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Reconfigurable Micro-mould for the Manufacture of Truly 3D Polymer Microfluidic Devices

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Abstract
This paper concerns the concept, the design and the manufacturing steps for the fabrication of a precision mould for micro-injection moulding of truly three dimensional microfluidic devices. The mould was designed using the concept of replaceable cavities to enable the flexible development of the complex microfluidic device and to reduce machining time and therefore costs during the prototyping, testing and subsequent production phase. The precision machining technique used for the cavity manufacture was micromilling.

Keywords:
Mould, Micromachining, Microfluidics

1 INTRODUCTION

The demand for low cost, high quality miniature parts in the medical technology sector is rapidly growing and the ability to introduce new microparts in the market is dependent on finding methods for the manufacture of parts in high-volume and at low cost but ensuring high product reliability. These characteristics are particularly important for those medical products where devices must be disposable for safety considerations.

Micro-injection moulding (µ-IM) is a microreplication technique that offers mass-production capabilities for polymer parts at relatively low cost, short-cycle times (few seconds), full-automation, accurate replication and good dimensional control. Hence, micro-injection moulding is currently used commercially for the production of a number of biomedical miniaturised devices. Similarly to conventional Injection Moulding, µ-IM is a technology in which a thermoplastic material is fed in the form of granules into the plasticating unit and then injected at high pressure into a mould, which is the inverse of the desired shape. The molten polymer freezes into the mould becoming a solid part and is then released from the mould by opening the mould and ejecting the plastic part with a set of ejection pins. The whole process is normally very fast with production cycles of a few seconds. In µ-IM, the mould cavities contain features of micrometre (µm) dimensions which need to be completely filled by the polymer melt. In many cases this requires the process to be adapted by removing air entrapped in the small features and by using additional heating elements to account for the very fast cooling of the injected melt into the small, cold mould micro-features. Moreover, in order to ensure proper cavity filling, high injection speeds and pressures are required. The machines for performing microinjection moulding need to possess the following characteristics:

- small plasticating units to avoid prolonged residence of the polymer melt which could result in material degradation

- precise and repeatable shot volume control to carefully meter the volume of material required. No material cushion must reside in the injection unit in order to ensure material uniformity.

- adjustable injection speed and pressure

- precise mould alignment and gentle open/close mould movements to avoid deformation of the small mould features.

One of the focal points of the work currently ongoing within the Precision Engineering Centre at Cranfield University is the investigation of µ-IM as a potential technology for high-volume manufacture of a specific category of biomedical devices commonly called microfluidic devices or “lab-on-a-chip”. Lab-on-a-chip is a term for devices that integrate multiple laboratory functions on a single chip of only millimeters to a few square centimeters in size and that are capable of handling extremely small fluid volumes down to less than picolitres. This category of products is being widely investigated at a prototype level. However, examples of polymer microfluidic devices successfully introduced in the market are very few.

Since the introduction of lab-on-a-chip devices in the early 1990s, glass has been the dominant substrate material for their fabrication [1] because of its material properties and because of the fabrication methods which were well established in the semiconductor industry; however, the cost of producing systems in glass is driving commercial producers to seek other materials. Commercial manufacturers of microfluidic devices see many benefits in employing plastics. Polymers are a group of materials offering several advantages over other conventional materials such as glass, silicon or other metals [2] eg a wide variety of properties which are tuneable, relatively low costs, relative simplicity of processing and accurate repeatability in high-volume production.

As part of the EPSRC funded project, 3D-Mintegration (EP/C534212/1), a multidisciplinary team based at Cranfield University and Herriot Watt University has identified and designed a versatile, generic module for

use in the preparation of blood samples necessary for a number of lab-on-a-chip diagnostic devices based on blood analysis. The element under consideration is a blood/plasma separator aimed at producing high-efficiency plasma separation in the simplest designs to compete with conventional plasma extraction such as centrifugation, blood filtration or CD-like platforms [3]. The biomechanical Fahraeus and Zweifach-Fung effects are combined in the device design to produce a separation between blood cells and plasma within the microchannels. No filtration is used at any stage of the process which results in a clog-free system. The method benefits from the natural plasma "skimming effect" in microchannels of dimensions below 300 µm [4], [5], [6].

This paper describes the design and the manufacturing steps of a truly 3D microfluidic device for blood/plasma separation. The expression "truly 3D" here refers to those plastic parts produced by µ-IM which have geometrical design such that they would not normally be demouldable. A way to overcome this limitation is to produce the 3D parts by lamination.

The polymer microfluidic device was designed for functionality, manufacturability by µ-IM and easy assembly. Moreover, the micromould was designed as a set of replaceable inserts with the aim of minimising the mould manufacturing costs and increasing the responsiveness of the process to subsequent changes and adaptation.

2 MICROFLUIDIC DEVICE DESIGN

The initial design proposed [8] was based on a 2,5D structure (fig. 1) characterised by a 25µm constriction in the whole blood inlet channel, followed by several bifurcating plasma subchannels 20µm wide and deep. The separation of the whole blood (which in first approximation can be seen as a suspension of red blood cells in plasma) into its basic components of red blood cells and plasma is made possible in the microchannel structure by biomechanical effects. The performances of the systems are believed to be governed by the channel width ratios and the length of the constrictions; however there is currently no definite design rule for determining the exact channel dimensions required for achieving efficient separation.

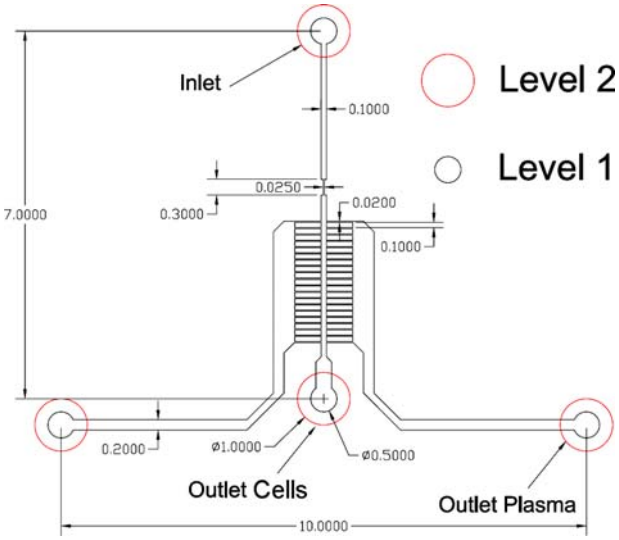

Fig. 1: Design of a 2,5D microfluidic device for plasma/blood separation [8]

The initial 2,5D design concept was reconsidered and a new 3D design was proposed. The 3D design was developed by re-conceptualising the 2D channels as 3D "disk spaces" around the inlet channel. A cross section of the design is shown in fig.2.

The polymer chosen for the plastic parts was poly-methylmethacrylate (PMMA) because of its good haemocompatibility and because it is suitable for direct welding techniques.

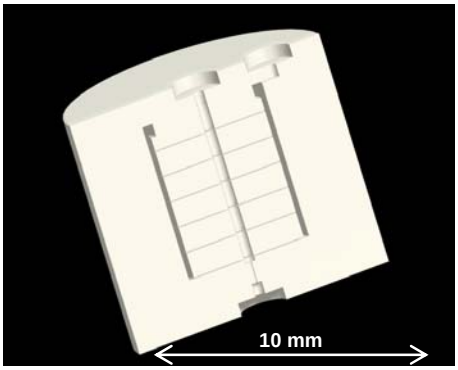

Fig.2: Design of the 3D microfluidic device for plasma/blood separation.

The 3D microfluidic device was designed by lamination of 5 PMMA discs all produced from the same polymer shot during the micro-injection moulding process. This device, which consists of one unit for the constriction channel, two separation discs each equivalent to a plasma subchannel in the 2,5 D design, one blood inlet and one blood/plasma outlet, has a number of benefits compared to the 2,5D version:

- Overall volume optimisation which allows a more compact product

- Use of 2 of the functional layers to act as a top and bottom lid for the device, thereby avoiding the need for manufacturing the lid in a separate process

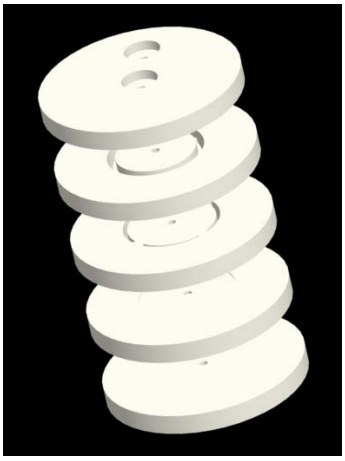

Fig.3: Laminated structure of the 3D microfluidic device

- Optimisation of the area involved in the separation (small channels in the 2,5D design which become thin discs in the 3D design)

- Modularity via the addition of separation units in the basic module to incorporate extra separation channels if required (fig.2).

- Potential for integration of other modular units in series with the blood separation module (for example, mixing units, detection, etc).

The initial dimensions as proposed by the designers in the 2,5D model were reconsidered bearing in mind the available manufacturing processes for micromoulds and the relative lack of clear design guidelines for optimising the required dimensions of the microchannels. The new

proposed critical dimensions are shown in fig. 4. Experimental trials will determine the tolerances required on the critical dimensions.

3 DESIGN FOR MANUFACTURING BY MICRO-INJECTION MOULDING

The 3D microfluidic device was designed for being manufactured by µ-IM using a Battenfeld Microsystems 50. The 5 PMMA slices comprising the final 3D device were designed to be moulded in one shot with the aim of minimising the variability from shot to shot that can occur during the moulding process. The restriction in the maximum polymer shot volume, which is approximately 1.1cm^3 for the particular model available at Cranfield University, was also taken into account for the parts design.

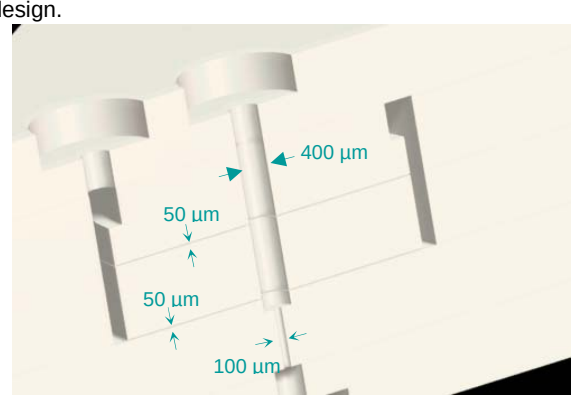

Fig. 4: Critical dimensions in the 3D microfluidic device

With regard to the micromould, this was manufactured adapting an existing two plate mould for cost considerations. This posed two major constraints: 1) the accessible surface area was restricted to about 25x25mm^2 and 2) the 5 slices were designed with features on one side only to comply with the pre-existing two plate mould.

4 DESIGN FOR ASSEMBLY AND JOINING

The plastic microfluidic device was designed for easy assembly. The overall size of the device (10X5mm) allows manual handling during the assembly trials (process which is expected to become fully automated during production cycle). Moreover the device has rotational symmetry of the parts around the central channel requiring alignment only of the central axis. The most critical part for alignment is the 100µm constriction; however this was designed so that it is completely within one side of the plastic inserts and overlaps with a much larger feature (the large inlet channel which has a diameter of 400 µm – bottom disc in figure 3 and 4).

The joining process is seen as a very critical step as the device must be leak-proof for correct functioning. Two different joining techniques will be evaluated: Transmission Laser Welding (TLW) and ultrasonic welding. It is expected that ultrasonic welding will prove to be more successful during the initial trials because of the relatively ease of tuning of the process parameters, however TLW will also be investigated because it holds the potential for a clean and fast serial production joining method for microfluidic devices.

The polymer material selected for the device manufacture (PMMA) is in principle suitable for both techniques.

5 MICROMOULD MANUFACTURE

The mould insert was designed as a set of 5 interchangeable elements (fig. 5 and 6).

Fig. 5: Solid model of the micromould insert. The shading is used to indicate the different parts of the mould and not to represent different materials

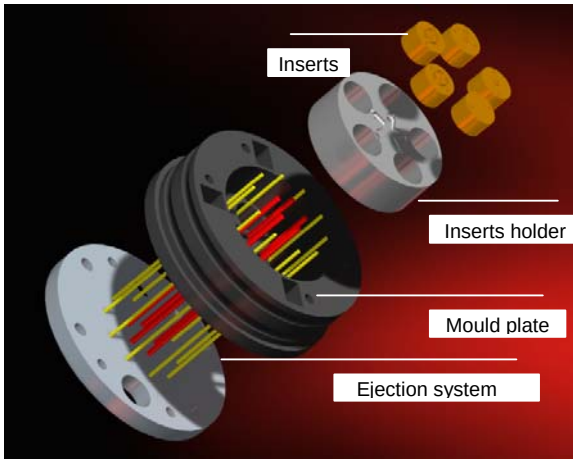

Fig. 6: Exploded micromould assembly including ejection system, insert holder and five inserts

A configuration based on replaceable inserts such as the one here proposed has potentially a number of advantages in particular during the prototyping and pre-production stages. First, it allows optimisation of the microfluidic device design which will be discussed below. This is crucial in particular for blood microfluidic devices where the support from simulations or modelling is absent because of the limited knowledge of the blood rheology in microchannels and because of the difficulties in simulating complex fluids such as blood. A similar problem also exists in the simulation of the polymer flow behaviour in microstructured inserts. Flow simulation software programs have proved very successful with conventional mouldings and allow for investigating the feasibility of a micromoulding process for component manufacture without a costly R&D moulding trial. However these software packages cannot be applied to micro moulding as they lose accuracy when considering micro-scale flows [7].

To overcome these limitations micromoulders typically rely on the feedback from the moulders to optimise the mould tools. This requires measuring the first runs of polymer parts to correlate against predictions and re-machining the mould cavity to specifications. However because of the complexity of the manufacturing processes and the dimension of the cavity it can be very difficult, costly and time consuming to modify an existing

micromould. Developing a mould in which the cavities are replaceable is therefore highly desirable; however this poses new challenges during the micromould manufacture because of the tight tolerances required between inserts and inserts holder to prevent polymer flash which may occur because of the high pressure, high speed conditions of the µ-IM process. Also the ejection system needs to travel a more complex path through the various parts. This creates new requirements during the micromoulds manufacturing and assembly steps to ensure a smooth ejection process.

Both inserts holder and inserts were fabricated in Alumold 1-500 (Alcan). From a functional point of view this type of aluminium was selected because it is appropriate for injection-moulds and can be utilised as an alternative to the more commonly used steel. From a machining point of view Alumold 1-500 was selected because it is a highly machinable type of Al and is suitable for micromilling, polishing and, if required, for subsequent diamond turning. Diamond turning is not suitable for machining of steels because of the extensive diamond tool wear.

All the five inserts were fabricated by micromilling with a Kern micromilling centre using the CAD/CAM software Cimatron E7.1. This software package supports the micro milling functions, produces optimal tool paths and the CNC programme for making the precise mould inserts. Fig. 8 shows an SEM micrograph of one of the 5 inserts and fig. 9 the model of the respective plastic part.

The cutting strategy for each insert consisted of a roughing step and a subsequent finishing step to remove the top 0.1mm layer. Both roughing and finishing steps were performed using tungsten carbide flat-end milling cutters. The process parameters for cutting the insert of fig. 8 including the 4 slots are shown in table 1. The overall machining time was 15 minutes.

	Roughing		Finishing	
Tool diameter (mm)	Feed rate (mm/s)	Rotational speed (rpm)	Feed rate (mm/s)	Rotational speed (rpm)
2	200	5000	/	/
1.5	200	8000	150	8000
1 (4 slots)	200	8000	200	8000

Table 1: Micromilling process parameters

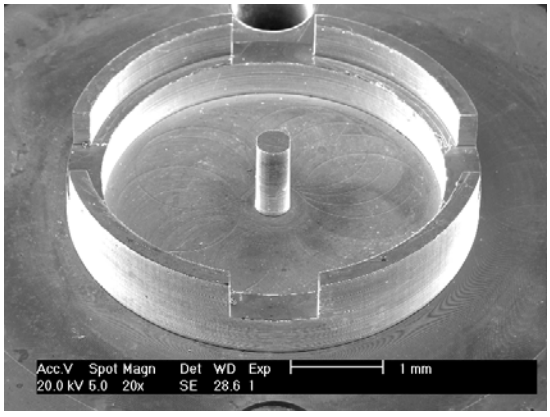

Fig. 8: Metal micromould

Fig. 9: plastic part replicating the mould of fig 8.

The holes visible at the top and bottom of the micrograph in fig. 8 were machined for the ejection system.

Once completed each inserts' outside diameter was machined to fit the insert holder with a H7/h6 sliding fit.

6 CONCLUSIONS

This paper describes the design and manufacture of a micromould for the manufacture of a polymer 3D microfluidic device.

- The 3D polymer device was designed for functioning as a blood/plasma separator for a lab-on-a-chip diagnostic device and was achieved by lamination of 5 layers.

- The micromould was designed as a set of replaceable inserts to allow for adaptations in the microfluidic design during the research, development and prototyping stages.

- The mould cavities were manufactured using a micromilling centre by adapting a two plate mould designed to fit onto a Battenfeld Microsystem 50 micro-injection moulding machine.

- The efficiency of the product development stage is believed to be greatly improved by the use of moulds with replaceable inserts. This allows easier testing of the design prototypes especially in those products where clear design guidelines are not available.

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