ACCOUNTS
of chemical research

Materials for Microfluidic Chip Fabrication

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RECEIVED ON NOVEMBER 27, 2012

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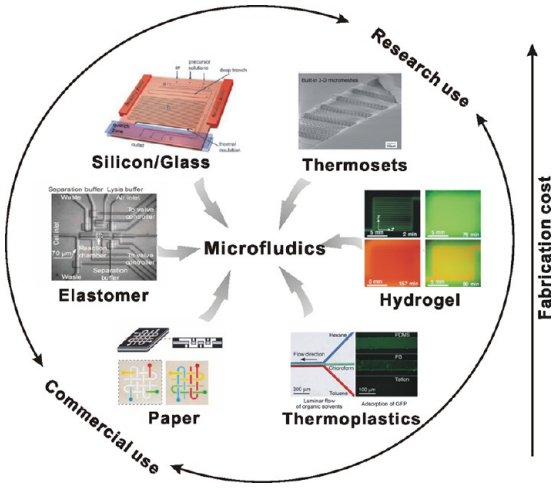

Through manipulating fluids using microfabricated channel and chamber structures, microfluidics is a powerful tool to realize high sensitive, high speed, high throughput, and low cost analysis. In addition, the method can establish a well-controlled microenivroment for manipulating fluids and particles. It also has rapid growing implementations in both sophisticated chemical/biological analysis and low-cost point-of-care assays. Some unique phenomena emerge at the micrometer scale. For example, reactions are completed in a shorter amount of time as the travel distances of mass and heat are relatively small; the flows are usually laminar; and the capillary effect becomes dominant owing to large surface-to-volume ratios. In the meantime, the surface properties of the device material are greatly amplified, which can lead to either unique functions or problems that we would not encounter at the macroscale. Also, each material inherently corresponds with specific microfabrication strategies and certain native properties of the device. Therefore, the material for making the device plays a dominating role in microfluidic technologies. In this Account, we address the evolution of materials used for fabricating microfluidic chips, and discuss the application-oriented pros and cons of different materials.

This Account generally follows the order of the materials introduced to microfluidics. Glass and silicon, the first generation microfluidic device materials, are perfect for capillary electrophoresis and solvent-involved applications but expensive for microfabriaction. Elastomers enable low-cost rapid prototyping and high density integration of valves on chip, allowing complicated and parallel fluid manipulation and in-channel cell culture. Plastics, as competitive alternatives to elastomers, are also rapid and inexpensive to microfabricate. Their broad variety provides flexible choices for different needs. For example, some thermosets support in-situ fabrication of arbitrary 3D structures, while some perfluoropolymers are extremely inert and antifouling. Chemists can use hydrogels as highly permeable structural material, which allows diffusion of molecules without bulk fluid flows. They are used to support 3D cell culture, to form diffusion gradient, and to serve as actuators. Researchers have recently introduced paper-based devices, which are extremely low-cost to prepare and easy to use, thereby promising in commercial point-of-care assays.

In general, the evolution of chip materials reflects the two major trends of microfluidic technology: powerful microscale research platforms and low-cost portable analyses. For laboratory research, chemists choosing materials generally need to compromise the ease in prototyping and the performance of the device. However, in commercialization, the major concerns are the cost of production and the ease and reliability in use. There may be new growth in the combination of surface engineering, functional materials, and microfluidics, which is possibly accomplished by the utilization of composite materials or hybrids for advanced device functions. Also, significant expanding of commercial applications can be predicted.

The technology of microfluidics has experienced explosive growth after its debut in 1990s; now it is spreading into chemical, biological, and medical research areas and showing great potential in miniaturized, portable, and low-cost commercial devices.[1−3] A significant feature of microfluidics is that the material of the device dominates its functions. In this Account, we portray the evolvement of materials exploited for microfluidic devices; with systematic comparison of application-oriented pros and cons of different materials, we hope to provide a guide for choosing chip materials.

Published on the Web 06/11/2013 www.pubs.acs.org/accounts
10.1021/ar300314s

Based on George Whitesides' definition, microfluidics is "the science and technology of systems that process or manipulate small (10^{-9} to 10^{-18} liters) amounts of fluids, using channels with dimensions of tens to hundreds of micrometres."[2,3] Some unique phenomena emerge at such scale. For instance, reactions are completed in a shorter amount of time as the travel distances of mass and heat are relatively small; the flows are laminar because of low Reynolds number in microfluidic channels; capillary effect becomes dominant owing to large surface-to-volume ratios.[2,4] In the microscale, the surface properties of the device material are greatly amplified, which can either realize unique functions or lead to problems that would not be encountered at macroscale;[5] the materials largely determine the function of the devices.

Another attractive feature of microfluidic systems is their power to realize sophisticated functions as the device could contain complicated channel structures and integrate with sensors and operators.[6−10] However, to realize certain functions, special attention should be paid on choosing the right material for the device as it endows the inherent property of the device and determines the applicable microfabrication approaches as well (Table 1).

In the past two decades, various materials have been introduced in microfluidics. Although there are some excellent reviews on specific technologies with certain materials,[11,12] few of them provide the overview of the orientation and development of microchip materials even though choosing the right material is the first and usually a crucial step for a microfluidic chip.

This Account presents the evolvement of materials employed for microchip fabrication; their pros and cons as well as suitable applications are systematically discussed. Instead of trying to provide a complete survey, we focus on the general criteria for choosing chip materials, and the underlying reasons and considerations. Noting that modification of various materials have been reviewed in many excellent papers,[13,14] we do not particularly discuss it here.

1. Inorganic Materials

Before the concept of "microfluidics" was introduced, microchannels had already been used, for example, glass or quartz capillaries for gas chromatography and capillary electrophoresis (CE), and flow reactors micromachined in metal; they contributed to the incubation of microfluidics. Sparked by the microfabrication technologies in the semiconductor industry, the first-generation microfluidic chips were prepared in silica or glass.[1,3]

TABLE 1. Overview of Materials for Microfluidic Device Fabrication

property	silicon/glass[a]	elastomers	thermoset	thermoplastics	hydrogel	paper
Young's (tensile) modulus (GPa)	130−180/50−90	~0.0005	2.0−2.7	1.4−4.1	low	0.0003−0.0025
common technique for microfabrication[b]	photolithography	casting	casting, photopolymerization	thermomolding	casting, photopolymerization	photolithography, printing
smallest channel dimension	<100 nm	<1 μm	<100 nm	~100 nm	~10 μm	~200 μm
channel profile	limited 3D	3D	arbitrary 3D	3D	3D	2D
multilayer channels	hard	easy	easy	easy	medium	easy
thermostability	very high	medium	high	medium to high	low	medium
resistance to oxidizer	excellent	moderate	good	moderate to good[c]	low	low
solvent compatibility	very high	low	high	medium to high	low	medium
hydrophobicity	hydrophilic	hydrophobic	hydrophobic	hydrophobic	hydrophilic	amphiphilic
surface charge	very stable	not stable	stable	stable	N/A	N/A
permeability to oxygen (Barrer[d])	<0.01	~500	0.03−1	0.05−5	>1	>1
optical transparency	no/high	high	high	medium to high	low to medium	low

[a]Photosensitive glass can be considered as thermoset. [b]Most of the materials can be fabricated by laser ablation, but compared with those obtained with lithographic or molding methods the ablated features usually have a rougher surface and are often misshaped. [c]Excellent for Teflon. [d]1 Barrer = 10^{-10} [cm^3 O_2(STD)] cm cm^{-2} s^{-1} $cmHg^{-1}$.

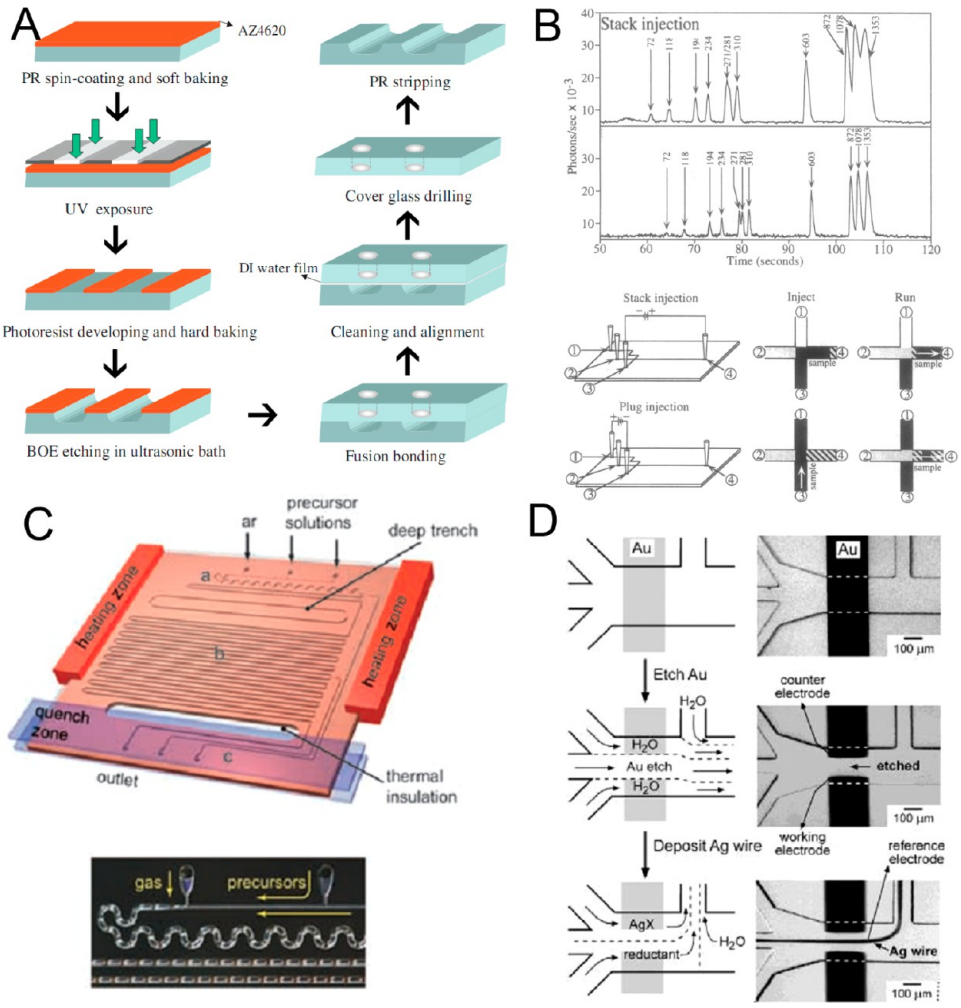

FIGURE 1. (A) Fabrication of glass microchips using wet-etching and fusion bonding methods. (B) Rapid separation on glass microfluidic chip with CE. (C) High-temperature reaction in microdroplets on a glass chip. (D) In-situ metal etching and deposition on a glass substrate using laminar flow. Panel (A) reproduced with permission from ref 15. Copyright 2001 IPO Publishing. Panel (B) reprinted from ref 18. Copyright 1994 National Academy of Sciences. Panel (C) reprinted with permission from ref 19. Copyright 2005 John Wiley and Sons. Panel (D) reprinted with permission from ref 20. Artwork originally published in Science **1999**, *285*, 83−85. Copyright 1999 American Association for the Advancement of Science.

Silica and glass is normally processed with standard photolithography (Figure 1A):[15] a thin layer of photoresist is applied to the wafer and subjected to an ultraviolet exposure, which transfers the micropattern on a transparency mask to the photoresist layer; the photoresist is developed to generate a mask for etching; after microchannels are formed, the photoresist is removed and the channels are sealed with a flat substrate, for example, through a fusion bonding process. Differently, photosensitive glass (rarely used glass in the field) can form microchannels with laser direct writing (LDW),[16] However, LDW is serial-processing (thus is slow) and relies on expensive equipment.

Glass is optically transparent and electrically insulating; as an amorphous material, etched glass channels have rounded sidewalls unless with special etching techniques.[17] In contrast, silicon is opaque and vertical channel sidewalls are created in crystalline silicon. Owing to their resistance to organic solvents, ease in metal depositing, high thermoconductivity, and stable electroosmotic mobility, silicon and glass are commonly used although many other chip materials have been introduced afterward.

One major application of glass chips is CE. Compared with standard CE, on-chip CE is lower in cost, easier to parallel, and offers valve-free injection by directly utilizing the electroosmotic flow, which can separate analytes within seconds (Figure 1B).[18] Due to its high thermoconductivity and stable electroosmotic mobility on its surface, glass microchannel provides better performance than chips in other materials. Other important applications of glass/silicon devices are derived from their thermostability and solvent

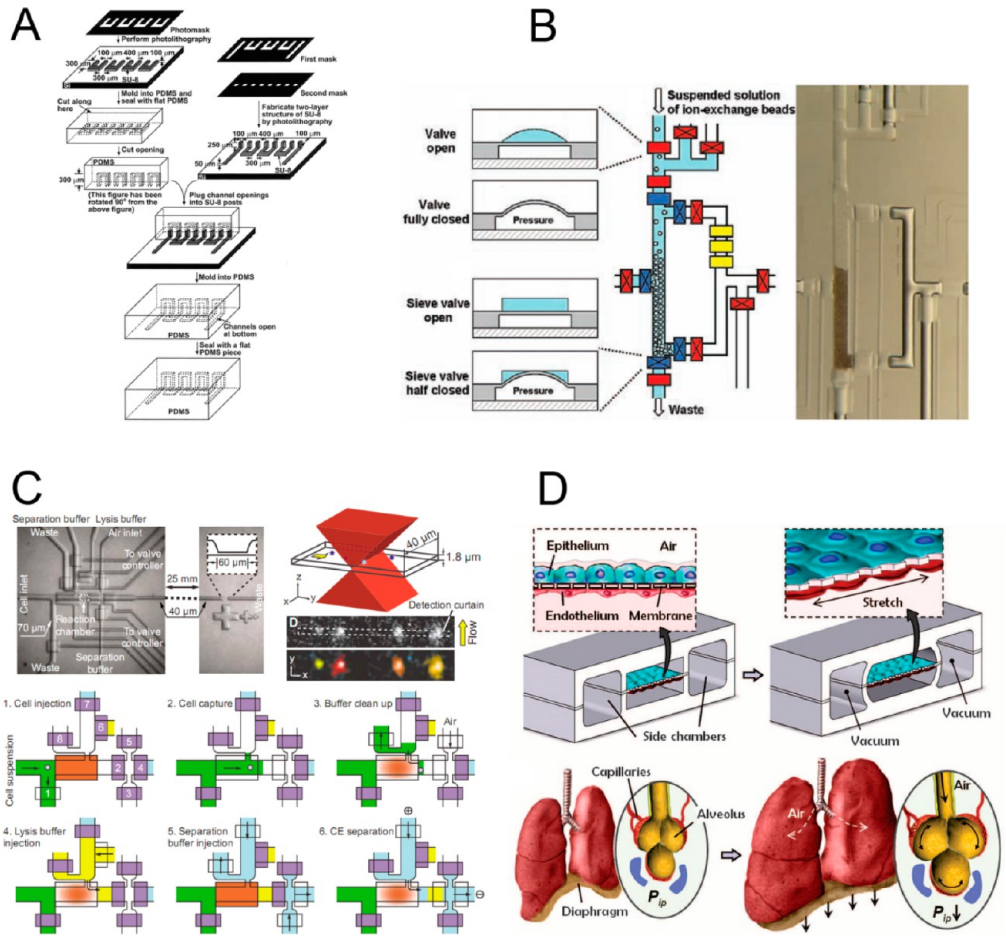

FIGURE 2. (A) Fabrication of 3D microchannels in PDMS. (B) Microsized pneumatic valves in PDMS for manipulating fluids and particles. (C) Complicated manipulation of picoliter fluids on a PDMS device. (D) Application of PDMS 3D structure and deformation of PDMS structure to mimic the function of lungs. Panel (A) reprinted with permission from ref 26. Copyright 2003 American Chemical Society. Panel (B) reprinted with permission from ref 27. Copyright 2005 American Association for the Advancement of Science. Panel (C) reprinted with permission from ref 28. Copyright 2007 American Association for the Advancement of Science. Panel (D) reprinted with permission from ref 29. Copyright 2010 American Association for the Advancement of Science.

compatibility. Typical applications include on-chip reactions (Figure 1C),[19] droplet formation,[6] and solvent extraction and in situ fabrication (Figure 1D).[20]

However, every coin has two sides—the hardness of glass and silicon also poses limits to their broad application in microfluidics. One problem is the high cost of fabrication: each chip is made from the beginning; dangerous chemicals are involved (e.g., HF) and thus require protective facilities; finally, the bonding of such chips is difficult (high temperature, high pressure and super clean environment are normally required). Additionally, effective valves cannot be easily achieved in glass/silicon chips. Hybrid chips [e.g., glass-elastomer; see section 5, point (1) below] can facilitate valve fabrication but may compromise the advantages of glass or silicon. What's more, because glass or silicon is not gas permeable, their chips with enclosed channels and chambers cannot be used for long-term cell culture.

These limitations motivated the development of other chip materials that can be easily fabricated and are compatible for broader biological applications.

2. Elastomers and Plastics

Polymer-based chips were introduced several years later after silicon/glass chips. The vast variety of polymers offers great flexibility in choosing suitable material with specific properties.[11,21] Compared with inorganic materials, polymers are easy to access and inexpensive, and therefore have become the most-commonly used microchip materials. According to their physical properties, polymers can be classified into three groups: elastomers, thermosets, and thermoplastics.

2.1. Elastomers. Elastomers consist of cross-linked polymer chains that are normally entangled; they can stretch or compress when external force is exerted, and return to the original shape when the external force is withdrawn.

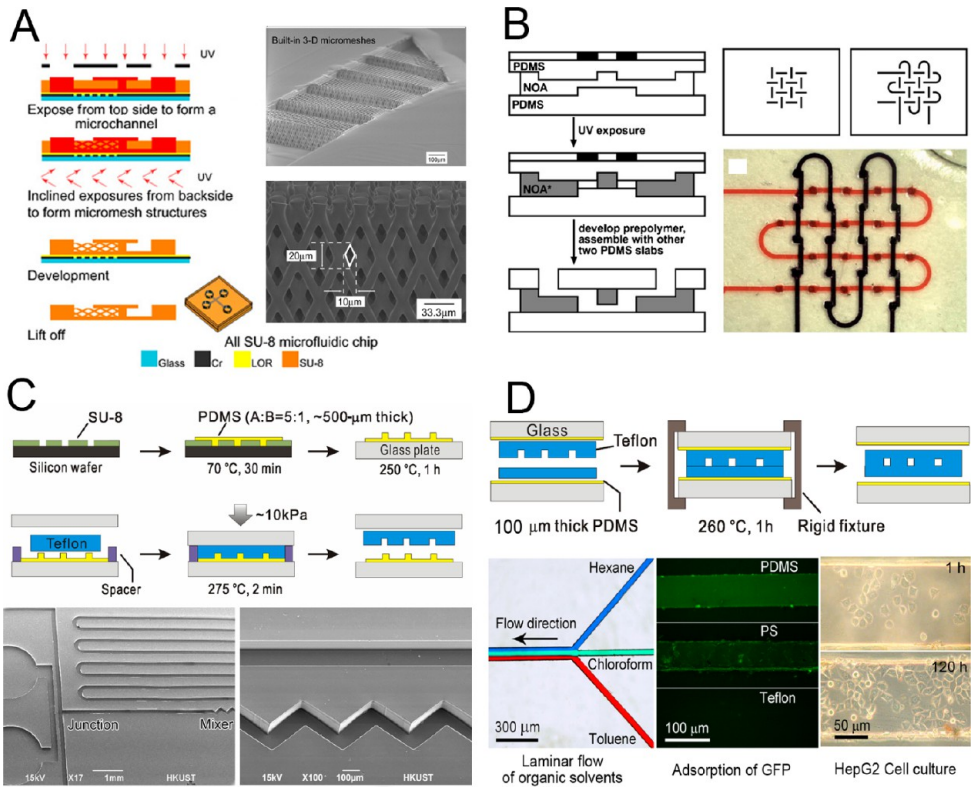

FIGURE 3. (A) Microchannel made entirely with SU-8, with in situ fabricated 3D fine structures. (B) 3D microfluidic channel fabricated in thermoset NOA. (C) Microfabrication of thermoplastics with high temperature transfer molding method. (D) Microfluidic chip fabricated entirely using Teflon PFA. Panel (A) reprinted with permission from ref 43. Copyright 2006 IOP Publishing. Panel (B) reprinted with permission from ref 44. Copyright 2010 AIP Publishing. Panels (C) and (D) reproduced from ref 46. Copyright 2010 National Academy of Sciences.

The most popular elastomer in microfluidics is polydimethylsiloxane (PDMS).[22,23]

A significant superiority of PDMS is its ease and low cost of microfabrication.[24] Liquid PDMS prepolymer is thermally cured at mild temperatures (40−70 °C), and it can be cast with nanometer resolution from photoresist templates, which are easier and cheaper to prepare than silicon or glass templates;[25] its low surface tension greatly facilitates its peeling from templates after being cured. PDMS chip can be reversibly and conformally sealed to another piece of PDMS, glass, or other substrates by simply making contact.[24] It is also convenient to irreversibly bond PDMS to PDMS, glass, or silicon by plasma oxidizing the PDMS surface or using a thin layer of PDMS as glue.[24] Multilayer channel structures were fabricated by simply stacking many PDMS pieces with through holes to connect different layers (Figure 2A).[26] The convenience in fabrication, with other advantages discussed below, makes PDMS the most popular material in research laboratories.[24]

Another advantage of PDMS comes from its high elasticity. Quake et al. developed an integrated valve based on two layers of microchannels,[30] which allows high-density integration of valves (1×10^6 valves/cm^2) with picoliter to femtoliter dead volume, and realized parallel and complicated on-chip manipulation (Figure 2B,C).[27,28] Among many valve designs, this one has become currently the most widely used in the microfluidics field. The design has been adapted for various applications, for example, as an on-demand filter[27,31] or to realize controllable deformation (Figure 2D).[29]

In contrast to glass, silicon, and other hard materials [(e.g., poly(methylmethacrylate) (PMMA) and polycarbonate (PC)], PDMS is gas permeable (which is crucial for long-term cell culture in sealed microchannels); also its surface is compatible for cell culture. Compared with macroscale culture, the microchip provides a well-controllable microenvironment. For example, gradients and oscillations as well as complicated media changing schemes can be easily achieved.[32] It is worth noting that cell behaviors on plain PDMS can be different from those on rigid substrate or on textured or modified PDMS.[33,34]

Because of these traits, PDMS devices are broadly used in biorelated research, primarily, cell culture, cell screening, and biochemical assays.[10,33,35] Specifically, the capability

of handling picoliter to femtoliter volume makes it superior in single-cell analysis.[28,36]

Despite its popularity, PDMS also has notable limitations.[37] At the molecular level, PDMS is a porous matrix of Si−O backbones covered with alkyl groups. This structure allows permeation of gases, which facilitates cell culture; however, it also leads to some major problems: the incompatibility with organic solvents, and the incapability to support certain quantitative experiments owing to three effects—the absorption of small hydrophobic molecules into channel walls, the adsorption of biomolecules onto channel walls, and the change in concentration of solution by water evaporation through channel wall (this property has been exploited for protein crystallization[38]). Various modification strategies have been introduced, but still cannot fully overcome these drawbacks.[13,39−41] Therefore, applications of PDMS devices are restricted in aqueous solutions.

2.2. Thermosets. Before their introduction into microfluidics, thermosets (e.g., SU-8 photoresist and polyimide) have already served as negative photoresists; later they were adapted for the fabrication of microchannel structures.[42] When heated or radiated, the thermosetting molecules cross-link to form a rigid network that cannot soften before decomposition. That is, thermosets cannot be reshaped once cured. Normally, these materials are stable even at high temperatures, resistant to most solvents, and optically transparent. With proper bonding methods, microfluidic chips can be fabricated entirely in thermosets.[21] One major advantage of thermosets is for true 3D microfabrication using photopolymerization (Figure 3A).[43] Another advantage is their high strength, which allows the fabrication of high-aspect ratio and free-standing structures (Figure 3B).[44] Because of their high stiffness, thermosets are improper for the fabrication of the diaphragm valve mentioned above; also with their high cost, their applications in microfluidics are limited.

2.3. Thermoplastics. Different from thermosets, thermoplastics can be reshaped after being cured. Because of their wide use in industry, plentiful experience has been accumulated with thermoplastics. Thermoplastics distinctly soften at glass transition temperature (T_g), making them processable around this temperature. They can be reshaped multiple times by reheating, which is important for the convenience of their molding and bonding. Typical themoplastics for microchips are PMMA, PC, polystyrene (PS), polyethylene terephthalate (PET), and polyvinylchloride (PVC).[21] In general, they show a slightly better solvent compatibility than PDMS—fair resistance to alcohols, but incompatible with most other organic solvents such as ketones and hydrocarbons. Because they are barely permeable to gas, their sealed microchannels and microchambers are unsuitable for long-term cell study. Additionally, diaphragm valves are difficult to realize in these materials because of their rigidity.

Different from elastomers and thermosets, thermoplastics are normally purchased as solid and fabricated by thermomolding.[21] Thermomolding can produce thousands of replicas at high rate and low cost, but it requires templates in metal or silicon for using at high temperatures (to allow ample plastic flow); it is excellent for commercial production but not economical for prototypic use. Rapid prototyping using transfer molding, developed by Whitesides and Xia, uses PDMS as replication intermediate and enables the transfer of micropatterns to thermoplastics from easy-to-prepare photoresists.[25] This technique is limited to thermoplastics with T_g's below 150 °C because PDMS releases gas during molding at higher temperatures. Recently, by adjusting the curing formula and modified procedure, we have raised the maximum working temperature of PDMS for transfer molding to 350 °C, which is enough for almost all existing thermoplastics (Figure 3C).[45,46]

Not as convenient as PDMS, thermoplastics cannot form conformal contact with other surfaces. Typical strategies for sealing their channels include thermobonding and glue-assisted bonding.[47,48] The thermobonding of thermoplastics generally requires much milder conditions than those used for glass, that is, lower temperature and pressure without cleanroom environments.

Depending on their applications, the surface of thermoplastics can be modified by dynamic coating or surface grafting.[47] Covalent modified surfaces are generally more stable for thermoplastics than PDMS. For example, after treatment with oxygen plasma, their surfaces can retain hydrophilicity for up to a few years. Also, they can be easily integrated with electrodes for flexible circuits; one related application is digital microfluidics that can manipulate droplets by electrowetting.[49]

Two particular perfluorinated polymers, perfluoroalkoxy (Teflon PFA) and fluorinated ethylenepropylene (Teflon FEP), are thermoprocessable and can be used for microfluidic structures. All Teflons are extremely inert to chemicals and solvents, and ultimately nonsticky and antifouling. Importantly, they are optically transparent, soft enough to make diaphragm valves, and moderately permeable to gases. Although their melting temperatures are high (over 280 °C), with the high-temperature thermomolding technique mentioned above,[45] we can generate delicate microstructures with nanometer resolution in them and

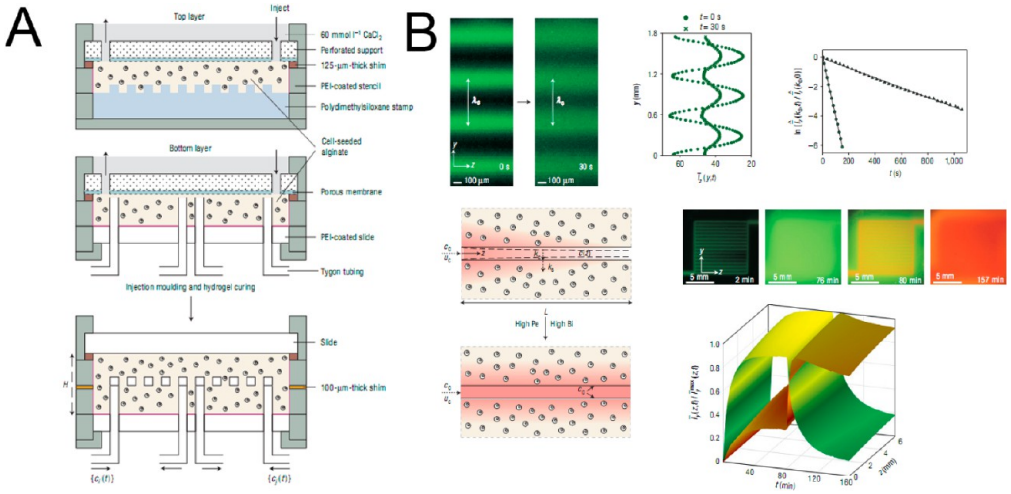

FIGURE 4. (A) Microfluidic device fabricated in alginate gel with embedded cells for culture. (B) Diffusion of molecules through channel wall into alginate gel. Reprinted with permission from ref 52. Copyright 2007 Nature Publishing Group.

thermally bond them to form various microfluidic devices.[46] The resulting whole-Teflon chips show excellent compatibility with organic solvents, outstanding antifouling properties, and amenability for cell culture (Figure 3D).

3. Hydrogels

With its explosive advancement, microfluidics has been increasingly involved in biological/medical research and biomimicking.[9] Hydrogels, resembling the extracellular matrix, have been widely used to embed cells for various applications; microchannels can be built in the hydrogels for delivery of solutions, cells, and other substances.[9,50] Hydrogels are 3D networks of hydrophilic polymer chains that span in aqueous medium, of which over 99% content can be water. They are highly porous with controllable pore sizes, allowing small molecules or even bioparticles to diffuse through. The combination of aqueous nature and high permeability makes hydrogels perfect for encapsulating cells for 3D culture.[9] However, the diffusion of nutrition and oxygen through bulk gel is not yet adequate to support thick layer cell culture; the cells may behave differently along the gradient, and typically, necrosis starts to occur at the depth of several hundred micrometers.[51] The introduction of microfluidic channels into the bulk gel matrix could realize rapid mass transfer through the bulk, offering similar function as the natural bifurcating vasculatures, thereby allowing bulk 3D culture of cells (Figure 4).[52]

For cell-culture-based experiments, another important factor is the compatibility between the substrate and the cells. Hydrogels are generally biocompatible, even though they show different affinity to animal cells.[53] Animal-derived hydrogels, for example, Matrigel and collagen, contain factors that promote cell adhesion and proliferation. In contrast, plant-derived hydrogels, for example, alginate and agarose, as well as synthesized hydrogels, for example, PEG and polyacrylamide, lack cell adhesion sites; however, adhesion sites could be grafted back in a controlled manner.

Owing to low density at the macromolecule scale (and low strength), hydrogels support only lower resolution (micrometer scale) in microfabrication than other polymers (nanometer scale). In addition, hydrogels with cells encapsulated may not be compatible with some microfabrication processes. The reported strategies[54] fall into two groups. One is the direct writing method, including LDW and gelation of gel solution from a moving nozzle, which can generate arbitrary 3D structures with low speed. The other involves two steps: generation of channels followed by channel sealing. Most hydrogels are gelled at mild conditions in aqueous solutions; thus, they can be molded from masters made of almost any material insoluble in water. In contrast to the ease in molding, the bonding is challenging. Normally, hydrogels generally do not stick with simple contact. Reported bonding strategies include (1) melting a thin layer of the bonding surface by heating or chemicals right before attaching and (2) utilizing a second linking agent at the interface.

The applications of hydrogel devices are mostly cell-related. In contrast to PDMS devices, they are more commonly used to study tissue-level cell culture, for example, 3D cell culture for tissue-engineering research.[9,54,55]

4. Paper

Before the introduction of paper-based devices, most microfluidic devices were prepared with sealed channels. However,

channels do not have to be sealed; a paper-based device is a good example (Figure 5A).[56] Paper is a highly porous matrix made of cellulose, excellent in wicking liquids. When certain areas of a paper are modified hydrophobically, aqueous solution applied to the paper will be precisely guided through the hydrophilic region by the capillary effect. Paper-based microfluidic devices are promising in portable and low-cost analysis, especially for bioassay-based personalized medical care.[56,57]

The fabrication of paper-based microfluidic devices is simple. In general, any method that generates hydrophobic patterns on paper is feasible. The reported methods[58] can be divided into two groups. Lithographic methods apply polymer solution to a paper and subsequently remove the formed coating from certain regions where channels are defined. These methods are relatively high-resolution but expensive, and the properties of the channel area once covered by polymer solution may have already been altered. In contrast, the printing (cutting) methods, requiring simpler equipment, directly generate hydrophobic barriers without pre-exposure of the channel area to reagents.

On the contrary, the applicable detection methods are relatively limited, owing to the presence of fabric matrix in the channel area. Reported detection strategies include colorimetry, luminescence, and electrochemical detection.[58] Among them, colorimetry is the most commonly used, and can be the primary strategy for commercial applications because of its minimal requirement of equipment and its convenience to realize telemedicine by capturing an image of the detection zones.[57]

The utilization of paper as chip material leads to several advantages: (1) the microchannel acts as passive pump dispenser without the need of power or external components; (2) the channels have a large surface-to-volume ratio which benefits surface-related applications, and can be used to store reagents by simply drying the soaked area; (3) paper is one of the cheapest materials for microfluidics, and fabrication by printing is convenient and low-cost; (4) paper can be easily stacked to form multilayer microfluidic channels (Figure 5B) or to realize 3D cell culture;[60] and (5) paper can filter out particles in the sample, for example, remove blood cells from blood.

However, the challenges are just as obvious. (1) The sensitivity of detection is often unsatisfactory, as the fabric matrix of the channel can block the internal signal and dilute the sample during transportation. (2) Liquids with low-surface tension may not be well confined in the channel defined by hydrophobicity. (3) Few typical microfluidic applications (e.g., CE, droplets and laminar flow) have been demonstrated on paper chips. (4) High-density integration is

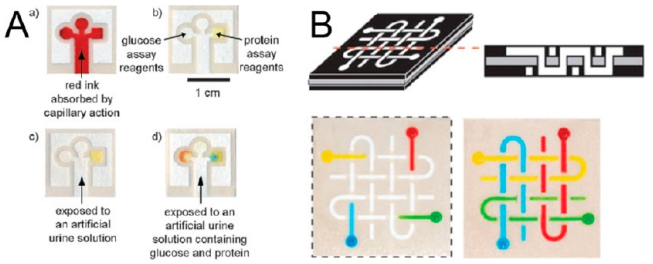

FIGURE 5. Paper based microfluidic chips. (A) Bioassay on a paper-chip. (B) Multilayer channel fabrication. Panel (A) reprinted with permission from ref 56. Copyright 2007 John Wiley and Sons. Panel (B) reproduced from ref 59. Copyright 2008 National Academy of Sciences.

hard to realize; the reported minimum channel width is around 200 μm, while 20 μm wide channels are common for other materials. (5) There is a lack of convenient strategy to integrate small-sized valves. (6) The evaporation of liquid from open channels also poses a problem.

5. Hybrid and Composite Materials

The materials mentioned above can be combined into one hybrid chip to exploit their advantages.[7] Instead of trying to list the various combinations, we summarize the concepts for determining the combinations based on the desired functions. In general, the secondary material should realize new function without largely compromising the desired property from the primary material.

(1) Sandwiching soft films between hard chips to form diaphragm valves (Figure 6A). The channels need to withstand the pressure for operating the valves (over tens of kPa). The most commonly used combination is glass−PDMS, as etched channels in glass are naturally rounded,[17] the ideal profile for the diaphragm valve.

(2) Incorporating channels with substrates patterned with metal electrodes (Figure 6A). Glass is often used to integrate metal electrodes into polymer-based devices.[61] If optical detection is needed, indium tin oxide (ITO) coated glass is an excellent candidate as it is easy to pattern by lithography to form transparent electrodes.[62]

(3) Combining different materials to adjust the permeability of channel walls at certain regions. Here a "permeable material", mostly porous, is employed as part of the channel wall to act as a barrier to bulk flow but to allow mass transfer by diffusion. This setup has been used to assist on-chip extraction and cell culture.[29] This strategy was extended to generating concentration gradients in static solution. By applying a concentration difference of solutions at the two sides of a hydrogel, a gradient can form therein.

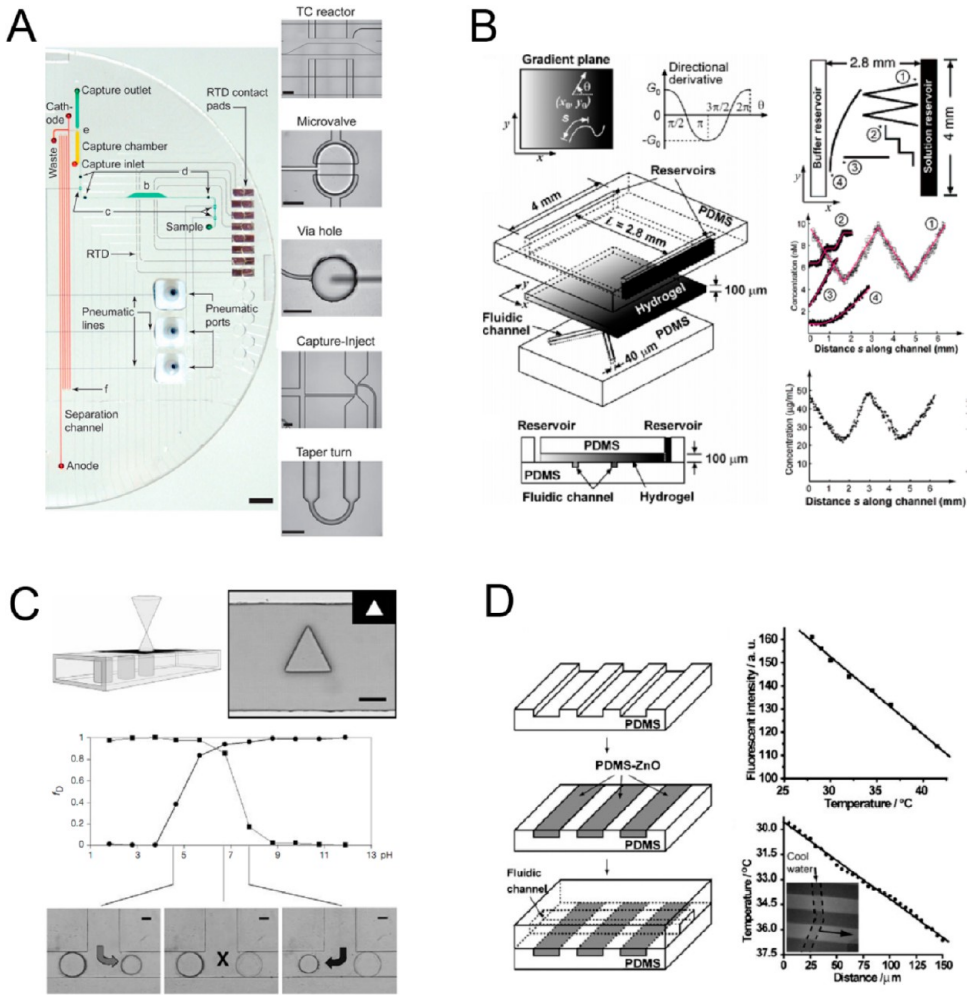

FIGURE 6. (A) Glass−PDMS hybrid chip with integrated valves and electrodes. (B) PDMS−hydrogel hybrid chip for gradient generation. (C) In-situ photocured hydrogel structure as pH-sensitive valves for automatic flow manipulation. (D) PDMS-ZnO composite as in-situ temperature sensor on a PDMS chip. Panel (A) reproduced from ref 7. Copyright 2006 National Academy of Sciences. Panel (B) reprinted with permission from ref 63. Copyright 2006 American Chemical Society. Panel (C) reprinted with permission from ref 69. Copyright 2000 Nature Publishing Group. Panel (D) reproduced from ref 67. Copyright 2009 John Wiley and Sons.

TABLE 2. Applications of Microfluidic Systems Made of Different Materials

applications	silicon/glass	elastomers	thermoset	thermoplastics	hydrogel	paper
CE	excellent	moderate	good	good	N/A	N/A
electrochemical detection	good	limited	moderate	moderate	no	moderate
organic synthesis	excellent	poor	good	moderate to good	N/A	N/A
droplets formation[a]	excellent	moderate	good	good	N/A	N/A
PCR	excellent	good	good	good	N/A	N/A
protein crystallization	poor	good	poor	moderate	N/A	N/A
bioculture	moderate	good	moderate	moderate	excellent, 3D	good, 3D
cost of production	high	medium	high	low	medium to high	low
reusability	yes	no	yes	yes	no	no
disposable device use	expensive	good	expensive	good	hard to store	good

[a]In the cases of droplet microfluidics, biological or chemical reactions are confined to individual droplets, and the surface properties of the device material only affect the generation of the droplets.

The gradient can be transferred into free solutions in microchannels attached to the hydrogel (Figure 6B).[63]

(4) Implanting photocurable material to achieve in situ fabricated structures.[64] This strategy could help to generate complicated structures and motion components in a microchannel. Depending on the properties of the materials, the trigger signal could be chemical, thermal, electrical, or optical (Figure 6C).[69]

Besides, the materials can also be doped with additives to provide demanded functions.[65] Recently, nanomaterial-doped composites have attracted increasing attention in microfluidics.[66] Polymers cured from liquid are convenient to dope therefore promising for this application (Figure 6D).[67,68]

Conclusions and Outlook

The evolution of chip materials reflects the two major trends of the microfluidic technology: powerful microscale research platforms and low-cost, portable analyses. For laboratory research, choosing materials generally needs to compromise the ease in prototyping and the performance of device, while in commercialization the major concerns are the cost of production and the ease and reliability in use. Such difference leads to varied preference in materials for device fabrication. Current trends seem to be that glass/silicon and PDMS are commonly used in research laboratories while plastics and paper are more promising for commercial devices. Each material has its pros and cons. Glass, silicon, and Teflon represent the most inert materials to chemicals and solvents; PDMS is easy to prototype and to fabricate complicated fluid circuits with various integrated components; normal thermoplastics are excellent for commercial mass production of standard microfluidic devices; hydrogels are more suitable for biological applications; and paper is highly promising for commercial disposable bioassays (Table 2). Finally, all the materials can be modified or combined to fabricate more powerful devices for specific aims.

K.R. acknowledges the constructive discussion with Dr. Xuan Mu at Institute of Basic Medical Sciences, Chinese Academy of Medical Sciences. We acknowledge support from Hong Kong RGC (#605210 and #N_HKUST617/09).

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FOOTNOTES

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The authors declare no competing financial interest.

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