Shrinky-Dink microfluidics: 3D polystyrene chips

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We present a novel approach for the ultra-rapid direct patterning of complex three-dimensional, stacked polystyrene (PS) microfluidic chips. By leveraging the inherent shrinkage properties of biaxially pre-stressed thermoplastic sheets, microfluidic channels become thinner and deeper upon heating. Design conception to fully functional chips can thus be completed within minutes.

Introduction

To fully realize the long-heralded potential of microfluidics for diagnostics, bio-analytical assays, and chemical synthesis, we must develop ways to rapidly prototype new and increasingly complex chips without compromising important material properties. Although silicon, glass, and quartz have attractive material properties, complex and expensive processing steps are required to develop intricate patterns into these substrates.[1] Whitesides' introduction of polydimethylsiloxane (PDMS) catalyzed exponential progress in the field of microfluidics by enabling rapid prototyping *via* soft lithography.[2] Soft lithography accelerates chip fabrication from months (using standard silicon technology) to typically less than 2 days. However, the inherent material properties of this polymer present significant limitations. Hydrophobic molecules absorb easily into the porous PDMS matrix, potentially affecting results, intolerable in many analytical applications.[3] Moreover, PDMS swells in organic solvents and has inherently unstable surface properties, reverting rapidly to its hydrophobic state post-oxidation.[4] Due to its high elasticity, channels tend to expand and contract with applied pressure. These aforementioned limitations have precluded industry adoption of PDMS for applications in drug discovery and other sensitive assays.[5] Thus, PDMS has been largely relegated to academic prototyping.

Instead, industry relies on plastics, such as polystyrene (PS), the material standard in drug discovery for cell-culture dishes and microtiter plates (*e.g.*, for enzyme-linked immunosorbent assay (ELISA) applications). PS is optically transparent, biocompatible, inert, rigid, and its surface can be readily functionalized.[6] Its hydrophobic surface can be easily made hydrophilic by various physical and chemical means, including: corona-discharge, gas plasma, and irradiation. However, the high-tooling investments typically necessary to realize intricate chips from such plastics (*e.g.*, injection molding, hot embossing) have precluded academic adoption.

To overcome this persistent chasm between academic prototyping and industry standards, various approaches have been investigated. For example, to obviate the time and expense required to develop embossing tools, Koerner *et al.* developed epoxy resins stamps.[7] Sudarsan *et al.* developed PS-based thermoplastic elastomer gels to create viscoelastic 3D stacked chips using a molding approach.[8] Huang *et al.* developed a DNA synthesizer by molding perfluoropolyether (PFPE), resistant to organic solvents.[9] Most recently, Fiorini *et al.* developed improvements in thermoset polyester for microfluidic devices.[10] Zhao *et al.* demonstrated high-aspect ratio microstructures using reactive ion etching of shrinkable PS films, but did not develop complete chips with this approach.[11,12]

We present a new method to develop PS microfluidic chips. Our direct-write approach differs from molding and hot embossing in that we leverage the inherent shrinkage properties of biaxially pre-stressed thermoplastic sheets; therefore, upon heating, etched microfluidic channels become thinner and deeper than the tooling. Our approach to ultra-rapidly write complex microfluidic patterns directly into PS requires no capital investment or equipment. This technique, which is even faster than soft lithography, includes a simultaneous rapid bonding step. Complex multi-layered microchips can thus be completed in a matter of minutes (Fig. 1).

'Shrinky-Dinks' is a children's toy. These pre-stressed transparent PS sheets retract upon heating. We leverage this property

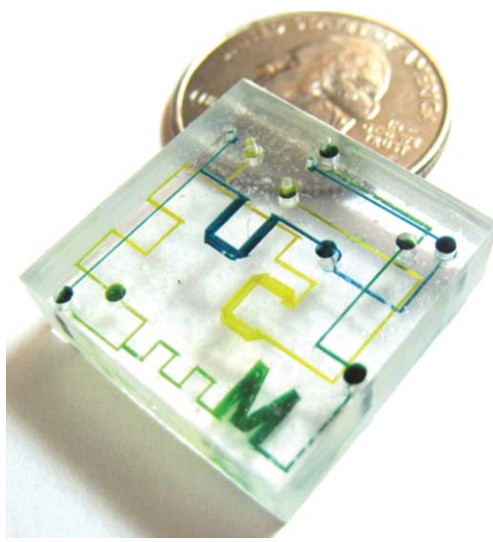

Fig. 1 3D Polystyrene microfluidics. Micromixer, demonstrating the blue (U) and yellow (C) channels on different layers mix on a 3rd layer to form the green M.

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by engraving channels (using syringe tips) that we subsequently shrink to a fraction of their size. Notably, as the channels shrink in width, they increase in height. Upon heating to its glass transition temperature (3–5 min, 160 °C), the engravings shrink isotropically in plane by almost 50% and correspondingly increase in height by over 700% ($n = 20$). While we previously demonstrated that Shrinky-Dinks make effective molds for PDMS by printing on them,[13] we have now improved our technique such that we can directly pattern the PS and rapidly bond them for functional chips, eliminating several fabrication steps, and essentially, the need for PDMS altogether.

Experimental

To create 3D chips, each layer of the chip is first scribed manually and interconnects holes are punched through (Fig. 2). As the channels shrink in width, they increase in height (Fig. 3). We can achieve channels as thin as 8 μm, with controllable channel depths (from 50–600 μm) and shapes, dependent on applied scribing pressure and tip shape (Fig. 4). This proof of principle approach was achieved by manually scribing with various luer stubs, razor blades, and syringe needles (16–25 gauge tips (Instech Soloman, Plymouth, PA) and BD (Franklin Lakes, NJ)). Instead of just cutting the surface, it is important that the channel material be removed. Wells and other designs are also achievable with this simple process. The surface is then rinsed and dried with compressed air to remove any debris. This method can be readily adapted to milling machines or computer-controlled plotters that directly write patterns. Thus even multi-height channels (by varying the applied pressure), typically laborious to achieve with lithography, can be easily realized.

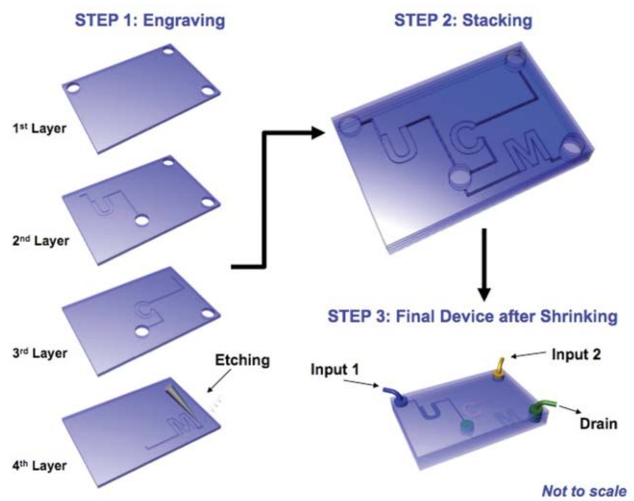

Fig. 2 Process flow for 3D microfluidic chips. Each layer is scribed (using a syringe tip) and interconnect holes are punched. The layers are then aligned and placed in the oven for simultaneous shrinking and bonding.

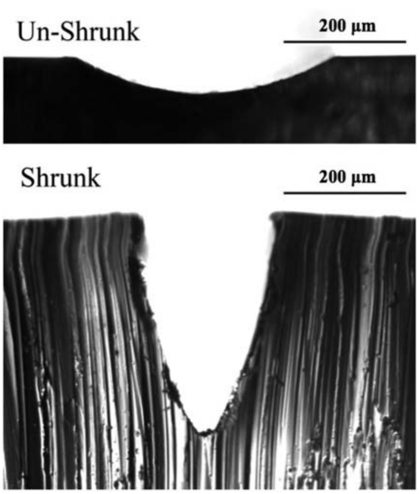

Fig. 3 Before and after cross-sections of a channel. Note the shrinkage in width and corresponding increase in height.

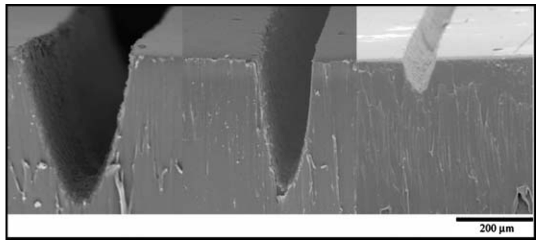

Fig. 4 Different channel widths and heights. SEMs of channels demonstrating different channel shapes achievable using a simple scribing technique.

We achieve strong bonding by heating (160 °C) the patterned unshrunk PS sheet on top of another unshrunk sheet for irreversible cross-linking. In this way, we fabricate stacked chips, in which microfluidic channels traverse several layers. Alignment between several layers can be maintained during the bonding process by constraining the vias with catheter pins or by applying a small amount of super-glue to the corners of each layer, to ensure all the layers shrink together without shifting.

Results and discussion

We are thus now able to rapidly fabricate complex designs, including a functional 3D vortex mixer, in which vortices at low Reynolds numbers can be controllably formed within the vias of the layers (Fig. 5). While our observations are still preliminary, this could prove quite important. Micromixing,

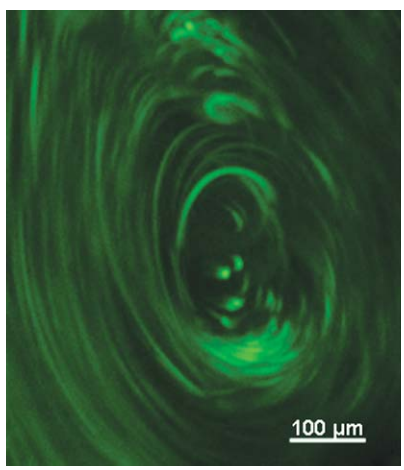

Fig. 5 Microvortex (maximum intensity projection of 30 fps video) of fluorescent polystyrene bead streak-lines, representative of the vortices observed in the vias (see Fig 2) connecting the layers.

though fundamental to almost every miniaturized biological and chemical analysis system, still poses a considerable challenge in 2D due to the inherent laminar flow regime.[14] Whereas this problem can be alleviated with 3D designs, to date, developing 3D micromixers, and 3D chips in general has been difficult due to alignment and bonding issues.[15,16]

Because this is a children's toy, the shrinkage tolerance from sheet to sheet is less-than-ideal for applications that require highly controlled channel sizes (though sufficient for many microfluidic applications); this can be overcome by using more precisely pre-stressed thermoplastic sheets.

Analogous to stacked integrated circuits, such complex 3D chips will allow for faster reaction times, increased miniaturization, and increased processing power. In addition, eliminating the need for PDMS greatly increases the range of applications for which microfluidic chips can be utilized. Combining simple and rapid fabrication, three-dimensional complexity, chemical compatibility and optical transparency (unlike stacked silicon chips) will undoubtedly help usher microfluidics from the prototyping stage to its full potential of miniaturizing systems to address critical biomedical issues.

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