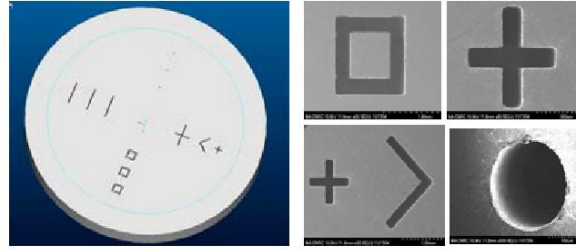


Fig. 4 Micro-cavities with different geometries used for testing the filling behaviour of polymers [64]

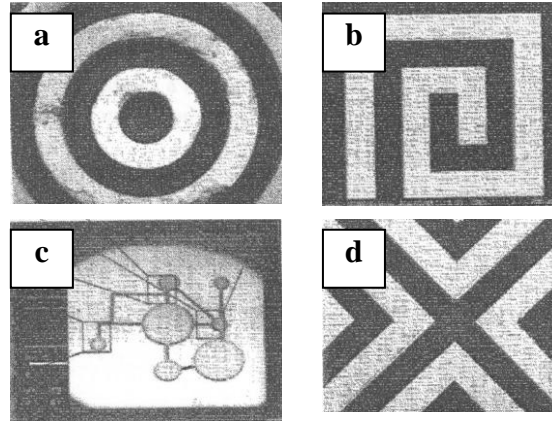


Fig. 5 Testing shapes for demoulding. (a) Circular (b) Meander (c) Microfluidic (d) Ray [72]

In another attempt to investigate dimensional and aspect ratio limits, different geometrical shapes with aspect ratios of 5 were tested for filling with Polylactic acid (Fig. 4). It was shown that square shapes were easier to completely fill without premature freezing than cylindrical shapes.

The authors also reported that features that are farthest from the centrally located gate fill more than those closer to the gate. This is because the farther features have a lower thermal gradient and higher temperature that facilitates their filling. This was verified by numerical simulation, which showed that the polymer tends to fill the relatively thick substrate before completely filling the features, so the farthest features usually contain the hottest material and require less pressure during the holding stage to fill than the features closest to the gate [64].

The effect of geometric shape on demoulding quality has also been studied by comparing the quality of circular, meander, microfluidic and ray shapes (Fig. 5) [72]. The ray shape proved to be optimum for demoulding conditions due to the shrinkage pattern it takes.

III. Micro-Moulds & Inserts

3.1 Special features of moulds for micro-injection moulding

Moulds made for micro-injection moulding of microfluidic parts are in principle similar to moulds made for conventional injection moulding. They usually consist of a fixed part and one or more moving parts, depending on the design. Finished parts are demoulded with ejector pins that are usually controlled hydraulically and electrically. However, moulds made for microinjection moulding have special features [27,40]. For example, moulds can be controlled by the Variotherm process. This process permits heating rates of the order of several tens of Kelvins per second, and hence imposes no significant change in the process time compared to conventional injection moulding. The Variotherm process raises the mould temperature instantly above the polymer T_g during injection to prevent early freezing. During cooling, the mould temperature is decreased below the T_g to assist part solidification [27].

In addition to Variotherm, evacuation of the mould is done by air evacuation with evacuation rates that can reach up to 25 m³/h in some systems [73]. Air evacuation is used rather than air vents used in conventional injection moulding. This is because the vents used in conventional injection moulding are larger in size than some of the cavity features in micro-injection moulding, i.e. they will simply be clogged with polymer melt. In addition, micro-cavities may form air pockets that cannot be released while the polymer is flowing in the mould, so the mould has to be evacuated just before injection [3].

Due to the size of the mould cavity and features, adapted mould sensors are used, because conventional sensors are not always suitable to micro-features. For example, pressure sensors with front diameters down to 1 mm and pressure range up to 2000 bar are currently available for measuring cavity pressures in micro-injection moulding [74].

Special ejector/withdrawal design is important, so that microfeatures are not deformed due to the induced friction

between the mould and the part as discussed earlier in section 2.2.

3.2 Inserts for micro-injection moulding

For moulds used in micro-injection moulding, especially for microfluidic applications, micro-cavities are usually produced on an insert, which is then fitted in the main mould body. While the mould is made of steel, as in conventional injection moulding, inserts can be manufactured of other materials, depending on the technology used. This is because hardened steel, which is the commonly used material for mould-making, requires specialised, and hence expensive, tools for machining micro-sized channels and features.

The use of insert moulds also reduces the over-all cost of process set up where the finalised mould design is produced by a number of iterative steps in which parts are moulded and the mould design is then changed.

3.2.1 Special considerations about manufacturing inserts

Some considerations are recommended for manufacturing/processing inserts for micro-injection moulding [40]. An insert should exhibit extremely smooth side walls to avoid friction during demoulding. Although suggested wall roughness have not been reported in the literature, the inner walls of the insert should be smooth enough to prevent form-locking, i.e. the case where the part cannot be demoulded or the structures will be ripped or sheared off during demoulding [61]. A small inclination angle, preferably greater than $\frac{1}{4}^\circ$ [39], is also desirable, if this does not unduly impact on the functionality of the microstructures to be moulded.

In addition, the mould insert should ensure replication of the micro-features over many moulding cycles and withstand lateral and normal forces during injection and demoulding. In practice this is achieved by choosing a material that is hard and ductile enough for the mould insert.

The surface properties of the mould affect demoulding during micro-injection moulding. The effect of surface treatment has been investigated in the literature, where a tool coated with diamond-like carbon (DLC) was compared with an uncoated identical tool [75]. Measurements of demoulding forces showed that surface treatment significantly reduces demoulding forces.

3.2.2 Manufacturing inserts for micro-injection moulding

Several manufacturing techniques are used to produce inserts with micro-cavities. The choice of the technique depends on the dimension/geometry of the structure, the accuracy requirements and the fabrication costs. Manufacturing techniques include e-beam writing, lithography, electroforming processes (e.g. LIGA techniques, laser ablation) and precision engineering techniques (e.g. micromilling and electro discharge machining (EDM)) [26]. Other advanced processes include laser machining, ion machining and ultrasonic machining [18].

Some complex moulds require the combination of different processes in a modular way by combining components made by LIGA or laser ablation with components made by mechanical treatment [26].

3.2.3 Capabilities of manufacturing methods

Summaries of the capabilities of different manufacturing techniques are readily available in the literature [4,76]. Several comparison tables have been presented. For example, Rötting, et al, tabulated different processes in terms of choice of geometry, minimum feature size, height, total surface area, aspect ratio, life time, cost and availability [62]. High-speed cutting (HSC) milling, grinding, Erosion and UV-LIGA have been compared in terms of reproducibility, minimum roughness, minimum groove width, minimum step width and maximum aspect ratio [40]. An extensive evaluation of the common manufacturing techniques, such as electroplating, EDM and the developing processes, such as laser technology is available [40]. The capabilities of precision manufacturing methods in terms of their geometric limitations ($2\frac{1}{2}$ D vs. 3D structures) have been compared [77].

3.2.4 Challenges facing mould and insert manufacturing

It has been pointed out that the wide range of technologies available makes it practically impossible for any small or medium enterprise to have all technologies in house. It is therefore required to solve the problem of the availability of mould inserts on an industrial scale which includes comparatively short delivery times, a reproducibility in the manufacturing process and the guarantee of certain quality parameters of the mould insert [62].

Another challenge is the successful integration of pieces made with different insert-manufacturing technologies to create a micro-mould [18].

In a recent study, hybrid tooling was presented, in which tools are manufactured with combination of micro-machining techniques and tested by replication of several polymers. Comparison criteria were feature size, aspect ratios and surface finish [78].

Concerning mould manufacturing, one of the main challenges is to modify the mould design to allow for more complex processes versions of the micro-injection moulding process. New mould designs have been tested to allow for

micro assembly injection moulding (μ AIM), a process for combining two components in one process step [79-81]. The mould was designed such that the cavity holding the insert was interchangeable. This enabled some of the time-consuming steps of the moulding process (i.e. demoulding the part, positioning the integrated elements inside the cavity, heating the cavity) to be done out of the process cycle, while the other cavity was being injected. Some of the process steps were automated, such as the cavity replacement process. This modification in the mould design enabled the process to produce micro-parts with joint-like movable components, fluidic hollow structures by lost-core technology and overmoulding of wires and optical fibres [82,83]

Some recent studies have focused on the problems caused by using ejector pins for demoulding the parts. Other alternatives are under investigation such as vacuum or ultrasonic ejection [72].

IV. Material Selection for Polymeric Microfluidic Devices

Selecting the appropriate polymer to micro-inject microfluidic components is one of the most challenging tasks in process design for microfluidics, because several considerations have to be taken into account. These include the effect of polymer on achievable part tolerance, costs and the meeting of material property requirements.

4.1 Material requirements for microfluidics

In the case of parts with microfeatures, like microfluidic devices, material requirements have been discussed by several authors in the literature [10,21,27,30,45]. For example, the material should possess appropriate mechanical properties. Although microfluidic devices are not usually subject to severe mechanical stresses, mechanical properties could be of interest if the chip is to be stacked with other units or integrated within a larger cell. Thermal properties are also important, especially when the microfluidic device is subject to elevated temperatures while in service. In order to avoid softening of the device, and subsequent deformation in features, glass transition temperature T_g , melt temperature T_m and thermal expansion coefficient will be critical. In addition, the ability of the polymer to dissipate heat is important in order to avoid local high temperatures in the device when it is subject to high temperatures while in service. In addition to thermal properties, chemical resistance to certain solvents or strong acids can be required if chemical reactions are taking place in the microchannels. Chemical resistances of several micro-mouldable polymers to different chemical substances have been compared [30]. The authors adopted a qualitative poor-to-excellent scale in comparing the polymers.

During the processing of the polymer, dimensional stability and accuracy are key properties for microfluidic polymers. They include, for example, reproducibility, tendency to shrinkage and warpage, as presented previously in section 2.

If electrical connections are integrated with the microfluidic device, additional attention should be paid to the electrical properties of the polymer. It should possess good insulating properties, such that currents are allowed to pass only through the microfluidic substance moving in the channels.

Biological applications require the polymer to be biocompatible, and permeability could also be demanded if living cells are involved.

In addition to the previous conditions, optical properties might be significant if optical monitoring is involved. Amorphous polymers are usually used in such cases. For optical properties, charts comparing five common polymers (PMMA, COC, PC, MABS, SBS) in terms of transmittance and replication quality have been produced [47]. Transmittance was compared by the value of transmission percentage at a wavelength of 590 nm, whereas replication quality was compared by the depth of filling in nm.

Special microfluidic applications like micro-pumps require additional properties for the polymer. Such properties include hardness, surface charge, molecular adsorption and electro-osmotic flow mobility.

4.2 Material requirements for manufacturability

Micro-injection moulding is a process that involves severe operation conditions in terms of temperatures (up to few hundred degrees) and pressures (up to tens of mega-Pascals). In addition, being a viscoelastic material, polymeric melts experience shear-thinning, i.e. a decrease in viscosity with increase in shear rate. Thus, radical changes in the material properties are expected due to high shear-rates resulting from flow in to micro cavities. Therefore, the polymer selected should be appropriate for micro-injection moulding. Generally speaking, all standard thermoplastic materials suitable for conventional injection moulding can be used for micro-injection moulding [9], provided that some manufacturability conditions are met [28,42,84,85]. For example, the polymer should possess low viscosity and hence good flow properties. Therefore, most of the materials used today in micro-injection moulding are low-viscosity formulations of standard polymers.

High mechanical strength is also recommended in order for the moulded part to resist mechanical stresses associated with demoulding friction or ejector forces. This is especially important for high-aspect-ratio structures, where a larger surface of contact between the mould and the polymer imposes higher frictional resistance while

demoulding. Thus, small structures are often torn off at high-aspect ratios [42,86].

The polymer should be compatible with the mould material, as during processing, polymers may have different effects on the mould material. Also the material should not leave deposits in the mould. For example nickel mould inserts are not affected by moulding PC even after 10,000 moulding cycles [28]. On the other hands, it has been reported in the literature that polymers containing aggressive chemicals can lead to corrosion in the inserts. This causes rough mould surfaces leading to aggressive demoulding and damage to structural details in the sub-micrometer range [28]. No list of specifically aggressive chemicals was available in the literature covered in this review.

Taking into consideration the radical temperature changes in the Variotherm process, it is recommended that the polymer has a narrow temperature interval between free-flowing and solidification. Rapid solidification is thus required.

When it comes to the pellet size, The polymer pellets should be of size small enough to fit within the flights of the smaller conveying screws generally required for micromoulding, to ensure proper melting of the polymer [87]. (This issue of developments in pellet size is further discussed in section 4.4.2.). In addition, if the polymer is filled, the size of the filler particles should be less than the size of the minimum microstructure; otherwise reproducibility will be affected.

4.3 Polymeric materials used in micro-injection moulding

A number of authors have reported on the mouldability of particular engineering plastics. Table 3 summarises polymers that have been reported as mouldable by the micro-injection moulding process. Most of the known engineering plastics appear on this list.

Among the listed materials, some have been specifically recommended for medical applications, because they comply with the approval criteria of the European regulatory agencies, such as POM, PPS, PBT and LCP [86].

In addition to the listed materials, thermoplastic elastomers, such as polyurethanes, were recently reported to be injection mouldable with high-aspect-ratio features [88].

Class	Polymer	Full name	References
Amorphous	PMMA (Acrylic)	Polymethylmethacrylate	[9,27,28,30,37,42,47,69,72,89,90]
	PC	Polycarbonate	[9,10,19,22,24,28,30,37,42,47,72,89-92]
	PSU	Polysulfon	[9,10,28,42,89]
	PS	Polystyrene	[9,19,37,42,93]
	COC	Cyclic Olefin Copolymer	[10,19,33,42,47,90,91]
	COP	Cyclic Olefin Polymer	[94]
	PPE (PPO)	Polyphenylene Oxide	[9,10,26,42]
	PEI	Polyetherimide	[9,10,26,42]
	PAI	Polyamide imide	[10,42]
	MABS	Methylmethacrylate Acrylonitrile-Butadiene-Styrene	[47]
	SAN	Styrene Acrylonitrile	[94]
	SBS	Styrene-Butadiene-Styrene	[47]
	ABS	Acrylonitrile-Butadiene-Styrene	[92,95,95]
Semicrystalline	LCP	Liquid Crystal Polymer	[9,10,42,87]
	PP	Polypropylene	[9,42,67,92,95,96]
	PE	Polyethylene	[9,19,20,42,69]
	POM (Acetal)	Polyoxymethylene	[9,10,19,26-28,42,67,68,70,72,84,89,95]
	POM-C	Polyoxymethylene (Carbon-filled)	[28]
	PBT (Polyester)	Polybutylene Terephthalate	[9,10,19,26,42]
	PBT-HI	Polybutylene Terephthalate (filled with 15% glass fibre)	[10]
	PA 6 (Nylon)	Polyamide 6	[42]
	PA 12	Polyamide 12	[9,10,28,89]
	PA 12 -C	Polyamide 12 (Carbon-filled)	[28]
	PVDF	Polyvinylidene Fluoride	[28,89]
	PFA (Teflon)	Perfluoroalkoxy	[89]
	PEEK	Polyetheretherketone	[9,10,26,28,42,87]
	PLA (Polyester)	Polylactic Acid (Polylactide)	[64]

Table 3 Polymers for micro-injection moulding

4.4 Comparing the performance of polymers in micro-injection moulding

Generally speaking, selecting the right polymeric material for micro-injection moulding microfluidic devices is an issue that is still under investigation. The available reported data have been collected through experiments done under different processing conditions with different types of machines and microfluidic feature designs. Thus, it will be of

great benefit to set a standard method by which polymer materials can be compared objectively for micro-injection moulding.

Several comparisons of the performance of different polymers in micro-injection moulding are now available in the literature. For example, commonly available polymers have been compared in terms of structure quality, filling properties and demoulding [28]. In this case, the authors adopted a qualitative approach in comparison, which was dependent on experience rather than reported measurements. Other authors have reported that the choice of materials can affect the quality of the produced parts in terms of dimensional stability, shrinkage, warpage and filling high aspect-ratios. For example, Weber, et al, tested six polymers for the manufacture of micro-sized features [26]. The experiments indicated that PBT and PEEK gave the best results for filling small V-grooves. This was represented in complete filling of the mould insert, minimum radius of curvature at the edges, and homogenous surface profile. With respect to shrinkage, LCP experienced the minimum percentage shrinkage of approximately 0.5%, whereas POM showed maximum percentage shrinkage of approximately 2%.

It has been reported [42] that the best filling results for micro-injection moulding were obtained with POM, PA and PBT for semicrystalline materials, and PC and PMMA for amorphous polymers. Numerical measurements, however, were not been reported by the authors.

In another filling experiment, it has been noted that PP and HDPE showed unusual flow behaviour in filling high-aspect-ratio structures. For PP, SEM micrographs of structures of aspect ratio 6 showed spherical or nipple-shaped protrusions on the flow fronts. For HDPE, the moulded micro-walls were tilted, and the surfaces at the base of the micro-walls were cambered [48].

Changing the processing parameters can affect the performance of the material. For example, one experiment has shown that changing the melt-zone temperature T_m , affects POM, but it does not affect other materials such as PP and ABS, from which it was deduced that some materials are more sensitive to temperature than others [67].

4.5 Ongoing developments in materials for micro-injection moulding

4.5.1 Developing new materials

The demand for developing special materials tailored for micro-injection moulding is increasing. However, although many developments have been achieved in micromoulding in terms of machine and processing capabilities, development of special polymers is lagging behind. The main reason for this is the small size of the part, which causes the demand for the material to be relatively low. If the size of a single part is between 0.001g and 1g, neglecting the weight of the sprue tree, the production of a million parts requires, at the most, 1 ton of starting material [27]. Under such low-material-demand conditions, it is sometimes difficult to find a supplier who is ready to deliver such small amounts of special polymers [28].

When parts with micro-structures are produced in larger quantities, the demand for special materials will increase. Material suppliers may find it more feasible to develop new materials when market consumption reaches several hundred tonnes per year [42,84].

4.5.2 Filled polymers for microfluidics

Fillers can enhance polymer properties in terms of, for example, mechanical properties, thermal properties and electrical properties. Filled polymers are currently being tested for micro-injection moulding of microfluidic applications. Carbon-filled POM and PA 12 have already being tested for microfluidics in addition to glass-fibre-filled PBT [28]. It is important that the filler size is smaller than the micro-structures of the part in order to maintain accurate reproducibility. New filler concepts are based on small-dimensioned fillers that provide the micro structure with high stiffness and strength while maintaining adequate reproduction fidelity compared with unfilled polymers [42].

Another developing area within the use of fillers is the introduction of nano-filled polymers. Filling polymers with nanoclay particles, for example, is a promising area in research, and the nano-composite market is expected to grow to over 25% a year to reach \$250 million in 2008 [97]. Polymer nano-fillers, such as nanotals, carbon nanotubes and graphite platelets, are currently used to enhance properties of polymeric materials in applications such as food-packaging, automotive and electronics, where nano-fillers are currently used to enhance material properties including lighter weight, added durability, dimensional stability, better temperature resistance, enhanced surface finish and surface aesthetics and easier processing [97]. The amount of improvement achieved is dependent on the application and the nano-filler used. It was not possible within the available literature covered in this review to find details as to how nano-fillers can enhance the properties of micromoulded microfluidic devices.

4.5.3 Two-component micro-injection moulding and hybrid microstructures for microfluidics

Multi-component micro-injection moulding is a developing method allowing for the possibility of connecting different materials within one part, thus combining different material properties. Possibilities include connecting conductive/insulating, hard/soft or magnetic/nonmagnetic combinations. For example, it has been reported in the literature [98] that it was possible to micro-injection mould insulating macro-structures over a conductive substrate.

The part was then coated with a metal layer by electroforming, and the two-component thermoplastic part was separated afterwards.

Another research group introduced the process of micro assembly injection moulding (μ AIM), which combines different materials by overmoulding. A set of articles was published detailing the methodology of this process in terms of the different materials combined, the investigation of the bonding strength and the potential applications for such a technology [79-83].

V. Micro-Injection Moulding Machines

5.1 Introduction

Micro-features have always been a challenge for injection machines, because of the requirement to completely fill cavities in the micro-range before the material starts to solidify. This is specifically critical for microfluidic devices where there is a large change in thickness between the substrate and the microfeatures. In fact, this challenge appeared before the spread of micro-injection moulding, when the same problem was to be solved for thin-wall injection moulding. At this stage it was required to completely fill 2-D thin-walled geometries before the frozen layers begin to block the cavity. Such thin-walled parts were used in producing laptops and mobile phones. Conventional machines were able to overcome this problem by changing certain parameters such as injection pressure and speed [99]. Increasing the injection pressure forces the material to flow into the thin cavities when its resistance to flow increases due to premature freezing. This technique can, however, result in high stresses and sink marks in the part. Increasing the injection speed enhances the filling process because it decreases the viscosity of the polymer melt due to the shear-thinning effect associated with viscoelastic materials [99].

The same approach was adopted to allow conventional injection machines to produce 3-D micro-sized parts. Machines used for producing CDs proved to be qualified for producing low-aspect-ratio structures [99]. In addition, injection moulders produced large, but precise, sprues to achieve the necessary shot weights, because the minimum shot weights were larger than the part size [100].

Structures with higher aspect ratios required further modifications [69]:

1. Applying vacuum to ventilate the mould.
2. Increasing the mould temperature to the melt temperature of the polymer to avoid premature freezing.
3. Correctly timing the switchover between the injection pressure and holding pressure, so that the holding pressure is applied to compensate for part shrinkage before the materials is frozen.

Nevertheless, modifications in the machine design proved to be necessary, especially after the increase in market demand for products with microfeatures of complex design, higher aspect ratios (larger than 2) and sub-micron precision [26].

5.2 Modifications made for micro-injection moulding machines

Based on the set of problems discussed in the previous section, several technical modifications were necessary to manufacture injection machines capable of producing micro-parts:

5.2.1 Smaller injection (plastification) unit

In order to decrease the residence time to prevent material degradation, a smaller plastification unit was introduced to provide a shot size of 5 cc or less. Because the most efficient operating range of most injection units is 20% to 80% of the allowable stroke, a typical injection unit size would be 30 cc or smaller [101].

Decreasing the size of the plastification unit requires the reduction of the screw size and also changes in its design parameters, such as residence time, length to diameter ratio (L/D ratio), root diameter, and compression ratio. Strength is the primary limitation to screw diameter, because the screw should withstand the torque required to convey the solid material through the transition zone. In addition, the standard pellet size imposes limits on the screw flight size. In micro-injection moulding, typical injection unit diameters are 14 and 18 mm with L/D ratios of 15 to 18.

In addition, decreasing the screw size makes it important to increase the linear injection speed in order to maintain the same filling rate. A target linear speed is larger than 200 mm/s for a screw diameter of 18 mm or less to achieve a fill time less than 0.2 seconds [101].

5.2.2 Lower tonnage

Injection moulding of small parts usually requires less projected area, which is the area of the mould surface occupied by the part cavity. Therefore a clamping unit with lower tonnage was required [102]. Both mechanical toggle systems and hydraulic clamp mechanisms are suitable for micro-injection moulding. The former system is less complicated, where as the latter is more accurate for small shot sizes [101].

5.2.3 Advanced control system

An accurate control system was necessary to meter smaller shot sizes. The accuracy depends on the control system response time and the resolution of the positional indicator [101]. In addition, accurate parameter-control is required

for better reproducibility [10], especially in the changeover from injection to holding pressure [27].

5.2.4 Variotherm system (temperature variation program) [26]

In this system the mould is heated up to nearly the melt temperature, and when the mould is completely filled, it is cooled down rapidly using additional cooling lines inside the tool [10,23]. This system is a basic requirement to decrease the cycle time for producing microfluidic parts with structural dimensions of several tens to several hundreds of micrometers, from aspect ratios of three to five, or extreme precision requirements of 1 μm [84].

The use of a rapid thermal process (RTP) has been investigated, in which the surface is heated with IR radiation using a high power halogen lamp [90].

5.2.5 Air evacuation

In order to avoid air vents that have sizes similar to some microstructures, the mould cavity has to be evacuated using an external evacuation system [23,26].

5.2.6 Handling and inspection

This should be integrated into the machine system for correct positioned removal of the part [27]. In addition, a robotized vacuum-suction system was integrated in some machines to demould the part, handle it and quality-inspect it against a video camera [19].

Several additional enhancements have been introduced to micro-injection machines, including turning-tables to optimize the cycle time. A clean-room environmental cell is sometimes added to create a controlled working environment. A detailed description of machine developments is provided in the literature [103].

Future enhancements for micro-injection moulding focuses on decreasing the sprue size and developing plastification units suitable for providing small amounts of melt using, for example, ultrasonic energy [104,105].

It should be noted that microfluidic devices can still be produced using conventional injection machines, provided that the optimum operational conditions are selected. In fact, several of the reported experiments used in this review are performed with conventional machines [48,51,106,107]. Conventional machines are usually used when a large-area mould is required. This is particularly important for the production of microfluidic devices with relatively large substrates, or where mass-production demands multi-cavity design. As mentioned in section 5.1, using conventional machines to produce microfluidic devices would require processing principles similar to those used for thin-wall moulding, such as increased injection pressure, increased melt temperature or high injection speed. Optimizing these parameters results in a decreased melt viscosity that allows the polymer to fill relatively thin-walled, large-area cavities. Another option would be to implement Variothermal process for the mould by locally heating specific areas of the mould and maintaining the mould temperature above the T_g of the polymer during the injection process.

In the recent years there has been a trend towards the development of electric-hydraulic hybrid type machines or all-electrical machines [108]. It was reported in 2004 that all-electric machines hold a 75% share of the Japanese market and 30% of the US market [109]. Electric machines use servomotors to drive processes, such as injection, clamping and plastifying. The main advantages of electric machines vs. hydraulic machines are higher precision, clean environment without hydraulic oil, etc., low noise-level and energy efficiency [108-111]. A comparison between a number of injection moulding machines was reported in the literature. Four machines, two of which were electric, were compared in terms of performance factors, including process variation and energy consumption [111]. It was shown that electric machines are more reliable, in that they exhibit less variation over a number of process measurements, which was reflected in better repeatability. In addition, it was shown that hydraulic machines consume more power than electric machines by a factor of 3.6. On the other hand, electric machines are more expensive relative to hydraulic machines [109,111].

5.3 Micro-injection machine manufacturers

Several manufacturers began to produce injection machines tailored specifically for micro-parts. An example for this was a partnership project that was introduced to produce machines with specifications suitable for micro-injection moulding, including their design, styling and manufacture, as well as handling, testing and assembly [14]. The Austrian project group involved Battenfeld Kunststoffmaschinen GmbH, of Kottlingbrunn, HB-Plastic GmbH, of Korneuburg, Inocon Technologie, of Attnang Puchheim and Zumtobel Staff GmbH of Dornbirn. In 1985 Battenfeld presented an injection unit for micro-parts with weights of 0.5 to 4 g: the Micromelt unit. With other partners, it could produce a unit capable of producing weights down to 0.1 g known as the Microsystem 50 [14]. Another example is the cooperation project between the Institute for Plastics Processing (IKV) at Aachen University of Technology (RWTH) and Ferromatik Milacron Maschinenbau GmbH in Germany. They were able to produce a plastification unit with a shot weight of 0.1 to 1 g [100]. A detailed description of the Milacron machine is in the literature [102].

Comparison between different machine types available in the market and their capabilities are available in several references [4,84,112].

VI. Optimization of Process Parameters

Common processing parameters usually include melt temperature, mould temperature, injection speed, injection pressure, holding pressure, injection profile controlled either by speed or pressure and cooling time, in addition to the possibility of changing the material type. The part quality can be measured in terms of complete filling, dimension stability, mechanical properties or any other parameter depending on the product.

6.1 Early experiments

In initial studies made to investigate process-parameter effects, the main method was by changing one parameter at a time and observing its effect on the part quality. This method was useful for injection moulders in making some basic conclusions about the role of each parameter by its own.

For example, low mould temperatures offer a short cycle time, but can cause premature freezing [69]. Thus, the injection rates have to be high enough to allow for complete filling before freezing. In addition, because of the viscoelasticity of polymeric melts, high temperatures allow for complete penetration without the need for high speeds. Thus, it was deduced that injection speed and melt temperature at various stages within the process are the most important parameters of the injection process.

In another experiment [22] the parts did not completely fill, except when the mould was heated up to a temperature above the T_g of the polymer, which illustrates that the mould temperature affected the filling depth of the polymer. This relation between the mould temperature and the filling depth was also shown in another experiment [20] where an attempt was made to overcome the hesitation effect caused by the viscoelastic nature of the polymer melt, which was preventing the filling of high-aspect-ratio cavities. It was concluded that the ideal situation will be reached when having a hot mould during injection stage and a cold mould during the cooling stage. This concept has been adopted by several machine manufacturers in the form of a Variotherm system.

The effect of holding pressure was also investigated [21]. Birefringence was used to evaluate the effect of process parameters on the residual stresses in the moulded parts. Holding pressure was shown to provide better replication by eliminating material shrinkage, but at the expense of residual stresses. Recent experiments showed that mould temperature significantly improves optical properties of microstructured PC parts [113].

6.2 Design of Experiments (DoE) approach

The studies previously cited show that several parameters can affect the part quality. In fact, the interaction of more than one parameter may affect both the filling behaviour and the part quality. However, testing of all the possible combinations of the different parameters is not practical in terms of time and resources. Therefore, it was required to find a statistical method that has the capability of accounting for the interaction between different parameters and at the same time optimizing the experimental work so that only the important parameters were investigated. Hence, the Design of Experiment approach has become widely used in experiment assessments of micro-injection moulding.

Table 4 compares a number of designed experiments conducted by different research groups. The experiments presented indicate that many parameters can play a role in the part quality either independently or interactively. The table also shows that the main results of each set of experiments are different. This indicates that the part quality is not only a factor of processing parameters. Other factors play a significant role such as the material used (rheological behaviour), the geometry of the mould, the selected response (quality parameter) and the surface finish of the mould. It is therefore advisable to run a designed experiment to optimize the process whenever an element is changed, such as the mould geometry or the polymeric material. Further study and investigation is required in this area.

6.3 In process monitoring of process parameters

Multiple-sensors and data-acquisition systems have been used to monitor the change in processing parameters during the different stages of injection moulding. It was reported in a series of articles that several additional sensors could be used to monitor the change in, for example, injection pressure, cavity pressure, displacements and velocity of the injection pin, temperature in both halves of the mould and the injection force [16,114,115].

In addition, in-process rheometry has been used to monitor the change in the strain rates during processing [86].

Ultrasonic probes are currently used to evaluate the part quality in terms of filling incompleteness, polymer degradation and melt flow speed [116,117].

6.4 Summary

From the previous discussion, it can be deduced that determining the most effective process parameters for micro-injection moulding is a topic that needs further investigation. Although several experiments have been done, even with the same type of machine, results are often different. This could be because studies were carried out under different experimental conditions (e.g. different polymers or test part structures were used) [95].

There is, however, a general agreement in the literature that the mould temperature should exceed the no-flow temperature of the polymer, but the most influential processing parameters are still a subject of debate.

This emphasises the idea that part quality is a factor of different parameters interacting with each other. Processing conditions, materials used, geometrical shapes and even the machine type are all significant in determining the quality

of the final product. In addition, the most significant parameters can vary depending on which output parameter is chosen for evaluating the part quality. Output parameter may include, for example, a specific dimension, a weight or a tolerance. How these parameters interact together is an issue that needs further research.

It seems that the DoE approach is the most suitable strategy to deal with the considerable amount of variables available. However, the experiments need to be well planned, so that only the significant properties are identified without affecting the resolution of the results.

Running a DoE requires a mould to have been designed and built, such that it is ready for running the experiments. This is one limitation of the method, because the results obtained for specific geometrical shape are not necessarily valid for another shape. Thus, for design of moulds for microfluidic parts, it would be of great help if a simulation package were to be available, where it was possible to simulate the effect of changing processing parameters on the quality of parts of different geometrical designs. With the existence of such a package, it would also be possible to investigate post-ejection properties such as residual stresses, warpage, etc.

Tested factors	Response	Materials	Main results	Ref.
Melt temp., injection pressure, holding pressure, injection speed and mould temp.	Filling quality of micro-featured channels	PC, SBS, MABS, COC and PMMA	Melt temp. and mould temp. are most significant parameters.	[47]
Injection time, injection pressure, injection temp. and mould temp.	3D numerical simulation of part filling.	PS, PC and PMMA	The mould temp. is the most important parameter. It must be higher than material T_g .	[118]
Injection speed, holding pressure time, metering size, melt temp. and mould temp.	Part weight and dimensions	PC and POM	Metering size and holding pressure are most significant. The interaction between both is also important	[119]
Injection speed, mould temp., melt temp. and holding pressure.	Complete filling of donut-shaped parts	PS and PC	Injection speed and holding pressure are the most influential, while melt temp. and mould temp. have less influence.	[120]
Melt temp., mould temp., injection speed, holding pressure, air evacuation and the size of features.	Complete filling of high-aspect-ratio rods.	PP, POM and ABS	Melt temp. and injection speed are key factors for PP and ABS. Mould temp. is also significant in case of POM.	[121]
Injection speed, shot size, vacuum, holding pressure, piston diameter	Micro-feature height.	PC	The diameter of the piston, shot size, injection speed and mould temperature are significant parameters.	[24]
Melt temp., mould temp., injection speed and distance between micro-features	Complete filling of micro-structures.	PP, POM and ABS	Injection speed and melt temp. are influential in case of POM and ABS with some side effects. Mould temp. improves filling for some shapes. Distance between micro-features is not influential.	[95]
Melt temp., mould temp., injection speed and surface finish	Flow length along a micro-channel into a flat cavity.	PP, ABS and PC	The high levels of all processing parameters result in better filling. Surface finish is related to level of turbulence in melt flow.	[92]
Melt temp., mould temp., injection speed and holding pressure	Weld-line formation	PS	Injection speed and mould temperature have the main effect on weld-line placement and orientation.	[122]
Injection pressure, melt temp., mould temp. And flow ratio	Flow length	PP	Melt temp. and injection pressure are the most significant factors.	[123]
Holding pressure, filling flow rate and mould temperature	Filled volume fraction of microfilters	COC	Flow rate found to be the most important processing parameter	[124]

Table 4 A summary of different designed experiments to identify significant processing parameters

VII. Modelling and Numerical Simulation

This section illustrates the areas in which numerical simulation can be useful in micromoulding of microfluidic devices, and it points out the simulation requirements specific to micro-scale processing. Some simulation experiments are also presented, in addition to the potential areas for improvement.

7.1 Applications of numerical simulation

The ability to numerically simulate micro-injection moulding would allow for the following major goals to be achieved [98,125,126]:

1. To visualize the flow and predict the last-filled sections of the mould. This is usually done by the short-shots method, where the mould is filled with different amounts of the material to see how the flow proceeds during injection. This is useful to identify defects that are usually associated with the last filled parts like incomplete filling, weld lines and voids.
2. To economically optimize the design of the mould. Because it is usually expensive to manufacture injection-moulding moulds, it would be very useful to simulate different geometrical designs, sprue and gating systems, flow-paths to determine the optimum mould design before manufacturing.
3. To simulate the thermal conditions of the flow during filling and cooling which would be useful in estimating the cycle time and determine the processing bottlenecks.
4. To assist designed experiments in determining the most influential processing parameters on the part quality.
5. To identify post-processing properties, such as residual stresses, shrinkages and warpage.

7.2 Special considerations for simulating micro-injection moulding

Simulating injection moulding has always been a challenge even at the macro-scale processes. This is because many variables are involved in the process and also because of the non-Newtonian nature of polymers. Micro-injection moulding poses an extra challenge for simulation programs, because different physical concepts are involved on the micro-scale, which makes it unfeasible to scale down macro-physics simulations [87].

Several factors affect the accuracy of modelling micro-injection moulding, which include [125,127]:

1. In conventional injection moulding, two-dimensional modelling is common, which neglects the effect of side and end surfaces. This is not accurate for micro-injection moulding because three-dimensional modelling becomes significant. This is because on the micro-scale it is not possible to approximate the flow shape to flow between two parallel plates. Thus, the Hele-Shaw approximation, which has been used several times to simulate micro-injection moulding, is not suitable for simulating micromoulding conditions such as fountain-flow and transverse pressure gradients. In addition, this approximation simplifies the modelling near corners, bifurcations and changes in the part thickness.
2. Some effects that are neglected in conventional injection moulding become significant in the micro-scale due to the increased surface-to-volume ratio, such as surface roughness, surface tension, heating of the melt by viscous friction and cooling of the melt front due to increased heat loss. In addition, models should account for the differences in dynamics of heat and mass transfer in the micro-scale. The heat transfer coefficient, for example, was shown to be significant on the micro-scale [107].
3. The viscoelastic nature of the polymeric melt becomes more significant at the micro scale because of the high shear rates involved in, for example, narrow gates. It has been mentioned in the literature that increasing the shear rate decreases the melt viscosity to values that are different from those that may be specified in data sheets. Experiments showed that reducing the gate sizes from 0.1651 mm to 0.0381 mm can decrease some physical properties by 5% to 7% [87].
4. Meshing elements should be chosen with particular care, because two-dimensional elements conventionally used on macro-scale, for example shell elements, give over-predicted filling.
5. Special processing conditions, such as the Variotherm processes, or evacuating the mould prior to filling, should be considered in modelling.

7.3 Examples of simulation experiments

Several attempts have been made to simulate micro-injection moulding using a variety of packages for different purposes.

One of the earliest attempts [127] was undertaken using I-DEAS Master Series™ Thermoplastic Moulding version 1.3c to optimize the design of the mould, runner and gates, to define and optimize the process parameters and to predict problems associated with warpage and shrinkage during cooling. It was noticed that on the micro-scale, an increase in the significance of some factors appears which affects the accuracy of the software predictions. One factor, for example, is the large surface-to-volume ratios of micro parts, which make surface phenomena dominate the filling and cooling behaviour [127]. The Hele-Shaw approximation was used with shell elements. The simulation over-predicted the length of the short-shots. This was probably because of the two dimensional simplification of the geometry. In which all the surface effects were calculated only for the top and bottom of the mid-surface of the mesh element, whereas side and end effects were ignored.

In another experiment [39] 2-D simulation software C-MOLD ver. 2000 (Moldflow Corp.) was used to determine the most influential processing conditions. It was concluded that the injection speed, feature width and mould temperature were important for mould filling.

ABAQUS has been used to simulate the temperature distribution in the tool during the different steps of the cycle [66]. The filling was simulated by Moldflow. It was observed that it was possible to predict qualitative properties such as welding lines, but numerical values of filled volume, for example, could not be simulated as precisely as required [128]. It was proposed that the packages designed for macroscopic applications could not be relied for micro-scale processes, and it was pointed out that the development of software tools specifically tailored to micro-applications is one of the main future tasks.

The use of software such as C-MOLD to analyse the effect of different gate geometries and locations on the final part has been discussed. In the particular geometrical shape simulated, changing the size and position of the gate in addition to changing the material eliminated the knit line and flow hesitation [85].

Complex shapes and high-aspect-ratio micro-features have also been simulated.

C-MOLD 2000 was used to simulate the filling of micro-gears [44]. A 2-D mid-plane mesh structure was applied to represent a 3-D melt flow. The simulation was in agreement with the experimental design showing that the teeth of the gear were the last parts to be filled

The effect of micro-scale phenomena on micro-injection moulding has been investigated [77]. These phenomena include size-dependent viscosity (i.e. the change in the fluid viscosity from the wall to the middle of the flow stream in microchannels), wall slip (i.e. the tendency of polymeric melts to slip over solid walls during flow in microchannels when the shear stress becomes higher than a critical value) and surface tension. Simulation was used to identify the most influential parameters in micro-injection moulding [118]. The Navier-Stokes equations were used for modelling the flow of PS, PC and PMMA, and the simulation showed that the mould temperature was the most effective parameter on part quality. A finite element code with a 3D solution approach was used [64] to simulate the filling of different shapes relative to their positions to the gate, and it was shown that the features far from the gate experienced more complete filling, because the material far from the gate required a smaller pressure drop in order to fill the features.

Several other simulation experiments were also reported in the literature [107,129-134].

7.4 Ongoing developments

As mentioned in section 7.3, it has been shown by different researchers that commercial simulation programs for conventional injection moulding have drawbacks when used in simulating micro-injection moulding. Some packages over-predict the filling of the cavity. Other packages give acceptable qualitative simulation results, but fail to give reliable quantitative values [46,91,98,125,126]. Therefore, two approaches are currently followed:

The first approach is to develop finite-element codes specifically for simulating micro-injection moulding, instead of using commercial packages. Attempts are made to add the special modifications associated with scaling down the physics from the macro-scale. For example, a finite element code was used to simulate three-dimensional non-Newtonian non-isothermal flow in micro-injection moulding. This was achieved by solving the momentum, mass and energy equations [125].

The second approach is to try and develop the currently available packages, so that they can simulate micro-injection moulding. An example of this is a combined project [135] in which a code was written that enables Moldflow system to accurately simulate the last place to fill in a micromoulded part. This replaces the method of using progressively short-shots of a real micro part in a real micromould.

VIII. Post-Ejection Processes for Microfluidic Parts

It is normally desired to obtain the final product with the least number of processing steps in order to limit time and error sources. Microfluidic devices, however, usually need extra processes before they are ready for use. Such processes may include, but are not limited to, sealing, coating, drilling holes and connecting inlets and outlets, depending on the application. Other logistic problems are also relevant to post-ejection processes, such as handling and inspection. Literature about these processes is currently scarce, either because such processes are still being researched or because they exist as in-house knowledge of commercial companies.

8.1 Handling the ejected parts

Given that the produced part can be very small in size, special care is required when handling, especially if other processes are still in line. Part handling is challenging given the sizes of micromoulded components. Micromoulders use different handling techniques depending on the product. Many micromoulders use edge-gated runners to carry parts from one location to another, and such runners are used as part of the automation process. In other cases customized end of arm tooling, vacuum systems, reel-to-reel take-up equipment and blister packs are used [18].

8.2 Inspection and metrology

The technique for evaluating the quality of the part varies depending on the parts' application. The quality parameter for microfluidic applications can be, for example, the micro-channel width, the tolerances or the filled aspect-ratio. Inspection can take place as a part of the process by using, for example, an in-line video camera.

However, in-line quality control may not be enough for some purposes, such as surface finish or material morphology within the component [16,136], and in this case further inspection has to be done with specialized equipment. Inspection techniques in measuring small micromoulded parts require customized vices, tweezers, and fixturing [112]. Moreover, there is limited availability of inspection equipment that is capable of measuring to sub-micron tolerances [18], and therefore most of the time functional tests were performed.

Quality assurance with regard to specific processing issues may require the use of specialized equipment. An example of this is the use of a laser profilometer to check warpage by measuring deviation in the flat surface of the

part [26]. A 3D-measurement for the geometric dimensions of the part can be made by using a confocal microscope with suitable image-processing software [62]. In addition, Atomic Force Microscopy (AFM) has been used for surface inspection and characterization, and Scanning Electron Microscopy (SEM) for observing 3-D details and evaluating dimensions [16,136,137]. Although SEM is a standard imaging technique, it is not the best method for measurement of three-dimensional features. Contact-probe methods, such as micro-coordinate measurement machines (μ -CMM) have been commercially developed for three-dimensional dimensional metrology.

8.3 Measurement of mechanical properties

Due to the small sizes involved, conventional mechanical testing techniques such as tension and bending tests cannot be readily applied to micro-features of micro-fluidic parts. Nano-indentation can be used to investigate the mechanical properties such as the modulus of elasticity. For example, the relation between the processing conditions, the level of crystallization of the micromoulded part and the modulus measured has been investigated and reported in a set of articles [16,115,136,138,139].

8.4 Sealing the device

It is important to be able to seal the microfluidic device so that leakage is prevented. Different techniques are being developed to find applicable sealing techniques. Adhesives, different variants of welding or lamination are some examples ¹⁰². MILDENDO GmbH introduced a method that does not involve a third material, which is useful for biocompatible applications [62].

Although sealing polymers is challenging, it is much easier than sealing silicon or glass to other substrates [30], because most polymers have T_g s between 120 and 180°C, so relatively low-temperature annealing could be used for assembly. Using the same technique for glass or quartz, the temperature would be raised to approximately 600°C [57]. A polymer with a lower T_g can be used to ensure that there is no deformation in the micro-channels during sealing process. Elastomeric polymers such as PDMS have excellent adhesion to a wide variety of substrate materials and can be used to enclose micro-channels with a non-permanent seal. In cases where permanent sealing is required, it can be performed by plasma oxidation of PDMS surfaces.

Different sealing techniques were tested for biological microfluidic devices [140]. For example, thermal diffusion bonding (TDB) results in low strength and moderate distortion, when the device is bonded below T_g . In this case TDB at or very near T_g results in increased bond strength but excessive deformation. Another example is solvent-assisted bonding, which allows low distortion, high strength bonding at low temperatures and pressures.

An economical approach to the sealing problem would be to find a method by which micro-injection moulding and sealing can take place in the same process. A method has been introduced in which it is possible to inject the microfluidic circuit and cover it at the same process, which is known as in-line covering. It was done by mounting both the microfluidic-substrate mould and the lid mould on a rotating table. After moulding the substrate it is not ejected, but the table rotates such that the lid is moulded and held at the fixed part of the mould. Finally, the table rotates again bringing the substrate opposite to the lid, and they are pressed together using temperature and ejected as one single part [40].

Most of the sealing techniques mentioned in the literature are associated with specific cases. The choice of the optimum sealing technique is therefore dependent on the application. Several questions have to be considered when attempting to seal a polymer microfluidic device:

- Is it possible to bond the lid to the substrate without using a third material? Examples include thermal-diffusion bonding [38,140-144], laser welding [5,145], ultrasonic welding [146] and mechanical clamping [106,147,148].
- If a layer of a bonding material is to be used, how would this affect the cross-sectional area of the micro-channel? Would excess bonding material flow into the micro-channel areas?
- If heating is involved in bonding, would this distort the micro-features on the substrate or affect the mechanical properties of the polymer chip?
- Is the bonding technique only applicable for joining two parts of the same polymeric material, or is it possible to use it with different polymers or a polymer and another material?
- Is the bond strength high enough to resist the pressure caused by injecting microfluids in the channels?
- Is the bonding material, if any, compatible with the microfluids biologically and chemically?
- Can the existence of bonding material affect the flow of the microfluid (for example by surface tension)?
- If bonding requires the use of solvents, are they compatible with the polymer of the device?
- Will the bonding interfere with other “add-ons”, for example electrodes?

These are examples of questions that can pose a challenge in finding the right bonding technique. The answers will depend on the product itself and its technical requirements. Some sealing techniques for polymeric microfluidic devices are reviewed in the literature [145,149].

8.5 Additional processes

Additional post-ejection processes are sometimes required, which, in addition to inspection and sealing, are known as back-end processing. For example, holes can be used to connect the part to a macro-sized substrate, or they can be used as reservoirs. They can be drilled mechanically or by laser ablation, but problems may appear due to the

formation of burrs by the drilling process, which prevents the bonding between the moulded part and the other piece. In addition to hole formation, dicing of individual devices out of a wafer can be done easily and quickly using, for example, a CO₂-laser. Mechanical sawing can also be used, but it is slower and may restrict the possible design. In some cases, additional activation of the polymer surface or deposition of biologically active molecules on the polymer-surface might be needed [40].

IX. Outlook for the micro-injection moulding of microfluidic devices

Significant developments have been recently combined to make micro-injection moulding a stable high-volume process for manufacturing disposable microfluidic devices. Several problems have been successfully overcome by improvements made to the process or to the equipment. Micro-injection moulding is currently used for commercial microfluidic applications. However, challenges remain which require further investigation and research, and for many of these challenges very little information is available in the literature. This is because most of the current research activities are driven by the needs of new products or specific applications, and, furthermore, some of the achievements obtained are not published for commercial reasons.

Design and geometry

Concerning the microfluidic circuit design and geometry, it was not possible from the covered literature to identify a standardized approach for designing a microfluidic circuit to be manufactured by micro-injection moulding. Most of the design aspects discussed in the literature are concerned with individual problems, such as gate-placing or “hesitation-effect” problems, or concerned with specific products.

General design recommendations used in conventional injection moulding can be useful in micro-injection moulding, such as uniform part thicknesses, gate and runner positioning, cooling system distribution and ejection points. In addition, the effect of shrinkage on part demoulding and shape stability becomes significant with higher aspect ratios.

Special design recommendations need to be identified for microfluidic circuits, such as the minimum channel dimensions, maximum aspect ratios, spacing between channels, surface roughness, flow direction and position of the ejection points.

A broader challenge would be to set standards for designing integrated microfluidic circuits, which more than one function is integrated into the chip. This will involve significant changes in the process to take account of the insert/capsulation technique.

Techniques for modifying the surface properties of polymeric microfluidic devices are not well-established as the case in glass. Special techniques for improving the surface properties of micro-featured polymer surfaces need to be investigated.

Micro-injection moulding of truly 3D components is an open topic for research. Most microfluidic devices currently produced by micro-injection moulding are limited to 2½ D structures. This limits the design options of the system, and necessitates the use of post processing assembly.

Moulds and Inserts

Developments in precision engineering have allowed for several techniques to produce microfeatures. Laser ablation, LIGA and micro-machining are few examples of commonly used methods

Insert fabrication techniques have different limitations in terms of achievable minimum dimensions, fabrication time, economical feasibility, dimensional accuracy or finishing quality. It may be required to integrate several fabrication techniques, i.e. hybrid tooling, in order to overcome the limitations of each individual process. This requires choosing a suitable insert material and a cost-effective fabrication procedure.

Changing the mould design enables micro-injection moulding to produce more complex products. Micro-assembly injection moulding is an example for a process that can be used for integrating elements into the plastic chip. A proper mould design is required to allow for the assembly process to take place without significantly affecting the total cycle time.

Material selection

Generally speaking, most of the commonly known engineering plastics are already used in micro-injection moulding. Thermoplastic elastomers have also been used. Some challenges still exist with respect to polymer selection. Designed experiments show that a single polymer can have different filling quality for different part shapes or aspect ratios. In addition, for a specific geometrical shape, using different polymers results in different part qualities in terms of filling and shrinkage. This interaction between the type of polymer moulded and the quality of the part produced makes it a challenging task to determine a specific material for a certain application without testing it under different conditions.

Trial and error is usually the standard method used to select the optimum material.

No standardized methodology has been adopted to test the behaviour of different materials with respect to certain common microfluidic geometries, such as channels or reservoirs for example. Filled polymeric materials have not been widely tested for micro-injection moulding. Nano-clay particles, carbon nanotubes or metallic fillers may be of use to enhance specific properties in the microfluidic circuit. Considering the high shear rates involved in micro-injection moulding, problems such as particle distribution or migration in micro-moulded filled polymers should also be investigated.

Moulding Machines

Moulding Machines have been greatly developed during the past few years, and several manufacturers are currently offering machines for industrial-scale production. Screw-over-plunger design, small plastification units, advanced control, the Variotherm system and clean-room environments are some of the enhancements made specifically for micro-injection moulding. A major challenge would be the successful integration of additional elements to the microfluidic chip. This would allow the commercial use of microfluidic devices to cover more complex structures and applications.

Process parameters

Several experiments and approaches have been adapted to determine the most influential processing parameters, but the results are sometimes in conflict. There is common agreement that heating the mould temperature above the T_g of the material enhances the product quality considerably.

The interactions between the processing parameters, material properties and part geometry are still largely to be investigated. The Design of Experiment (DoE) approach seems to be the most appropriate strategy to investigate such complex interactions. Nevertheless, being a statistical method, the accuracy of the results depends on the number of runs allowed and the tolerance ranges specified. In addition, a DoE is normally performed for certain circuit designs. Hence, the results obtained might not be applicable for other designs because of the change in, for example, surface properties or shear rates induced in the mould.

Post-Ejection processes

The function of the microfluidic device determines the number and type of post-ejection processes required before the device is ready for use. Some processes are common among most of the devices such as quality inspection, testing specific properties and sealing. Special processes may be needed such as drilling holes or metallization.

Sealing of microfluidic circuits is a factor of different interacting parameters. Preventing leakage and ensuring compatibility of the lid and seal with the material and the micro-fluid are some of the challenges that are subject to research. Integrating the sealing process within a mass-manufacturing process would be a major development in microfluidic manufacturing.

Integrated microfluidic devices

Integrating different components by micro-injection moulding is a potential area for development. Integrating external functional elements within a mass-production process like micro-injection moulding would allow for many complex microfluidic prototypes to be realized on a commercial scale. Two component micro-injection moulding is a developing field, and having it as an established process requires changing the design of the mould and machine parameters to allow for an automated process for series production. In addition, micro-assembly injection moulding is a promising technology for producing hybrid microstructures. Movable parts, hollow structures and overmoulded fibres are currently being developed. The technology has not yet been applied for microfluidic applications as far as the literature covered in this review is concerned, which makes it an open area for further investigation. A number of integrated microfluidic devices were produced by mass-manufacturing techniques, such as micro-injection moulding and hot-embossing, but this discussion is beyond the scope of this paper.

X. Conclusion

This review intended to present the state-of-the-art technology of micro-injection moulding for microfluidic devices and to present potential developments and research gaps. The recent decade has witnessed major developments in the technology that made it one of the most preferred high-volume techniques for fabricating microfluidics. The technology offers several advantages in terms of mass-manufacturability, variety of materials and accurate replication of micro-scaled features, and it is currently being used commercially for producing some types of microfluidic systems. Further technologies are being developed to allow for precise heating and metering of polymer for better control of the process.

A number of limitations, however, need to be overcome before the wide-scale fabrication of microfluidic devices can be realized by micro-injection moulding. The nature of end-shape processes puts limitations on the allowed geometrical designs to ensure smooth demouldability. In addition, polymers in general have limitations in terms of operation temperature and electrical properties that prevents them from replacing glass or silicon in specific applications. The optimization of the process parameters, especially for high aspect ratios, is essential for parts with acceptable quality. Finally, taking into consideration the complexity of integrated microfluidic systems, especially for applications like bio-MEMS, it is important to develop in-line integration techniques to allow the mass-fabrication of polymeric microfluidic devices that are economically feasible for commercial use.

5

10

References

- [1] Becker H. Microfluidics: A Technology Coming of Age. Medical Device Technology 2008; 19: 21-24.
- 5 [2] Bourdon R, Schneider W. A systematic Approach to Microinjection Moulding. Business Briefing: Medical Device Manufacturing & Technology 2002: 1-3.
- [3] Hecke M, Schomburg W. Review on Micro Molding of Thermoplastic Polymers. J. Micromech. Microengineering 2004; 14(3).
- [4] Giboz J, Copponnex T, Mélé P. Microinjection Molding of Thermoplastic Polymers: A Review. J. Micromech. Microengineering 2007;17(6).
- 10 [5] Becker H, Gärtner C. Polymer Microfabrication Methods for Microfluidic Analytical Applications. Electrophoresis 2000; 21(1): 12-26.
- [6] Reyes D, Iossifidis D, Auroux P, Manz A. Micro Total Analysis Systems. 1. Introduction, Theory, and Technology. Anal. Chem. 2002; 74(1): 2623-2636.
- 15 [7] Zhang C, Xu J, Ma W, Zheng W. PCR Microfluidic Devices for DNA Amplification. Biotechnol. Adv. 2006; 24: 243-284.
- [8] Fiorini GS, Chiu DT. Disposable Microfluidic Devices: Fabrication, Function, and Application. BioTechniques 2005; 38: 429-446.
- [9] Weber L, Ehrfeld W. Molding of Microstructures for High-tech Applications. Proceedings of the 56th Annual Technical Conference (ANTEC 1998). Part 3 (of 3); 26 April 1998 through 30 April 1998; Atlanta, GA, USA.
- 20 [10] Niggemann M, Ehrfeld W, Weber L. Fabrication of Miniaturized Biotechnical Devices. Proceedings of SPIE - The International Society for Optical Engineering; 21 September 1998 through 22 September 1998; Santa Clara, CA.
- [11] Hanemann T, Pfleging W, Haußelt J, Zum K. Laser Micromaching and Light Induced Reaction Injection Molding as Suitable Process Sequence for the Rapid Fabrication of Microcomponents. Microsystem Technologies 2002 01/22; 7(5): 209-214.
- 25 [12] Becker H, Heim U. Hot Embossing as a Method for the Fabrication of Polymer High Aspect Ratio Structures. Sens Actuators A Phys 2000 7 June 1999 through 10 June 1999; 83(1): 130-135.
- [13] Grande JA. Micro-Thermoforming Makes Its Debut. Plastics Technology 2006 11; 52(11): 37-41.
- [14] Kukla C, Loibl H, Detter H, Hannenheim W. Micro-injection Moulding - The Aims of a Project Partnership. Kunsts Plast Eur 1998; 88(9): 6-7.
- 30 [15] Angelov A, Coulter, J. Micromolding Product Manufacture - A Progress Report. Proceedings of the Annual Technical Conference, (ANTEC 2004); 16 May 2004 through 20 May 2004; Chicago, IL.
- [16] Whiteside B, Martyn M, Coates P, Allan P, Hornsby P, Greenway G. Micromoulding: Process Characteristics and Product Properties. Plast. Rubber Compos. 2003; 32(6): 231-239.
- 35 [17] Martyn M, Whiteside B, Coates, P, Allan P, Greenway G, Hornsby, P. Aspects of Micromoulding Polymers for Medical Applications. Proceedings of the Annual Technical Conference, (ANTEC 2004); 16 May 2004 through 20 May 2004; Chicago, IL.
- [18] Bibber D. Advanced Micromolding Applications. Proceedings of the Annual Technical Conference, (ANTEC 2005); 1 May 2005 through 5 May 2005; Boston, MA.
- 40 [19] Tom A, Layser G, Coulter J. Mechanical Property Determination of Micro Injection Molded Tensile Test Specimens. Proceedings of the Annual Technical Conference, (ANTEC 2006); 7 May 2006 through 11 May 2006; Charlotte, NC; 2006.

- [20] Yao D, Kim B. Injection Molding High Aspect Ratio Microfeatures. J Inject Molding Technol 2002; 6(1): 11-17.
- [21] De Mello A. Plastic fantastic? Lab Chip Minituarisation Chem. Biol. 2002; 2(2).
- [22] Wimberger-Friedl R. Injection Molding of Sub- μ m Grating Optical Elements. J Inject Molding Technol 2000; 4(2): 78-83.
- 5 [23] Piotter V, Guber AE, Hecke M, Gerlach A. Micro Moulding of Medical Device Components. Business Briefing: Medical Device Manufacturing & Technology, 2004; <http://www.touchbriefings.com/pdf/954/piotter.pdf>. Accessed February 2007.
- [24] Pirskanen J, Immonen J, Kalima V, Pietarinen J, Siitonen S, Kuittinen M, et al. Replication of Sub-micrometre Features Using Microsystems Technology. Plast. Rubber Compos. 2005; 34(5-6): 222-226.
- 10 [25] Mazzeo A, Dirckx M, Hardt, D. Process Selection for Microfluidic Device Manufacturing. Proceedings of the Annual Technical Conference, (ANTEC 2007); 6 May 2007 through 11 May 2007.
- [26] Weber L, Ehrfeld W, Freimuth H, Lacher M, Lehr H, Pech B. Micromolding: A Powerful Tool for Large-scale Production of Precise Microstructures. Proceedings of SPIE - The International Society for Optical Engineering; 14 October 1996 through 15 October 1996; Austin, TX, USA.
- 15 [27] Weber L, Ehrfeld W. Micro-moulding - Processes, Moulds, Applications. Kunsts Plast Eur 1998; 88(10; Munich, Germany): 60-3.
- [28] Ruprecht R, Hanemann T, Piotter V, Haußelt J. Polymer Materials for Microsystem Technologies. Microsystem Technologies 1998; 5(1): 44-48.
- [29] Bartels Mikrotechnik GmbH. Available at: www.bartels-mikrotechnik.de Accessed 2009.
- 20 [30] Becker H, Locascio L. Polymer Microfluidic Devices. Talanta 2002; 56(2): 267-287.
- [31] ThinXXS Microtechnology AG. Available at: www.thinxxs.com Accessed 2009.
- [32] Piotter V, Hanemann T, Ruprecht R, Haußelt J. Microinjection Moulding of Medical Device Components. Business Briefing: Medical Device Manufacturing & Technology 2002: 63-66.
- 25 [33] Kim D, Lee S, Ahn C, Lee J, Kwon T. Disposable Integrated Microfluidic Biochip for Blood Typing by Plastic Microinjection Moulding. Lab Chip Miniaturisation Chem.Biol. 2006; 6(6): 794-802.
- [34] Micralyne Inc. Available at: <http://www.micralyne.com> Accessed 2009.
- [35] Abbott Laboratories. i-STAT. Available at: <http://www.abbottpointofcare.com/istat> Accessed 2009.
- [36] Microfluidic ChipShop GmbH. Lab-on-a-Chip Catalogue 01/2009. Available at: <http://www.microfluidic-chipshop.com> Accessed 2009.
- 30 [37] Gottschlich N. Production of Plastic Components for Microfluidic Applications. Business Briefing: Future Drug Discovery, 2004; http://www.touchbriefings.com/pdf/855/fdd041_greiner_tech.pdf. Accessed 2007.
- [38] Boone T, HughFan Z, Hooper H, Ricco A, Tan H, Williams S. Plastic Advances Microfluidic Devices. Anal. Chem. 2002;74(3).
- 35 [39] Yu L, Koh C, Lee L, Koelling K, Madou M. Experimental Investigation and Numerical Simulation of Injection Molding with Micro-features. Polym.Eng.Sci. 2002; 42(5): 871-888.
- [40] Bourdon R. Short Cycles for Injection Moulded Microfluidics Parts. Kunsts Plast Eur 2003; 93(9): 9,11+33.
- [41] Xu G, Kim D, Koelling K, Lee L. Flow Dynamics in Injection Molding with Microfeatures. Proceedings of the Annual Technical Conference, (ANTEC 2005); 1 May 2005 through 5 May 2005; Boston, MA.

- [42] Schneider C, Maier G. Small, but Potent: Special Plastics for Injection Moulding Microparts. *Kunstst Plast Eur* 2001; 91(3): 27-28.
- [43] Gerlach A, Knebel G, Guber AE, Hecke M, Herrmann D, Muslija A, et al. Microfabrication of Single-use Plastic Microfluidic Devices for High-throughput Screening and DNA Analysis. *Microsystem Technologies* 2002;7(5-6):265-268.
- [44] Zhao J, Mayes R, Chen G, Chan PS, Xiong ZJ. Polymer Micromould Design and Micromoulding Process. *Plast.Rubber Compos.* 2003;32(6):240-247.
- [45] Song S, Lee KY. Polymers for Microfluidic Chips. *Macromol.Res.* 2006;14(2):121-128.
- [46] Stange T. Development and Production of Microfluidic Chips Made of Polymers. *Am. Biotechnol.Lab.* 2002; 20(8): 8-10.
- [47] Mönkkönen K, Hietala J, Pääkkönen P, Pääkkönen E, Kaikuranta T, Pakkanen T, et al. Replication of Sub-micron Features Using Amorphous Thermoplastics. *Polym.Eng.Sci.* 2002; 42(7): 1600-1608.
- [48] Liou A, Chen R. Injection Molding of Polymer Micro- and Sub-micron Structures with High-aspect Ratios. *Int J Adv Manuf Technol* 2006; 28(11-12): 1097-1103.
- [49] Angelov A, Coulter J. The development and Characterization of Polymer Microinjection Molded Gratings. *Polym. Eng. Sci.* 2008; 48(11): 2169-2177.
- [50] Macintyre D, Thoms S. The Fabrication of High Resolution Features by Mould Injection. *Microelectron Eng.* 1998; 41-42: 211-214.
- [51] Pranov H, Rasmussen H, Larsen N, Gadegaard N. On the Injection Molding of Nanostructured Polymer Surfaces. *Polym.Eng.Sci.* 2006; 46(2): 160-171.
- [52] Angelov A, Coulter J. A feasibility Study for Sub-100 nm Polymer Injection Molding. *Proceedings of the Annual Technical Conference, (ANTEC 2007); 6 May 2007 through 11 May 2007.*
- [53] Gadegaard N, Mosler S, Larsen NB. Biomimetic Polymer Nanostructures by Injection Molding. *Macromol. Mater. Eng.* 2003; 288(1): 76-83.
- [54] Erickson D, Li D. Integrated Microfluidic Devices. *Anal. Chim. Acta* 2004; 507(1): 11-26.
- [55] Soper S, Henry A, Vaidya B, Galloway M, Wabuyele M, McCarley R. Surface Modification of Polymer-based Microfluidic Devices. *Analytica Chimica Acta* 2002 10/11; 470(1): 87-99.
- [56] Whitesides G. The Origins and the Future of Microfluidics. *Nature* 2006; 442(7101): 368-373.
- [57] Soper SA, Ford S, Qi S, McCarley R, Kelly K, Murphy M. Polymeric Microelectromechanical Systems. *Anal. Chem.* 2000;72(19).
- [58] Raviwongse R, Allada V. Artificial Neural Network Based Model for Computation of Injection Mould Complexity. *Int. J. Adv. Manuf. Technol.* 1997; 13(8): 577-586.
- [59] Little G, Tuttle R, Clark D, Corney J. A Feature Complexity Index. *Proc. Inst. Mech. Eng. Part C J. Mech. Eng. Sci.* 1998; 212(5): 405-412.
- [60] Rosen D, Dixon J, Poli C, Dong X. Features and Algorithms for Tooling Cost Evaluation in Injection Molding and Die Casting. *Proceedings of the ASME International Computers in Engineering Conference and Exposition; 2 August 1992 through 6 August 1992; New York, NY, United States: Publ by ASME; 1992.*
- [61] Greener J, Wimberger-Friedl R. *Precision injection molding: process, materials, and applications*. Cincinnati: Hanser Gardner Publications; 2006.
- [62] Rötting O, Röpke W, Becker H, Gärtner C. Polymer Microfabrication Technologies. *Microsystem Technologies*

2002; 8(1): 32-36.

[63] Madou M, Lee L, Koelling K, Lai S, Koh C, Juang Y, et al. Design and Fabrication of Polymer Microfluidic Platforms for Biomedical Applications. Proceedings of the Annual Technical Conference, (ANTEC 2001); 3: 2534-2538.

5 [64] Derdouri A, Ilinca F, Hétu J. Microinjection Molding of Microstructures - Experimental and Numerical Simulation. AIChE Annual Meeting, Conference Proceedings; 30 October 2005 through 4 November 2005; Cincinnati, OH.

[65] Wimberger-Friedl R, Balemans W, Van Iersel B. Molding of Microstructures and High Aspect Ratio Features. Proceedings of the Annual Technical Conference, (ANTEC 2003); 4 May 2003 through 8 May 2003; Nashville, TN.

10 [66] Piotter V, Mueller K, Plewa K, Ruprecht R, Haußelt J. Performance and Simulation of Thermoplastic Micro Injection Molding. Microsystem Technologies 2002; 8(6): 387-390.

[67] Sha B, Dimov S, Griffiths C, Packianather M. Micro-injection Moulding: Factors Affecting the Achievable Aspect Ratios. Int J Adv Manuf Technol 2006.

15 [68] Ong N, Zhang H, Woo W. Plastic Injection Molding of High-Aspect Ratio Micro-rods. Mater.Manuf.Process. 2006; 21(8): 824-831.

[69] Despa M, Kelly K, Collier J. Injection Molding Using High Aspect Ratio Microstructures Mold Inserts Produced by LIGA Technique. Proceedings of SPIE - The International Society for Optical Engineering; 21 September 1998 through 22 September 1998; Santa Clara, CA, USA.

20 [70] Kemmann O, Schaumburg C, Weber L. Micro Moulding Behaviour of Engineering Plastics. Proceedings of SPIE - The International Society for Optical Engineering; 30 March 1999 through 1 April 1999; Bellingham, WA, United States: 464-471.

[71] Hörr, M. Grundlagenuntersuchungen durch Strukturdefinition beim Mikrospritzgießen im Rahmen des LIGA-Prozesses. Darmstadt: Fachhochschule Darmstadt; 1997.

25 [72] Michaeli W, Gärtner R. New Demolding Concepts for the Injection Molding of Microstructures. J. Polym. Eng. 2006; 26(2-4): 161-177.

[73] SMS Group. Battenfeld Service Manual, Version MB4GBV20 10/03. 2006.

[74] Kistler Instrument Corporation. <http://www.kistler.com>; Accessed Feb. the 27th, 2007.

[75] Griffiths C, Dimov S, Brousseau E, Chouquet C, Gavillet J, Bigot S. Micro-Injection Moulding: Surface Treatment Effects on Part Demoulding. 4M2008 Proceedings; 9th - 11th September; UK: Whittles Publishing; 2008.

30 [76] Bissacco G, Hansen H, Tang T, Fugl J. Precision Manufacturing Methods of Inserts for Injection Molding of Microfluidic Systems. ASPE Spring Topical Meeting on Precision Micro/Nano Scale Polymer Based Component & Device Fabrication; April 2005.

[77] Yao D, Kim B. Simulation of the Filling Process in Micro Channels for Polymeric Materials. J Micromech Microengineering 2002; 12(5): 604-610.

35 [78] Tosello G, Fillon B, Azcarate S, Schoth A, Mattsson L, Griffiths C, Staemmler L, Bolt P. Hybrid Tooling Technologies and Standardization for the Manufacturing of Inserts for Micro Injection Molding. Proceedings of the Annual Technical Conference, (ANTEC 2007); 6 May 2007 through 11 May 2007.

[79] Michaeli W, Rogalla A, Ziegmann C. Processing Technologies for the Injection Moulding of Hybrid Microstructures. Macromol.Mater.Eng. 2000; 279: 42-45.

40 [80] Michaeli W, Ziegmann C. Micro Assembly Injection Moulding for the Generation of Hybrid Microstructures. Microsystem Technologies 2003; 9(6-7): 427-430.

- [81] Michaeli W, Opfermann D. Bonding Strength in Micro Injection Assembly Moulding. Proceedings of the Annual Technical Conference, (ANTEC 2005); 1 May 2005 through 5 May 2005; Boston, MA.
- [82] Michaeli W, Opfermann D. Micro Assembly Injection Moulding. Microsystem Technologies 2006; 12(7): 616-619.
- 5 [83] Michaeli W, Opfermann D. Increasing the Feasible Bonding Strength in Micro Assembly Injection Molding Using Surface Modifications. Proceedings of the Annual Technical Conference, (ANTEC 2006); 7 May 2006 through 11 May 2006; Charlotte, NC; 2006.
- [84] Weber L, Ehrfeld W. Micromoulding: Market Position and Development Potential. Kunststoffe 1999;89(10):192-202.
- 10 [85] Clay J, Heggs R. Material Challenges in Medical Micromolding Applications. Proceedings of the Annual Technical Conference, (ANTEC 2002); 5-9 May 2002
- [86] Martyn M, Whiteside B, Coates P, Allan P, Greenway G, Hornsby P. Micromoulding: Consideration of Processing Effects on Medical Materials. Proceedings of the Annual Technical Conference, (ANTEC 2003); 4 May 2003 through 8 May 2003; Nashville, TN.
- 15 [87] Tolinski M. Macro Challenges in Micromolding. Plast.Eng. 2005; 61(9): 14-16.
- [88] Yoon S-H; Alabran M, Lee J, Mead J, Barry C, Carter D. Micro-Injection Molding of High Aspect Ratio Features with Thermoplastic Polyurethanes. Proceedings of the Annual Technical Conference, (ANTEC 2007); 6 May 2007 through 11 May 2007.
- 20 [89] Ruprecht R, Bacher W, Haußelt J, Piotter V. Injection Molding of LIGA and LIGA-similar Microstructures Using Filled and Unfilled Thermoplastics. Proceedings of SPIE - The International Society for Optical Engineering; 23 October 1995 through 24 October 1995; Austin, TX.
- [90] Kim S, Trichur R, Beaucage G, Ahn C, Kim B. New Plastic Microinjection Molding Technique for Extremely Tall Plastic Structures Using Remote Infrared Radiation Heating Method. Proceedings of the 10th Solid-State Sensor, Actuator and Microsystems Workshop; June 2-6, 2002.
- 25 [91] Chen S, Chang J, Chang Y, Chau S. Micro Injection Molding of Micro Fluidic Platform. Proceedings of the Annual Technical Conference, (ANTEC 2005); 1 May 2005 through 5 May 2005.
- [92] Griffiths C, Dimov S, Brousseau E, Hoyle R. The Effects of Tool Surface Quality in Micro-Injection Moulding. J. Mater. Process. Technol. 2007; 189(1-3): 418-427.
- 30 [93] Miller T, Fontaine J. Performance and Materials for High Performing Injection Molded Optical Elements. Proc Conf Plast Portable Wireless Electron 1999; 25 January 1999 through 26 January 1999 (Brookfield, CT, United States): 37-42.
- [94] Kalima V, Pietarinen J, Siitonen S, Immonen J, Suvanto M, Kuittinen M, et al. Transparent Thermoplastics: Replication of Diffractive Optical Elements Using Micro-injection Molding. Opt Mater 2007; 30(2): 285-291.
- 35 [95] Sha B, Dimov S, Griffiths C, Packianather M. Investigation of Micro-Injection Moulding: Factors Affecting the Replication Quality. J Mater Process Technol 2007; 183(2-3): 284-296.
- [96] Zhang K, Lu Z. Analysis of Morphology and Performance of PP Microstructures Manufactured by Micro Injection Molding. Microsyst Technol 2008; 14(2): 209-214.
- [97] Stewart R. Nanomaterials: Still Climbing the Steep Curve of Material Development. Plastics Engineering April 2006;:12-20.
- 40 [98] Piotter V, Finnah G, Oerlygsson G, Ruprecht R, Haußelt J. Special Variants and Simulation of Micro Injection Moulding. Injection Moulding 2005: Collected Papers of the 5th International Conference, Copenhagen, Denmark; March 1-2, 2005.

- [99] Fassett J. Thin wall molding: differences in processing over standard injection molding. Proceedings of the Annual Technical Conference, (ANTEC 1995); 7 May 1995 through 11 October 1995; Boston, MA, USA.
- [100] Spennemann A, Michaeli W. Process Analysis and Machine Technology for the Injection Molding of Microstructures. Proceedings of the Annual Technical Conference, (ANTEC 1999); May 2-6, 1999.
- 5 [101] Shepard T, Dunn D. Micro-injection Molding of Medical Products: Machine Specification and Process Simulation. Proceedings of the Annual Technical Conference, (ANTEC 1995); 1995.
- [102] Catanzaro J, Kadykowski B. Micor Molding - "A New Way". Proceedings of the Annual Technical Conference, (ANTEC 2002); 3:2627-2633.
- 10 [103] Tipler P, Manser P. Developments in Micromoulding. Proceedings of Polymer Processing Engineering 01; Bradford; UK; June 2001 UK; 2001.
- [104] Michaeli W, Spennemann A. A New Injection Molding Technology for Micro Parts. J Polym Eng 2001; 21(2-3): 87-98.
- [105] Michaeli W, Spennemann A, Gärtner R. New Plastification Concepts for Micro Injection Moulding. Microsyst Technol 2002; 8(1): 55-57.
- 15 [106] Liu M-K, Huang K-S, Chang J-Y, Wu C-H, Lin Y-C. Using a CD-like Microfluidic Platform for Uniform Calcium Alginate Drug Carrier Generation. Proceedings of SPIE - The International Society for Optical Engineering; 22 January 2007 through 24 January 2007; San Jose, CA; 2007.
- [107] Yu L, Lee L, Koelling K. Flow and Heat Transfer Simulation of Injection Molding with Microstructures. Polym. Eng. Sci. 2004; 44(10): 1866-1876.
- 20 [108] Chang P, Hwang S, Lee H, Huang D. Development of an External-type Microinjection Molding Module for Thermoplastic Polymer. Journal of Materials Processing Technology 2007 4/12; 184(1-3): 163-172.
- [109] Strassner J. Precision as a Competitive Edge. Demagpress 2004:3-4.
- [110] Wang Y-D, Chang P-Q, Wu Y-F, Hwang S-J, Hwang, D-Y, Cheng, R-W. Design and Fabrication of an All-electric Tiebarless Injection Molding Machine. 2005 IEEE International Conference on Mechatronics, ICM '05; 10 July 2005 through 12 July 2005.
- 25 [111] Kelly A, Woodhead M, Coates P. Comparison of Injection Molding Machine Performance. Polymer Engineering & Science 2005; 45(6): 857-865.
- [112] Bibber D. Micro Molding Challenges. Proceedings of the Annual Technical Conference, (ANTEC 2004); 16 May 2004 through 20 May 2004; Chicago, IL.
- 30 [113] Murakami O, Yamada K, Kotaki M. Replication and Optical Properties of Injection Moldings with Microstructures. Proceedings of the Annual Technical Conference, (ANTEC 2007); 6 May 2007 through 11 May 2007.
- [114] Zhao J, Chen G, Juay Y. Development of Process Monitoring Technologies for Polymer Micro Moulding Process. Available at: <http://www.simtech.a-star.edu.sg/Research/TechnicalReports/TR0321.pdf> .Accessed 2nd of March, 2007.
- 35 [115] Whiteside B, Martyn M, Coates P. Micromoulding: Process Evaluation. Proceedings of the Annual Technical Conference, (ANTEC 2004); 16 May 2004 through 20 May 2004; Chicago, IL.
- [116] Ono Y, Cheng C, Jen C, Tatibouët J, Héту J. Ultrasonic Technique and Probes for Monitoring Surface Imperfection of Microfluidic Plastic Devices During Injection Molding. Proceedings of the Annual Technical Conference, (ANTEC 2005); 1 May 2005 through 5 May 2005; Boston, MA.
- 40 [117] Whiteside B, Brown E, Ono Y, Jen C, Coates P. Polymer Degradation and Filling Incompletion Monitoring for Micromolding Using Ultrasound. Proceedings of the Annual Technical Conference, (ANTEC 2005); 1 May 2005 through 5 May 2005; Boston, MA.

- [118] Shen Y, Yeh S, Chen S. Three-dimensional Non-Newtonian Computations of Micro-injection Molding with the Finite Element Method. Int. Commun. Heat Mass Transf. 2002;29(5):643-652.
- [119] Zhao J, Mayes R, Chen G, Xie H, Chan P. Effects of Process Parameters on the Micro Molding Process. Polym. Eng. Sci. 2003; 43(9): 1542-1554.
- 5 [120] Aufiero R. The Effect of Process Conditions on Part Quality in Microinjection Molding. Proceedings of the Annual Technical Conference, (ANTEC 2005); 1 May 2005 through 5 May 2005; Boston, MA.
- [121] Sha B, Dimov S, Griffiths C, Packianather M. Micro-injection Moulding: Factors Affecting the Achievable Aspect Ratios. Int J Adv Manuf Technol 2007; 33(1-2): 147-156.
- 10 [122] Tosello G, Gava A, Hansen H, Lucchetta G. Influence of Process Parameters on the Weld Lines of a Micro Injection Molded Component. Proceedings of the Annual Technical Conference, (ANTEC 2007); 6 May 2007 through 11 May 2007.
- [123] Jung W-C, Heo Y-M, Shin K-H, Yoon G-S, Chang S-H. An experimental study on micro injection parameters. Proceedings of the Annual Technical Conference, (ANTEC 2007); 6 May 2007 through 11 May 2007: 638-642.
- 15 [124] Lee B, Hwang C, Kim D, Kwon T. Replication Quality of Flow-through Microfilters in Microfluidic Lab-on-a-chip for Blood Typing by Microinjection Molding. J Manuf Sci Eng Trans ASME 2008;130(2):0210101-0210108.
- [125] Ilinca F, Héту J-F, Derdouri A. Numerical Simulation of the Filling Stage in the Micro-Injection Molding Process. Proceedings of the Annual Technical Conference, (ANTEC 2004); 16 May 2004 through 20 May 2004; Chicago, IL.
- 20 [126] Kemmann O, Weber L, Jeggy C, Magotte O. Simulation of the Micro Injection Molding Process. Proceedings of the Annual Technical Conference, (ANTEC 2000): 576-580.
- [127] Hill S, Kämper K, Dasbach U, Döpper J, Ehrfeld W, Kaupert M. An Investigation of Computer Modelling for Micro-Injection Moulding. Proceedings of Microsym'95; September 1995.
- 25 [128] Norajitra P, Muller K, Ruprecht R, Haußelt J. Computersimulation zur Verbesserung der Wirtschaftlichkeit beim Spritzgießen von Kunststoffmikrostrukturen. Proceedings of Werkstoffwoche 1996, Symposium 8; DGM-Informationsgesellschaft Verlag; 1996.
- [129] Shen YK, Wu WY. An Analysis of the Three-dimensional Micro-Injection Molding. Int. Commun. Heat Mass Transf. 2002; 29(3): 423-431.
- [130] Young W. Simulation of the Filling Process in Molding Components with Micro Channels. Microsystem Technologies 2005; 11(6): 410-415.
- 30 [131] Mehta N, Barry C, Bibber D, Tully D. Validation of Flow Simulation for Micromolded Parts. Proceedings of the Annual Technical Conference, (ANTEC 2003); 4 May 2003 through 8 May 2003; Nashville, TN; 2003.
- [132] Shen Y, Chien H, Lin Y. Optimization of the Micro-Injection Molding Process Using Grey Relational Analysis and MoldFlow Analysis. J Reinf Plast Compos 2004; 23(17):1799-1814.
- 35 [133] Majmundar R, Asthana A, Ghuman B, Barry C. Comparison of Predicted and Experimental Filling of Micromolded Parts. Proceedings of the Annual Technical Conference, (ANTEC 2005); 1 May 2005 through 5 May 2005; Boston, MA.
- [134] Sammoura F, Kang J, Heo Y, Jung T, Lin L. Polymeric Microneedle Fabrication Using a Microinjection Molding Technique. Microsyst. Technol. 2007; 13(5-6): 517-522.
- [135] Kirkland C. A first in Micromold Flow Analysis. Injection Molding Mag. May 2003.
- 40 [136] Whiteside B, Martyn M, Coates P, Greenway G, Allen P, Hornsby P. Micromoulding: Process Measurements, Product Morphology and Properties. Plast. Rubber Compos. 2004; 33(1): 11-17.

- [137] Martyn M, Whiteside B, Coates P, Allan P, Hornsby P. Studies of the Process-property Interaction of the Micromoulding Process. Proceedings of the Annual Technical Conference, (ANTEC 2001); 5-9 May 2001. Brookfield Center, CT, USA.
- 5 [138] Greenway G, Allan P, Bevis M, Hornsby P. The Mechanical Testing of Micro Injection Mouldings. Proceedings of the Annual Technical Conference, (ANTEC 2001); 5-9 May 2001.
- [139] Greenway G, Allan P, Hornsby P. The Characterisation and Physical Testing of Micro-mouldings. Proceedings of the Annual Technical Conference, (ANTEC 2003); 4 May 2003 through 8 May 2003; Nashville, TN.
- 10 [140] Morales A, Simmons B, Wallow T, Campbell K., Mani S, Mittal B, et al. Injection Molded Microfluidic Devices for Biological Sample Separation and Detection. Proceedings of SPIE - The International Society for Optical Engineering; 25 January 2006 through 25 January 2006; San Jose, CA.
- [141] Mair D, Geiger E, Pisano A, Fréchet J, Svec F. Injection Molded Microfluidic Chips Featuring Integrated Interconnects. Lab Chip Miniaturisation Chem. Biol. 2006; 6(10): 1346-1354.
- [142] Hecke M, Guber A, Truckenmüller R. Replication and Bonding Techniques for Integrated Microfluidic Systems. Microsystem Technologies 2006; 12(10-11): 1031-1035.
- 15 [143] Sung W, Lee G, Tzeng C, Chen S. Plastic Microchip Electrophoresis for Genetic Screening: The Analysis of Polymerase Chain Reactions Products of Fragile X (CGG)_n Alleles. Electrophoresis 2001; 22: 1188-1193.
- [144] Lee S, Kim S, Kang J, Ahn C. A Polymer Lab-on-a-chip for Reverse Transcription (RT)-PCR Based Point-of-care Clinical Diagnostics. Lab Chip Miniaturisation Chem.Biol. 2008; 8(12): 2121-2127.
- 20 [145] Yussuf A, Sbarski I, Hayes J, Solomon M. Sealing and Bonding Techniques for Polymer-Based Microfluidic Devices. Swinburne University of Technology; <http://www.swin.edu.au/iris/pdf/profiles/AbdirahmanYussuf.pdf> Accessed: March 2007.
- [146] Noerholm M, Bruus H, Jakobsen MH, Telleman P, Ramsing NB. Polymer Microfluidic Chip for Online Monitoring of Microarray Hybridizations. Lab Chip Miniaturisation Chem. Biol. 2004; 4(1): 28-37.
- 25 [147] Blattert C, Jurischka R, Schoth A, Kerth P, Menz W. Fabrication and Testing of Novel Blood Separation Devices Based on Microchannel Bend Structures. Progress in Biomedical Optics and Imaging - Proceedings of SPIE; 13 December 2004 through 15 December 2004; Sydney, NSW.
- [148] Klepárník K, Horký M. Detection of DNA Fragmentation in a Single Apoptotic Cardiomyocyte by Electrophoresis on a Microfluidic Device. Electrophoresis 2003; 24(2): 3778-3783.
- 30 [149] Tahhan I, Blattert C, Jurischka R, Schoth A, Kerth P, Reinecke H. Improved and Simple Sealing of Microfluidic Structures. 2005 3rd IEEE/EMBS Special Topic Conference on Microtechnology in Medicine and Biology; 12 May 2005 through 15 May 2005.