Title: A rapid-prototyped moulding system towards optimised scalable fabrication of elastomeric microfluidic devices

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Abstract
3D printing and makerspace technologies are increasingly explored as alternative techniques to soft lithography for making microfluidic devices, and for their potential to segue towards scalable commercial fabrication. Here we considered the optimal application of current benchtop 3D printing for microfluidic device fabrication through the lens of lean manufacturing and present a straightforward but robust rapid prototyped moulding system that enables easy estimation of more precise quantities of polydimethylsiloxane (PDMS) required per device to reduce waste and importantly, making devices with better defined depths and volumes for (i) modelling gas exchange and (ii) fabrication consistency as required for quality-controlled production. We demonstrate that this low-cost moulding step can enable a 40 – 300% reduction in the amount of PDMS required for making individual devices compared to the established method of curing approximately 30 grams of PDMS prepolymer overlaid on a 4” silicon wafer master in a standard plastic petri dish. Other process optimisation techniques were also investigated and are recommended as readily implementable changes to current laboratory and foundry-level microfluidic device fabrication protocols for making devices either out of PDMS or other elastomers. Simple calculators are provided as a step towards more streamlined, software controlled and automated design-to-fabrication workflows for both custom and scalable lean manufacturing of microfluidic devices.

Keywords: lab on a chip, microfluidics, 3D printing, process optimisation, translation, manufacturing, fabrication methodology

Introduction
Lab-on-a-chip and micro total analysis devices have been revolutionary for many research disciplines by enabling assays and studies to be conducted using micro-scale volumes of reagents. Through offering more resource-efficient means of studying novel reactions and processes, microfluidic technologies have burgeoned across multidisciplinary applications, spanning from analytical chemistry, biology and engineering to more emergent fields including synthetic biology and prebiotic chemistry. However, the translation of microfluidic devices to commercial production and the level of implementation of current standard laboratory consumables e.g. flasks and petri dishes has been limited due to the inherent challenges in upsampling established soft lithography fabrication techniques to achieve ‘low cost’ device batch processing beyond foundry-level initiatives. Furthermore, there is currently a lack of consensus on standardised device designs, geometries and means of connecting devices to flow systems which is necessary for developing manufacturing systems for commercial production of devices and microfluidic components. This issue is partially
due to two intersecting categories of researchers seeking to apply microfluidics: those interested in designing and studying custom flow configurations to meet the requirements of a particular application, and those who would prefer fully developed and validated plug and play systems. While the spectrum shifts as the field of microfluidics grows, the former category dominates the current state of the field. Given the sheer diversity of applications, myriad microfluidic device configurations are possible which may be modular or customized with any number of components and features e.g. ports, valves, mixers and particles traps. A convergence on assay-specific or basic channel configurations for relatively simpler applications may eventuate in tandem with new solvent resistant materials amenable for mass manufacturing. Until then, it is currently more convenient and economical for researchers to design and make their own devices rather than attempt to source prefabricated devices with the exact features and geometries required as these are likely not available to purchase as off the shelf products. This has led to a circular issue for attaining consensus on standard device designs and geometries, which is ultimately required to meet economies of scale for commercialised production of microfluidic devices. Earlier open repository initiatives such as Metafluidics 5-6 (and now journal-based repositories) were established to encourage design sharing and gathering consensus on microfluidic device designs. However, the immediate end-user market is still for custom devices, which is fundamentally at odds with high-throughput manufacturing. Therefore, the extant paradigm of soft lithography pioneered by Xia and Whitesides 7 currently remains the most straightforward means of prototyping microfluidic devices for the individual researcher for studying novel application-specific channel configurations, features and their effects, and is entirely suitable for the research and development ecosystem and proof of concept stage of a product lifecycle. Devices are formed by curing an elastomer, most commonly polydimethylsiloxane, on a relief template of the inverse pattern of the channel design, which is created by etching or patterning photore sist on a silicon wafer or other flat substrates. Alternative elastomers and thermoplastics may also be used 8-9. Once prototypes are validated, devices may be fabricated with more inert and solvent-resistant materials such as PTFE, polycarbonate and glass, which are compatible with mass-manufacturing methods e.g. injection moulding and machining.

The recent advent of affordable 3D printers and makerspaces have made traditional manufacturing techniques e.g. machining and laser cutting more accessible 10-11; these have been actively explored as means to progress from soft lithography to high throughput fabrication 12. 3D printing (3DP) has been particularly investigated for fabricating standalone millifluidic devices or microfluidic device moulds 10, 13-14. However, the print resolutions of current desktop filament-based fused deposition modelling (FDM) and stereolithography (SLA) 3D printers is limited by virtue of their respective print mechanisms and are suboptimal for producing the micro and nanoscale features that can be achieved by photolithography 10. Also, 3D printing materials may have low chemical resistance 15, leach small molecules that interfere with biological processes 16 and are not optically clear, which preclude devices from imaging studies. Nevertheless, these technologies have motivated an evolution from laboratory-based to dedicated start-up level fabrication of custom OEM devices e.g. Darwin Microfluidics and Fluigent. Here we deconstructed the established soft lithography workflow to identify process improvements, grounded in lean manufacturing principles, that may bridge the gap between laboratory-level fabrication and upscaled manufacturing of custom devices. Namely, these are: (i) better estimation and use of more defined quantities of PDMS per device, (ii) known and replicable device volumes, and (iii) more optimal use of PDMS and silicon wafer templates to align with overarching goal of microfluidics to reduce reagents and material waste. To achieve this, we also considered the optimal integration of current desktop 3D printing where the surface texture of the printed model will not affect microscale features. Here we present a 3D moulding system (Figure 1) to cast PDMS devices with well-defined volumes and depths, which is necessary for both
modelling gas exchange and quality control. Simple calculators are provided to determine mould dimensions based on the geometry of the channel design, volume of PDMS and size of silicon wafer required, scaled by PDMS curing temperature and associated shrinkage as measured by Madsen et al. As a demonstration of the technique, this moulding method enabled easy fabrication of devices with dimensions of 21 mm (width) x 32 mm (length) x 4 mm (height) using just 3.5 grams of PDMS, compared to approximately 5 grams of PDMS per equivalent device assuming optimal spacing of up to 6 designs on one wafer via the conventional method of using 30 grams to cover a standard 4 inch (100 mm) diameter silicon wafer. The 3D printed outer moulds can be easily cleaned and are reusable for making devices with similar X-Y dimensions.

![Diagram of the moulding process](image)

**Figure 1.** This 3D printed outer mould allows devices to be fabricated with exact quantities of PDMS (or other elastomers) to achieve desired heights. A calculator for substrate and mould dimensions and amount of PDMS required is provided in Supplementary Document.

**Soft lithography & optimising the use of silicon wafers**

**Device-specific substrate sizing**

For researchers new to microfluidics, ample excellent resources exist that detail the concept and process of soft lithography, including. Briefly, a microfluidic master template is created by UV curing photoresist as an inverse pattern of the fluid channels onto a flat substrate. 3” and 4” diameter silicon wafers are typically used as the preferred substrate for photolithography as they are polished down to be perfectly flat and smooth, which is necessary for producing micro and nano-scale features. The conventional approach to optimising the use of a single wafer is to fit and arrange multiple templates on a single wafer depending on their X & Y dimensions. A 5-10 mm gap is recommended between the outermost channels of each pattern to ensure that there is adequate space to trim out individual devices and accommodate fluidic connectors, which typically occur at the edges of the device. It was envisaged that silicon wafers can be sized to provide just the area needed for moulding a chip, which is convenient for making or re-making individual devices compared to having to cast PDMS across an entire wafer, especially when multiples may not be required for preliminary design evaluation. The size of the wafer required can be calculated by
adding a 5 mm margin to both directions of the X and Y dimensions of the device, and an additional 3.5-4 mm rim on each side to accommodate a 3D printed mould with 1.5-2 mm thick walls, and account for meniscal edge effects (Figure 1). A simple calculator is provided (Supplementary Document) to determine the minimum dimensions of the wafer needed as well as dimensions for a corresponding 3D printed outer mould by entering the maximum X and Y dimensions of a device channel design. After calculating the required dimensions of the substrate, guide positions were marked along the edge of a whole silicon wafer with permanent marker. A wafer piece was then cut by positioning the wafer on layer of paper towel, then notching the edge at the mark with a diamond tip scribing pen and pressing the tip of the pen down at the notch to cleave the wafer along the crystal plane (Supplementary information 1). This method allowed for clean orthogonal pieces to be cut. Spare wafer pieces can be stored and cleaved to size as needed. The wafer can also be placed on a sheet of adhesive film for stability during cleaving and to catch fragments. It is anticipated that this process can be automated with programmable dimension fitting and is applicable for sectioning alternative substrates.

**Photoresist handling, dispensing and storage**

The most common photoresist used for microfluidics soft lithography is SU-8, a liquid epoxy-based UV-cured resin, which is typically spin-coated onto a silicon wafer to attain an even layer. SU-8 may also be dispensed via constant-volume injection and allowed to self-level \(^{23}\), or manually spread with guide walls for higher-viscosity formulations to obtain layer thicknesses of up to 1500 \(\mu\)m \(^{24}\). However, the process of spin-coating is inherently wasteful, which led to the development of photoresist films such as SUEX, ADEX or custom thick sheet dry films (TDFS) that are laminated onto the substrate. The advantage of dry resists including simpler solvent-free processing, ready fabrication of multilayer and high-aspect ratio features, homogeneous and controlled layer thickness (corresponding to channel height), and reduced waste from liquid handling and spin-coating \(^{25}\). However, these films are relatively expensive due to niche early market, production and supply-demand factors as with off-the-shelf microfluidic devices. Care must be taken to remove any dust or particulate material between the sheet and substrate, and a yellow-light cleanroom is still recommended for processing.

A standard 4” wafer typically requires 3-5 mL of resist for spin-coating. However, repeatedly opening a bottle of resist will speed up evaporation of the solvent component, causing it to thicken, as well as increased the risk of light and particulate contamination. Therefore, once a new stock bottle (1 L) of resist was opened, aliquots were decanted into smaller 250 mL capped amber glass bottles in a yellow light cleanroom (CASLEO, School of Chemical Engineering, UNSW Sydney, Australia) to reduce the rate of solvent evaporation and for ease of dispensing. These 250 mL bottles can be opened sequentially and further decanted into 30-50 mL capped amber glass bottles, which should be sufficient for covering the entire surface of approximately ten 4” silicon wafers depending on the viscosity of the resist. As with photolithography processes, decanting and handling of SU-8 and photoresists must be carried out in a yellow light room, ideally a clean-room facility. If smaller amber glass bottles cannot be sourced, normal capped clear glass bottles can be completely covered with aluminium foil to protect the photoresist from light exposure during storage. Aliquots stored in smaller amber glass bottles would also benefit from additional protection with a layer of aluminium foil as the walls of smaller bottles may be thinner than those of the stock bottles. If the stock or aliquot SU-8 has noticeably thickened, or the spin-coat layer thickness is significantly higher than manufacturer calibration curves, SU-8 can be thinned and/or diluted with cyclopentane. Calibration of spin speed to layer thickness \(^{26}\) is then necessary as the resulting viscosity may be lower than that of the original stock resist.
Given the viscosity of SU-8 photoresists, directly pouring the resist from a small bottle onto the centre of the silicon wafer in a continuous action is recommended over dispensing the resist with a transfer pipette as the action of pipetting introduces air bubbles into the resist, which then need to be removed by either manually rupturing them with a needle after spin-coating or dragged towards the edge of the wafer. Either method of removing bubbles (and any remaining microbubbles) can leave artefacts within the milieu of the resist that interfere with photolithography and the downstream resolution of the SU-8 master. Also, more viscous resists may be difficult to dispense from the pipette and so is wasted. Pouring enough resist (approximately 3-5 mL) from the smaller aliquot bottle to cover approximately \( \frac{1}{2} \) of the area of the wafer substrate is typically adequate for spin-coating.

**Precoating silicon wafers with photoresist towards upscaled manufacturing**

Adhering the photoresist to the wafer (whether in liquid or dry film form) and subsequent processing of the photomask remains the rate-limiting step for soft lithography. Dry film resists were developed for greater convenience and less use of solvents over liquid photoresists but still requires manual handling and sizing over substrates. A logical extrapolation for workflow streamlining would be a ready-to-use photolithography substrate, i.e. a substrate that has been precoated with photoresist and which can be resized if desired, such as for the moulding system described here. Therefore, to investigate the viability of precoating silicon wafers with resist as a step towards a potentially scalable commercial product, quadrants of 4” diameter wafers were coated in two grades of SU-8 with different viscosities: SU-8 2015 (thinner) and SU-8 2075 (thicker). In a photolithography facility (CASLEO, The University of New South Wales, Sydney, Australia), the resists were spin-coated onto clean and dry wafer segments to approximately 45 µm and 50 µm respectively and soft-baked to set the resist. The coated wafers were then stored in foil-covered petri dishes and could be cleaved into desired dimensions for photolithography as for uncoated wafers (Supplementary Information 2, 3). While edge effects from spin-coating liquid resists are unavoidable, dry resists can be prelaminated onto wafers as a future alternative. To test the viability of the resist, a coated wafer that had been stored for one week was used to make a photolithography master and PDMS devices were successfully cast (Supplementary Information 6.2). Several artefacts resembling small spheres of cured resist were present on the edges of some of the SU-8 master channel features, which could be manually removed and had negligible impact on the surface resolution of a PDMS device cast using the master (Supplementary Information 6.2). Although care was taken to not expose any of the resist to normal (shorter wavelength) light, the artefacts may either be due to resist degradation over time, photocrosslinking from a monitor screen or condensation and crosslinking of the epoxy polymers as the solvent component evaporates during application and storage (the foil-covered petri dishes were not tightly sealed). Uncured resist following photolithography was otherwise thoroughly removed with developer as with freshly cured resist. While further work is required to determine proper storage techniques and shelf life, this work shows that precoating substrates with photoresist is possible and has potential for batch coating as a foundry-level or commercial operation.

**3D printed outer moulding system**

A drawback of soft lithography is that it requires the use of copious quantities of PDMS. Another issue is that the heights of single-layer devices and devices constructed from building up individually layers of PDMS are variable, which is not conducive for the precise modelling of gas exchange and study of oxygen-sensitive processes. Therefore, an outer moulding system was conceived where 3D printed frames could be used to hold well-defined quantities of PDMS for casting devices with controlled depths, volume and hence less PDMS waste. As proof of concept, rectangular moulds
with dimensions optimised for a simple mixing device design were printed with polylactic acid (PLA) and acrylonitrile butadiene styrene (ABS) using benchtop FDM printers as well as in stereolithography resin. PLA was initially chosen as it is one of the most accessible standard filament-extrusion printer materials. PLA is biodegradable and has lower toxicity compared to other FDM thermoplastics and stereolithography printer resins, which makes it more user and environmentally friendly and better suited for moulding devices for biological applications. Furthermore, its high hydrophobicity was hypothesized to facilitate the easy release of cured PDMS devices without requiring additional surface treatment steps. PLA also has a lower glass transition temperature than ABS, another common FDM filament material, which allows it to be readily printed on an unheated stage, have higher bonding strength between layers and be less prone the warping and delamination issues commonly encountered with ABS. Nevertheless, moulds were 3D printed with PLA, ABS and stereolithography resin as a representative sample of print materials and 3D printers commonly available at most makerspace facilities for comparison and analysis of potential leachates. The specifications of each are presented in Table below:

Table 1. Specifications for outer moulds printed in ABS, PLA and resin as a representative sample of accessible FDM and stereolithography (SLA) 3D printers

<table>
<thead>
<tr>
<th>Material</th>
<th>Printer Make/Model</th>
<th>Type</th>
<th>Layer thickness/print resolution (mm)</th>
<th>Fill density</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABS (white)</td>
<td>Ultimaker3</td>
<td>FDM</td>
<td>0.1</td>
<td>20%*</td>
</tr>
<tr>
<td>PLA (green)</td>
<td>Prusa3</td>
<td>FDM</td>
<td>0.2</td>
<td>20%*</td>
</tr>
<tr>
<td>Resin</td>
<td>Formlabs Form3</td>
<td>SLA</td>
<td>0.05</td>
<td>100%</td>
</tr>
</tbody>
</table>

PLA models were printed without supports while ABS required a primer layer to initialize and adhere the print to the stage. Due to low model complexity, both FDM models were set up to print with the bottom perimeter of the frame contacting the stage. SLA model was offset at a slight angle off the stage to mitigate planar spot focussing issues and hence improve print resolution. All support contact points were kept on the outside of the mould to ensure that the inner faces are free from surface artefacts that may impede the release of a PDMS or elastomeric device from the mould.

Postprocessing and treating 3D printed outer moulds

After printing, the resin mould was thoroughly rinsed with isopropanol to remove liquid resin residue, then UV cured for an additional 20 minutes to the recommended time to ensure that no uncured resin may potentially interfere with PDMS curing. Any support structures were then removed from the moulds. No support structure was necessary for printing the PLA moulds, while the initialising layer for the ABS mould was easily peeled off. The models may also be sanded with fine grain sandpaper to obtain a smoother finish. The resin moulds were then plasma cleaned and surface treated with trimethylchlorosilane to reduce adhesion to PDMS and facilitate device release. A resin mould was left untreated for analysis of leachates.

Leak-proofing 3D printed moulds

To effectively contain liquid PDMS when casting devices, the bottom rim of 3DP moulds must be flat and sit flush to the surface of a silicon wafer/base master mould. However, the top and bottom faces of the extrusion-based 3D printed moulds may not be perfectly flat due to printer-dependent deposition processes, print conditions, the stage material and contact points between the model and the stage and/or support structures (determined by print setup). For example, the number and position of support structures may leave artefacts, the first layers of filament extrusion printers may
fuse to the stage and peel if a support is not included in print model setup, the pressure exerted by a print nozzle during deposition of molten filament in FDM printing may create ridges, and the UV-curing and heat post-processing of stereolithography printed resin models may lead to warpage. These artefacts can create small gaps through which liquid PDMS can leak through when casting devices even at higher temperature cures (up to the glass transition temperature of the 3DP mould material) over the course of several hours. Therefore, a straightforward method for creating a leak-proof seal at the mould-master interface was devised where the bottom rim (face) of the 3D printed frame was dipped into liquid PDMS prepared for making a device (Supplementary information 5, 6). The frame was then positioned PDMS-coated side down on the silicon wafer master on a polystyrene petri dish, then cured together at 60°C for 15-20 minutes in an oven. A maximum curing temperature of 60°C was selected as a balance between curing efficiency and the glass transition temperature of PLA (50-80°C). Once the rim of PDMS was set, the rest of the PDMS was poured into the mould and cured. The viscosity of PDMS allows self-levelling under the weight of the frame. Any PDMS exudate along the internal contact edge is either incorporated into the main body of the device or if external to the frame, is easily removed with a scalpel. This sealing step was effective at preventing PDMS leakage for all 3DP moulds printed with PLA, ABS and resin and does not require the use of other materials e.g. silicone-based sealants which may leach small molecules that could potentially interfere with PDMS curing, sensitive biological assays or chemical reactions.

Leachates from 3D printed moulds

It is well established that 3D printing resin, FDM filament materials and SU-8 moulds and PDMS itself leach small molecules including uncured monomers, photo initiators, colourants and acrylates/epoxy backbone polymer chains, which can interfere with sensitive biological assays and chemical reactions. The degree of leaching is dependent on 3DP material and PDMS curing temperature. Therefore, a study was conducted to assess and compare any leachates from the common 3DP materials (ABS, PLA and resin) if they are used for the outer moulding system to inform potential chemical interference and whether additional processing steps are necessary, as well as correlate to existing literature. Sample 5 mm thick PDMS devices were cast in rectangular 3DP moulds on a polystyrene petri dish to reduce interference from SU-8, then incubated in Milli-Q water at a concentration of 1 µL per mm³ for 24 hours at room temperature, 37°C and 60°C to cover a range of device operational conditions. The samples were then analysed with liquid chromatography-mass spectrometry (LC-MS) (Supplementary information 7).

[Spectra to be retrieved and analysed January 2022]

Fabricating PDMS microfluidic devices with the moulding system

Methodology run-through

As silicon wafers tend to be segmented circles in shape, curved edge pieces are potentially wasted. The 3DP outer moulds can theoretically be designed to fit any corresponding shape and size of a piece of silicon wafer. However, as a test of the robustness of the methodology and whether the rectangular PLA moulds could be reused for non-orthogonal wafer sections with similar dimensions to those determined by the calculator, devices were fabricated on a master made with a curved corner piece of a silicon wafer. Briefly, a perimeter piece wafer with a curved corner was spin coated with SU-8 2015, and a simple channel resist template was created via photolithography (Supplementary Information 3). The silicon master was then silanized (Supplementary Information 4). PDMS was prepared by mixing prepolymer and curing agent in the standard 10:1 ratio, then degassed under vacuum for 30 minutes (Supplementary Information 5). The rim of a PLA 3DP mould was coated with PDMS as previously described, then positioned on the irregular wafer
(Supplementary Information 6). The wafer-less region was filled in with an additional droplet of PDMS using a standard pipette, then cured together with the 3DP mould and master during the sealing step. The rest of the PDMS was then poured into the mould and the chip was cured at 60°C for 4 hours and the process was repeated. Devices were easily removed from the non-orthogonal wafer and PLA moulds. The curved corner portion and any rim residue was trimmed off with a scalpel to obtain a flat device, then inlet and outlets were formed with a biopsy punch. Finished devices were then bonded to glass slides via oxygen plasma treatment. The process is summarized in Figure 2.

![Figure 2](image)

**Figure 2.** (a) PLA 3DP mould and irregular photolithography master; (b) the bottom rim of the 3DP mould was coated with PDMS and cured against the master with the top right corner filled in with PDMS; (c) the rest of the PDMS was then poured into the mould and cured; (d) the device was easily extracted from the mould and master; (e) edge residue was trimmed, inlets and outlets were formed and the corner infill piece was removed to obtain a flat device; (f) finished device was plasma bonded to a glass slide and flow tested.

**Bonding the devices and integrating fluidic connectors**

After removal from the 3DP mould and master, any PDMS edge residue on the device was easily trimmed off with a scalpel. Inlets and outlet ports were formed by punching holes through the entire thickness of the device with biopsy punches (alternatively, ports may be formed by microdrilling). As the design system accounts for the position of inlet and outlet ports, the thickness of the PDMS device is theoretically the same at all connection points. The meniscal edges of the device can be trimmed down if a perfectly flat device is required. However, the meniscus is effective at holding small volumes of PDMS or sealant should any additional steps be required to permanently bond tubing or connectors to the device such as for high-pressure applications 38, negating the need to refit finished devices into the mould, although that is readily possible if an additional layer of PDMS thicker than the height of the meniscus (2-3 mm) is required.
Coating Glass Coverslips with PDMS

Some applications require fluidic channels to be comprised of the same material in order to have the same surface properties after treatment and/or functionalization, i.e. glass slides or cover slips need to be coated with PDMS to enclose PDMS device channels. Cover slips are preferred for imaging as their thinness is more compatible with smaller objective working distances. For coating, PDMS may be directly spin coated onto thicker glass slides, or glass coverslips may be overlaid on a layer of PDMS spin coated on a silanized silicon wafer, then cured. However, cover slips are prone to breakage during the extraction step due to their low fracture toughness and the strong adhesion between elastomeric PDMS and the wafer surface. It was thought that the smaller surface area of sectioned wafers may facilitate handling and extraction of individual coated slips, resulting in less breakage and hence more efficient production of PDMS-coated glass substrate. To test the hypothesis, silicon wafer pieces were silanized then spin coated with PDMS. A 22 mm x 22 mm coverslip was lightly pressed into the PDMS layer and cured at 120°C on a hotplate for 5 minutes. The PDMS-coated slip readily peeled off the smaller wafer, where the PDMS overhang along the edges of the wafer provided an easy area to roll and grip the PDMS sheet. Excess PDMS around the cover slip layer was then removed (Supplementary information 8). Six coverslips were consecutively prepared without shattering using the smaller sized silicon substrates, where the number of intact slides per number coated indicates the efficacy of this method. While efficacy also depends on individual skill and improves with practice, the approach gives a similar time-material-cost benefit as using a whole wafer. Given that PDMS porosity is affected by the polymer to curing agent ratio, a key advantage of using smaller PDMS coating substrate is that allows the same batch of PDMS for making an individual device to also be used for coating the sealing slide, therefore ensuring compositional homogeneity and hence material and surface properties throughout a device.

Other process improvements

Silicon wafer master reinforcements

Silicon wafers used for making photoresist master moulds have thicknesses in the order of several hundred microns to 1 mm, which makes them quite fragile and amenable to breaking when peeling cured PDMS devices from the master due to adhesion between the cured elastomer and the surface of the silicon. Photoresist master moulds are commonly treated with trichloromethylsilane or perfluorinated silane to reduce this surface adhesion and aid the release of PDMS devices. However, the silicon wafers are still prone to breakage during device removal, particularly with inexperience. The larger the contacting surface area between cured PDMS and the wafer, the more adhesion and the greater the risk of breaking the wafer or PDMS coated glass slides. Using smaller optimised wafer pieces for the moulding step proposed by this work mitigates the risk of wafer breakage effectively. However, for whole wafers and larger sized masters, the risk of breakage can be further reduced by bonding the back of the wafer to a glass petri dish via heat or a thin layer of epoxy for reinforcement (Supplementary 9). The entire dish and wafer can then be silanized for easier release of devices. This reinforcing step is easy and inexpensive to implement and provides self-contained storage of custom sectioned or whole silicon master moulds. Alternatively, standalone photoresist masters may be stored on double sided adhesive tape in a folder system between moulding devices.

Surface finishing for devices directly cast from 3D printed moulds

While resin-based SLA printers offer higher resolution than filament extrusion (FDM) printers, their resolution depends on the laser spot size, energy and polymerization mechanism itself. A resolution of 25 µm renders the process unsuitable for fabricating micron scale relief templates as the surface texture produced from non-feature regions are technically microchannels, which would create
leakage issues along the axis of the print texture from the main channel features. This concept is illustrated in Figure 3. As a circumvention and investigation of low-cost fabrication, Felton et al. suggest only printing the relief channel features, then bonding these to a glass slide to form a master template. However, this approach is still best suited for millifluidic scale devices. For larger scale devices cast from 3DP moulds, the surface texture of the bottom face may be smoothed out by spin coating PDMS on a petri dish to a maximum thickness of 25 µm, stamping a freshly cured PDMS device on the spin-coated PDMS layer to fill in the print surface texture, then bonding the device to a glass slide, dish or another piece of PDMS (Figure 3). Koschwanez et al. recommends spin coating PDMS (standard 10:1 curing ratio) for 5 minutes at 1000 rpm to obtain a thickness of approximately 25 µm, which is sufficient for filling in the surface texture. Thicker layers are not recommended as excess can flow into and/or clog channel features.

Figure 3. Overview of steps to fill in the surface texture of devices cast from 3D printed moulds by stamping the device in a thin layer of spin coated PDMS. Cross sectional view is shown.

Conclusions and future directions

The process of soft lithography has traditionally relied on adapting a protocol at a postprocessing stage in order to obtain devices of certain dimensions, when a more effective manufacturing approach is to engineer the intended outcome from the start of the process. This work explored how the current design and fabrication workflow for making PDMS microfluidic devices from either photoresist masters or 3D printing can be optimised and improved, with potential forward compatibility with upscaled lean manufacturing processes. Here a moulding system was developed as an immediate integration of benchtop 3D printing and conventional soft lithography, and is comprised of a 3D printed volume delimiting mould, substrate and PDMS volume optimally sized to intended device dimensions. We demonstrated that this straightforward moulding system is an effective means of estimating precise quantities of PDMS (or other elastomers) and silicon wafer substrate required to form individual devices of known and/or consistent dimensions as necessary for quality control. The rectangular 3DP moulds can be applied on whole wafers with multiple SU-8 templates, or on sized silicon masters with individual templates. While individual rectangular moulds were investigated here, the concept of a volume-delimiting mould can be extended to a multicompartment grid to simultaneously cast multiple devices on whole silicon wafers or larger substrates. Both the 3DP moulds and sized masters can be offered as a packaged product for those interested in casting devices in PDMS or elastomers, or along with fabricated devices. The overall moulding system can readily be applied from laboratory to start-up level operations for the creation of custom devices, with potential for automation and scaling. For example, the calculator can be programmed into an integrated software interface to dimension 3D printed mould design files for 3D printing, and photoresist-coated substrates for cleaving, laser cutting or CNC milling. It is anticipated that with microfluidic design consensus, advancements in solvent resistant materials and manufacturing technologies, soft lithography may be superseded by a primarily automated workflow where more durable templates are stamped into PDMS/elastomers that have been volume injected.
into a multicompartment grid-like mould to simultaneously mould multiple devices. In the meantime, the low-cost rapid prototyped moulding system described here is recommended for streamlined quality-controlled fabrication of elastomeric microfluidic devices, which can inform further development towards full process automation.

Acknowledgements
Many thanks to Prof. Kourosh Kalantar-Zadeh and Dr. Jiong Yang (CASLEO, School of Chemical Engineering, University of New South Wales) for supporting the photolithography component this work, 3D printer custodians Gabriel Graterol Nisi (UNSW Makerspaces) and Christopher Lee (School of Chemistry, University of New South Wales) for their assistance with attaining high quality 3D printed models, and the Bioanalytical Mass Spectrometry Facility (Mark Wainwright Analytical Centre, University of New South Wales).

Contribution Statement
CP ideated the moulding system, developed the methodologies, prepared the supplementary information and wrote the manuscript. AF edited the manuscript and provided feedback.

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