

Bonding of thermoplastic polymer microfluidics

Chia-Wen Tsao · Don L. DeVoe

Received: 20 August 2008 / Accepted: 20 October 2008 / Published online: 13 November 2008
© Springer-Verlag 2008

Abstract Thermoplastics are highly attractive substrate materials for microfluidic systems, with important benefits in the development of low cost disposable devices for a host of bioanalytical applications. While significant research activity has been directed towards the formation of microfluidic components in a wide range of thermoplastics, sealing of these components is required for the formation of enclosed microchannels and other microfluidic elements, and thus bonding remains a critical step in any thermoplastic microfabrication process. Unlike silicon and glass, the diverse material properties of thermoplastics opens the door to an extensive array of substrate bonding options, together with a set of unique challenges which must be addressed to achieve optimal sealing results. In this paper we review the range of techniques developed for sealing thermoplastic microfluidics and discuss a number of practical issues surrounding these various bonding methods.

Keywords Adhesive bonding · Thermal fusion bonding · Solvent bonding · Welding · Surface treatment and modification

1 Introduction

Thermoplastics are a class of synthetic polymers which exhibit softening behavior above a characteristic glass

transition temperature (T_g) resulting from long-range motion of the polymer backbone, while returning to their original chemical state upon cooling. Thermoplastic polymers differ from elastomer or thermoset plastics by their ability to be softened or fully melted and reshaped upon heating, while remaining chemically and dimensionally stable over a wide range of operational temperatures and pressures. Together with the availability of tailored chemophysical properties, this characteristic makes thermoplastics highly adaptable for use as substrates for microfluidic applications. Compared with more traditional microfluidic materials such as silicon and glass, thermoplastics offer substantially lower raw material costs and lower manufacturing costs. Just as the fabrication of microfluidic devices in elastomeric polymers such as polydimethylsiloxane (PDMS) typically involves a simple casting process to transfer patterns from a mold to the elastomer (Xia and Whitesides 1998), microchannel fabrication in thermoplastics has been reported using a variety of replication methods including hot (Martynova et al. 1997) or cold (Xu et al. 2000) embossing, injection molding (McCormick et al. 1997), or thermoforming (Giselbrecht et al. 2006). More recently, hot roller embossing into polymer foils using high throughput reel-to-reel processing promises further reductions in fabrication costs for mass produced thermoplastic microfluidics (Velten et al. 2008). In addition to replication-based fabrication, thermoplastics are also amenable to direct machining techniques such as laser ablation and mechanical micromilling. These various fabrication methods are well established and summarized in recent review articles (Becker and Gartner 2000, 2008; Becker and Locascio 2002; Rotting et al. 2002; Reyes et al. 2002; Rossier et al. 2002; Chen et al. 2008a).

Due to these advantages, the popularity of thermoplastics for microfluidic applications has grown significantly in

C.-W. Tsao (✉)
Department of Mechanical Engineering,
National Central University, Jhongli 32001, Taiwan
e-mail: cwtsao@ncu.edu.tw

D. L. DeVoe
Department of Mechanical Engineering,
University of Maryland, College Park, MD 20742, USA

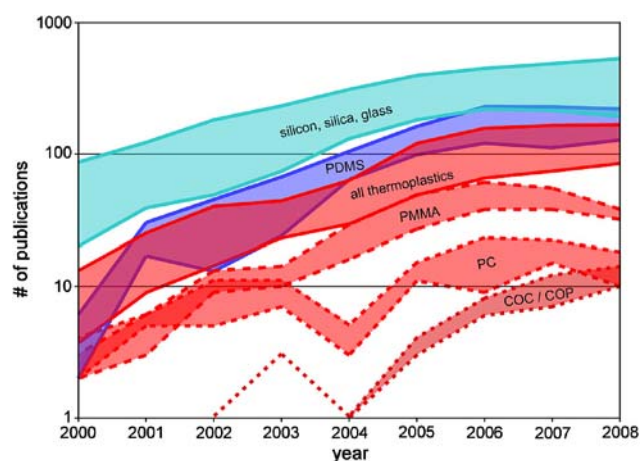


Fig. 1 Approximate numbers of annual publications referencing different materials for microfluidics. Maximum and minimum values defining the ranges were extracted from the Thomson Reuters ISI and NIH PubMed databases, respectively. Data for 2008 is projected based on reference counts from the first half of the year

recent years. As revealed by a search of the Thomson Reuters ISI and National Institutes of Health PubMed databases (Fig. 1), silicon and silica remain the dominant materials for microfluidics, second only to PDMS which experienced explosive growth following the introduction of soft-lithography-based elastomer casting in the late 1990s (Xia and Whitesides 1998). While the use of PDMS far surpasses that of any single thermoplastic commonly used for microfluidics including polymethylmethacrylate (PMMA), polycarbonate (PC), and cyclic olefin polymers (COP) or copolymers (COC), the more general class of thermoplastics reveals a strong growth trend, reflecting expanding research attention towards these materials for microfluidic applications.

Early developments in thermoplastic microfluidic systems were largely focused on the use of PC and PMMA due to their wide availability in a variety of grades with high optical transmission in the visible wavelengths, good solvent and chemical compatibility, and well-characterized molding parameters. More recently, cyclic olefins (COC and COP) have emerged as highly attractive microfluidic materials, with high optical clarity into the deep-UV range (~ 250 nm) (Piruska et al. 2005), low water absorption, and exceptionally good resistance to a host of solvents including organics such as acetonitrile commonly used in liquid chromatography (Ro et al. 2006). A short list of other engineering thermoplastics which have been used for microfluidic chips include polystyrene (PS), polyetheretherketone (PEEK), various polyesters, polyethylene terephthalate (PET), parylene and fluoropolymers such as polytetrafluoroethylene (PTFE) and fluorinated ethylene propylene (FEP). Due to the prevalence of optical detection in microfluidic systems, many thermoplastics used for lab-on-a-chip systems are amorphous materials that are transparent over a wide wavelength range. One exception is PET, which can be either transparent or opaque, depending on grade and processing conditions (Strong 2000). A chart summarizing several important material properties for common microfluidic thermoplastics is provided in Table 1. The qualitative metrics shown in this chart are neither comprehensive nor definitive, and are provided only as a general guide for material evaluation. In particular, note that solvent resistance can be highly dependent upon the solvent type, e.g. hydrocarbons, alcohols, ketones, etc.

Regardless of the fabrication method employed, the sealing of the open microchannels is necessary to produce

Table 1 Summary of physical properties for common microfluidic thermoplastics

Polymer	Acronym	T_g (°C)	T_m (°C)	CTE (10^{-6}°C^{-1})	Water absorption (%)	Solvent resistance	Acid/base resistance	Optical transmissivity	
								Visible	UV ^a
Cyclic olefin (co)polymer	COC/COP	70–155	190–320	60–80	0.01	Excellent	Good	Excellent	Excellent
Polymethylmethacrylate	PMMA	100–122	250–260	70–150	0.3–0.6	Good	Good	Excellent	Good
Polycarbonate	PC	145–148	260–270	60–70	0.12–0.34	Good	Good	Excellent	Poor
Polystyrene	PS	92–100	240–260	10–150	0.02–0.15	Poor	Good	Excellent	Poor
Polypropylene	PP	–20	160	18–185	0.10	Good	Good	Good	Fair
Polyetheretherketone	PEEK	147–158	340–350	47–54	0.1–0.5	Excellent	Good	Poor	Poor
Polyethylene terephthalate	PET	69–78	248–260	48–78	0.1–0.3	Excellent	Excellent	Good	Good
Polyethylene	PE	–30	120–130	180–230	0.01	Excellent	Excellent	Fair	Fair
Polyvinylidene chloride	PVDC	0	76	190	0.10	Good	Good	Good	Poor
Polyvinyl chloride	PVC	80	180–210	50	0.04–0.4	Good	Excellent	Good	Poor
Polysulfone	PSU	170–187	180–190	55–60	0.3–0.4	Fair	Good	Fair	Poor

T_m melting temperature, CTE coefficient of thermal expansion

^a high UV transmissivity often requires the selection of special polymer grades, e.g. without stabilizers or other additives

the final enclosed fluidic paths, and thus a critical step in the fabrication process invariably involves bonding a capping layer to the microchannel substrate. Depending on the functional requirements of the final microfluidic system, there are a number of considerations that must be taken into account when selecting and implementing an appropriate bonding method. Bond strength is a critical consideration, with some applications requiring interfacial bond energies on par with the cohesive strength of the bulk substrate material, and others benefiting from relatively weak and reversible bonds. Bond interfaces must provide suitable chemical or solvent compatibility to prevent degradation during use, without compromising dimensional control of the microchannels due to deformation during the bonding process. Other important considerations for the bond interface include surface chemistry, optical properties, and material compatibility and homogeneity of the channel sidewalls. Additional issues such as manufacturability and compatibility with world-to-chip interconnects can also limit the selection of bonding methods for specific microfluidic applications. For example, the use of a thin laminating film to seal microchannels may be inappropriate when there is a need for a thicker sealing layer to support large access reservoirs or other fluidic connections to the embedded channels.

Microfluidic bonding techniques may be categorized as either indirect or direct. Indirect bonding involves the use of an adhesive layer to seal two substrates and encapsulate microchannels fabricated in one or both of the substrates. In contrast, direct bonding methods mate the substrates without any additional materials added to the interface. While direct bonding is arguably a form of adhesive bonding, where the bulk polymer itself comprises the adhesive, it is distinguished by its ability to produce microchannels with homogeneous sidewalls, whereas indirect bonding methods require an intermediate adhesive that results in channel sidewalls with different chemical, optical, and mechanical properties than the bulk polymer.

In general, bonding forces between mating surfaces arise from either molecular entanglement or charge interactions. Entanglement can occur by mechanical interlocking of diffusion between the surfaces, while bonding due to charge interactions can result from electrostatic or chemical (covalent) bonding, acid-base interactions, or van der Waals forces (Schultz and Nardin 1994; Pocius 2002). For example, thermoplastic bonding methods like thermal fusion bonding, solvent bonding, localized welding and surface treatment and modification bonding are mainly achieved by molecular entanglement. Adhesive bonding is achieved from charge interactions.

High interfacial compatibility is optimal allowing efficient intermixing or interaction of polymer chains during thermoplastic bonding process. This is due to the fact that

both polymers use the same internal bond structures. In most cases, bonding at high temperature can greatly enhance polymer entanglement and interaction at the bonding interface resulting in high bond strength. However, unlike macro-scale devices, bonding methods for microfluidic chips must be adapted and optimized for the demanding task of enclosing micron-scale, or even sub-micron-scale, fluidic channels without excessive deformation of the channel cross-sections. Thus, excessive heating and melting of thermoplastic are usually undesired. In low temperature bonding applications, high surface wettability is preferred to promote more intimate contact between mating surfaces during the bonding process. However, most thermoplastic polymers are formed from hydrocarbons with additional atomic components such as oxygen and nitrogen, resulting in low-energy hydrophobic surfaces with poor wettability, limiting the strength of bonds which may be readily formed. To overcome this limitation, a variety of direct and indirect bonding methods have been reported for thermoplastic microfluidics that leverage techniques developed for traditional thermoplastic manufacturing.

Here we explore the range of bonding techniques that have been used for sealing thermoplastic microfluidics and describe issues that impact ongoing developments in the field. In addition to reviewing the background and state-of-the-art in thermoplastic bonding methods for microfluidics, practical issues which must be considered are discussed.

2 Indirect bonding

2.1 Adhesive bonding

Due to the simplicity of adhesive bonding, this approach has been widely used for sealing thermoplastic microfluidic chips. One of the simplest adhesive bonding techniques is the use of glues, i.e. liquid adhesives that set through the evaporation of solvent, or epoxies and acrylates that cure (polymerize and crosslink) after mixing with a catalyzing agent. This technique has been discussed as a viable approach to polymer microfluidic bonding (Becker and Gartner 2000; Rotting et al. 2002), but there are few published examples where this strategy has been successfully employed, likely due to the challenge of channel clogging. More commonly, adhesive bonding is performed by applying a thin layer of a high viscosity liquid adhesive which forms a bond after curing by UV light irradiation. UV-curing adhesives are generally manufactured from synthetic resins containing photoinitiators to enhance resin crosslinking upon exposure to specific wavelengths of light. While a wide range of UV-curable adhesives is available, they are most commonly derived from polyester or acrylate resins which possess a surface energy less than

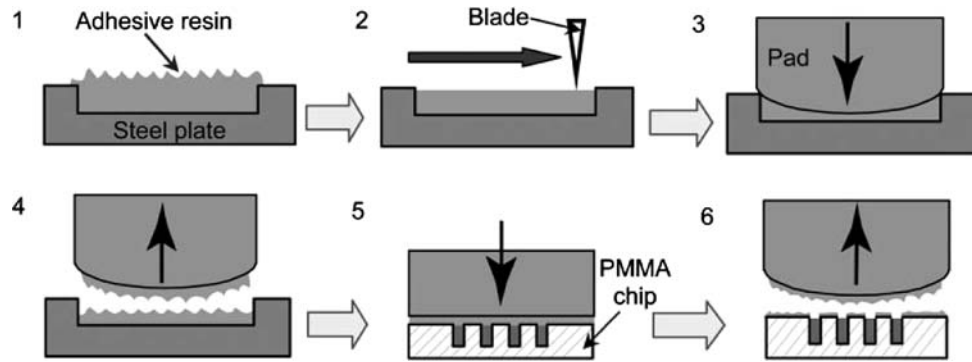


Fig. 2 Adhesive application using a contact printing process. Adhesive was poured on steel plate with a hollow and spread over the plate using a blade (step 1, 2). Adhesive was applied on the silicon rubber pad (step 3, 4). The adhesive on the silicone pad was deposited on the

PMMA chip, the adhesive thickness on PMMA chip was nearly one-fourth of the hollow depth and excessive adhesive was removed by sacrificial channels (step 5, 6). (Dang et al. 2005). Reproduced by permission of The Royal Society of Chemistry

the critical wetting tension of most typical thermoplastics except olefin thermoplastics like COC and PS, thereby ensuring spontaneous wetting of the microfluidic chip surfaces (Pocius 2002). Regardless of the method used to activate the liquid adhesive, several approaches have been described to prevent adhesives from clogging the microchannels. Dang et al. reported a contact printing process in which adhesive layer can be precisely controlled by the stainless steel plate hollow and use sacrificial channel network design to remove air bubbles and excessive adhesive, ensuring that the adhesive cannot enter the channels (Fig. 2) (Dang et al. 2005). A further benefit of this approach is that with the exception of the exposed thickness of the adhesive layer, the resulting microchannels possess homogeneous surface properties. Similar results have been achieved by using screen printing to apply adhesive onto the cover plate prior to bonding (Han et al. 2003), although careful alignment between microchannels and adhesive patterns is required in this latter approach.

In a related method a microchannel substrate is placed beneath a cover plate with a small gap separating the mating surfaces (Lu et al. 2008). A UV-curable adhesive resin introduced into reservoirs in the cover plate wicks into the 5–10 μm gap due to capillary action. When reaching the 250 μm width and 100 μm depth microchannel, the resin stop flowing into microchannel due to the capillary pressure drop, thus prevent leakage of resin into the channels (Fig. 3). Similarly, hydroxyethyl methacrylate (HEMA) monomer mixed with a photoinitiator was directly injected into microchannels formed in a PMMA substrate loosely capped with a second PMMA plate (Lai et al. 2004). The adhesive entered the interstitial region between the plates, while excess HEMA within the microchannels was flushed using N_2 gas before UV curing. In addition to the use of epoxies and other liquid adhesives, partially-cured PDMS has also been investigated as an

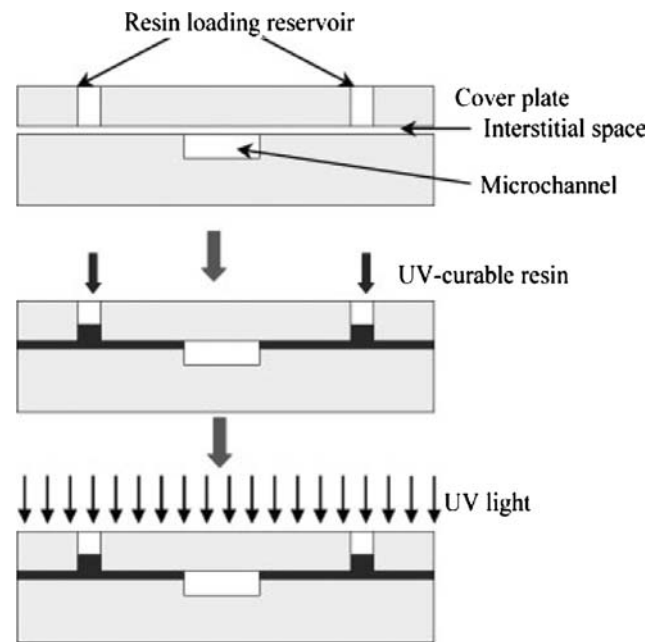


Fig. 3 UV-curable adhesive application using capillarity-mediated resin introduction (Lu et al. 2008). Copyright Wiley-VCH Verlag GmbH & Co. KGaA, reproduced with permission

adhesive layer for bonding PMMA microfluidic substrates (Chow et al. 2006).

Another common method for adhesive bonding is the use of lamination films. This approach is attractive for several reasons. Commercial laminators are inexpensive and simple to use, and many different laminate material options with film thickness as low as 40 μm are available. The process is also high throughput and scalable, making laminate sealing well suited for mass production of thermoplastic microfluidics. Pressure sensitive adhesive films use a polymer layer which can flow at room temperature, allowing effective wetting of the bonding surface to encourage a strong bond. While pressure sensitive films are

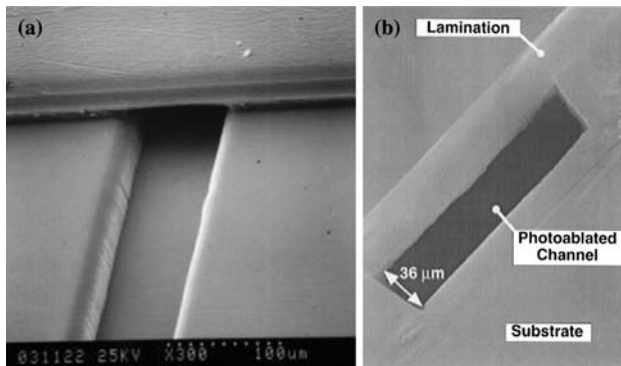


Fig. 4 Lamination film sealing based on **a** pressure sensitive film (Huang et al. 2007), and **b** thermal lamination film (Roberts et al. 1997) (copyright Wiley-VCH Verlag GmbH & Co. KGaA, reproduced with permission)

available in both solvated liquid form and as dry lamination films (Fig. 4a) (Huang et al. 2007), microfluidics applications most commonly employ the latter. Lamination using thermally-activated adhesives is another approach demonstrated for sealing thermoplastic microfluidics (Fig. 4b) (Roberts et al. 1997; Klank et al. 2002). Thermal lamination films consist of a polymer layer coated with an adhesive resin which is activated at elevated temperatures, typically on the order of 100–150°C. Several variants on the basic lamination process have been reported. These include the use of a thin COC sheet plasticized using a solvent mixture as an adhesive lamination film (Paul et al. 2007), and the use of dry lamination films formed from an uncrosslinked photopatternable resin (SU-8) spun onto a PET backing sheet against a second layer of fully cross-linked SU-8 which was also used to define the microchannels (Abgrall et al. 2006). The unexposed SU-8 behaved as a thermoplastic which reflowed during the bonding process. In a related lamination process, standard laser printer toner was used as a binding agent, allowing printed transparency films to be bonded by thermal lamination with the toner acting as both adhesive and microchannel sidewalls (do Lago et al. 2003).

3 Direct bonding

3.1 Thermal fusion bonding

During direct thermal bonding, substrates are heated to a temperature near or above the T_g of one or both of the substrate materials, while applying a pressure to increase mating contact forces. The combined temperature and pressure can generate sufficient flow of polymer at the interface to achieve intimate contact, with interdiffusion of polymer chains between the surfaces leading to a strong

bond. Under ideal conditions, the resulting bond strength can reach the cohesive strength of the bulk material. An important advantage of direct thermal bonding is that the microchannels possess homogeneous surface properties when identical materials are used for both the microchannel and capping substrates. This feature, together with the relatively high bond strengths and overall simplicity of the approach, have made direct thermal bonding the most common method for sealing microfluidic chips. Thermal fusion bonding of various thermoplastics has been widely demonstrated, including PC (Li et al. 2004; Buch et al. 2004; Wang et al. 2005; Park et al. 2008; Shadpour et al. 2007; Wang et al. 2008), PMMA (Chen et al. 2003; Arroyo et al. 2007; Kelly and Woolley 2003; Liu et al. 2008; Nie and Fung 2008; Nikcevic et al. 2007; Sun et al. 2006; Tan et al. 2008; Yao et al. 2005; Zhu et al. 2007), and COC (Ahn et al. 2004; Bhattacharyya and Klapperich 2006; Riegger et al. 2007; Tsao et al. 2008; Steigert et al. 2007; Fredrickson et al. 2006; Olivero and Fan 2008). Direct thermal bonding of a wide range of polymers including polystyrene, nylon, polysulfone (Shadpour et al. 2006) as well as polystyrene and copolyester (Locascio et al. 1999) have also been explored. Several fluoropolymers have also been successfully bonded using the thermal fusion method (Taberham et al. 2008). Thermal bonding can also be readily applied to bonding dissimilar materials. For example, PVDC films have been used as low temperature sealing layers to thermally bond PC substrates (Hromada et al. 2008). When thermal bond dissimilar material, the bonding temperature need to set near or above their T_g s. So, thermoplastic with similar T_g s are preferred to prevent channel distortion on the lower T_g substrate.

One major challenge of thermal fusion bonding is channel deformation caused by un-optimized temperature and pressure. Thus, properly controlling temperature, pressure, and time is critical to achieve high bond strength while limiting deformation of the embedded microchannels due to bulk polymer flow. For this reason the use of a programmable hot press (Li et al. 2004, 2005, 2008; Buch et al. 2004; Nie and Fung 2008; Bhattacharyya and Klapperich 2006; Hromada et al. 2008; Tsao et al. 2007), commercial bonding system (Arroyo et al. 2007; Abgrall et al. 2007), or more recently, high throughput roller laminator (Fredrickson et al. 2006; Olivero and Fan 2008) is generally preferred. However, for relatively low density channel designs, heating a pair of substrates which have been manually aligned and clamped together before being placed in an oven can provide a simple method for prototyping thermal bonded chips (Park et al. 2008; Shadpour et al. 2007; Kelly and Woolley 2003; Sun et al. 2006; Shadpour et al. 2006; Locascio et al. 1999; Taberham et al. 2008).

Several general methodologies have been explored to reduce the degree of channel collapse during thermal bonding. The first approach relies on the use of high bond temperatures as high as 58°C above the substrate T_g , while applying low pressures to limit substrate deformation (Sun et al. 2006; Tan et al. 2008). Using this approach, excellent stability of channel cross-sections can be attained, as revealed in Fig. 5 for the case of laser micromachined channels in PMMA (Sun et al. 2006). Alternately, bonding substrates using high pressures but at temperatures well below T_g has also proven useful for reducing channel collapse while achieving stable bonds (Park et al. 2008; Ahn et al. 2004). The bonding strength is lower than the high bonding temperature ones but strong enough to ensure no fluid leakage.

Even when using a well characterized commercial hot press, selecting process parameters to limit channel collapse during thermal bonding is a critical step which must be optimized for each application. For a specific type of thermoplastic, different material grades can require significant adjustments to the bonding parameters due to variations in T_g and flow properties. Optimal process values can even vary between different polymer lots, requiring that experimental conditions be monitored and adjusted on an ongoing basis. Before bonding, the substrates should be as flat, clean, and dry as practicable. When possible, bonding should be performed in a cleanroom environment to prevent particulates from becoming trapped within the sealed microchannels. When a high degree of flatness cannot be achieved for the initial thermoplastic plates, thermally conductive silicone pads may be placed on either side of the bonding substrates to help evenly redistribute pressure over the full substrate area during bonding.

3.2 Solvent bonding

A chemical acts as a solvent for another material when the molecules of each material do not exhibit a tendency to

separate from one another, i.e. when the total molecular force of attraction between the dissimilar materials is greater than the force of attraction for each material alone (Brydson 1999). For interactions between organic solvents and polymers, solubility can be adequately described by the Hildebrandt parameter (δ), defined as the square root of the cohesive energy density for each molecular system (Hildebrandt and Scott 1949). The cohesive energy, dictated by attractive molecular forces for each material, can be determined from the material's energy of vaporization (U_{vap}) defined as the difference between the latent heat of vaporization ($\cdot H^\circ$) and the mechanical work resulting from evaporation. This latter term is approximately equal to the product of the gas constant (R) and the absolute temperature (T) so that

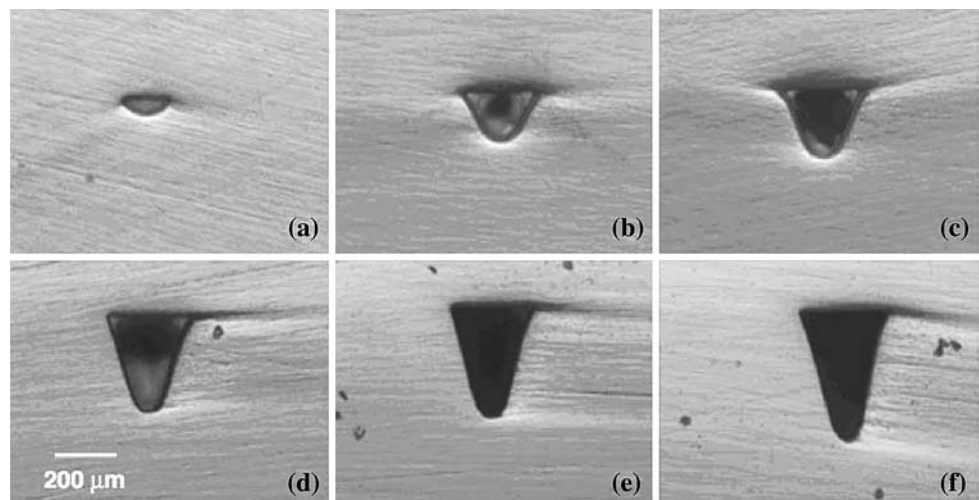
$$U_{\text{vap}} = \cdot H^\circ - RT \quad (1)$$

The energy of vaporization divided by the molar volume of the solvent (v) yields the cohesive energy density, and the Hildebrandt solubility parameter is defined as the square root of this quantity, i.e.

$$\delta = [(\cdot H^\circ - RT)/v]^{1/2} \quad (2)$$

with units of $(\text{J}/\text{cm}^3)^{1/2}$ or $\text{MPa}^{1/2}$. Thus the Hildebrandt parameter provides a measure of the cohesive molecular forces for both solvent and solute. If the cohesive forces for each material are similar, their molecules can readily co-exist and dissolution of the solute will occur (Hildebrandt and Scott 1949). For amorphous non-polar polymers, the cohesive forces between the materials can be approximated as the geometric mean of the individual cohesive forces. In this case, a material will act as a good solvent for a given material when the Hildebrandt parameters for the materials are nearly equal to one another (Brydson 1999). For amorphous polar polymers, a modified model for solubility developed by Hansen that segregates individual terms due to dispersion forces, dipole-dipole interactions, and

Fig. 5 Cross-sectional views of enclosed laser micromachined PMMA channels, with increasing depth from **a–f**, thermally bonded at 180°C, well above T_g , using a low bonding pressure below 20 kPa (Sun et al. 2006). Copyright IOP Publishing Ltd., reproduced with permission



hydrogen bonding may be applied (Hansen 1969). A summary of solubility parameters for common thermoplastic polymers and organic solvents is shown in Table 2.

Solvent bonding of thermoplastics takes advantage of polymer solubility in selected solvent systems to achieve entanglement of polymer chains across the interface. When a thermoplastic surface is solvated, polymer chains become mobile and can readily diffuse across the solvated layer, leading to extensive intertwining of chains between the surfaces and resulting in exceptionally strong bonds. Depending upon the specific approach used, solvent bonding can be a high throughput process that is readily scalable from prototyping to mass production. Solvent may be applied to the polymer substrates in either liquid or vapor phase. In general, liquid phase application is performed using polymer/solvent systems with dissimilar solubility parameters in order to prevent excessive solvent uptake into the polymer matrix which could lead to channel deformation during bonding. Excessive solvent absorption can also be prevented by using very short solvent exposure times. For example, when using acetone ($\delta \sim 20.4$) to solvent bond PMMA ($\delta \sim 20.1$), limiting solvent exposure of the microchannels to less than 3 s was shown to be necessary to prevent channel deformation (Shah et al.

2006). Vapor phase application can avoid this issue by allowing more controllable exposure of solvent molecules to the polymer surface.

As evident from Table 2, appropriate solvents are available for bonding a wide range of microfluidic thermoplastics. In practice, the majority of reported solvent bonding work for microfluidic applications has focused on PMMA. Solvent bonding of PMMA has been performed by simply immersing the chips in ethanol for 10 min before mating them together under pressure (Klank et al. 2002). Because the solubility parameters of PMMA and ethanol are substantially different, the immersion process could be performed without significant channel deformation. Solvent bonding of PMMA chips has also been explored using either ethanol, methanol, or isopropanol (Hsu and Chen 2007), with the solvent applied to the capping layer by quickly dipping the polymer chip into a solvent bath. The chips were immediately removed and bonded to the microchannel plates using different pressures, temperatures, and times to determine optimum process conditions. The bond strength of optimum process exhibit as high as 23.5 MPa. Direct application of acetonitrile (Sun et al. 2007) and a solvent system comprising an aqueous solution of dimethyl sulfoxide (DMSO) and methanol (Brown et al. 2006) have also been reported for PMMA bonding. In the latter example, softening of the PMMA was shown to be limited to only the first 50 nm of the surface following 30 min exposure to the solvent mixture (Brown et al. 2006).

Enhanced solvation of chip surfaces by isopropanol has been explored by controlling the solvent temperature to adjust its co-solubility with PMMA (Ng et al. 2008). In one interesting approach, a mixture of ethylene dichloride and ethanol was used as an azeotropic solvent (Lin et al. 2005, 2007). An azeotropes is a mixture in which the ratio of constituents in the vapor phase is equal to the ratio in the liquid phase upon boiling. In the case of ethylene dichloride and ethanol, the azeotrope possesses a characteristic boiling point below that of either individual component in the mixture. The ethylene dichloride ($\delta \sim 20$) acted as a solvent for the PMMA substrates, while the ethanol ($\delta \sim 26$) served to prevent microchannel clogging. Because the composition of the solvent mixture remains unchanged during evaporation, the constant ratio of ethanol ensured that channel deformation was avoided during the drying process.

In addition to controlling the solvent composition, exposure time and temperature, other approaches to increasing bond strength while preventing unwanted deformation of enclosed PMMA microchannels during solvent bonding have been reported. One approach involved an initial deposition of a thin layer of isopentylacetate onto a glass plate, which was then used as a stamp

Table 2 Solubility parameters for selected thermoplastic polymers and organic solvents (Brydson 1999; Barton 1991; Fitzpatrick and Dean 2002)

Thermoplastic	δ [(J/cm ³) ^{1/2}]
PTFE	12.6
PE	16.3
PP	16.3
COC	17.7
PMMA	20.1
PS	18.7
PVC	19.4
PC	19.4
PET	21.8
Solvent	δ [(J/cm ³) ^{1/2}]
Cyclohexane	16.7
Methylene dichloride	19.8
Ethylene dichloride	20.0
Acetone	20.4
<i>n</i> -Hexanol	21.8
Isopropanol	23.4
Acetonitrile	25.1
Ethanol	26.0
Dimethyl sulfoxide	26.7
Methanol	29.6
Water	47.7

to apply a controlled dose of solvent to the chip containing microchannels (Fig. 6) (Griebel et al. 2004). Sacrificial phase change materials have also been explored as a highly robust solution for preventing channel collapse even after extended solvent exposure. In this approach, open microchannels filled with liquid wax (Kelly et al. 2005) or water (Koesdjojo et al. 2008) are cooled to solidify the sacrificial material. When directly applying either acetonitrile (Kelly et al. 2005) or ethylene dichloride (Koesdjojo et al. 2008) to the chip surfaces, the sacrificial materials prevent solvation of the channels walls, and thus channel deformation can be virtually eliminated. The process flow for the sacrificial frozen water process is depicted in Fig. 7.

Solvent bonding has also emerged as an important method for sealing COC microchannels. Because COC is compatible with typical solvents used in high performance liquid chromatography (HPLC) such as acetonitrile, microfluidic systems based on COC are attractive for chip-HPLC applications. However, pressure-driven HPLC requires high internal pressures on the order of 10–40 MPa, well beyond the typical limits of microfluidic chips bonded by adhesives or thermal bonding techniques. Solvent bonding is uniquely suited for achieving adequate bond strength for these applications.

In one example of COC solvent bonding, a tailored mixture of ethanol and decalin was used to introduce a well-defined volume of solvent into a COC chip surface by timed immersion (Wallow et al. 2007). The solvent mixture exhibited case-II permeation, in which the solvated region of the polymer surface is separated from the unsolvated bulk by a sharp boundary. Using this approach, cohesive failure was observed for internal channel pressures around 10 MPa. The deposition of solvents from the vapor phase onto COC chips has also been described (Ro et al. 2006;

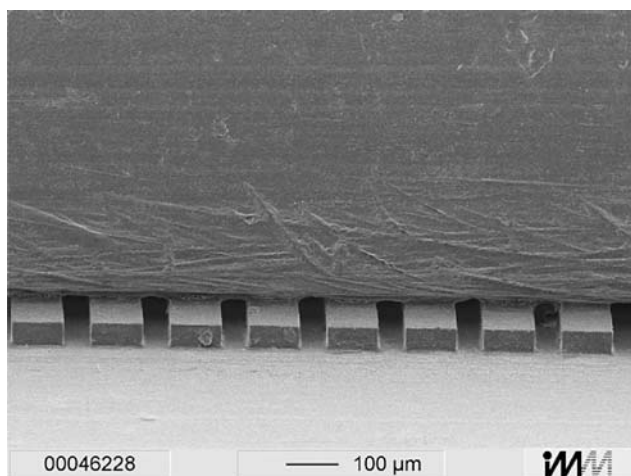


Fig. 6 PMMA electrophoresis chip bonded using isopentylacetate deposited by solvent stamping (Griebel et al. 2004). Reproduced by permission of The Royal Society of Chemistry

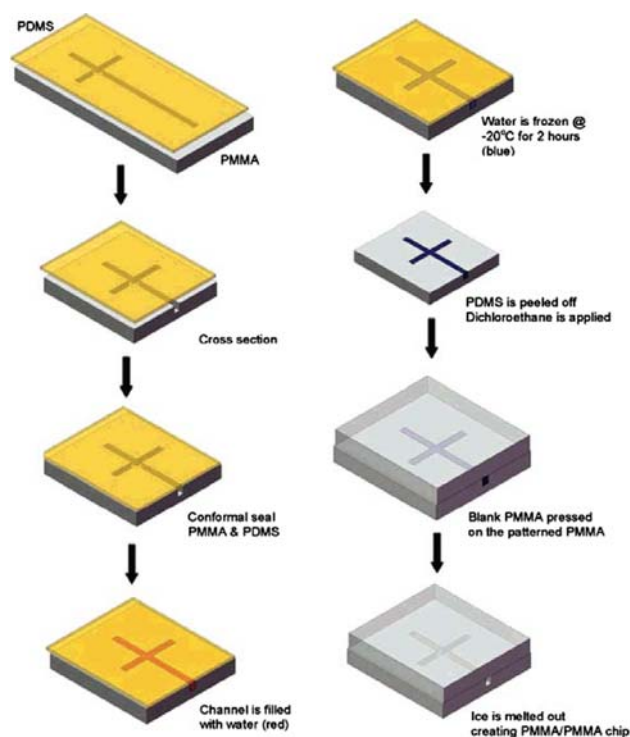


Fig. 7 Solvent bonding process employing frozen water as a sacrificial layer to preserve the dimensional stability of the enclosed microchannels (Koesdjojo et al. 2008)

Mair et al. 2007; Chen et al. 2008; Liu et al. 2007; Morales et al. 2006). Mair et al. reported a 50% bond strength enhancement by irradiating the bonded chip with deep UV light after solvent exposure step. Maximum burst pressures of 34.6 MPa (Mair et al. 2007) has been reported for COC chips bonded by 90 s cyclohexane vapor exposure and subsequent 15 min deep UV irradiation.

3.3 Localized welding

A common non-adhesive and non-mechanical method for bonding macroscale thermoplastic components is the introduction of ultrasonic energy to induce heating and softening at the interface of the mating parts. An advantage of this method is that energy can be introduced locally for targeted bonding of specific regions, or globally for uniform bonding of all mating interfaces (Strong 2000). Efficient ultrasonic welding of PMMA and PEEK microfluidic components has been demonstrated using a commercially available welding system operating at 35 kHz (Truckenmuller et al. 2006a, b). By mechanically machining the microchannel chip and cover plate to contain energy directors and structures to guide the melt flow during bonding, and by optimizing the welding parameters including force, power and time, precise bond results were achieved (Fig. 8).

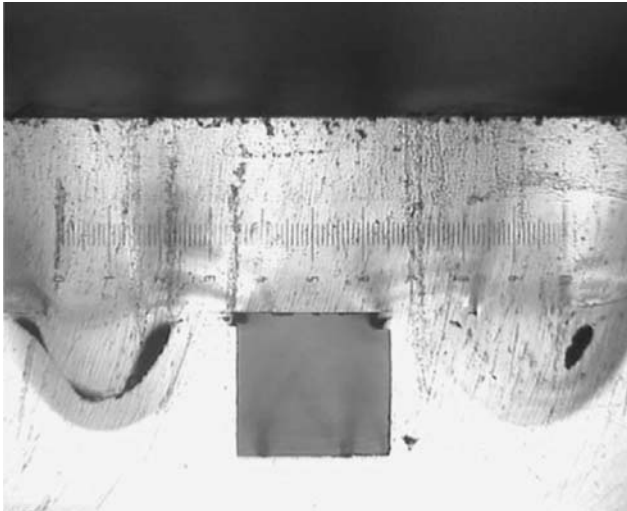


Fig. 8 Cross-section of a PMMA microchannel ca. 500 μm square sealed by ultrasonic bonding, with deformed energy concentration structures evident on either side of the channel opening (Truckenmuller et al. 2006a). Copyright Elsevier, published with permission

An alternative method to achieve localized welding of thermoplastics is the use of microwave energy to heat embedded metal films located between the desired bond surfaces. In one example of this method, a 100 nm layer of chromium/gold was deposited onto an embossed PMMA substrate, which was mated to a cover plate also coated with a 100 nm metal film (Lei et al. 2004). The metal layers were mated together and the stack was placed in a microwave chamber operating near 2.4 GHz. While PMMA is transparent at this frequency range, the metal films efficiently absorbed the incident RF energy, leading to melting of the gold layer and localized bonding of the polymer. Full sealing was achieved with 10 W power in only 120 s. In related work, microwave energy was employed to seal both PMMA and PC microfluidic substrates using a layer of polyaniline, a conductive polymer, deposited by screen printing onto the substrates (Yussuf et al. 2007). Bond strengths on the order of 1–2 MPa were realized using this method.

Infrared (IR) laser welding has also been used to achieve localized sealing of microfluidic chips (Kim and Xu 2003). In this approach, an IR-transparent thermoplastic layer is placed on top of an opaque thermoplastic substrate. Using a 1,100 nm laser focused through the transparent layer to heat the opaque layer at the interface between the substrates, high resolution local bonding was achieved.

While these bonding techniques provide interesting options for highly localized welding of thermoplastics, they have not been widely adopted for general microfluidic bonding applications. There are several likely reasons for this. While ultrasonic welding offers further advantages including compatibility with essentially any thermoplastic, the ability to weld dissimilar plastics, and the ability to

weld plastics to other materials including metals, a disadvantage is the need for special chip designs to effectively direct and focus energy at the desired weld points. This requirement complicates the use of ultrasonic welding for efficient chip prototyping. Microwave RF bonding requires the additional step of metal deposition, which constrains the fabrication process and may not be suitable for applications where the metal can contaminate the system or act as an electrical shunt. Finally, laser bonding imposes unwanted constraints on the substrate materials by necessitating materials with different absorption characteristics.

3.4 Surface treatment and modification

Increased surface energy serves to improve the wettability between mating surfaces, enabling more intimate contact and ultimately enhancing mechanical interlocking and interdiffusion of polymer chains between the surfaces. Higher surface energies can also improve bonding through the generation of electrostatic interactions, and surfaces possessing high specific energy in the form of polar functional groups can produce hydrogen or covalent bonds across the interface are capable of providing bond strengths exceeding the cohesive strength of the bulk polymer. Surface treatments are widely used in macro-scale polymer engineering to increase surface energy prior to bonding. Examples include solvent or acid treatments (Wu 1982), surface grafting (Uyama et al. 1998; Hu and Brittain 2005), and both vacuum (Kruse et al. 1995; Collaud et al. 1994) and atmospheric (Shenton et al. 2001) plasmas. For microfluidic applications, plasma activation is commonly used to modify PDMS surfaces with silanol groups (Eddings et al. 2008), resulting in covalent bond between mating elastomer layers, and this technique has been widely applied to thermoplastic microfluidics as well. Energetic ions, electrons, and UV photons in plasmas can possess sufficient energy to break chemical bonds on the target surface, producing highly reactive free radicals which assist in forming the desired charged surface groups and increasing the overall energy density of the surface. Plasma modification has been reported as a method for reducing processing temperatures and improving bond strength for microfluidic chips fabricated from a range of thermoplastics including PMMA (Abgrall et al. 2007; Brown et al. 2006; Lee et al. 2005; Johansson et al. 2002; Kettner et al. 2006; Pepin et al. 2002), COC (Ahn et al. 2004; Johansson et al. 2002; Puntambekar et al. 2002; Nikolova et al. 2004; Bhattacharyya and Klapperich 2007), PC (Wang et al. 2008; Klintberg et al. 2003), PS (Bhattacharyya and Klapperich 2007), and PET (Wu et al. 2002) using both oxygen and ambient air plasmas. Notably, Bhattacharyya and Klapperich reported a two to threefold improvement in bond strength for COC and PS surfaces exposed to a 10 W air plasma source followed

by thermal bonding at the same temperatures as untreated surfaces (Bhattacharyya and Klapperich 2007).

A simpler alternative to plasmas for the enhancement of thermoplastic surface energy is the application of ultraviolet light. Exposure of thermoplastic surfaces to UV energy is well known to result in photodegradation, with the primary mechanism due to photo-oxidation and scission of polymer chains on the surface (Emanuel and Buchachenko 1987). In general, exposure to light in the range of 300–400 nm is generally sufficient to break chemical bonds within most thermoplastics (Allen and Edge 1992). Together with the formation of lower molecular weight radicals resulting from chain scission, a coupled consequence of UV radiation is a reduction in glass transition temperature at the exposed polymer surface. Because the thickness of the affected polymer layer is determined by the optical absorption length, the thermomechanical properties of the bulk polymer remain essentially unchanged by UV exposure. Truckenmuller et al. demonstrated that the T_g for PMMA surfaces can be reduced by approximately 60 K using this method (Truckenmuller et al. 2004), enabling UV-exposed microfluidic chips to be bonded at temperatures well below the bulk T_g , without significant channel deformation or reduced bond strength. This same approach has been successfully applied to low temperature bonding of variety of PMMA (Witek et al. 2004; Truckenmuller et al. 2004), PC (Park et al. 2008), and celluloseacetate (Truckenmuller et al. 2004) microfluidic devices.

More recently, a surface treatment combining UV light and exposure to photogenerated oxygen radicals has been shown to provide exceptionally high bond strengths for thermoplastic microfluidics using low process temperatures

(Liu et al. 2008; Tsao et al. 2007; Bhattacharyya and Klapperich 2007). This method is derived from a UV/ozone exposure technique originally developed for the removal of organic contaminants from semiconductors as an alternative to oxygen plasma ashing (Bolon and Kunz 1972; Sowell et al. 1974; Vig and LeBus 1976; Vig 1985). Using a low-pressure mercury lamp to expose a substrate in an air-filled chamber at atmospheric pressure, light output at a wavelength of 184.9 nm is absorbed by oxygen in the air, resulting in the generation of ozone. Light at 253.7 nm is absorbed by the ozone, leading to breakup of the ozone and production of atomic oxygen. Hydrocarbons at the substrate surface are rapidly oxidized due to the presence of elemental oxygen, together with the fact that most hydrocarbons also absorb the 253.7 nm radiation from the UV source. The UV/ozone exposure can also break polymer chains and insert oxygen-containing functional groups (Peeling and Clark 1983), substantially increasing surface energy. Bond strength measurements performed on PMMA and COC chips have revealed substantial improvements in bond strength compared to untreated surfaces. Even when bonding at room temperature, UV/ozone treated surfaces provide bond strengths approaching those of the native surfaces bonded near their glass transition temperatures (Fig. 9). When bonding at 90°C, the UV/ozone treated PMMA and COC chips exhibited bond strengths 10–100 times higher than their native counterparts.

In general, surface treatments performed by plasma, UV, or UV/ozone exposure can significantly improve bond strengths for thermoplastic microfluidics. For prototyping, the high throughput and minimal equipment requirements for UV or UV/ozone exposure make this a particularly

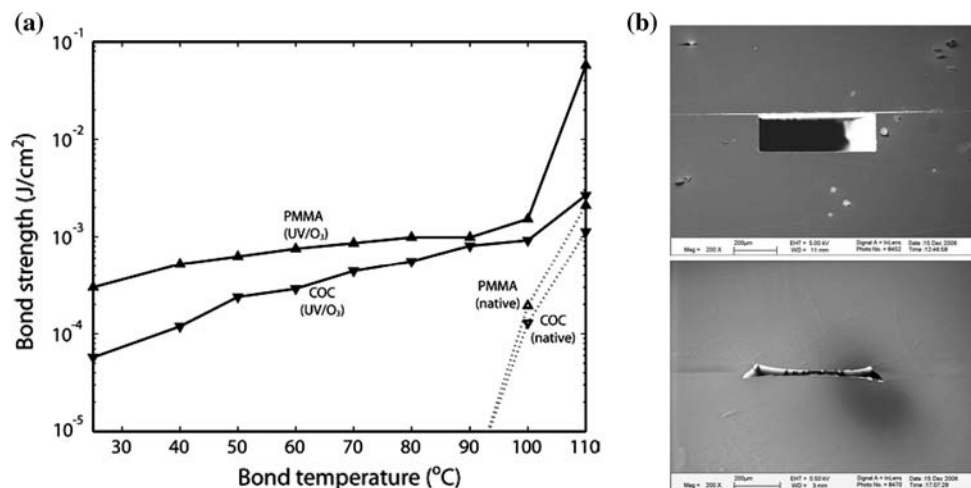


Fig. 9 **a** Bond strength of PMMA and COC substrates following 24 min UV treatment, compared with native polymer surfaces, and **b** SEM images of 500 μm wide, 180 μm deep PMMA microchannels bonded at 60°C following UV/ozone treatment (*top*), or at 100°C with no treatment (*bottom*). While substantial collapse of the channel is

evident for the untreated chip, the treated channel exhibits no measurable deformation while providing higher bond strength than the untreated chip (Tsao et al. 2007). Reproduced by permission of The Royal Society of Chemistry

practical approach to surface activation prior to thermal bonding. Commercial UV/ozone instruments are significantly less expensive than typical plasma systems. It should be noted that ozone is a carcinogen, and proper ventilation of exhaust gas during chip exposure should be addressed before using these tools.

The effects of surface modifications on microchannel wall chemistry are another important consideration. For example, enhanced hydrophilicity can enable simple channel priming via surface tension-driven wetting, while charged surface groups resulting from plasma, UV, or UV/ozone exposure can produce undesirable electrostatic interactions with analyte molecules and excessive or poorly controlled electroosmotic flow. In one recent study, UV/ozone treatment was found to nearly double the zeta potential for the channel sidewalls in PMMA and COC microfluidic chips. However, aggressive flushing of the channels with DI water can alleviate this problem, and in fact the charged surface may be used for further modifications such as attachment of polyvinyl alcohol (PVA) which can reduce the zeta potential well below that of the native polymers (Tsao et al. 2007).

4 Conclusion and outlook

Thermoplastics offer a very promising alternative to silicon, quartz, glass, and elastomer materials for microfluidic applications, with benefits including a wide range of material properties, low material costs, and compatibility with manufacturing methods which are scalable from laboratory prototyping to full scale mass production. Just as replication-based methods borrowed from macro-scale thermoplastic manufacturing have been modified for the fabrication of microchannels, established thermoplastic bonding methods have also been adapted to the particular challenges of sealing these miniaturized fluidic components.

Thermal fusion bonding, and solvent bonding remain the most prevalent bonding methods applied to thermoplastic microfluidics, while the importance of adhesive bonding has been greatly reduced by ongoing improvements in the former bonding techniques. Welding using ultrasonic or laser energy to thermally fuse defined chip regions remains a niche fabrication method that offers particular utility for applications which can benefit from localized bonding. Surface modifications are playing an increasingly important role in thermoplastic microfluidic bonding, enabling high bond strengths with low process temperatures, while also providing benefits for downstream surface modifications. Although surface modifications have been discussed here in terms of their application to thermal fusion bonding, these treatments can also be used for increasing surface energy prior to other bonding methods in order to

improve wettability and generate charged moieties for enhanced bond strength.

A chart summarizing thermoplastic bonding techniques for microfluidic device is listed in Table 3. This chart provides qualitative comparison between each bonding technique. In general, each bonding technique offers particular advantages and disadvantage that must be considered in the context of specific microfluidic applications. An obvious example is that recent advances in solvent-based thermoplastic microfluidic bonding methods have been driven in large part by the need for compatibility with high pressure liquid chromatography. Beyond considerations of bond strength, evaluation of the effects of different bonding methods of the thermoplastic surfaces is needed to understand whether desirable surface properties can be retained or enhanced, and whether undesirable properties can be reduced using a given bonding process.

It is clear that the thermoplastic bonding technique need further advanced to superior compatibility to meet various microfluidic applications with high bond strength, high dimensional and environmental stability without reducing its native material performance after bonding. In addition, with more and more thermoplastic microfluidics to be commercialized, low infrastructure cost, reliable and high yield thermoplastic bonding technique to be developed in near future is foreseeable. In addition, as widespread commercial adoption of thermoplastic microfluidic systems move closer to reality, the need for bonding methods which are compatible with high throughput manufacturing will increase. A harbinger of this trend can be seen in the emergence of tape-based imprinting techniques as an ultra-low cost solution for mass fabrication of thermoplastic microfluidic chips, although current methods for bonding these devices are limited to lamination or low strength thermal sealing. This limitation unnecessarily constrains the types of applications which this fabrication approach can address. Compatible high throughput methods for surface treatments and substrate bonding are needed to meet this demand. For examples, corona discharge treatments offer a simple and high throughput alternative to plasma or UV/ozone exposure for increasing thermoplastic surface energy prior to thermal bonding, while also being amenable to integration with in-line heated roller bonding as an alternative to the use of planar presses for thermal fusion bonding. Solvent bonding may also prove suitable for high throughput microfluidic chip processing through the use of vapor deposition or carefully tailored solvent mixtures with well-defined solvent uptake into the bulk polymer. Regardless of the bonding method, manufacturing scale-up always imposes its own unique set of challenges during process development. As these issues are addressed, further improvements in the robustness and performance of thermoplastic sealing techniques will result.

Table 3 Overview of thermoplastic bonding technique for microfluidic device

Bonding method	Bonding strength	Bonding quality	Process complexity	Bonding time	Cost ^a	Advantage	Limitation	Suitable material	References
Adhesive printing bonding	High	Fair	Medium–high	Short–medium	Low–medium	Low temperature, high bond strength, low channel clogging, controllable adhesive thickness	Scarification channel (contact printing) or printing mask (screen printing) required	PMMA, COC	Dang et al. (2005), Han et al. (2003)
Adhesive interstitial bonding	High	Fair	Low	Short	Low	Simple, fast, low temperature, high bond strength, low channel clogging, low cost	Adhesive loading reservoirs or flush adhesive out of channel needed	PMMA	Lu et al. (2008), Lai et al. (2004)
PDMS-interface bonding	Medium	Low	Medium	Long	Medium	Low temperature, compatible with PDMS microfluidics	PDMS layer may squeeze into channel	PMMA	Chow et al. (2006)
Lamination film bonding	Medium	Fair	Low	Short	Low	Simple, fast, low cost, low temperature, no adhesive clogging	Lamination film may be embedded inside channel	PMMA, PC, PS, PET	Huang et al. (2007), Roberts et al. (1997), Klank et al. (2002)
Thermal fusion bonding	Medium	Fair	Low	Long	Low–medium	Simple, homogeneous channel, compatible with various material	Channel deformation from un-optimized process condition	PMMA, PC, PS, nylon, COC, PSU	Li et al. (2004), Buch et al. (2004), Wang et al. (2005), Park et al. (2008), Shadpour et al. (2007), Wang et al. (2008), Chen et al. (2003), Arroyo et al. (2007), Kelly and Woolley (2003), Liu et al. (2008), Nie and Fung (2008), Nikevic et al. (2007), Sun et al. (2006), Tan et al. (2008), Yao et al. (2005), Zhu et al. (2007), Ahn et al. (2004), Bhattacharyya and Klapperich (2006), Riegger et al. (2007), Tsao et al. (2008), Steigert et al. (2007), Fredrickson et al. (2006), Olivero and Fan (2008), Shadpour et al. (2006), Locascio et al. (1999), Taberham et al. (2008), Hromada et al. (2008)

Table 3 continued

Bonding method	Bonding strength	Bonding quality	Process complexity	Bonding time	Cost ^a	Advantage	Limitation	Suitable material	References
Solvent bonding	High	Fair	Low	Low	Low	Simple, fast, low temperature, high bond strength, low cost	Soften polymer surface may collapse channel from un-optimized process	PMMA, PC, COC	Ro et al. (2006), Klank et al. (2002), Hsu and Chen (2007), Sun et al. (2007), Brown et al. (2006), Ng et al. (2008), Lin et al. (2005), Lin et al. (2007), Griebel et al. (2004), Wallow et al. (2007), Mair et al. (2007), Chen et al. (2008), Liu et al. (2007), Morales et al. (2006)
Solvent bonding with sacrificial material	High	Good	High	Medium	Low	High bond strength, low cost, low channel collapse and clogging	Sacrificial material need applied into channel before bonding and removed after bonding	PMMA	(Kelly et al. (2005), Koesdjojo et al. (2008)
Localized welding	Medium	Fair	Medium–high	Medium	Medium	Low temperature, localized bonding	Energy director (ultrasonic welding) or metal layer (microwave welding) are required	PMMA, PEEK	Truckenmuller et al. (2006a, b), Lei et al. (2004), Yussuf et al. (2007), Kim and Xu (2003)
Surface treatment bonding	Medium–High	Good	Medium	Medium	Medium–high	Low temperature bonding, low channel deformation	Surface chemistry changed after treatment	PMMA, PC, COC PS, PET	Wang et al. (2008), Liu et al. (2008), Ahn et al. (2004), Tsao et al. (2007), Abgrall et al. (2007), Brown et al. (2006), Wu (1982), Uyama et al. (1998), Hu and Brittain (2005), Kruse et al. (1995), Collaud et al. (1994), Shenton et al. (2001), Lee et al. (2005), Johansson et al. (2002), Kettner et al. (2006), Pepin et al. (2002), Puntambekar et al. (2002), Nikolova et al. (2004), Bhattacharya and Klapperich (2007), Klinitberg et al. (2003), Wu et al. (2002), Raghavan et al. (2000)

^a Cost includes material cost and equipment cost

References

- Abgrall P, Lattes C, Conederal V, Dollat X, Colin S, Gue AM (2006) A novel fabrication method of flexible and monolithic 3D microfluidic structures using lamination of SU-8 films. *J Micromech Microeng* 16(1):113–121
- Abgrall P, Low LN, Nguyen NT (2007) Fabrication of planar nanofluidic channels in a thermoplastic by hot-embossing and thermal bonding. *Lab Chip* 7(4):520–522
- Ahn CH, Choi JW, Beaucage G, Nevin JH, Lee JB, Puntambekar A, Lee JY (2004) Disposable Smart lab on a chip for point-of-care clinical diagnostics. *Proc IEEE* 92(1):154–173
- Allen NS, Edge M (1992) *Fundamentals of polymer degradation and stabilization*. Elsevier, New York
- Arroyo MT, Fernandez LJ, Agirregabiria M, Ibanez N, Aurrekoetxea J, Blanco FJ (2007) Novel all-polymer microfluidic devices monolithically integrated within metallic electrodes for SDS-CGE of proteins. *J Micromech Microeng* 17(7):1289–1298
- Barton AFM (1991) *Handbook of solubility parameters and other cohesion parameters*. CRC Press, Boca Raton
- Becker H, Gartner C (2000) Polymer microfabrication methods for microfluidic analytical applications. *Electrophoresis* 21(1):12–26
- Becker H, Gartner C (2008) Polymer microfabrication technologies for microfluidic systems. *Anal Bioanal Chem* 390(1):89–111
- Becker H, Locascio LE (2002) Polymer microfluidic devices. *Talanta* 56(2):267–287
- Bhattacharyya A, Klapperich CM (2006) Thermoplastic microfluidic device for on-chip purification of nucleic acids for disposable diagnostics. *Anal Chem* 78(3):788–792
- Bhattacharyya A, Klapperich CM (2007) Mechanical and chemical analysis of plasma and ultraviolet-ozone surface treatments for thermal bonding of polymeric microfluidic devices. *Lab Chip* 7(7):876–882
- Bolon DA, Kunz CO (1972) Ultraviolet depolymerization of photoresist polymers. *Polym Eng Sci* 12(2):109
- Brown L, Koerner T, Horton JH, Oleschuk RD (2006) Fabrication and characterization of poly(methylmethacrylate) microfluidic devices bonded using surface modifications and solvents. *Lab Chip* 6(1):66–73
- Brydson J (1999) *Plastic materials*. Butterworth-Heinemann, Oxford
- Buch JS, Kimball C, Rosenberger F, Highsmith WE Jr, DeVoe DL, Lee CS (2004) DNA mutation detection in a polymer microfluidic network using temperature gradient gel electrophoresis. *Anal Chem* 76:874–881
- Chen ZF, Gao YH, Su RG, Li CW, Lin JM (2003) Fabrication and characterization of poly(methyl methacrylate) microchannels by in situ polymerization with a novel metal template. *Electrophoresis* 24(18):3246–3252
- Chen Y, Zhang LY, Chen G (2008a) Fabrication, modification, and application of department of analytical poly(methyl methacrylate) microfluidic chips. *Electrophoresis* 29(9):1801–1814
- Chen G, Svec F, Knapp DR (2008b) Light-actuated high pressure-resisting microvalve for on-chip flow control based on thermo-responsive nanostructured polymer. *Lab Chip* 8(7):1198–1204
- Chow WWY, Lei KF, Shi GY, Li WJ, Huang Q (2006) Microfluidic channel fabrication by PDMS-interface bonding. *Smart Mater Struct* 15(1):S112–S116
- Collaud M, Groening P, Nowak S, Schlappbach L (1994) Plasma Treatment of Polymers - the Effect of the Plasma Parameters on the Chemical, Physical, and Morphological States of the Polymer Surface and on the Metal-Polymer Interface. *J Adh Sci Technol* 8(10):1115–1127
- Dang F, Shinohara S, Tabata O, Yamaoka Y, Kurokawa M, Shinohara Y, Ishikawa M, Baba Y (2005) Replica multichannel polymer chips with a network of sacrificial channels sealed by adhesive printing method. *Lab Chip* 5(4):472–478
- Eddings MA, Johnson MA, Gale BK (2008) Determining the optimal PDMS-PDMS bonding technique for microfluidic devices. *J Micromech Microeng* 18(6)
- Emanuel NM, Buchachenko AL (1987) *Chemical Physics of Polymer Degradation and Stabilization*. VNU Science Press, Utrecht
- Fitzpatrick LJ, Dean JR (2002) Extraction solvent selection in environmental analysis. *Anal Chem* 74(1):74–79
- Fredrickson CK, Xia Z, Das C, Ferguson R, Tavares FT, Fan ZH (2006) Effects of fabrication process parameters on the properties of cyclic olefin copolymer microfluidic devices. *J Microelectromech Syst* 15(5):1060–1068
- Giselbrecht S, Gietzelt T, Gottwald E, Trautmann C, Truckenmuller R, Weibezahn KF, Welle A (2006) 3D tissue culture substrates produced by microthermoforming of pre-processed polymer films. *Biomed Microdevices* 8(3):191–199
- Griebel A, Rund S, Schonfeld F, Dorner W, Konrad R, Hardt S (2004) Integrated polymer chip for two-dimensional capillary gel electrophoresis. *Lab Chip* 4(1):18–23
- Han J, Lee SH, Puntambekar A, Murugesan S, Choi J-W, Beaucage G, Ahn CH (2003) UV adhesive bonding techniques at room temperature for plastic lab-on-a-chip. In: *Proceedings of 7th International Conference Micro Total Analysis Systems*. Squaw Valley, CA, pp 1113–1116
- Hansen CM (1969) The universality of the solubility parameter. *Ind Eng Chem Prod Res Dev* 8:2–11
- Hildebrandt J, Scott R (1949) *The solubility of non-electrolytes*. Reinhold, New York
- Hromada LP, Nablo BJ, Kasianowicz JJ, Gaitan MA, DeVoe DL (2008) Single molecule measurements within individual membrane-bound ion channels using a polymer-based bilayer lipid membrane chip. *Lab Chip* 8(4):602–608
- Hsu YC, Chen TY (2007) Applying Taguchi methods for solvent-assisted PMMA bonding technique for static and dynamic mu-TAS devices. *Biomed Microdevices* 9(4):513–522
- Hu SW, Brittain WJ (2005) Surface grafting on polymer surface using physisorbed free radical initiators. *Macromolecules* 38(15):6592–6597
- Huang F-C, Chen Y-F, Lee G-B (2007) CE chips fabricated by injection molding and polyethylene/thermoplastic elastomer film packaging methods. *Electrophoresis* 28(7):1130–1137
- Johansson BL, Larsson A, Ocklind A, Ohrlund A (2002) Characterization of air plasma-treated polymer surfaces by ESCA and contact angle measurements for optimization of surface stability and cell growth. *J Appl Polym Sci* 86(10):2618–2625
- Kelly RT, Woolley AT (2003) Thermal bonding of polymeric capillary electrophoresis microdevices in water. *Anal Chem* 75(8):1941–1945
- Kelly RT, Pan T, Woolley AT (2005) Phase-changing sacrificial materials for solvent bonding of high-performance polymeric capillary electrophoresis microchips. *Anal Chem* 77(11):3536–3541
- Kettner P, Pelzer RL, Glinsner T, Farrens S (2006) New results on plasma activated bonding of imprinted features for Bio MEMS applications. *J Phys Conf Ser* 34:65–71
- Kim J, Xu XF (2003) Excimer laser fabrication of polymer microfluidic devices. *J Laser Appl* 15(4):255–260
- Klank H, Kutter JP, Geschke O (2002) CO₂-laser micromachining and back-end processing for rapid production of PMMA-based microfluidic systems. *Lab Chip* 2(4):242–246
- Klintberg L, Svedberg M, Nikolajeff F, Thornell G (2003) Fabrication of a paraffin actuator using hot embossing of polycarbonate. *Sens Actuators A Phys* 103(3):307–316
- Koesdjojo MT, Tennico YH, Reincho VT (2008) Fabrication of a microfluidic system for capillary electrophoresis using a two-

- stage embossing technique and solvent welding on poly(methyl methacrylate) with water as a sacrificial layer. *Anal Chem* 80(7):2311–2318
- Kruse A, Kruger G, Baalmann A, Hennemann OD (1995) Surface pretreatment of plastics for adhesive bonding. *J Adh Sci Technol* 9(12):1611–1621
- do Lago CL, da Silva HDT, Neves CA, Brito-Neto JGA, da Silva JAF (2003) A dry process for production of microfluidic devices based on the lamination of laser-printed polyester films. *Anal Chem* 75(15):3853–3858
- Lai S, Cao X, Lee LJ (2004) A packaging technique for polymer microfluidic platforms. *Anal Chem* 76(4):1175–1183
- Lee GB, Lin CH, Lee KH, Lin YF (2005) On the surface modification of microchannels for microcapillary electrophoresis chips. *Electrophoresis* 26(24):4616–4624
- Lei KF, Ahsan S, Budraa N, Li WJ, Mai JD (2004) Microwave bonding of polymer-based substrates for potential encapsulated micro/nanofluidic device fabrication. *Sens Actuators A Phys* 114(2–3):340–346
- Li Y, Buch JS, Rosenberger F, DeVoe DL, Lee CS (2004) Integration of isoelectric focusing with parallel sodium dodecyl sulfate gel electrophoresis for multidimensional protein separations in a plastic microfluidic network. *Anal Chem* 76:742–748
- Li JH, Chen D, Chen G (2005) Low-temperature thermal bonding of PMMA microfluidic chips. *Anal Lett* 38(7):1127–1136
- Lin C-H, Fu L-M, Tsai C-H, Chao C-H, Lan C-W (2005) Low azeotropic solvent sealing of PMMA microfluidic devices. In: *The 13th international conference on solid-state sensors, actuators, and microsystems (transducers 05)*, Seoul, Korea, pp 944–947
- Lin CH, Chao CH, Lan CW (2007) Low azeotropic solvent for bonding of PMMA microfluidic devices. *Sensors and Actuators B-Chemical* 121(2):698–705
- Liu J, Ro KW, Nayak R, Knapp DR (2007) Monolithic column plastic microfluidic device for peptide analysis using electrospray from a channel opening on the edge of the device. *Int J Mass Spectrom* 259(1–3):65–72
- Liu J, Yang S, Lee CS, DeVoe DL (2008) Polyacrylamide gel plugs enabling 2-D microfluidic protein separations via isoelectric focusing and multiplexed sodium dodecyl sulfate gel electrophoresis. *Electrophoresis* 29(11):2241–2250
- Locascio LE, Perso CE, Lee CS (1999) Measurement of electroosmotic flow in plastic imprinted microfluid devices and the effect of protein adsorption on flow rate. *J Chromatogr A* 857(1–2):275–284
- Lu C, Lee LJ, Juang Y-J (2008) Packaging of microfluidic chips via interstitial bonding technique. *Electrophoresis* 29(7):1407–1414
- Mair DA, Rolandi M, Snauko M, Noroski R, Svec F, Frechet JMJ (2007) Room-temperature bonding for plastic high-pressure microfluidic chips. *Anal Chem* 79(13):5097–5102
- Martynova L, Locascio LE, Gaitan M, Kramer GW, Christensen RG, MacCrehan WA (1997) Fabrication of plastic microfluid channels by imprinting methods. *Anal Chem* 69(23):4783–4789
- McCormick RM, Nelson RJ, Alonso-Amigo MG, Benvenuto J, Hooper HH (1997) Microchannel electrophoretic separations of DNA in injection-molded plastic substrates. *Anal Chem* 69(14):2626–2630
- Morales AM, Simmons BA, Wallow TI, Krafcik KL, Domier LA (2006) Low distortion, high strength bonding of polymer microfluidic chips exploiting case II permeation. In: *10th international conference on miniaturized systems for chemistry and life sciences*. 1:155–157
- Ng SH, Tjeung RT, Wang ZF, Lu ACW, Rodriguez I, de Rooij NF (2008) Thermally activated solvent bonding of polymers. *Microsyst Tech Micro Nanosyst Inf Storage Process Syst* 14(6):753–759
- Nie Z, Fung YS (2008) Microchip capillary electrophoresis for frontal analysis of free bilirubin and study of its interaction with human serum albumin. *Electrophoresis* 29(9):1924–1931
- Nikcevic I, Lee SH, Piruska A, Ahn CH, Ridgway TH, Limbach PA, Wehmeyer KR, Heineman WR, Seliskar CJ (2007) Characterization and performance of injection molded poly(methylmethacrylate) microchips for capillary electrophoresis. *J Chromatogr A* 1154(1–2):444–453
- Nikolova D, Dayss E, Leps G, Wutzler A (2004) Surface modification of cycloolefinic copolymers for optimization of the adhesion to metals. *Surf Interface Anal* 36(8):689–693
- Olivero D, Fan ZH (2008) Chips & tips: lamination of plastic microfluidic devices. *Lab Chip*. http://www.rsc.org/Publishing/Journals/lc/Chips_and_Tips/lamination.asp
- Park DSW, Hupert ML, Witek MA, You BH, Datta P, Guy J, Lee JB, Soper SA, Nikitopoulos DE, Murphy MC (2008) A titer plate-based polymer microfluidic platform for high throughput nucleic acid purification. *Biomed Microdevices* 10(1):21–33
- Paul D, Pallandre A, Miserere S, Weber J, Viovy J-L (2007) Lamination-based rapid prototyping of microfluidic devices using flexible thermoplastic substrates. *Electrophoresis* 28(7):1115–1122
- Peeling J, Clark DT (1983) Surface ozonation and photo-oxidation of polyethylene film. *J Polym Sci A Polym Chem* 21(7):2047–2055
- Pepin A, Youinou P, Studer V, Lebib A, Chen Y (2002) Nanoimprint lithography for the fabrication of DNA electrophoresis chips. *Microelectron Eng* 61–2:927–932
- Piruska A, Nikcevic I, Lee SH, Ahn C, Heineman WR, Limbach PA, Seliskar CJ (2005) The autofluorescence of plastic materials and chips measured under laser irradiation. *Lab Chip* 5(12):1348–1354
- Pocius AV (2002) *Adhesion and adhesives technology: an introduction*. Hanser/Gardner Publications, Cincinnati
- Puntambekar A, Murugesan S, Trichur R, Cho HJ, Kim S, Choi J, Beaucage G, Ahn CH (2002) Effect of surface modification on thermoplastic fusion bonding for 3-D microfluidics. In: *Proceedings of the 6th International Conference on Micro Total Analysis Systems Nara, Japan*, pp 425–427
- Raghavan D, VanLandingham M, Gu X, Nguyen T (2000) Characterization of heterogeneous regions in polymer systems using tapping mode and force mode atomic force microscopy. *Langmuir* 16(24):9448–9459
- Reyes DR, Iossifidis D, Auroux PA, Manz A (2002) Micro total analysis systems. 1. Introduction, theory, and technology. *Anal Chem* 74(12):2623–2636
- Riegger L, Grumann M, Steigert J, Lutz S, Steinert CP, Mueller C, Viertel J, Prucker O, Ruhe J, Zengerle R, Ducree J (2007) Single-step centrifugal hematocrit determination on a 10- μ S processing device. *Biomed Microdevices* 9(6):795–799
- Ro KW, Liu H, Knapp DR (2006) Plastic microchip liquid chromatography-matrix-assisted laser desorption/ionization mass spectrometry using monolithic columns. *J Chromatogr A* 1111(1):40–47
- Roberts MA, Rossier JS, Bercier P, Girault H (1997) UV laser machined polymer substrates for the development of microdiagnostic systems. *Anal Chem* 69(11):2035–2042
- Rossier J, Reymond F, Michel PE (2002) Polymer microfluidic chips for electrochemical and biochemical analyses. *Electrophoresis* 23(6):858–867
- Rotting O, Ropke W, Becker H, Gartner C (2002) Polymer microfabrication technologies. *Microsystem Technologies* 8(1):32–36
- Schultz J, Nardin M (1994) Theories and mechanisms of adhesion. In: Mittal APAKL (ed) *Handbook of adhesive technology*. Marcel Dekker, New York, pp 19–33
- Shadpour H, Musyimi H, Chen JF, Soper SA (2006) Physicochemical properties of various polymer substrates and their effects on

- microchip electrophoresis performance. *J Chromatogr A* 1111(2):238–251
- Shadpour H, Hupert ML, Patterson D, Liu CG, Galloway M, Stryjewski W, Goettert J, Soper SA (2007) Multichannel microchip electrophoresis device fabricated in polycarbonate with an integrated contact conductivity sensor array. *Anal Chem* 79(3):870–878
- Shah JJ, Geist J, Locascio LE, Gaitan M, Rao MV, Vreeland WN (2006) Capillarity induced solvent-actuated bonding of polymeric microfluidic devices. *Anal Chem* 78(10):3348–3353
- Shenton MJ, Lovell-Hoare MC, Stevens GC (2001) Adhesion enhancement of polymer surfaces by atmospheric plasma treatment. *J Phys D Appl Phys* 34(18):2754–2760
- Sowell RR, Cuthrell RE, Mattox DM, Bland RD (1974) Surface Cleaning by Ultraviolet-Radiation. *J Vac Sci Technol A* 11(1):474–475
- Steigert J, Haerberle S, Brenner T, Muller C, Steinert CP, Koltay P, Gottschlich N, Reinecke H, Ruhe J, Zengerle R, Ducree J (2007) Rapid prototyping of microfluidic chips in COC. *J Micromech Microeng* 17(2):333–341
- Strong AB (2000) *Plastics Materials and Processing*. Prentice-Hall, Upper Saddle River
- Sun Y, Kwok YC, Nguyen NT (2006) Low-pressure, high-temperature thermal bonding of polymeric microfluidic devices and their applications for electrophoretic separation. *J Micromech Microeng* 16(8):1681–1688
- Sun XH, Peeni BA, Yang W, Becerril HA, Woolley AT (2007) Rapid prototyping of poly(methyl methacrylate) microfluidic systems using solvent imprinting and bonding. *J Chromatogr A* 1162(2):162–166
- Taberham A, Kraft M, Mowlem M, Morgan H (2008) The fabrication of lab-on-chip devices from fluoropolymers. *J Micromech Microeng* 18(6):064011
- Tan HY, Loke WK, Tan YT, Nguyen N-T (2008) A lab-on-a-chip for detection of nerve agent sarin in blood. *Lab Chip* 8(6):885–891
- Truckenmuller R, Henzi P, Herrmann D, Saile V, Schomburg WK (2004) A new bonding process for polymer micro- and nanostructures based on near-surface degradation. In: 17th IEEE International Conference on Micro Electro Mechanical Systems, pp 761–764
- Truckenmuller R, Henzi P, Herrmann D, Saile V, Schomburg WK (2004b) Bonding of polymer microstructures by UV irradiation and subsequent welding at low temperatures. *Microsyst Technol* 10(5):372–374
- Truckenmuller R, Ahrens R, Cheng Y, Fischer G, Saile V (2006a) An ultrasonic welding based process for building up a new class of inert fluidic microsensors and -actuators from polymers. *Sens Actuators A Phys* 132(1):385–392
- Truckenmuller R, Cheng Y, Ahrens R, Bahrs H, Fischer G, Lehmann J (2006b) Micro ultrasonic welding: joining of chemically inert polymer microparts for single material fluidic components and systems. *Microsyst Tech Micro Nanosyst Inf Storage Process Syst* 12(10–11):1027–1029
- Tsao CW, Hromada L, Liu J, Kumar P, DeVoe DL (2007) Low temperature bonding of PMMA and COC microfluidic substrates using UV/ozone surface treatment. *Lab Chip* 7(4):499–505
- Tsao C-W, Liu J, DeVoe DL (2008) Droplet formation from hydrodynamically coupled capillaries for parallel microfluidic contact spotting. *J Micromech Microeng* 18:025013
- Uyama Y, Kato K, Ikada Y (1998) Surface modification of polymers by grafting. *Graf Charact Tech Kinet Model* 137:1–39
- Velten T, Schuck H, Richter M, Klink G, Bock K, Khan Malek C, Roth S, Schoo H, Bolt PJ (2008) Microfluidics on foil: state of the art and new developments. *Proc IMechE Part B J Eng Manuf* 222(1):107–116
- Vig JR (1985) Uv ozone cleaning of surfaces. *J Vac Sci Technol A Vac Surf Films* 3(3):1027–1034
- Vig JR, LeBus JW (1976) UV/ozone cleaning of surfaces. *IEEE Trans Parts Hybrid Packag PHP* 12:365–370
- Wallow TI, Morales AM, Simmons BA, Hunter MC, Krafcik KL, Domeier LA, Sickafoose SM, Patel KD, Gardea A (2007) Low-distortion, high-strength bonding of thermoplastic microfluidic devices employing case-II diffusion-mediated permeant activation. *Lab Chip* 7(12):1825–1831
- Wang Y-X, Zhou Y, Balgley BM, Cooper JW, Lee CS, DeVoe DL (2005) Electrospray interfacing of polymer microfluidics to MALDI-MS. *Electrophoresis* 26:3631–3640
- Wang YR, Chen HW, He QH, Soper SA (2008) A high-performance polycarbonate electrophoresis microchip with integrated three-electrode system for end-channel amperometric detection. *Electrophoresis* 29(9):1881–1888
- Witek MA, Wei S, Vaidya B, Adams AA, Zhu L, Stryjewski W, McCarley RL, Soper SA (2004) Cell transport via electromigration in polymer-based microfluidic devices. *Lab Chip* 4:464–472
- Wu S (1982) *Polymer Interface and Adhesion*. Marcel Dekker, New York
- Wu ZY, Xanthopoulos N, Reymond F, Rossier JS, Girault HH (2002) Polymer microchips bonded by O-2-plasma activation. *Electrophoresis* 23(5):782–790
- Xia Y, Whitesides GM (1998) Soft lithography. *Angew Chem Int Ed Engl* 37:550–575
- Xu JD, Locascio L, Gaitan M, Lee CS (2000) Room-temperature imprinting method for plastic microchannel fabrication. *Anal Chem* 72(8):1930–1933
- Yao LY, Liu B, Chen T, Liu SB, Zuo TC (2005) Micro flow-through PCR in a PMMA chip fabricated by KrF excimer laser. *Biomed Microdevices* 7(3):253–257
- Yussuf AA, Sbarski I, Solomon M, Tran N, Hayes JP (2007) Sealing of polymeric-microfluidic devices by using high frequency electromagnetic field and screen printing technique. *J Mater Process Technol* 189(1–3):401–408
- Zhu XL, Liu G, Guo YH, Tian YC (2007) Study of PMMA thermal bonding. *Microsyst Tech Micro Nanosyst Inf Storage Process Syst* 13(3–4):403–407