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An easy-to-use microfluidic interconnection system to create quick and reversibly interfaced simple microfluidic devices

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Abstract

The presented microfluidic interconnection system provides an alternative for the individual interfacing of simple microfluidic devices fabricated in polymers such as polymethylmethacrylate, polycarbonate and cyclic olefin polymer. A modification of the device inlet enables the direct attachment of tubing (such as polytetrafluoroethylene tubing) secured and sealed by using a small plug, without the need for additional assembly, glue or o-rings. This provides a very clean connection that does not require additional, potentially incompatible, materials. The tightly sealed connection can withstand pressures above 250 psi and therefore supports applications with high flow rates or highly viscous fluids. The ease of incorporation, configuration, fabrication and use make this interconnection system ideal for the rapid prototyping of simple microfluidic devices or other integrated systems that require microfluidic interfaces. It provides a valuable addition to the toolbox of individual and small arrays of connectors suitable for micromachined or template-based injection molded devices since it does not require protruding, threaded or glued modifications on the inlet and avoids bulky and expensive fittings.

Keywords: microfluidic interconnection, microfluidics, chip-to-world interface, modular microfluidic systems, polymer devices

S Online supplementary data available from stacks.iop.org/JMM/25/115010/mmedia

(Some figures may appear in colour only in the online journal)

Introduction

Interfacing microfluidic devices to external equipment remains a challenge that is yet lacking a widely accepted standard [1, 2]. While the development of applications for microfluidic devices is progressing, microfluidic technology is refined and re-invented alongside. Both the interdisciplinary nature and the vast variability in methodologies create a large amount of individual solutions to similar problems such as the chip-to-world interface [3]. Different requirements and desired levels of flexibility have given rise to numerous specialised interconnection systems used both for complex lab-on-a-chip systems and for simpler microfluidic devices that provide a proof-of-concept for a certain design or constitute the interface to other components such as biosensors. An excellent overview of the current state of the field can be found in a recent review [4].

A few commercially available platforms have emerged providing a standardised solution for the operation of devices from specific manufactures or devices that are designed to match a certain layout [5–7]. Some research groups have also developed interface platforms that can provide access to a large number of inlets simultaneously, for example in polydimethylsiloxane (PDMS) [8] or using an aluminium clamp and flanged polytetrafluroethylene (PTFE) tubing [9]. These components and platforms are generally rather large compared to the devices, and while the standardised layout is suitable for the routine operation of microfluidic devices it lacks the flexibility that is often necessary for early prototyping and the development of modular systems. The individual commercially available connectors such as Luer and Nanoport, on the other hand, need to be irreversibly glued or bonded to the devices. While there are solutions to overcome some problems associated with epoxy glues [10], the additional material can lead to chemical or thermal incompatibilities. As an alternative, the required protruding structures can be molded as part of the device, which avoids the adhesive but complicates fabrication and bonding procedures [11]. In either case, the added structures are generally large compared to inlet size and, in the case of the Luer connector, associated with large internal and dead volumes. Additionally, a wide variety of other solutions for individual connectors have emerged in recent years. Many are based on a press fit mechanism to interface needles or capillaries directly with PDMS devices [12–17] or using PDMS as a gasket material [18–20]. PDMS however is not chemically inert, which prohibits applications that use solvents, and usually these connectors suffer from low leakage pressures unless very thick layers are used. Furthermore, cored holes in PDMS films are difficult to reproduce with good quality and are easily damaged [12]. Press fit [11, 14] and interference fit [21, 22] mechanisms have also been presented using other materials such as SU-8, but these show low pressure tolerance and handling robustness [14] or are limited to being used as a chip-to-chip interface [22]. Interconnections that are composed of a number of materials such as metal needles, adhesives and other polymers that are irreversibly attached to devices are often not compatible with common sterilisation procedures such as autoclaving due to different thermal expansion coefficients hindering adequate cleaning for biomedical applications. Recently, the advent of additive manufacturing techniques (3D printing) has enabled novel approaches to microfluidic device design. No longer limited to planar designs with unidirectional feature definition, complexity no longer comes at the cost of tedious assembly and alignment. Naturally, this has given rise to additional solutions for the interfacing of microfluidic devices [23] and the development of modular systems [24]. In this paper we present a novel interconnection system based on an interference fit mechanism that does not require the use of o-rings or the assembly of an external platform, but is integrated into the device fabrication. The connection is chemically robust to the extent of the device material chosen for each application, fully reversible and can withstand pressures above 250 psi (1720 kPa), which was the limit of the used pressure test setup. Being composed of only two or three materials, that of the device, that of the plug and that of the tubing, which can be completely separated from each other, make this interconnection especially robust, easy to clean and sterilise, and thus compatible with most chemical or biological applications. It is intended for the quick, reversible and reliable interfacing of simple microfluidic devices providing high flexibility and ease-of-use. External tubing can be connected individually or in small arrays, with a small footprint and low dead volumes. We demonstrate its use in the attachment of standard PTFE tubing to devices fabricated in a variety of polymers. Different parts of the interconnection can be fabricated in the same or a combination of different materials to meet the requirements of the application, without compromising functionality. The connectors have been incorporated in continuous flow systems as well as to connect different modules into a combined microfluidic system.

Materials and methods

Design and function

The interconnection system was designed to directly interface PTFE tubing (Bola, Germany) with microfluidic devices fabricated in hard polymers, as opposed to rubber-like polymers such as silicones that readily form a seal, without using o-rings or glue. Each connector consists of three components: a socket, which is a modified fluid inlet on the device, the tubing itself and a small separate plug as shown in the technical drawing in figure 1.

Figure 2(a) shows how devices are interfaced with the tubing by inserting the plug, while the sequence 1–4 in figure 2 illustrates how the different parts of the interconnection interact and how the seal is formed. The function of the socket is to receive the tubing and to create the sealing interface between the inside of the tubing and the microfluidic channel. It is composed of a pin surrounding the inlet hole that matches the inner diameter of the tube and a surrounding trench, which receives the plug and fastens the tubing by an interference fit mechanism. The plug is a separate part that slides onto the tubing before attachment. To connect, the cleanly cut edge of the tube is first pushed onto the pin and then compressed into a tight seal when the plug is pushed into the socket. To release the tubing, the plug is simply lifted from the device by one of its edges. In this way the tubing can easily be removed or exchanged. Figure 2(b) shows the tubing/socket interface and illustrates the fluid path. The red marked area outlines the area in which recirculation can occur. Of course the size of this area depends on the used flowrate and the inner diameter of the inlet hole. For the size of interconnection presented here, the volume is estimated to lie between 25 and 50 nl.

Fabrication

All the parts and devices were designed using Autodesk AutoCAD 2012 and fabricated by CNC milling using EZ-CAM Express 15.0 to generate the instructions. For demonstration, three different materials were used, poly(methyl methacrylate) (PMMA), cyclic olefin co-polymer (COC, grade: Topas 5013-S-04) and polycarbonate (PC).

Fabrication of microfluidic devices

A typical microfluidic device of the type that we are considering here consists of a minimum of two layers of polymer: one layer that contains the channels system (bottom plate)

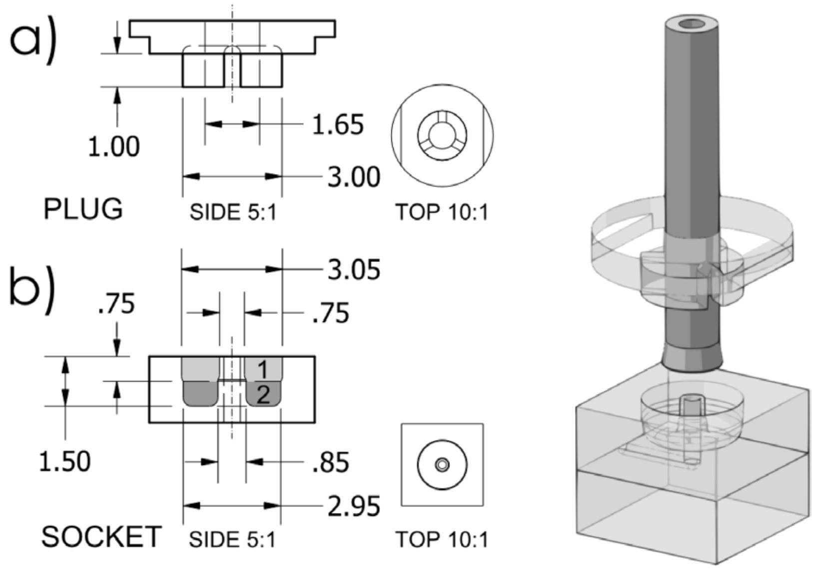

Figure 1. Technical drawings of the plug (a) and socket/inlet (b) and 3D model of the connector. The shaded areas labeled 1 and 2 in (b) mark the two-step pocket that creates the depression around the inlet hole. The drawing describes the standard connector used to interface the standard PTFE tubing (ID 0.8/OD 1.6). All dimensions are in mm. (The 3D CAD model of the connector is available in the supplementary material) (stacks.iop.org/JMM/25/115010/mmedia).

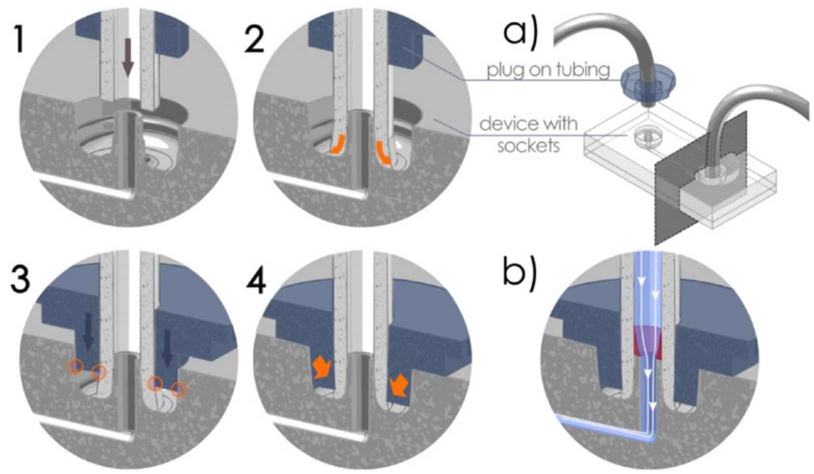

Figure 2. (1)–(4) Schematic illustration of the interference fit mechanism. First the tubing is inserted into the socket (1). It is pushed onto the pin surrounding the inlet where the edges deform outwards guided by the curved surface (2). Then the plug (blue) is pushed down, sliding along the tubing (3); the circles indicate where force is exerted. This force leads to an inward deflection of the interfering part of the plug exerting force on the tubing to form a tight seal and an outward force to fasten the connector in the socket (4). The connector can be removed by lifting the plug by its edge. (a) Schematic of a device with two sockets; the grey area illustrates the cut plane across the interconnection that is shown in the other images. (b) Flow path at the interface and recirculation area (red).

and one layer that contains the inlets (top plate). The plates are bonded together using thermal bonding for 15 to 20 min at 87 °C (PMMA), 120 °C (COC) and 105 °C (PC) for the three materials, respectively, and a pressure of approximately 500 N cm^{-2} for all of them. The devices were left to cool down to below 50 °C before releasing the bonding pressure. Bonding has not been found to have a negative effect on the function of the interconnection.

Fabrication of the socket

Each inlet hole in the top plate is surrounded by a socket. This ring-shaped depression is formed in a two-step pocketing process as denoted in figure 1(b). The first step creates a ring with an outer diameter (OD) slightly larger than that of the plug and an inner diameter (ID) slightly smaller than the ID of the tubing. In the second step a narrower ring is pocketed inside the first, with an OD slightly smaller than that of the plug and an ID slightly larger than that of the tubing. The edge that is formed in this way enables the transition from easy insertion of the tubing and plug to a tight fitting connection.

Fabrication of the plugs

The plugs are fabricated by micro milling from a 2 mm polymer plate. Figure 1(a) shows a technical drawing of the plug, which consists of a central hole that has an ID slightly larger than the OD of the tubing (1.65 mm for 1.6 mm tubing)

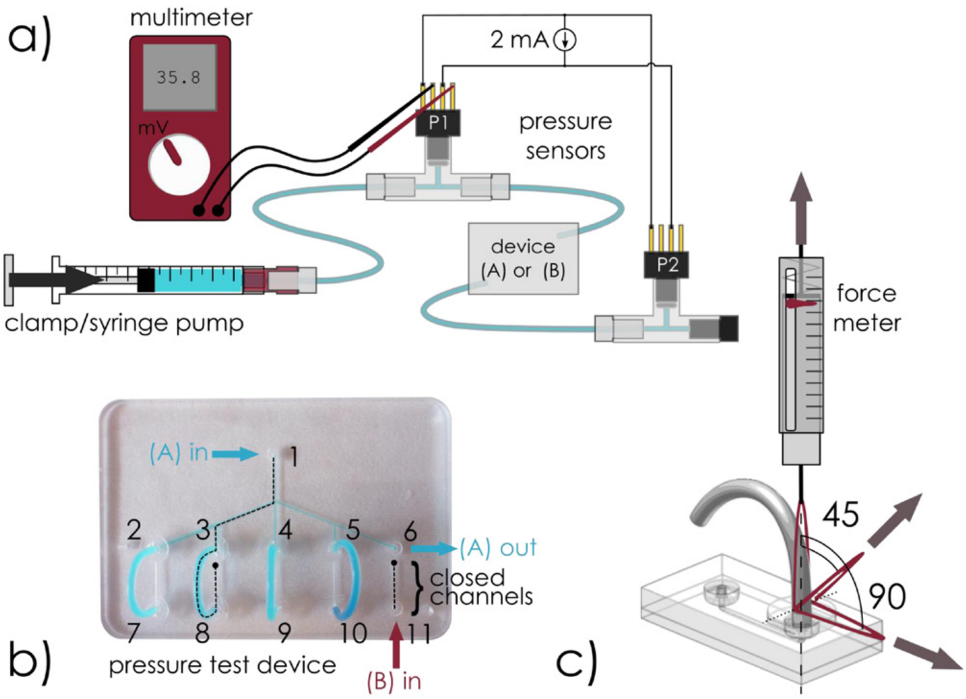

Figure 3. (a) Pressure tests were performed by applying pressure to a syringe, either by clamping or using a syringe pump, connected to a closed system. One (only P1) or two (P1 and P2) pressure sensors with a linear range up to 250 psi were flush mounted using T-junctions and excited by a constant current of 2 mA. Pressure was indicated as a voltage between the output terminals of the pressure sensor and read out using a voltmeter. (b) The device shows two possible configurations: (A) the pressure source is connected to a channel system with five outlets, one of which leads to P2 while the four others are connected to closed channels (indicating pressure by air-compression) or (B) the pressure source is connected to a single inlet ending in a closed channel. (c) For estimation of the force needed to dislocate the plug, a small hole is drilled into a piece of tubing to which a force meter is attached. When force is exerted on the force meter the force indicator is moved and retains its maximal value after release. The force was measured for three different angles with the surface normal as indicated: 0°, 45° and 90°.

which will receive the tubing. The hole is surrounded by a segmented ring (3 segments) on a circular base plate 6 mm in diameter with two edges that facilitate the lifting of the plug off the device. The segmentation enables the individual segments to deflect inwards when the plug is pushed into the socket, in this way holding the tubing in place and securing the seal.

Pressure and strain testing

To test the maximal operation pressure of the interconnection pressure tests were performed using uncompensated (no internal correction for temperature changes, this was done by monitoring the excitation voltage) gauge pressure sensors (Honeywell, 24PCGFH1G), which have a pressure limit of 250 psi or 17.2 bar. The sensors were operated by the application of a constant current of 2 mA and recording the output voltage using two Keithley 2400 sourcemeters. Sensor calibration was validated for up to eight bar prior to testing using a compressed air source with a calibrated pressure gauge. Linearity was assumed to hold up to the maximal given pressure range, and even though higher pressures could be obtained, 17.2 bar is given as the maximal value throughout this article. Two types of pressure tests were performed with a setup that is illustrated in figure 3(a).

Leakage pressure. The flow path for this test is denoted as (A) in figure 3(b). Two pressure sensors are used to monitor the pressure drop across the test device as well as to determine the maximal operation pressure. The first sensor is flush mounted using a T-junction (Upchurch scientific flangeless fittings) between a syringe pump and the device. The second one is mounted in the same way at the outlet with one terminal of the T-junction sealed. The device contains several channels in order to be able to test multiple connections at the same time (as in- and outlets respectively). The upper part contains a distribution channel, which splits the flow into five separate outlets (2–6). The lower part contains five closed channels with only one inlet each (7–11). By connecting every two out- and inlets via tubing, two connectors can be tested while the closed channel is filled with air and acts as a visual pressure indicator (an example of the flow path is shown as a dotted line). In this way, ten connectors are tested at the same time. The tubing and channels are filled with coloured water up to the inlets of the dead-end channels to visualise any leakage.

Leakage pressure after re-plugging. In a second pressure test the leakage pressure and the failure rate for connections that have been re-plugged multiple times without cutting a fresh edge of the tubing were investigated. For this, a number of individual inlets ending in dead-end channels are fabricated in PMMA, COC and PC. A pressure sensor is mounted, as described above, between the syringe pump and inlet. The syringe pump is used to gradually increase the pressure on the inlet, while monitoring the bottom of the inlet for any signs of leakage. A constant flowrate is used to increase the pressure up to the limit of the linear range of the pressure sensor (250 psi or 17.2 bar). In different tests the pressure was either increased stepwise (4 bar per step and kept for 5 min at each step or 1 bar steps and kept for 1 min at each step) or increased continuously (slowly: 5 μL min^{-1} or quickly: 100 μL min^{-1}) until the maximal value was reached. It was then kept at this maximal value for several minutes before decreasing the pressure again. Testing the connectors by slowly ramping up the pressure ensured that failure could be identified in cases where a certain time is required for it to be visible. If no failure occurs during a cycle, the tested connector is unplugged and re-plugged immediately. The test is then repeated in the same way until leakage occurs either while ramping up the pressure or during the time at maximal pressure. In case no failure occurs after eight cycle repetitions, the connector is unplugged and re-plugged five times before running the next pressure test. If failure occurs, a fresh edge is cut off the tubing and re-inserted into either the same or a different inlet for the next test.

Dislocation forces

The forces needed to dislocate plug and tubing from an interconnection were assessed to measure the robustness of the interference fit mechanism. To evaluate the strength of this interference fit plugs were fabricated within a small range of sizes (outer diameter of the rim: 2.99, 3.0, 3.01, 3.02, 3.03 mm) and the force needed to dislocate the connector or tubing was measured. For each size, four plugs were measured eight times each, cutting an edge off the used tubing for each test and using different sockets of the same size. The size of the socket has a nominal diameter of the outer edge of 3.05 mm decreasing to 2.95 mm in one step at the edge (see the technical drawing in figure 1(b)). A force meter equipped with a movable marker that shows the maximal applied force value after release is mounted between the devices and a handle to exert force as illustrated in figure 3(c). The devices are fixed in a clamp and the force on the tubing of the tested interconnection is exerted parallel to the direction of the tubing. The force is gradually increased until dislocation occurs. The force was measured for three different angles with respect to the surface normal: 0°, 45° and 90°.

Results

Fabrication

The three materials have been chosen for their use in different types of applications. While PMMA, being cheap and easy to machine using micro milling, is often the material of choice to test new concepts and make quick prototypes, other materials are likely required for specialised devices. PC is widely used in biomedical applications, where it is important to be able to sterilise devices according to standard protocols such as autoclaving. As a third material, COC was chosen due to its high chemical compatibility and excellent optical properties, which makes it suitable for analytical chemistry and optofluidic devices [25].

The socket was optimised for easy fabrication using a two-step pocketing process that results in an inner and an outer edge within the fastening depression. The size of these two edges was optimised to yield the best sealing behaviour by interaction with the inner diameter of the tubing on one hand, and to create a strong interference fit with the plug on the other hand. The width of the edge is 100 μm in both cases. The upper part of the central pin has a diameter that is 80 μm smaller than the ID of the tubing, while the lower part is 120 μm larger. This transition facilitates placement of the tubing and leads to the sealing deformation when the tubing is pushed down past the edge. On the outer part of the socket, the edge guides the plug and leads to an inward deflection of the segmented flange, which fastens the plug and tubing holding the interconnection in place. Using a 1 mm ball mill for the fabrication of these features additionally creates a rounded bottom at the base of the socket, providing a large sealing surface with the tubing. Furthermore, all the edges are curved, generating a smooth transition between guiding and sealing/fastening the surfaces.

The micro-milling parameters were individually adjusted according to the material and resulted in devices of comparable feature quality with PMMA showing the smoothest surface, while PC and COC are more prone to burring. Even though the shape of the connectors defines the sealing surfaces, we found that the different material properties do impact interconnection robustness in terms of reusability as discussed below.

The inlet structure is fully contained within the device without protrusions from the surface. This planar design offers the possibility to fabricate standard devices from templates that contain only the sockets and can readily be bonded to complementary parts with customised channel structures. In the same way, templates can be fabricated using injection molding with an invariable arrangement of inlets on one side combined with a variable channel system on the other side of the polymer plate. Such an approach is commonly used with Luer connections [26–29]. Using thermal bonding, ready-to-use prototypes can be produced in a quick manner. Since the tip of the inlet pin ends in the same plane as the surface of the device, pressure is applied evenly around the underlying channel structures to ensure sealing in the bonding process (images of the socket before and after bonding can be found in S3) (stacks.iop.org/JMM/25/115010/mmedia). In addition, the devices can be sealed with adhesive tape for storage or incubation, where the shape of the socket helps to prevent any spillage of liquid.

It was possible to directly reproduce the features for the socket and plug by stereolithographic 3D printing. The inlet to the microfluidic channel and the pin structure could be printed without collapsing, but structural quality was lacking. We believe that the correct sizes for a tight fitting interference fit can be achieved by the optimisation of exposure times and printing material, which has not been done at this time.

Pressure drop and pressure limit

In the first pressure test two pressure sensors, p1 and p2, were used to monitor the pressure drop Δp across the test device in order to ensure that the measured pressure values were

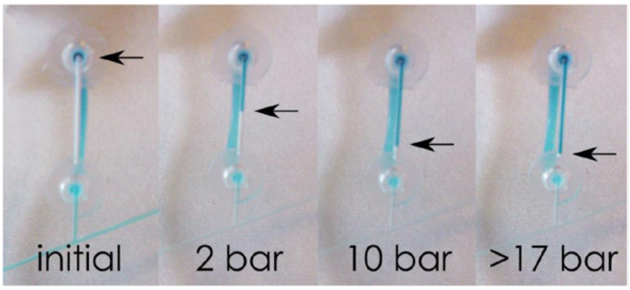

Figure 4. Close-up of one of the dead-end channels on the pressure test device. The compression of air in the channel indicates the applied pressure in the system. From this perspective (below the device) leakage can easily be spotted when inspecting the interconnection.

valid. Δp was found to be 9% ± 1% of p1 across the whole range up to 17 bar with a 2% decrease between the lowest and highest pressure (data not shown). The decrease indicates added pressure loss in the system at higher pressure, most likely due to deformation of the PTFE tubing along its length. The hydraulic resistance of the device and of the complete length of tubing between the device and the two sensors are of the same order of magnitude. We can therefore conclude that pressure p1 measured at the first sensor will correspond to the pressure at the first inlet to within a few percent. The closed channels were used as additional visual pressure indicators, to directly monitor that the pressure was the same in each branch (one channel at three different pressures is shown in figure 4).

The device was further used to test exposure to high pressure for an extended time. No leakage occurred after 12 h at 17 bar on any of the 11 newly connected interconnections in PMMA. Repeated tests of increasing the pressure to the maximal value and decreasing it again after 5 min showed no leakage.

Pressure testing of individual re-plugged interconnections

To determine the leakage pressure of the interconnection in different materials, individual or small sets of connectors were tested in the stepwise manner described above. The results are summarised in table 1. Since for most connectors, except two in the case of COC, no leakage occurred up to the limit of the testing system; the table further shows the average number of re-insertions after which leakage occurred (at any pressure) and the average pressure at which it occurred. The pressure here does not represent an actual pressure limit of the connector as it strongly depends on the number of re-insertions, i.e. the amount of damage inflicted on the tubing. It is to be expected that the robustness decreases for re-plugged tubing (with a necessarily deformed tip), but there are considerable differences for the three tested materials. For PMMA, a total of 36 connections were tested in this way until they failed after re-plugging (the details of this test are shown in figure S4) (stacks.iop.org/JMM/25/115010/mmedia). These connectors stay highly pressure tolerant for up to three re-insertions, where some of them start to fail at high pressures (between 14 and 17 bar). 36% of the connections could be re-plugged more than eight times without showing any sign of leakage even at maximal pressures. For COC about half of the connectors start to show a measureable leakage pressure (typically at 6 bar) after the first re-insertion, while this pressure drops further for failure at a later re-insertion. The performance of PC connectors lies in between that of PMMA and COC, where failure occurs typically within the first five re-insertions (except for some outliers that did not fail at all) at high pressures above 14 bar.

The data suggest that the quality of the micro milled inlet structure plays a major role in the reliability of the interconnection, as milling in PMMA produces the smoothest surface and least amount of burrs or cracking compared to PC and COC. Since the surface roughness affects the sealing behaviour, we propose that injection molded devices would improve the pressure tolerance of these materials even further and should be the fabrication method of choice if high pressures are expected in a system.

The spread of the data points for the PMMA connectors suggests that the damage induced by re-inserting the tubing does not systematically affect the connection and other factors such as the evenness of the cut and size of the plug will most likely have a larger impact on proneness to failure than the deformation of the tubing itself. Since leakage generally did not occur suddenly and with a large spillage, but after several seconds at maximal pressure, we suggest that small scratches on the tubing that are created by removing and re-inserting the tubing several times provide fluid paths for leakage. Since these scratches are induced by the inlet, the burrs and high surface roughness of the material have a large impact. Our tests show that while the freshly connected interconnection does not fail at extended times at high pressures, reliability is compromised if the deformed tubing is re-inserted several times.

Interference fit and dislocation force

The interconnection is secured by an interference fit between the plug and the outer edge of the socket. The data in figure 5 summarise the dislocation force measurements for three angles with respect to the surface normal (0, 45 and 90°). For a force parallel to the surface normal, the dislocation force increases with increasing plug diameter. Some outliers can be seen, which presumably represent plugs with fabrication defects. With decreasing size, the interference fit is not strong enough to hold the plug and tubing in place and the dislocation force drops. If force is exerted on the tubing at an angle of 45 or 90° by bending the tubing, the dislocation force levels off between 6 and 8 N, and does not increase above a plug size of 3.01 mm. Lower values are only found for the smallest plug. While the strength along the surface normal increases, bending of the tubing destabilises the connector and leads to easier dislocation. At even larger sizes above 3.03 mm, the plug can no longer be pressed all the way into the socket and dislocates easily (data not shown). As long as the plug can be fastened in the socket without dislocating when bending the tube (which is the case for too small or too large plugs) the strength of the interference fit does not impact the pressure tolerance of the interconnection. Tests performed with

Table 1. Summary of the pressure test. The pressure limit of the test system was 17.4 bar. The left column (A) shows that out of all tested connections only two fabricated in COC showed leakage (at 12 and 13 bar), while the rest did not leak even at an extended time at maximal pressure. The right column (B) shows the average number of times that a connector can be re-inserted without cutting a new edge off the tubing until leakage occurs and the average leakage pressure of this re-inserted connector. The numbers in brackets show the standard deviation of each average. There are major differences in the number of times a connector can be re-inserted without compromising pressure tolerance depending on the material. *For PC leakage was only observed at maximal pressure.

	(A) First connection (# leakage/# total tests)		(B) Re-inserted connection		
Material	Slow pressure increase	Quick pressure increase	Average # of re-insertions until leakage occurs	Average pressure [bar]	Total tests
PMMA	0/10	0/26	7.5 (2.8)	14.9 (4.8)	24
COC	2/15 (12.5 bar)	0/13	1.4 (0.7)	5.5 (2.8)	12
PC	0/15	0/15	3.2 (1.7)	17.2*	14

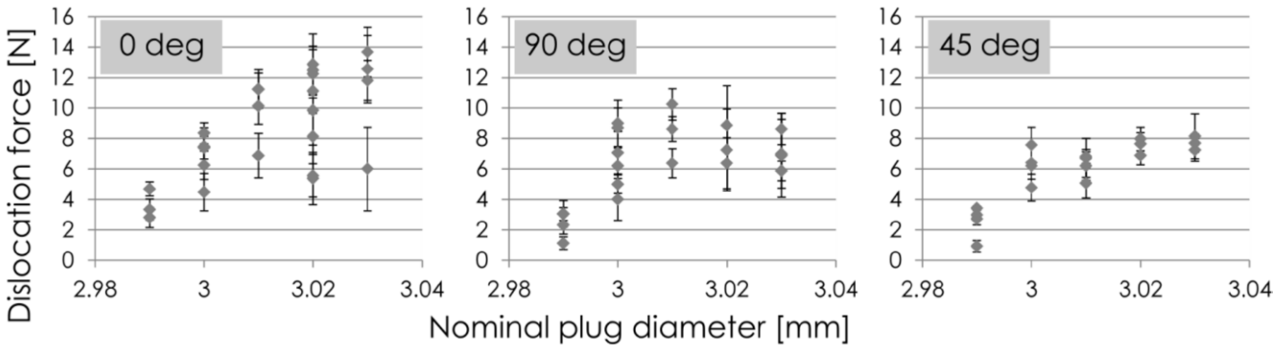

Figure 5. Dislocation force normal to the device surface for interconnections fastened with plugs of different sizes. Each point represents the average of eight (0 deg) or four (90 deg and 45 deg) dislocation force measurements for a single plug and a minimum of four plugs were tested for each nominal size. The strength of the interference fit increases with increasing plug size.

plugs of different outer diameters showed unchanged sealing behaviour. Overall, the data show that in the optimised case a dislocation force of 12.5 N on average can be achieved for a force normal to the surface. The data show that the optimal plug diameter is between 3.01 and 3.03 mm. It should be noted that no damage to the central part of the socket was observed after the experiments.

Application examples

Sensor integration and surface functionalisation in a flow cell

The interconnection system enables the fabrication of ready-to-use devices, which is especially useful for the integration and testing of silicon sensor devices that need to be reversibly interfaced with microfluidic flowcells for functionalisation and characterisation. Different flowcells have been developed to interface a silicon nanowire biosensor for the detection of proteins. A 4-chip flow cell, as shown in figure 6, was used to functionalise silicon surfaces using a pre-loaded protocol driven by a syringe pump. The reagents were loaded into a length of tubing separated by air bubbles, which is a common way to automate the execution of biological assay protocols for microfluidic systems [30]. The tubing could then be easily attached via the socket on the flow cell device to start the process. After execution the silicon chips were removed from the device for characterisation by atomic force microscopy, which would not be possible if they had been integrated into a permanent microfluidic chip.

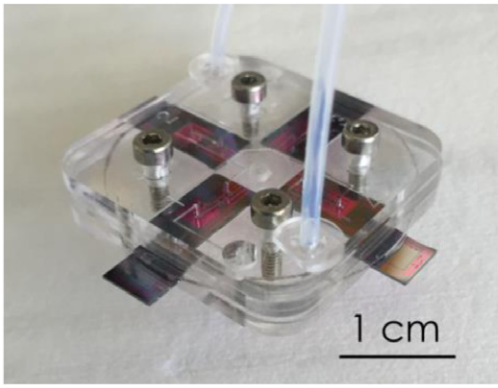

Figure 6. Flow cell to interface four silicon sensor chips in two separate flow streams, two sockets for in- / outlet can be seen in the front and back corner of the device. A PDMS sheet with channels in between the PMMA layers forms the sealing interface with the devices.

This application is an example of quick prototyping and testing of devices.

Brain slice culturing

For biomedical applications the devices need to be sterilised before use, which is often done by autoclaving. Therefore, all components must be able to tolerate a temperature of 120 °C for at least 15 min without deformation or delamination making composite interconnections (employing glues) less

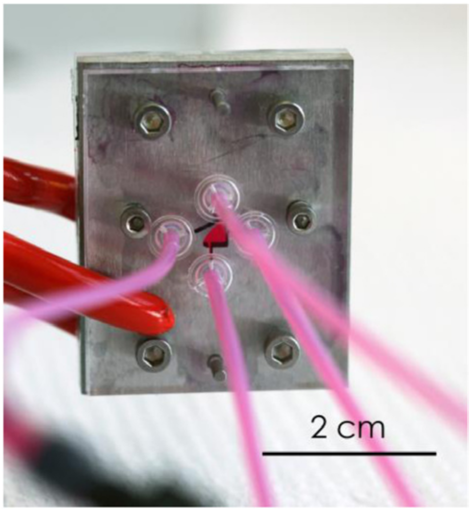

Figure 7. The working model of the RheoStream™, a microfluidic flow cell for complex rheology measurements has been interfaced using the interconnection system.

suitable. The interconnection system was used in the development of a microfluidic brain slice culturing device fabricated in PC where they proved to be superior to glued connectors and made it possible for the device to be operated without failure in a continuous flow driven by underpressure. The devices used perfusion of culture medium at a membrane interface to culture and monitor brain slices in a continuous flow system [31].

Complex rheology measurements

In addition to many biomedical applications, microfluidic tools are being developed for the on-line determination of fluid properties. Studying the rheology of complex fluids (such as non-newtonian fluids that show shear-thinning or thixotropy characteristics) can be achieved by the precise measurement of small pressure differences in a specially designed flow cell [32]. It is especially important to keep the system free of any pressure leakage and to have the possibility to operate with fluids of high viscosity. The interconnection system was used in the working model of the RheoStream™ measurement cell (shown in figure 7) and proved to be an easy-to-use and reliable interface for the continuous measurements of complex fluids.

Discussion

The interconnection is designed without a gasket or glue, which avoids introducing any additional material into the system. This increases the flexibility in terms of chemical compatibility, since the device material needs to be chosen according to the application, and chemically inert tubing such as PTFE is readily available. No further fabrication steps or additional assembly of the connector parts are necessary in addition to device manufacturing, which reduces the time and complexity of device preparation before use; the tubing can be plugged in directly in a few seconds. Different materials can be used both for the device and for the plug in the interconnection, three examples of which have been presented. While we focused on micro milling as a fabrication method, the design can be reproduced by additive manufacturing and could be adapted for injection molding. Although the work in this paper has been done exclusively with PTFE tubing, other polymers with similar properties could be used.

No special care needs to be taken for cleaning and sterilisation procedures, making the system especially suitable for biological applications. The internal volume of the interconnection is small, considering typical injection flow rates which can range from a few up to a few hundred μL min^{-1} for these types of devices. For example, in chemical microreactors for synthesis typical injection volumes can be 200 μL [33] with flow rates of several μL per minute or down to 0.1 μl min^{-1} [34], and are generally run for several minutes. For microfluidic cell culturing, sorting or filtering system flow rates span a range from 0.2 μL min^{-1} up to 450 μL min^{-1} and the systems are commonly operated for several minutes up to hours [35, 36].

A high-pressure tolerance of at least 17.2 bar for three tested materials (PMMA, COC and PC) makes the interconnection system suitable for applications that require high flowrates or very viscous fluids. Connectors can be un-plugged easily and can be re-plugged after a fresh edge has been cut off the tubing to ensure the highest possible reliability. Depending on the material, the re-plugged connection without a fresh edge can still withstand the same high pressures but may fail after several re-insertions. Compared to screwed connectors, which can typically withstand equally or even higher pressures, the presented structures have the advantage of a smaller size of the complete connector and especially of the socket compared to the threaded female part. In addition to the integrated socket it is also possible to fabricate the inlet separately and glue it using double-sided tape to devices where structuring of the inlet feature is not possible or not desirable, such as devices made of glass or thin sheets of polymer. Of course this simplified method is only applicable in a very limited number of cases, where the requirements for the material and performance are accordingly low, but it can offer an alternative to expensive and bulky commercial connectors. The dislocation test shows that interconnected devices are tolerant to device handling, which is important when devices are to be operated by people that are less familiar with microfluidics; this facilitates interdisciplinary research. It is common that especially in the prototyping stage microfluidic devices need to be tested and used by researchers other than the developers and simple operation is an important factor for the success of an experiment.

To obtain higher port densities, sockets can be spaced at a distance of the tubing diameter plus the diameter of the smallest milling tool use for the fabrication of the plugs, typically this would be 500 μm. Multiple plugs can then be included in a small plug array which has been tested and proven to work well for up to four plugs. Higher port densities are more strenuous for the plug material and make attachment of the tubing inconvenient. For devices with a large number of inlets, other interconnection options are available that provide better usability. Furthermore, the presented device allows for the direct interconnection of microfluidic modules either via lengths of tubing on a breadboard-like system or using a double-sided plug that enables the stacking of several devices with minimal flow volume in between modules (an example is shown in S5) (stacks.iop.org/JMM/25/115010/mmedia).

Conclusions

We have developed a microfluidic interconnection system with a high-pressure tolerance that is easily integrated with manufacturing of planar polymer devices. The size can be matched to integrate different sizes of tubing and fabricated in different materials, making it easy to tailor properties such as chemical resistance or temperature tolerance. It is very easy to use and offers high robustness. Since no irreversible assembly is required, the interconnection parts can be cleaned and sterilised separately, making the system suitable for biomedical applications in particular.

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