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REVIEW

Toward the commercialization of optofluidics

Chaolong Song[1] · Nam-Trung Nguyen[2] · Say Hwa Tan[2]

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Abstract Optofluidics is a marriage between the field of optics and microfluidics. This field aims at providing practical solutions with the integration of optical tools into lab-on-chip systems. Often, this results in opportunities for commercialization due to the advancement offered after the integration. Although numerous novel functions and properties have been demonstrated with the combination of optics and microfluidics, the market has witnessed only few transferals of optofluidic technologies from academic laboratories. This stemmed from a lack of a "killer applications" despite several decades of development. Therefore, it is necessary to have a retrospective review on this topic, particularly on the basic optofluidic components, to analyze what might be the hurdles to stop the market uptake of optofluidic devices. Specifically, this review paper is focused on discussion of optofluidic components in terms of fabrication standardization, device and operational cost and practicability for end users. It is believed that these factors play important roles in the market uptake of a novel technology. We then provide perspectives on how to align the development of optofluidics with the requirements imposed by the industry.

Keywords Optofluidics · Microfluidics · Lab-on-chip · Commercialization

1 Introduction

The field of microfluidics has been rising exponentially since the invention of ink jet by IBM (Bassous et al. 1977; Petersen and Petersen 1979). Microfluidics allows precise manipulation and processing of a small amount of fluid which is extremely desirable for applications in biomedical research and diagnostic (Gravesen et al. 1993; Sackmann et al. 2014; Whitesides 2006). With decades of development, a number of laboratory processes such as sample preparation, sorting, detection, analysis and treatment have been implemented on a single miniaturized system. This is often referred to as a lab-on-chip system or simply micro total analysis system (MicroTAS). However, majority of these proof-of-concept devices often remain in academic laboratories, and their progression to commercial products is still very limited (Blow 2009). The series of papers by Becker initiated the debate on the challenges and barriers pertaining to the slow market uptake of lab-on-chip technologies (Becker 2009a, b, c, d, 2010a, b, c). Consensus among the community perceived that two factors lacking sufficient attentions now need to be focused on: integration and standardization (Mohammed et al. 2015; Volpatti and Yetisen 2014).

Although a large number of microfluidic devices have been reported, most are individual functional components. The seamless integration of an entire assay procedure has only been treated as an afterthought (Chin et al. 2012). In particular, majority of the demonstrated devices still need external bulky equipment to perform actions such as fluid delivery, electrical power supplying or signal detection. This leads to an ironic argument that the device is only a chip in the lab, but not a lab-on-chip (Mohammed et al. 2015). Recently, the advent of optofluidics, which is a marriage between microfluidics and optics (Psaltis et al. 2006; Monat et al. 2007), aims to miniaturize the bulky optics, to

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✉ Chaolong Song
songcl@cug.edu.cn

[1] School of Mechanical Engineering and Electronic Information, China University of Geosciences (Wuhan), Wuhan, China

[2] Queensland Micro- and Nanotechnology Centre, Griffith University, 170 Kessels Road, Brisbane, QLD 4111, Australia

integrate the pertaining functions and to enable automated procedures, which ideally allow device operation without any microfluidics and optics expertise. A number of excellent review papers on the advancements of optofluidics exist in the literature. These reviews focused on specific applications, such as optofluidic sensors (Kim et al. 2017; Fan et al. 2008), spectrometers (Mak et al. 2013), cytometers (Zhang et al. 2016), and tweezers (Huang et al. 2014; Yang et al. 2016), or specific components, such as waveguides (Testa et al. 2016; Schmidt and Hawkins 2008) and lenses (Mishra et al. 2016; Nguyen 2010). Despite the systematic elaborations on the novelty and application aspects of optofluidics, none of reviews analyze the individual components or functions in terms of integration compatibility, practicability for end users outside laboratory environment, fabrication and operational cost, etc. which are factors of critical importance toward the commercialization of optofluidic technologies.

Figure 1 shows that the number of filed patents has overtaken the research articles number since the very beginning in the domain of microfluidics. In contrast, in the domain of optofluidics, the number of patents still falls behind the number of research articles after almost 20 years of development. One motivation of developing optofluidics lies in enhancing the integration level of microfluidic devices and thus pushing forward the commercialization of microfluidics. The technology can further miniaturize an entire lab-on-chip system. Configuring the optics using fluids instead of solids can significantly lower the device cost. Achieving self-tunability enabled by reconfigurable fluids is a convenient solution to finely align the optics inside a microdevice. Although the significance of commercializing optofluidics is obvious, the data in Fig. 2 imply that current in-lab optofluidic devices are still immature for market uptake. Therefore, at this point of time, we believe that it is necessary to have a retrospective view on the development of optofluidics and then to identify the challenges hindering the commercialization of optofluidics. In particular, the discussion will be focused on the fundamental optofluidic components which are basic elements of any optofluidic devices. We then provide a perspective on how these components can meet the requirements imposed by market uptake.

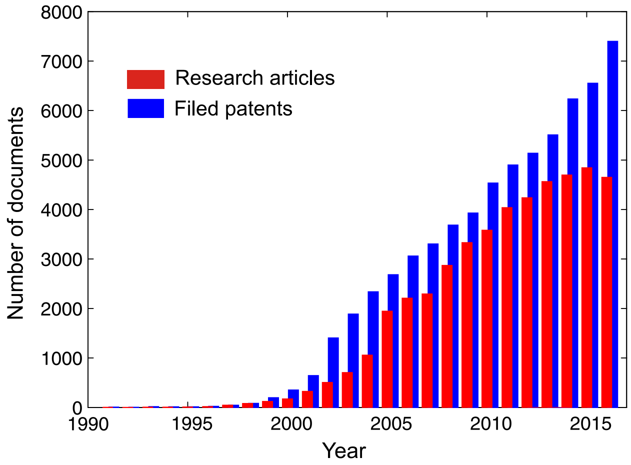


Fig. 1 The numbers of published research articles and filed patents in chronological order in the domain of microfluidics (data retrieved from Scopus May 26th, 2017)

Besides integration, standardization of materials and fabrication protocols is another important factor for the commercialization of technologies. This affects the integration compatibility and inevitably determines the cost structure for mass production and thus sets the threshold for market entrance. Hence, this review categorizes optofluidics in terms of fabrication materials, as solid-based, fluid-based and polymer-based optofluidic components. Another rationale for such a categorization is that each group can operate with a similar working mechanism to a certain extent. The fabrication protocols will be described and followed by the discussion on the device cost and its practicability. In contrast to the cost which can be directly evaluated as straightforward numbers, the practicability is tangible and thus difficult to assess. This review will qualitatively provide perspectives on the practicability in terms of three factors: (1) resistance to environmental disturbance, (2) tunability and (3) ease to operate for the end user. We emphasize here that the reason to take into account the tunability as a factor is that the miniaturized and integrated optical components do not have the luxury of position adjustment for optical alignment inside a microchip. Thus, the self-tunability is of critical importance to achieve precise light manipulation for practical use.

2 Solid-based optofluidics

The term "solid-based optofluidics" is referred to as those optofluidic components consisting of specific solid boundary and hollow chamber to be filled with various functional fluids. Their functions rely on the geometry and structure of interface between solid and fluid as well as the refractive index (RI) difference. And their mechanism to tune the optical properties can be achieved mainly by replacing the engaging fluids. This section discusses the solid-based optofluidic components by categorizing them according to their functionality. Under each category, we discuss how the components are fabricated and operated. Their practicability can subsequently be analyzed and summarized in Table 1.

2.1 Solid-based waveguide

Waveguide plays an important role in an optical system, equivalent to the channel or tube of the fluidic counterpart (Schmidt and Hawkins 2008). In contrast to traditional waveguides, optofluidic waveguides take advantage of hollow channel surrounded by a solid material with either higher RI or anti-reflection property. A simple way to realize an optical waveguide is using total internal reflection (TIR). TIR occurs when the light traveling from a material with higher RI (n_c) into a material with lower RI (n_{cl}) has an incidence angle larger than the critical angle. Filling a capillary tube with liquid is a simple method to implement liquid-core waveguide (Schelle et al. 1999). However, the implementation of waveguide in an optofluidic system is practically difficult since most of the solid materials used for MEMS and microfluidic fabrication possess a relatively higher RI (1.4–3.5) than the aqueous solutions (around 1.33) or other liquids (Testa et al. 2015). Datta et al. (2003) developed liquid-core waveguide on a silicon wafer by coating Teflon layer with RI around 1.30 on wet-etched channel wall. Due to low adhesion of Teflon AF on glass or silicon surface, additional coating of fluorocarbon film by PECVD is necessary to improve the adhesion.

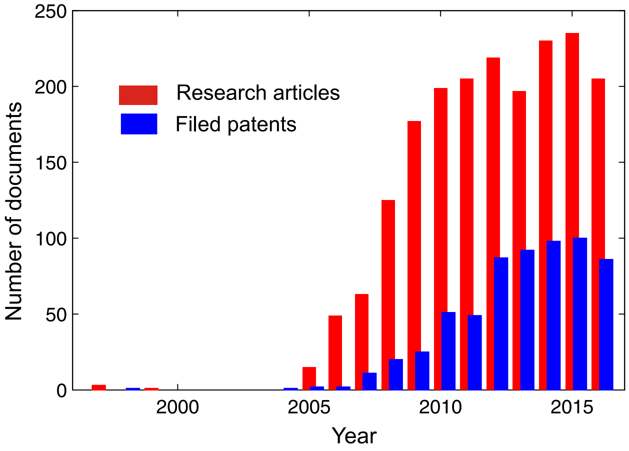
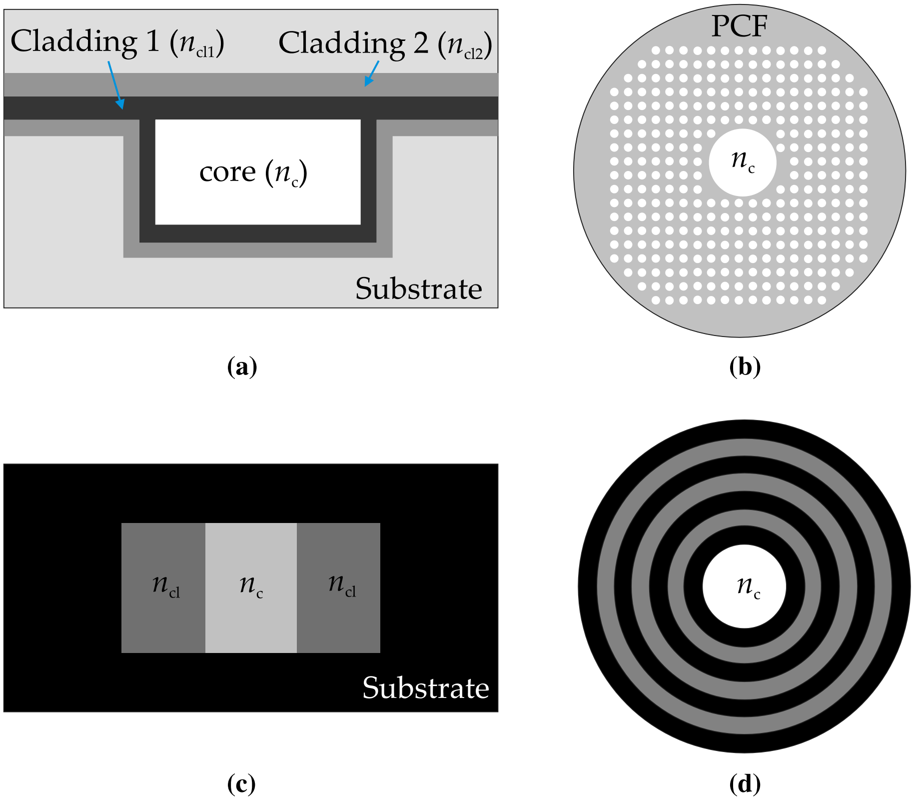


Fig. 2 The numbers of published research articles and filed patents in chronological order in the domain of optofluidics (data retrieved from Scopus on May 26th, 2017)

The concept and implementation of optically anti-reflective film has been well developed and commonly used in our daily life. Researchers applied such concept in the fabrication of optofluidic waveguide. For instance, liquid-core anti-resonant reflecting optical waveguides (ARROWs) can effectively confine the propagation of light within the liquid-core channel (Yin et al. 2004; Bernini et al. 2002). The cross section of the ARROW waveguide is illustrated in Fig. 3a. The claddings with multiple layers were designed in a way that they behave like a highly reflective Fabry–Perot cavity at transverse direction for a specific wavelength, so as to guide the light along the longitudinal direction. In such a configuration, alternating silicon nitride and oxide layers can be deposited on a silicon substrate using PECVD. The more periods of nitride and oxide layers, in principle, the less is the transverse loss, but also the more complex is the

Fig. 3 A schematic illustration of optofluidic waveguides (cross-sectional view): **a** ARROW waveguide, **b** photonic crystal fiber with hollow core, **c** liquid-core liquid-cladding (L^2) waveguide, **d** hollow-core Bragg fiber



fabrication. The compromise between the device performance and fabrication complexity needs to be balanced by the chip designers.

Besides ARROW, photonic crystal (Park et al. 2014; Tian et al. 2015; Wu et al. 2014; Ertman et al. 2017) and Bragg fibers (Passaro et al. 2008) with hollow cores are another two types of optofluidic waveguides, which take advantage of the periodic structures to prohibit the transmission of light at a certain frequency band gap. This band can be determined by the periodicity of the structure. However, these configurations cannot be easily integrated in planar structures for lab-on-chip applications.

2.2 Solid-based lens

A simple way to realize an integrated micro-lens is to develop it at the same time with the entire microfluidic system using the soft-lithography technique (Xia and Whitesides 1998). Camou et al. (2003) developed such an in-plane micro-lens in the same layer of the microfluidic channel (Fig. 4a). In this system, light can be delivered by an optical fiber inserted into a pre-defined channel perpendicularly aligned with the micro-channel. At the tip of this pre-defined channel, the PDMS was shaped to have a convex curvature. Because of the difference in RI between PDMS and air, light can be focused at the expected region in the micro-channel. Tuning the focus can be achieved either by designing lens with different curvatures or manually adjusting the position of the fiber tip. Later, Song et al. (2009a) applied such concept to the manipulation of a light beam by designing integrated telescopic compound lenses in a microfluidic system. Rosenauer and Vellekoop (2010) took advantage of such integrated lens for microfluidic cytometry application. Another solution to easily integrate a solid-based micro-lens can be by shaping the fiber tip using laser micro-machining technologies (Gissibl et al. 2016). Although the concept of such in-plane solid-based micro-lens offers good convenience for the system design and integration, it has its limitation with the tunability of optical properties due to the solid-based lens interface. Recently, Shi et al. (2016) reported a tunable Fresnel lens by pumping fluid into micro-channels with Fresnel plate structure, and its tunability can be achieved by dynamically adjusting RI of the fluid via a *Y*-shape mixer.

2.3 Other solid-based optofluidic components

Optical prism, as an important tool for spectrum analysis, can also find its applications in microfluidic systems. Llobera et al. developed a hollow prism chamber with flow inlet and outlet using soft lithography (Fig. 4b), and the chamber can be filled with the solution under investigation (Llobera et al. 2004, 2005). Any change in the solution concentration, or correspondingly the RI, would lead to the change in deviation angle of the light beam. On the one hand, this device can be used to manipulate the light propagation direction by replacing the liquid in the prism chamber. On the other hand, this liquid prism can also be used to measure the subtle change in RI of the liquid under investigation. Using it as a sensor, the authors achieved a detection limit of the solution concentration down to µM range.

As another example of the solid-based optofluidic components, Groisman et al. (2008) reportedly demonstrated a tunable optical switch using a brazed diffraction grating. The device was fabricated with a two-layer structure. The flow layer is fabricated using soft-lithography technique. The control layer with the grating was developed by firstly dipping a solid grating stamp into uncured PDMS and then thermally cured to solidify the grating structure of PDMS. The solid grating stamp is subsequently peeled off from

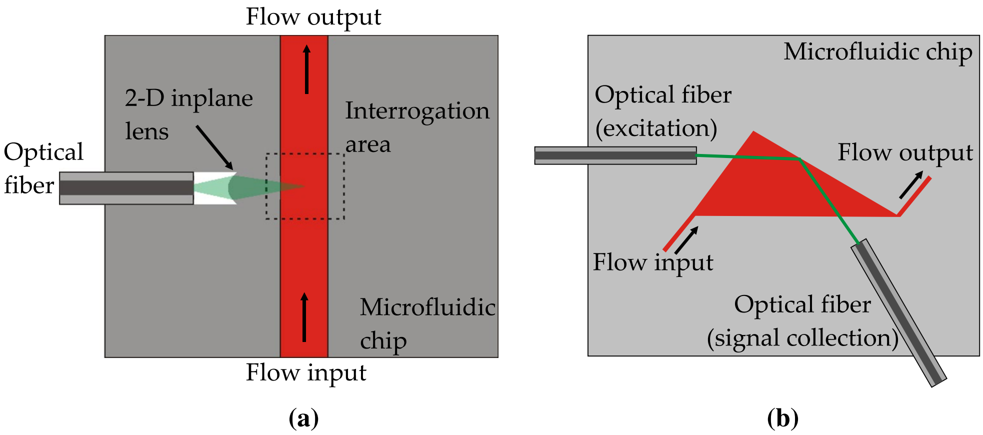


Fig. 4 Schematics of microfluidic systems with integrated optical components (*top view*): **a** A PDMS 2-D in-plane lens to focus light delivered by optical fiber into the microfluidic channel; **b** a hollow prism integrated in a PDMS-based microfluidic system for RI measurement

the PDMS layer before bonding the flow layer with the control layer. The mismatch of RI between PDMS and the filling liquid determines the diffraction angle of incident light, when the condition of diffraction maximum is met. The grating can achieve its tunability by re-filling the chamber with different liquids. Similar to the abovementioned prism, this type of grating can work either as a tunable actuator for manipulating the light beam or as a sensor for measuring the spectral response of the liquid analytes (Sarkar et al. 2016).

2.4 Summary on solid-based optofluidic components

The configurations of these solid-based optofluidic components share a common point. The functional solid interfaces are in contact with the fluid, and the optical properties can be tuned by replacing the contacting fluid. The advantages of such devices are: (1) the optofluidic components can be imprinted together with other modules in the same layer of the microfluidic platforms; (2) the tunability can be achieved by simply replacing the functional fluid; (3) the optofluidic components can function without consuming liquids at steady states; (4) the components possess relatively good stability and robustness to resist external vibrational noises due to the high stiffness of solid structures; (5) the process of simply filling and replacing fluids is easy to be implemented by the end users. However, the process of “replacing liquid” always takes time and slows down the response time. And after “replacing,” the residual fluid might mix with the new fluids, which affect the precision or accuracy of the device. Most importantly, the quality of the solid interface is dependent on the fabrication process. Producing an optically smooth interface can dramatically increase the fabrication cost of the device.

3 Fluid-based optofluidics

The term “fluid-based optofluidics” is referred to as those optofluidic components configured by fluid/fluid interface or refractive index gradient distributed in fluids. Their functions rely on the geometry and structure of the interface between two fluids or the refractive index (RI) distribution. The mechanism of tuning the optical properties can be achieved mainly by controlling the hydrodynamics or interfacial tensions. This section discusses the fluid-based optofluidic components by categorizing them according to their functionality. Under each category, we discuss how the components are fabricated and operated, based on which their practicability can be analyzed and summarized in Table 2.

3.1 Liquid-core/liquid-cladding (L^2) waveguide

The key challenge for a liquid-core/solid-cladding waveguide is that most liquids have RIs lower than those of the solid materials used for microfluidic fabrication. A liquid-core/solid-cladding structure cannot meet the TIR condition to confine the light within the liquid core. To overcome this challenge, the concept of liquid-core/liquid-cladding waveguide was proposed by Wolfe et al. (2004) (Fig. 3c). The device can be fabricated with standard soft-lithography technique. The waveguide employs three continuously pumping flows which merge into a straight-line channel. The central flow (core) with high RI is sandwiched by two sheath flows (claddings) with lower RI. Since the flow rates of the core and the claddings are independently controlled, the cross-sectional profile of the transmitted light can be manipulated by adjusting the widths of the core and the claddings. Moreover, the authors also demonstrated the control of the propagation direction of light by tuning the flow rate ratio between the two cladding flows. The tunability of this waveguide offers an excellent flexibility for on-chip light transportation, coupling and switching. The theory for the hydrodynamic spreading of such core/cladding microfluidic structure was reported by Wu and Nguyen (2005). Instead of controlling the flow rate, Tang et al. (2006) reported a tunable waveguide using temperature-based actuation. In their configuration, the RI of the fluid can be adjusted by pumping fluid with different temperatures. The transverse profile of the transmitted light can be tuned according to the change in RI distribution. The main drawback of this device is the decay of temperature gradient along the flow direction due to dissipation of heat, which leads to an unevenly distributed refractive index along the optical axis. Also, the temperature fluctuation of surrounding environment might also affect the performance of the device.

3.2 Fluid-based optofluidic lens

Solid-based optofluidic lenses have their inherent limitation in tuning the focus due to the fixed solid interface. Another drawback is that any irregularities on the solid interface would randomly scatter the light and thus affect the performance of the lens. Targeting those challenges, researchers have devoted a lot of efforts on developing the fluid-based optofluidic lenses which have naturally smooth lens interface, providing a more flexibly tunable curvature of the interface. The tuning mechanisms of these lenses can be generally categorized into two groups: (1) interfacial tension-based tuning and (2) hydrodynamic tuning.

3.2.1 Interfacial tension-based lenses

The balance between the applied pressure and the interfacial tension can be utilized to maintain and tune the curvature of a liquid lens interface. A spherical liquid-based microlens with pre-defined focal length can be achieved by filling uncured PDMS into microfluidic channels (Lien et al. 2003; Zhang et al. 2015). The interface curvature can be controlled by the surface interaction between the liquid and the channel wall. Silane was used to treat the hydrophobic PDMS channel and making it more hydrophilic for forming the lens interface. The different durations of the silane treatment may lead to the different curvatures of the PDMS lens interface. Thus, a programmable focal length can be obtained. One limitation of this method is the difficulty to pump the liquid PDMS into the micro-channel. Another drawback is that the liquid interface cannot be dynamically and continuously tuned since silane treatment is needed for each specific curvature of the lens interface.

To solve the above problems, several configurations have been proposed. Dong et al. developed a tunable microlens in a microfluidic platform fabricated using photopolymerization technique (Beebe et al. 2000). In particular, they manually pumped a liquid droplet into a micro-channel and utilized the pressure difference between the upper and lower interfaces to manipulate the interface curvature (Fig. 5a) (Dong and Jiang 2007). One challenge for the end users might be the critical requirement of experience-based manual operation control of the size of the droplet lens and to transport it to the designated position. Shi et al. (2010) developed a smooth lens interface between a fluid flow and air maintained by capillary forces. This concept does not require intensive manual manipulation but is at the expense of consuming functioning fluid at working state (Fig. 5b). To overcome these challenges, Mao et al. (2010) proposed to manipulate the liquid meniscus at a flared opening of a micro-channel. $CaCl_2$ solution was injected into the microfluidic channel as the working fluid. As fluid advances through the flange, the contact angle θ remains constant, while the curvature of the interface can be changed by adjusting the size of the protruding fluid (Fig. 5c). The advantage of this device lies in the convenient operation to form the required lens and no consumption of fluid at working state is needed. For further commercialization, a delicate pressure controller is needed to precisely and automatically advance the fluid in the micro-channel. The relationship between the applied pressure and the size of protruding fluid needs to be explored and calibrated. Another drawback of the above-mentioned lenses with pneumatic control of the fluid/air interface is the transient nature of the interface shape due to the porosity of PDMS as the structural material. Specifically, the lens interface may deviate from the designated shape for a given pressure after a period of time as the air escapes from the porous channel wall. Thus, novel structural materials need to be explored for the further translation of this technology for practical applications. Besides pneumatic control, stimuli-responsive hydrogels can be used to drive the re-shaping of liquid interface according to the variation of temperature or pH values (Dong et al. 2006). Electrowetting can also be used to adjust the interfacial force and thus the curvature of the liquid interface (Krupenkin et al. 2003; Krogmann et al. 2006). These working mechanisms require complex and delicate microstructures to induce the driving forces, which might pose challenges to scaling up for the mass production of the devices. Recently, Maxwell stress has been demonstrated to develop tunable aspherical lenses due to its effectiveness to balance the liquid interfacial tension on-demand (Mishra et al. 2014). However, the demonstrated devices can only manipulate light perpendicular to the device plane and thus might find difficulties in the applications of lab-on-chip systems. Microfluidic channels filled with liquid metal can effectively form electrodes and used to align the electric field parallel to the device plane (Ma et al. 2016; Eaker and Dickey 2016). Liquid–metal-based methods can be potential solutions for developing in-plane optofluidic components tuned by Maxwell stress.

3.2.2 Hydro dynamically tuned lenses

Hydrodynamic tuning of optofluidic lenses is a method that enables dynamically and continuously adjustable curvature of the lens interface. Mao et al. (2007) firstly proposed a hydrodynamically tunable optofluidic lens fabricated with standard soft lithography (Fig. 6a). The lens consists of two working fluids: water and $CaCl_2$ solution. The two-fluid flow was driven through a 90-degree curved micro-channel, and the $CaCl_2$ solution bows outward into water owing to the centrifugal force induced in the curve. By adjusting the flow rate ratio between these two fluids, different curvatures of the interface as well as different focal lengths can be obtained. Tang et al. (2008) developed an optofluidic lens with a liquid-core/liquid-cladding structure in a rectangular expansion chamber. A fluid with a higher refractive index works as the core stream. The one with lower refractive index serves as cladding stream. Manipulating the flow rate ratio between core and cladding streams can tune the curvature of the interface formed in the expansion chamber accordingly. Later, Song et al. (2009b, c, 2010b) found that the streamlines of the spreading flow in a circularly bounded chamber (Fig. 6b) present perfect arc shapes and can be mathematically described. As a result, the light path can be analytically predicted and taken into account at the early stage of the optical design. Combining the 90-degree curved micro-channel and a L^2-based structure,

Table 1 List of typical solid-based optofluidic components

Solid-based optofluidics	Working mechanism	Fabrication method	Structural material and cost (USD)	Functional fluid	Consuming fluid at working state	Remarks on practicability		
						Resistance to disturbance	Tunability	Ease to operate
Waveguide								
Teflon coated waveguide (Datta et al. 2003)	Total internal reflection	Wet etching, PECVD and Teflon coating	Teflon AF 2400, ~$110/g	DI water	No	Young's modulus of Teflon 11.8–14.3 MPa (Rae and Dattelbaum 2004)	Achieved by replacing fluids	Operate via pumping system, hands-on experience with microfluidics is not required
ARROW (Yin et al. 2004; Bernini et al. 2002)	Anti-reflection enabled by Fabry–Perot structure	Lithography and PECVD	SiO_2, Si_3N_4	DI water	No	Young's modulus of SiO_2 66.3 GPa Young's modulus of Si_3N_4 310 GPa	Achieved by replacing fluids	Operate via pumping system, hands-on experience with microfluidics is not required
Lens (Camou et al. 2003)	Curved shape of PDMS/air interface	Soft lithography	PDMS, ~$100/500 g	Air	No	Young's modulus of PDMS 8 kPa–1.72 MPa (Palchesko et al. 2012)	Focal length is fixed	No requirement for operation
Prism (Llobera et al. 2004, 2005)	Triangular shape of PDMS/fluid interface	Soft lithography	PDMS, ~$100/500 g	Water-based solution	No	Young's modulus of PDMS 8 kPa–1.72 MPa	Achieved by replacing fluids	Operate via pumping system, hands-on experience with microfluidics is not required
Grating (Groisman et al. 2008)	Blaze grating structure enable by PDMS/fluid interface	Soft lithography	PDMS, ~$100/500 g	Water-based solution	No	Young's modulus of PDMS 8 kPa–1.72 MPa	Achieved by replacing fluids	Operate via pumping system, hands-on experience with microfluidics is not required

Table 2 List of typical fluid-based optofluidic components

Fluid-based optofluidics	Working mechanism	Fabrication method	Structural material and cost (USD)	Functional fluid	Consuming fluid at working state	Remarks on practicability		
						Resistance to disturbance	Tunability	Ease to operate
Waveguide								
L^2 waveguide (Wolfe et al. 2004)	Total internal reflection	Soft lithography	PDMS, ~$100/500 g	DI water	Yes	Viscosity of water 0.89 cP	Tuned via control of flow rate	Operate via pumping system, hands-on experience with microfluidics is required
Refractive index gradient waveguide (Tang et al. 2006)	Refractive index gradient	Soft lithography	PDMS, ~$100/500 g	DI water	Yes	Viscosity of water 0.89 cP	Tuned via control of temperature of the pumping fluids	Operate via pumping system and temperature control, hands-on experience with microfluidics is required
Lens								
Interfacial tension tuned lens (Dong and Jiang 2007)	Deformation of droplet interface	Liquid-phase photopolymerization	Dimethacrylate, ~$40/100 mL	DI water	No	Surface tension of water 72.8 mN/m	Tuned via balance of air pressures	Manual manipulation of individual droplet in micro-channel is involved
Hydrodynamically tuned lens (Tang et al. 2008)	Hydrodynamically formed interface between fluid and fluid	Soft lithography	PDMS, ~$100/500 g	Cinnamaldehyde, ethylene glycol and ethanol	Yes	Viscosity of cinnamaldehyde 5.7 cP Viscosity of ethylene glycol and ethanol mixture 9.8 cP	Tuned via control of flow rate	Operate via pumping system, hands-on experience with microfluidics is required
Prism (Song et al. 2010a)	Triangular shape of fluid/fluid interface	Soft lithography	PDMS, ~$100/500 g	Benzyl alcohol and glycerol and water mixture	Yes	Viscosity of benzyl alcohol 5.0 cP Viscosity of glycerol and water mixture 9.0 cP	Tuned via control of flow rate	Operate via pumping system, hands-on experience with microfluidics is required

Rosenauer and Vellekoop (2009) constructed an optofluidic lens which can perform three-dimensional (3-D) focusing of light.

Optofluidic lenses based on hydrodynamic tuning offer a high level of automation, since the lens formation and tuning can be achieved by simply controlling the flow rate via external pumps. The shape of the lens can be well maintained through a long period of time as long as the flow rates of functional fluids are kept constant. However, from an economic point of view, continuous pumping of fluid without recycling and reuse unfortunately increases the operational cost of the devices.

3.3 Other fluid-based optofluidic components

3.3.1 Fluid-based optofluidic prism

Since most of the microfluidic structures are planar and flat, under such a scenario, the fluid dynamics can be simplified and described using the quasi-potential flow theory (Austin and Puchella 2009). According to the theory of potential flow, the shape of flow streamline is mostly determined by the geometries imposed by the boundaries. Hence, a proper design of the fluidic boundaries could shape and help to produce a desired interface of an optofluidic component. Inspired by this idea, Song et al. (2010a) designed a sector-shape microfluidic chamber to configure a L^2 tunable prism. In this configuration, the core and cladding flows merge and enter the sector-shape chamber, and the radial velocity of the flow field can be equalized by placing a row of pressure barriers at the outlet of the chamber (Fig. 7a). Due to the geometry of the chamber and the uniform radial velocity, the streamline (interface of the prism) can be straightened, thus producing a prism structure. The apex angle of the optofluidic prism can be easily tuned by adjusting the flow rate ratio between the core and cladding streams. Therefore, it can be used to maneuver the direction of a light beam on a chip and to analyze the light spectrum (Xiong et al. 2011). Compared to a solid-based optofluidic prism, this reconfigurable fluid-based prism can offer a faster response of light tuning by adjusting the flow rate ratio instead of replacing liquid in a hollow chamber. Because the tuning mechanism is based on the change in prism geometry, the tuning range of the fluidic prism can be larger than the solid-based one.

3.3.2 Fluid-based optofluidic grating

Unlike the solid-based optofluidic grating, the fluid-based gratings take advantages of the periodic structure of properly aligned droplets in micro-channel (Yu et al. 2010) or chamber (Hashimoto et al. 2006) (Fig. 7b). Instead of replacing the functional liquid to tune the grating, the pitch of the fluid-based grating can be adjusted by manipulating the size and separation distance of the droplet. The transmission light beam of the first order can swing at will with dynamically manipulating the droplet formation. In the field of droplet-based microfluidics, researchers have explored a variety of mechanisms for droplet manipulation (Xi et al. 2016; Chong et al. 2015; Murshed et al. 2009; Yit-Fatt et al. 2009; Say-Hwa et al. 2008) which can be used as the basis for a tunable grating.

3.3.3 Fluid-based optofluidic aperture

A simple method to integrate an optical aperture into a microfluidic system is to align two micro-channels with an interval between each other and fill the channel with black color liquid (Tang et al. 2008; Song et al. 2010b, 2011a). The gap allows light to pass through, whereas the black color liquid can absorb or reflect the light. However, the size of the aperture is fixed once the fabrication is completed. Song et al. (2011b) proposed to configure the aperture using liquid-core/liquid-cladding structure to develop a size-tunable aperture for lab-on-chip applications. Two cladding flows (black ink) sandwiching the core flow (transparent liquid) enter a rectangular chamber, and the L^2 flow spreads inside the chamber alike a portal allowing light to pass through in-between the two claddings. Adjusting the flow rate ratio between core and cladding flows tunes the size of the aperture and transmits the in-plane light with desired amount. To control the out-of-plane light, Yu et al. proposed a configuration, in which one chamber filled with opaque ink was superposed on an air-filled chamber, and a deformable diaphragm stayed between the two chambers (Hongbin et al. 2008). Deforming the diaphragm and pushing it to the top end of ink chamber squashes the ink at the central part of the chamber to the side to allow light to pass through. Besides this pneumatic actuation, several other mechanisms were also demonstrated to implement fluid-based tunable apertures, such as electro-wetting (Schuhladen et al. 2016), dielectric force (Tsai and Yeh 2010), magnetic force (Duduś et al. 2015) and capillary force (Muller et al. 2010).

3.4 Summary on fluid-based optofluidics

Traditional silicon-based micro-fabrication techniques can be used to create more complex or even three-dimensional photonic structures, which would bring more optical functionalities to the devices. However, the widely used fabrication method of fluid-based optofluidic devices has been soft lithography using PDMS as a structural material which is optically transparent to visible and near-infrared lights (Cai et al. 2008). One reason lies in the limitation posed by the intrinsic stiffness of silicon structures to conveniently make moving parts in the device such as fluidic valves. The required high temperature to bond silicon with glass also limits the manipulation of delicate surface chemistry

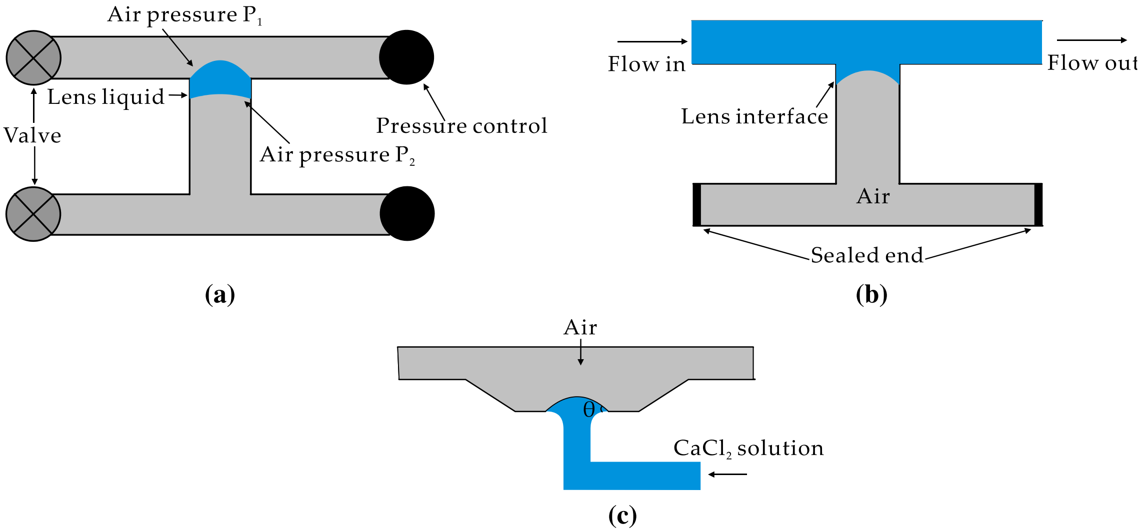
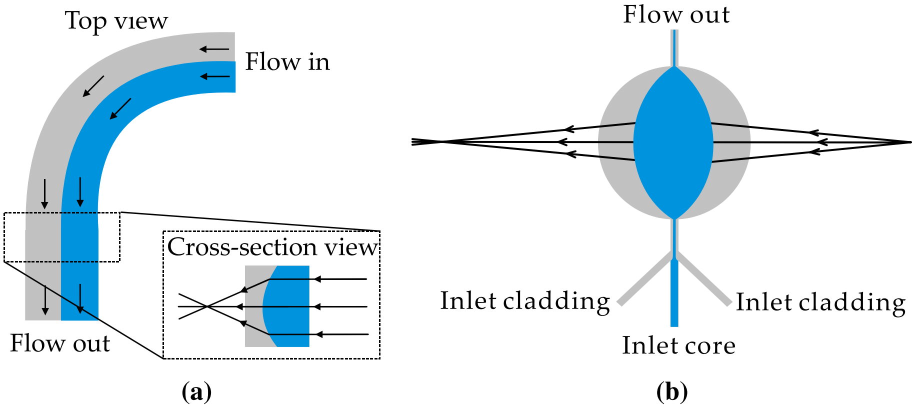


Fig. 5 Schematics of microfluidics-compatible liquid-based lenses (*top view*): **a** liquid lens tuned by controlling pressure difference; **b** liquid lens tuned by controlling the flow rate; **c** tunable micro-lens based on liquid meniscus

Fig. 6 Schematics of optofluidic lenses with hydrodynamic tuning: **a** optofluidic lens with a curved interface enabled by centrifugal effect; **b** optofluidic lens developed by the hydrodynamic spreading in a circular chamber



for biochemical applications. In contrast, polymers such as PDMS are more flexible for the development of fluidic structures and more biocompatible (Quake and Scherer 2000). Another reason for the intensive use of soft lithography and PDMS in academic laboratories might be the well-established fabrication procedures, good surface quality of the structures [important for light transmission (Song et al. 2010b)] and the small number of devices needed for experimental trials. However, this prevailing method is not preferred by the industry due to the higher cost of PDMS when compared to other cost-effective materials such as poly (methyl methacrylate) (PMMA) [another optically transparent material (Zidan and Abu-Elnader 2005)]. The use of PDMS also does not allow mass production of devices. In the perspective of commercialization and mass production, research efforts either need to be dedicated to explore scalable manufacturing methods of PDMS devices or diverted to investigating the feasibility of implementing the currently demonstrated optofluidic components or functions with more cost-effective structural materials.

Compared to solid-based optofluidics, fluid-based optofluidics presents more flexible tunability due to the easiness of deforming the fluid interface or manipulating the RI gradient in a flow field. The in situ control of the fluid allows dynamically and continuously tuning of optics, which enables a faster tuning response. Basically, the tuning response depends on the working mechanism of the device. For those devices actuated by continuous fluid flow, the tuning response depends on the flow rate and the length of tubing. The response time can be approximately estimated as the length of tubing divided by the flow velocity. The response time is on the order of few seconds considering the low Reynolds number in microfluidic channels. For devices actuated by immediate external driving forces, such as pneumatic pressure, Maxwell stress and magnetic force, the response time is a function of the magnitude of

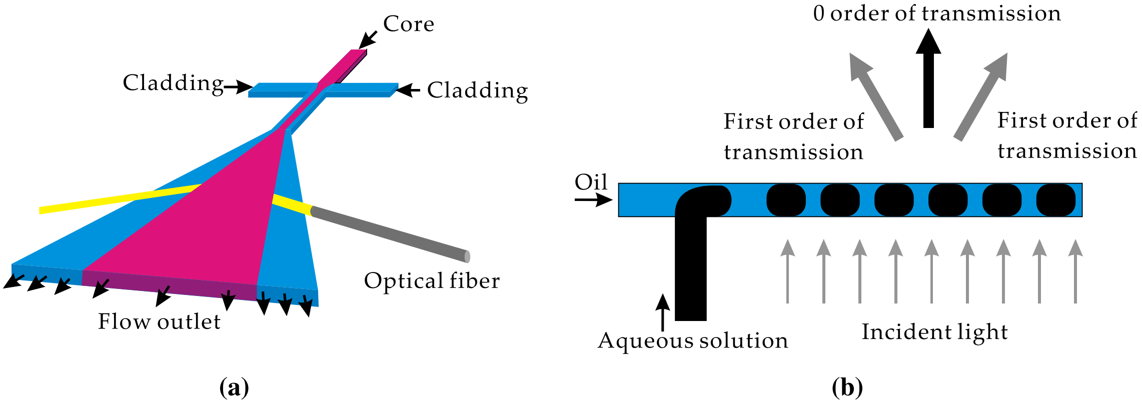


Fig. 7 Schematics of optofluidic components: **a** optofluidic prism with a L^2 configuration; **b** optofluidic grating structure generated by aligning a row of droplets in a micro-channel

the interacting force and the viscosity of the engaging fluid. Generally, the response time of the later can be much shorter than the former. The flexible tunability of fluid-based optofluidic components may come at the expense of reduced resistance to environmental disturbances, as any vibration-induced shear stress, which is very common especially in the context of field test, can enforce the fluid/fluid interface to deviate from the designated shape. And the deviation amount mostly depends on the viscosity of the fluid.

In terms of operation complexity for end users, the hydrodynamically tuned devices allow end users to switch on the optical functions by simply setting proper flow rates of the functional fluids from delivery systems. The operation of droplet lens formed in microfluidic networks might involve experience-based manual manipulation of the droplet position and delicate pressure control units to balance pressures for tuning optical properties as the change in interfacial force is in the order of 10^{-5} mN. However, the simplicity of hydrodynamically tuned devices comes at the expense of operational cost as the devices consume fluids during operation. Future research efforts can be devoted to the investigations of fluid recycling mechanism for the hydrodynamically tuned optofluidics. It is also worthy to explore novel methods to manipulate the fluid interface at the microscale for optofluidics, which actually has been intensively studied in the field of droplet-based microfluidics.

4 Polymer-based optofluidics

Although the fluid-based optofluidic components are more flexible in tuning their optics due to the adaptable deformation of the fluid, they are prone to undesired deformations as a result of environmental disturbance. Polymer-based optofluidic components can offer good tunability and at the same time possess resistance to the environmental disturbance to a certain extent. They are referred to as those with functional liquid sealed or embraced by an elastic polymer membrane, which is often PDMS at most of the time. The tunability can be achieved by deforming the elastic membrane and thus reshape the optical surface as well as the light beam profile.

So far, most applications of elastic diaphragms are with the development of tunable lenses (summarized in Table 3). Inspired by a human eye's crystalline lens, Ahn et al. demonstrated to use a deformable glass diaphragm with a thickness of 40 μm to enable a variable focal length of a single piece of lens (Ahn and Kim 1999). Silicone oil with a refractive index of 1.65 was employed as the functional liquid to match that of the glass diaphragm. An external pump was used to actuate the deformation of the diaphragm, which adjusts the curvature of the interface to achieve a tunable focal length. However, the high Young's modulus of the glass diaphragm can limit the tuning range of the lens. Only up to 50 μm of deformation for a 10-mm lens has been achieved. To overcome this challenge, several groups proposed and demonstrated lens interface using elastic membrane instead of glass (Fig. 8a) (Chronis et al. 2003; Zhang et al. 2003). Chronis et al. achieved up to 6 μm deformation for a 200-μm lens. Werber and Zappe (2005) also reported a microfluidic lens developed with dry-etched silicon substrate bonding to a piece of PDMS membrane. The spin-coated PDMS has smoothness up to 8 nm. Chen et al. propose to use a microlens film to serve as the membrane to obtain a shorter focal length (Jackie et al. 2004). These designs were based on a plano-convex structure, and the focal length is still quite large. Jeong et al. (2004) improved the design by combining a negative solid elastomer interface with a membrane to build a micro-doublet lens. The doublet lens can be tuned as either biconvex or meniscus (Fig. 8b). Zhang et al. (2004) further replaced the solid elastomer interface with another deformable membrane so as to tune the two lens interface independently (Fig. 8c).

Table 3 List of typical polymer-based optofluidic lenses

Polymer-based optofluidic lenses	Working mechanism	Fabrication method	Structural material and cost (USD)	Functional fluid	Consuming fluid at working state	Remarks on practicability		
						Resistance to disturbance	Tunability	Ease to operate
Ref. (Ahn and Kim 1999)	Deformation of glass membrane	Glass lapping and polishing, PECVD, wet etching	Glass, silicon	Silicone oil	No	Young's modulus of glass 112.6 GPa	Tuned via fluid pumping system and pressure sensor	Operate via pumping system, hands-on experience with microfluidics is not required
Ref. (Chronis et al. 2003a; Zhang et al. 2003)	Deformation of PDMS membrane	Soft lithography	PDMS, ~$100/500 g	Microscope immersion oil	No	Young's modulus of PDMS 8 kPa–1.72 MPa	Tuned via fluid pumping system and pressure sensor	Operate via pumping system, hands-on experience with microfluidics is not required
Ref. (Jeong et al. 2004)	Deformation of PDMS membrane combine with solid negative lens	Micromolding and photopolymer microdispensing	PDMS, ~$100/500 g	Water or oil	No	Young's modulus of PDMS 8 kPa–1.72 MPa	Tuned via fluid pumping system and pressure sensor	Operate via pumping system, hands-on experience with microfluidics is not required
Ref. (Zhang et al. 2004)	Deformation of PDMS membrane	Soft lithography	PDMS, ~$100/500 g	Water or sodium chromate solution	No	Young's modulus of PDMS 8 kPa–1.72 MPa	Tuned via fluid pumping system and pressure sensor	Operate via pumping system, hands-on experience with microfluidics is not required

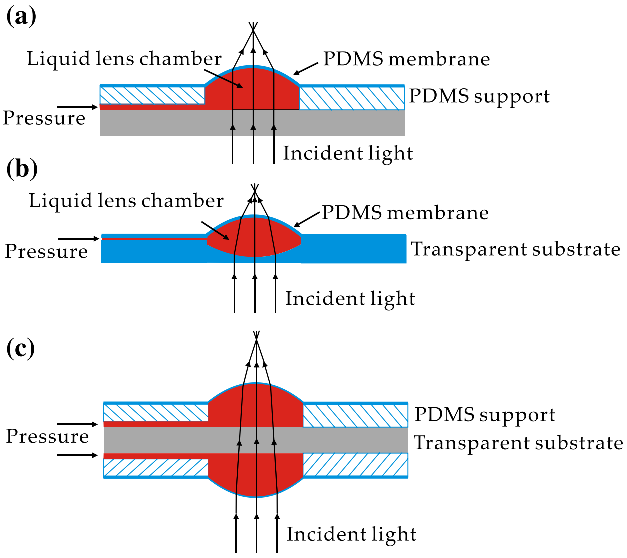


Fig. 8 Schematics of polymer-based optofluidic lenses

Since the deformation geometry of a circularly bounded diaphragm under uniform pressure is approximately hemispherical, such configurations are most suitable for lens development. The fabrication of such lenses is straightforward by creating a cylindrical chamber and sealing it with a deformable membrane. Depending on the size of the lens, different fabrication techniques can be applied. Micro-fabrication techniques, such as wet etching and soft lithography, can be used for the development of microlens arrays. For the applications with bulk imaging system, fineness of the chamber wall does not really matter, and thus, bulk molding techniques can be applied, such as polymer-based 3-D printing (Song et al. 2013b).

Compared to solid-based optofluidic lenses, the lenses with deformable diaphragm can have a tunable focus simply by controlling the pressure in the chamber without replacing the liquid. Thus, the response of tuning can be faster than the solid-based one. Compared to interfacial tension-based tuning lenses, the dynamical range of the actuation pressure is on the order of $\pm 10^4$ Pa and the force exerted on the diaphragm is on the order of 1 Newton (assuming the area of diaphragm is 1 mm^2). Thus, common pressure sensor combined with fluid pumping system can decently manipulate deformation of the diaphragm. Thus, the cost of entire operating system of polymer-based lenses can be much lower than that of interfacial tension-based lenses. In the perspective of operational cost, polymer-based lenses do not consume fluid as the hydrodynamically tuned lenses do. Owing to the lower cost and simple operation procedures, a number of companies have successfully commercialized polymer-based lenses, such as Varioptics, Optotune and TAG optics, whereas little market uptake of the fluid-based optofluidic components has been seen over the past decades.

Given the successful market uptake of polymer-based optofluidic lenses, most of their applications are with the improvements on bulk imaging modalities, such as phone cameras, microscopy systems and photoacoustic imaging systems. Only few applications have been reported for the integration of optical detection and manipulation into microfluidics using polymer-based optofluidics. Research efforts in the future can focus on the substitution of conventional microscopic system for lab-on-chip applications using polymer-based tunable lenses system. Multiple-layer structures might need to be developed and optimized for the entire integration of lab-on-chip system since the polymer-based lenses can only maneuver out-of-plane light, which may lead to fabrication complexity. Considering the high cost of conventional microscopic system, this substitution still holds its promise for market uptake.

5 Perspective

In principle, deformable and replaceable fluids offer greater flexibility for the reconfiguration of optics, which can never be achieved by solid-based optics. For example, a single piece of liquid imaging lens can possess the zoom function (Kuiper and Hendriks 2004; Chronis et al. 2003; Lee and Lee 2007; Song et al. 2013a), whereas compound lenses and locomotion of these lenses would be needed if the lenses were made of glass. However, any shear stress, no matter how small it is, would drive the fluid from its initial status to a certain deflection. The deflection depends on the viscosity of the liquid. This might make the optofluidic device vulnerable to environmental vibration. As mentioned above, the functioning part of an optofluidic component can be fabricated with one of the following materials or a combination of them: rigid solid, elastic polymer and fluid. The inherent nature of the three categories of materials determines the tunability and stability of the devices. The solid, with high stiffness, can hardly be expected to achieve the tunability through deflecting the solid surface, but the solid-based component would be more robust to resist the environmental disturbance. Fluid has the ease to realize reconfigurable tunability, but its configuration stability would be a big concern for chip designer. The properties of elastic polymer-based device stay between them and sometimes can be a compromising solution. The relationship between reconfigurable tunability and configuration stability is illustrated in Fig. 9. It is important to emphasize that device designers should properly balance the compromise between tunability and stability and select the optimum scheme for the integration of optofluidics according to the specific context of the applications. Besides the issue from environmental vibration, other

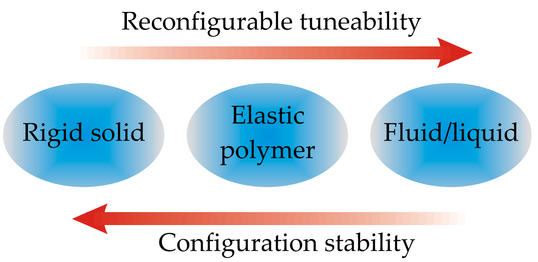


Fig. 9 An illustration on the relationship between reconfigurable tunability and configuration stability for different categories of materials

disturbances from the environment, such as temperature fluctuation, background light and vibration, also need to be taken care of when putting devices into real practice. The temperature change might lead to the shift of refractive index of fluids; extremely cold or hot environment might result in freezing or evaporation of fluids. The background light can disturb the fluorescence or interference signals. Thus, during the packaging stage of the device production, thermal isolation, lightproof or vibration isolation architectures need to be considered.

6 Conclusions

Recently, the attentions of research community have been diverted from solid-based to fluid-based optics by the insights into the unique properties of fluids: (1) replacing a liquid with another liquid inside an optical component can easily tune its optical performance or function; (2) gradients in optical properties can be created by the control of diffusion of two miscible fluids; (3) a smooth optical interface can be naturally formed between two immiscible liquids. These advantageous properties enabled by fluids provide opportunity to the optics to achieve a high level of tunability and performance. Meanwhile, the fabrication technologies in microelectromechanical system (MEMS) and microfluidics (Madou 2011) can be transferred to the fabrication of optofluidic components, significantly miniaturize them and possibly integrate multiple components on a single microchip in a compact way, improving the integration level of lab-on-chip systems and hence promoting the commercialization of lab-on-chip technologies.

In this context, we review the fundamental optical components, such as waveguide, lens, prism and grating, miniaturized using optofluidic technologies, and analyze them in terms of commercialization aspects. Currently, most optofluidic components are fabricated with PDMS using soft lithography that is actually not preferred by the industry due to its high cost and incompatibility for mass production. The main reasons might be the convenient fabrication procedures and good surface quality of structures which is critically important for light transmission. To meet the requirement for mass production, research efforts either need to be dedicated to explore scalable manufacturing methods of PDMS devices or diverted to investigate the feasibility of using cost-effective structural materials to host the currently demonstrated optofluidic components or functions.

Looking at the reconfigurable tunability (important for end users' practice) and configuration stability (important for the practice outside laboratory environment), we discussed both advantages and challenges of those optofluidic elements based on their unique features. We found that solid-based optofluidic components possess decent configuration stability due to relatively higher stiffness of the materials. Their tunability can be enabled by replacing the functioning fluids, though the replacing process takes time, which leads to a slow tuning response. Compared to solid-based optofluidic components, fluid-based ones possess a higher level of tunability owning to the simplicity of deforming the fluid using hydrodynamic or interfacial tension tuning. The response of tuning can be faster than the mechanism of "liquid replacing." However, the comfort to deform the fluid interface can also be a limitation when considering the vulnerability to resist environmental disturbances. Polymer-based optofluidic components might be a good solution with both good resistance to disturbance and tunability. So far, the demonstrated polymer-based components can only manipulate the out-of-plane light (the light traveling perpendicularly to the planar microfluidic platform), which might require designing the microfluidic modules on multiple layers for the integration with lab-on-chip systems.

In conclusion, recent development in the field of optofluidics brought in a number of novel, fundamental and miniaturized optical components which are ready for the integration into micro-systems. The integration of optics can help to greatly miniaturize the entire system, making the system portable and reducing its cost. On top of this, the alignment of optics can be implemented on chip by tuning the optical properties instead of manually adjusting the components. Thus, it is possible to make the optics alignment programmable using an external control system, which would offer more flexibility in control and more accuracy. We believe that continuing research efforts will improve many aspects of optofluidics toward the commercialization, such as recyclable fluid pumping system, chip packaging with anti-vibration, as well as micro-fabrication techniques for optically smooth channel side-wall.

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