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Optofluidics: the interaction between light and flowing liquids in integrated devices

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Optofluidics is a rising technology that combines microfluidics and optics. Its goal is to manipulate light and flowing liquids on the micro/nanoscale and exploiting their interaction in optofluidic chips. The fluid flow in the on-chip devices is reconfigurable, non-uniform and usually transports substances being analyzed, offering a new idea in the accurate manipulation of lights and biochemical samples. In this paper, we summarized the light modulation in heterogeneous media by unique fluid dynamic properties such as molecular diffusion, heat conduction, centrifugation effect, light-matter interaction and others. By understanding the novel phenomena due to the interaction of light and flowing liquids, quantities of tunable and reconfigurable optofluidic devices such as waveguides, lenses, and lasers are introduced. Those novel applications bring us firm conviction that optofluidics would provide better solutions to high-efficient and high-quality lab-on-chip systems in terms of biochemical analysis and environment monitoring.

Keywords: optofluidics; optical devices; microfluidic chip

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Introduction

Optofluidics is a newly developed technology associated with microfluidics and optics. It controls light and fluids at micro/nanoscale and exploits their interaction to produce novel instruments¹. Optofluidics can provide favorable circumstances for a number of traditional optical devices by manipulating small amount of liquids. This new technology enables scientists to solve many classical questions by new research instruments. Specially, fluids can be used to control light or also be exploited to carry substances being analyzed in optofluidic chips, making them adjustable, restructurable, and adaptive. Novel tunable optofluidic devices such as liquid waveguide^{2–4}, dye laser^{5–7}, lens^{8,9} and optical switches^{10–13} have been reported. The development of these devices opens a new chapter in manipulating light and fluids.

The key problem in modern optics is the interaction between light and matters. As shown in Fig. 1, the flowing liquids, as the "matter", are used to interact with light in the optofluidics. The fluids in the optofluidic chip are reconfigurable, non-uniform and usually carry cells or particles, which provides a novel idea in precise optical manipulation. In this paper, we summarized light modulation in inhomogeneous medium by unique fluid dynamic properties such as diffusion, heat conduction, centrifugal effect, the interaction between light and biochemical samples in liquid flows and others. First of all, the interaction between light and pure liquids is a research hotspot in optofluidics. In the pure liquid environment of the optofluidic system, there is convection and diffusion between different concentrations or different liquids. Using the convection and diffusion between the liquids of different concentrations and controlling the proper flow velocity, the natural smooth gradient concentration distribution and the step concentration distribution can be formed. Corresponding to this is the refractive index distribution, which is a crucial optical parameter. For example, the step index distribution can be produced by Dean flow in optofluidic system. It is gener-

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ated in the curved microchannel due to centrifugal effect, which achieves the three-dimensional (3D) spatial tunability of the fluid as it shown in Inset (i)-(1) of Fig. 1. The reconfigurability of fluids in optofluidic systems promotes broad applications such as reconfigurable lenses¹⁴, 3D dye lasers¹⁵. Moreover, the diffusion between miscible liquids or heat conduction in liquids can introduce the natural gradient index (GRIN) medium (Inset (i)-(2)). Light will bend in such flowing liquid, which can be applied for liquid GRIN lenses16,17, waveguides and liquid cloaks. Secondly, biochemical substances (cells, nanoparticles, etc.) can be carried in laminar flows (Inset (ii)). The transport of flowing fluids provides a novel tool detect and manipulate cells and particles¹⁸⁻²⁰. to Optofluidic delivers many merits to fast and accurate lab-on-a-chip systems of low cost and small size, making it potential applications for the next generation integrated optical devices, biological/chemical analyzers, and environmental monitoring²¹.



Fig. 1 | The principle of optofluidic chip and two kinds of interaction between light and flowing liquids. (i) The interaction of light and pure liquids. (1) Liquids with a step index profile. (2) Liquids with a GRIN distribution. (ii) The interaction of light and biochemical samples in flowing liquids.

The interaction between optics and pure liquids

It is critical that light interacts with pure liquids in optofluidics. In general, the liquid is heterogeneous. In Sun Tzu's *Art of War*, there is a well-known saying that the stream has no regular shape. In microfluidic chip, the shapes of fluids can be changed by hydrodynamic process. Reynolds number (Re number) is used for the flow patterns forecast in fluid mechanics, which is defined as: $\text{Re} = \rho VL / \mu (\rho$: the fluid density, *V*: the flow rate, *L*: the channel's hydraulic diameter, and μ : the fluid kinematic viscosity). The laminar will generate gently and predictably as Re<230, while the irregular turbulence will be formed as Re>4000. Usually, the state of flow is laminar in optofluidic systems, and maintains a stable state. The liquid profile is decided by convection-diffusion equation, and it can be described as²²:

$$\frac{\partial c}{\partial t} = D\nabla^2 c - v\nabla c + R \quad , \tag{1}$$

where *c* is the material concentration, *D* is the diffusion coefficient between fluids, *v* is the flow velocity, and *R* represents the source or sink of the quantity. In the equation, $D\nabla^2 c$ and $v\nabla c$ are respectively the contribution of diffusion and convection. Usually, the diffusion coefficient is constant in microfluidics, and there is no source or sink (*R*=0). For steady state, $\partial c / \partial t = 0$.

Step-index optical medium

When the miscible flows are at high flow velocity, the convection-diffusion process is dominated by convection. Smooth interface will be formed, and refractive index (RI) distribution shows nearly a step index profile. In the straight channel, the fluid interface is regulated by altering the flow rate or viscosity coefficient of fluids (two-phase flow). Additionally, Dean flow usually generates in an arc-shaped channel. The laminar flow deforms due to the centrifugal force, which can achieve the spatial adjustability (as seen in the Fig. 2(a)). Dean number (De number), a dimensionless parameter is utilized for describing the Dean flow²³, and De = $\delta^{0.5}$ Re, in which δ = *w* (channel width)/*R* (curvature radius). De number conveys the relationship between centrifugal force and viscous force.

The discovery of the Dean flow makes the 3D liquid operation possible. Light can be confined to a flowing stream and it can also be refracted and reflected at the interface of different streams. At present, a mass of devices have been reported, which have good potentials for biochemistry and medicine. The tunable optofluidic waveguide is a typical example²⁴⁻²⁶. In 2004, Wolfe et al. designed a liquid-liquid (L²) waveguide by deionized water (DI, n_1 =1.335) and calcium chloride solution (CaCl₂, $n_2=1.445)^{24}$. A step index distribution formed when the flow rates were high, and the light was confined in the core flowing streams with a higher RI. Both single mode and multimode 2D waveguides could be produced by this way. The position of core flow altered with the change of flow rates, and this feature was helpful to construct an optical switch. However, as the RI of the flowing liquids were usually smaller than that of solid substrate, there was serious optical leakage in such 2D liquid waveguides. To improve it, Yang et al. developed a novel 3D liquid waveguide based on Dean flow as shown in Fig. 2(b)¹⁵. Two flows were injected into the microchannel simultaneously. In the cured microchannel, they would reverse in rotation due to centrifugal effect, which formed a 3D waveguide. The core flow dissolving organic dyes was regarded as a laser medium, which produced stimulated emission by an external pump light. The Fabry-Pérot (F-P) microcavity with a pair of aligned gold-plated fibers could oscillate and amplify the fluorescence emission. The 3D core waveguide was of pure liquid structure in which the core flow was fully encased by the cladding

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Fig. 2 | (a) The schematic of 3D liquid remodelability in a curved channel by centrifugal effect. (b) A 3D optofluidic dye laser. Figure reproduced from: (b) ref.¹⁵, The Royal Society of Chemistry.

flow. The 3D dye laser had a higher slope efficiency and lower threshold than that of conventional 2D counterpart. Later, Li et al. proposed a 3D Y-type optofluidic waveguide, utilizing a symmetrical arc structure to form an adjustable Y-shaped 3D liquid waveguide²⁷. The experimental results showed that the diameter of the core flow could be consecutively regulated while the relative intensity of the two beam branches (with an angle of 10°) could also be adjusted from 0 to 1 by changing the flow rates.

Another application case of utilizing the Dean flow is the 3D lens. The solid microlens generally has a fixed focal length once it is fabricated, while the liquid microlens provides a greater flexibility²⁸. In 2007, Mao et al. proposed a 2D optofluidic cylindrical microlens by the Dean flow²⁹. Later, Rosenauer et al. reported a 3D optofluidic lens by two 90-degree curves microchannels and an expansion chamber³⁰. In 2017, Liang et al. combined the Dean flow and 3D circular micro-structure to design a 3D L² optofluidic biconvex lens³¹. By changing the flow rate, both the shape and focal length could be altered. The 3D lens was completely wrapped in the liquid, which greatly increased the resolution. The experimental results showed that the light was successfully focused from 3554 µm to 3989 µm, and the adjustable range of focal length was 435 µm. Its numerical aperture was 0.175-0.198. The resolution was increased by 1.79 times

compared to conventional 2D lens. It is potential for cell analysis in lab-on-chip systems.

Natural gradient optical medium

Gradient refractive index (GRIN) medium can gradually change the light path and help to create interesting optical devices. However, it is difficult to achieve in solid materials. Liquids are flexible to change their concentrations by mixing, diffusion or heat conduction. According to Equation (1), the convection-diffusion process will be dominated by diffusion as the flow rates of the miscible fluids are slow, the concentrations changed gradually in the microchannel. As the RI and the concentration is one-to-one match between each other, the GRIN distribution is naturally introduced (Fig. 3(a)).

A tunable 2D liquid GRIN lens was studied by Huang et al.³², which used liquid diffusion and did not need the cured lens surface. As shown in Fig. 3(b), the designed diffusion between CaCl₂ solution (n_1 =1.445) and DI water (n_2 =1.335) will produce hyperbolic secant distribution of RI, and it achieved a 2D light focusing. GRIN waveguides are another typical application by diffusion. In 2016, a multimode interference (MMI) hybrid optofluidic waveguide with self-imaging was designed by Shi et al.³³. Recently, Zhao et al. reported to use it for chemical reaction monitoring³⁴. These results confirmed such diffusion based on GRIN devices have wide potential applications



Fig. 3 | (a) The schematic design of liquid GRIN lenses. (b) The GRIN lens by diffusion. (c) The GRIN lens by heat conduction. Figure reproduced from: (b) ref.³², The Royal Society of Chemistry; (c) ref.³⁶, The Royal Society of Chemistry.

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in lab-on-chip community.

Besides diffusion, the heat conduction in liquids also affects the RI distribution. The heat conduction equation is³⁵:

$$\frac{\partial T}{\partial t} = \kappa \nabla^2 T - \nu \nabla T \quad , \tag{2}$$

where *T* represents the liquid temperature, *v* is the liquid mean flow rate, and κ is the thermal diffusivity. The thermal conductivity is usually greater than the molecular diffusion coefficient, the heat conduction has unique advantages over mass diffusion. The heat conduction in the liquids dissipates quickly, which in turn much less switching time comparing to diffused optical counterpart. Unlike diffusion, the heat conduction has a unique merit that the liquid can be recycled and does not produce wastes in principle^{36,37}.

Hence, the heat conduction is another good method to form GRIN devices. Chen et al. used a thermal gradient generated by a laser pump and a metal substrate to form a GRIN lens (Fig. 3(c))³⁶. The benzyl alcohol solution was utilized due to its relatively large RI change at a certain temperature difference. The results showed that the focal length of this thermal lens could be achieved 1.3 mm. To further simplify the operation, Liu et al. made an improvement in 2017³⁷. The thermal lens with a GRIN profile was just formed by thermal conduction between the same fluids with different temperatures. The benzyl alcohol at 100 °C (n_1 =1.50) and 0 °C (n_2 =1.55) was infused into the microchannel as the cladding flow and the core flow. When *Pe* number (a dimensionless number to describe the degree of convection-diffusion) was 230, a typical graded index lens was formed in the channel. The GRIN lens had a controllable focus in scope of 500 μ m and a minimum focal distance of 430 μ m. The adjustable GRIN lens was suitable for cell capture in its controllability. Compared to conventional solid optical tweezers, it can be applied to capture living cells in a microfluidic channel and manipulate cells in the range of 280 μ m in time.

Light propagates in a straight way in homogeneous medium while it bends in inhomogeneous medium (Fig. 4(a)). The GRIN distribution formed by liquids can be analogous to the quasi-conformal transformation optics (OCTO)³⁸. OCTO can control electromagnetic wave by inhomogeneous RI profile using isotropy medium, which represents a new direction of light manipulation. In previous studies, QCTO was usually fabricated by solid dielectric materials and it required complex manufacturing processes. It led high requirements on materials and preparation processes, and the device could not be adjusted in real time. The convective-diffusion between fluids can be used to form real-time adjustable transformation optics (TO), and the profile is analogous to the profile of QCTO with slow flow rate of liquid (diffusion dominated). Light in the fluids with GRIN distribution can realize TO waveguides^{39,40}, TO lenses³⁸, tunable visible cloaks⁴¹, and waveguide splitters⁴².

Yang et al. presented a diffused waveguide³⁹. By varying the flow velocity, spatially variable optical properties would be produced. And the new optical phenomena (self-focusing and interference) could be achieved (Fig. 4(b)). Besides, Liu et al. found that liquid TO waveguide could avoid light bend loss⁴⁰. Utilizing a reasonably low



Fig. 4 | (**a**) (1) Light propagates in a straight way in homogeneous liquid medium. (2) Light bends in inhomogeneous liquid medium. (**b**) The schematic diagram and experimental images of optofluidic waveguide based on QCTO, which can focus light. (**c**) A QCTO optofluidic waveguide, bending light at 90°, 180°, and 270°. (**d**) A tunable liquid cloaking. Figure reproduced from: (**b**) ref.³⁹, Macmillan Publishers Limited; (**c**) ref.⁴⁰, Optical Society of America; (**d**) ref.⁴¹, WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim.

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flow rate, the beam achieved the bend at 90° , 180° , and 270° (Fig. 4(c)). Thus, it imparts advance performance to liquid waveguides with low loss, low consumption, streamlined operation and real-time controllability, opening up more exploration paths in the TO field.

Invisible cloak is a classical application of TO and has great prospects in application. Zhu et al. used liquid dynamics to modulate a liquid shadow cloak in 2017⁴¹. In this experiment, a protrusion was designed as a hidden object at the entrance of the main channel. Three strands of fluid were injected at a low rate to form a GRIN profile in the microfluidic channel. When the liquid was inconsistent with the guasi-conformal-converted optical RI profile, the incident beam would be directly incident on the protrusion and scattered out, and it was in a "Cloak-off" state. Conversely, when the liquid coincided with the quasi-conformal-converted optical RI profile, the incident light would be reflected off without scattering and would hide the protrusion, which was the "Cloak-on" state (Fig. 4(d)). Compared with traditional solid materials (such as superconducting materials), liquid shadow cloak is simple in preparation, low in cost, and realizable in real-time reconstruction, it has become more and more valuable in the application of optical integrated devices.

Biochemical samples manipulation and

sensing in flowing liquids

Fluids are the natural carriers of biochemical samples. The manipulation and sensing for biochemical samples in flowing liquids is another research point in optofluidics. For example, the flow cytometry is a classical instrument which perfectly combines light and fluid, and it has been widely used in medical testing and biochemical analysis. Samples are confined in the core flow to be optical detected one-by-one using hydrodynamic focusing (Fig. 5(a))^{43,44}. The sample flow is sandwiched in the middle of the channel by the sheath flow. The flow rate can be adjusted to control the width of the core flow. Typically, the sheath flow takes up much larger volume of the whole channel than the sample flow by faster flow rates, pressing the sample flow into the narrower area of the channel.

In optofluidic research, the advanced on-chip flow cytometry is usually divided into two optical categories: one is detected by the traditional far-field scattering light⁴⁵⁻⁴⁷ and the other is detected by the near-field evanescent wave^{48,49}. For example, Yu et al. reported a cytometer to detect bacteriophage by the far-field scattering light and droplet optofluidic imaging (Fig. 5(b))⁴⁷. The sample alignment on both vertical and horizontal direction was realized by the flexible 3D hydrodynamic. This method could get a highly-focused central sample stream and flexible position change in the channel. Experimental results indicated that 4 µm polystyrene particles can be detected with 600/s. However, this flow cytometry collects scattered light or fluorescence from samples irradiated in the far field. For large collections of nanoparticles, only the average properties can be measured. The flow cytometry based on near-field evanescent wave can screen cells or particles at the single-cell level and record the fluorescence intensity in the evanescent field by photodetector, which greatly saves the response time.

In 2016, Liang et al. designed another kind of flow cytometer by two phase flow combined with the near-field evanescent wave to achieve nanoparticles detection and



Fig. 5 | (a) The schematic of the on-chip flow cytometry, which is detected in two ways. One is detected by the traditional far-filed scattering light, and the other is detected by the near-field evanescent wave. (b) The Schematic diagram (1) and experimental images (2, 3) of a label-free bacteriophage detection by using droplet optofluidic imaging and far-field scattering light. (c) The design (1) and experimental image (2) of the single nanoparticle detection by total internal reflection. Figure reproduced from: (a) ref.⁵¹, Springer Nature; (b) ref.⁴⁷, (c) ref.⁴⁹, The Royal Society of Chemistry.

counting (Fig. 5(c))⁴⁹. In a microfluidic channel, three fluids (the cladding flow is a mixed oil with a RI of 1.406 and a viscosity coefficient of 9.2 mPa·s; the sample flow and another cladding flow have a RI of 1.40, using an aqueous solution of ethylene glycol with a viscosity coefficient of 6.0 mPa·s) were simultaneously injected to form a narrow core stream (The width was 1 µm), and the nanoparticles were bound in the core flow. The two phase flow formed a naturally smooth surface and provided a good reflective difference interface for the total internal reflection. The skin depth of evanescent field was adjusted to about 1 µm. Thus, the sample would be fully detected in the detection area. This design opens up a new way to detect and count substances as small as nanoscale. Recently, evanescent wave is further developed to be applied to precisely monitor drug resistance⁵⁰. However, the flow cytometry based on the near-field evanescent wave has great limitations due to the small skin depth and complex operation process. To improve it and achieve greater throughput testing, Cheng et al. demonstrated an imaging flow cytometry combining a time-stretch microscopy⁵¹, which could achieve a high-throughput (> 10000 cells/s) while differentiate of the morphological and intracellular molecular variation.

Samples in flowing liquids can be exposed and manipulated by optical force for further applications such as trapping, sorting and aggregation. The optical scattering and gradient forces were first reported by Ashkin to trap microparticles in steady liquids⁵². Scattering force is related to the light intensity and accords with the direction of light propagation. It can be regarded as the momentum transmission by photons scattering. Gradient force is relative with the spatial gradient of light intensity and acts in the direction of the gradient⁵³. Precise manipulation of cells and particles can be achieved by optical force in flowing liquids. Optofluidics can provide a harmless and contactless method to manipulate particles and cells. Many related devices have been mentioned, such as optical stretchers^{54,55}, optical tweezers^{56,57}, optical lattices⁵⁸, optical chromatography⁵⁹ and so on. These findings laid the foundation for cell detection and intercellular contact.

The optical stretcher is a dual-beam light trap used to capture and stretch micron-sized particles of soft material, such as cells. The force used to capture and deform an object comes from the transfer of photon momentum on the surface of the object, which makes it a contactless tool in biophysics analysis. It is not easy to precisely align two laser beams, and the particle size can be manipulated at the micron level. Optical tweezers based on a single beam have the advantage that it is simpler to operate compared to optical stretchers. To make the trap stable, the single beam must be highly focused, trapping the particles close to the focus. The laser power of optical tweezers is low in order to avoid the damage of biomaterials caused by high focal intensity. And optical tweezers are usually be used to manipulate particles ranging in size from a few hundred nanometers to a few micrometers. However, handling much smaller dielectric objects requires stronger optical constraints and higher power. David Erickson's group solved the problem and realized the trapping of 75 nm dielectric nanoparticles and λ -DNA in sub-wavelength slot waveguides based on near-field technology⁶⁰. As shown in Fig. 6(a), the matters were confined inside the waveguide by near-field optical forces and they could be manipulated precisely by scattering/adsorption forces.

In addition, the optical force also can be used to sort particles and cells. In 2003, MacDonald et al. reported a method to sort particles in an optical lattice⁵⁸. When the different particles flown through the optical lattice (Fig. 6(b)), target particles were deflected and chose different trajectory by optical force. The different colloidal particles could be sorted according to the size or the refractive index difference. This method had close to 100% sorting efficiency with reasonable throughput. This approach had the ability of directly processing extended biomolecules. However, this method has some limitations in the manipulation of nanoparticles. Wu et al. integrated the optical force with the impinging streams in microfluidic device to realize the photodynamic screening of gold nanoparticles in fast flowing environment⁶¹. Two impinging streams could reduce the flow rate and extend the action time of the optical force in acting direction, achieving the separation of different gold nanoparticles (Fig. 6(c)). In flowing liquids, gold nanoparticles were also affected by liquid drag force except for optical force. The drag force could be derived from the Stokes Law and was given by $F_{\text{Flow}} = 6\pi\mu rv$, in which *r* was the particle's radius. As seen in the Fig. 6(c), the light force and the drag force are on the same line but in opposite directions. Gold particles of different sizes could be divided into two sides under their combined action. The method improved the accuracy, and the separation efficiency of 50/100 nm gold nanoparticles was as high as 92%. To achieve higher resolution, a new way to use quasi-Bessel beam was reported, which had a low numerical aperture (NA) and small focus (Fig. 6(d))⁶². Experimental results show that it separated individual nanoparticles with diameter ranging from 60 nm to 100 nm and resolution of 10 nm for the first time. Besides, optical chromatography, synthesizing light scattering force and fluid drag force has a broad application prospect in the separation of nanoparticles. Shi et al. reported a new way to control the dynamics and synergy between multiple particles combined optical lattice and optical chromatography (Fig. 6(e))⁶³. In this paper, the bacteria were conjugated to the antibody and captured using the optical lattice.

Optofluidics is a powerful stage for integration, other technology such as standing surface acoustic (SSAW)⁶⁴⁻⁶⁹ can be easily integrated in optofluidic chip. As similar cells usually overlap in size, density, and effective refractive index, combining the advantage of optical and acoustic methods to sort or trap cells in free-label, non-invasive

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Fig. 6 | (**a**) Biomolecules detection based on optical force in sub-wavelength slot waveguides. (**b**) Cells sorting in an optical lattice. (**c**) Gold nanoparticles sorting in flowing system. (**d**) Multi-range particles sorting by quasi-Bessel beam. (**e**) Microparticles sorting based on optical lattice and chromatography. (**f**) Cell sorting by a new method combing acoustic force and optical force. Figure reproduced from: (**a**) ref.⁶⁰, Macmillan Publishers Limited; (**b**) ref.⁵⁸, Nature Publishing Group; (**c**) ref.⁶¹, American Chemical Society; (**d**) ref.⁶², The Royal Society of Chemistry; (**e**) ref.⁶³; (**f**) ref.⁷⁰, The Royal Society of Chemistry.

way is promising. Hu et al. innovatively combined the sound and light for the first time to precisely separate the leukocyte subtypes⁷⁰. As presented in Fig. 6(f), a pair of parallel interdigital transducers (IDT) was used to generate acoustic surface standing waves. Conventional hydrodynamic focusing methods were inaccurate and induce extracellular pressure. Acoustic wave could focus cells gently in three dimensions and separate granulocyte. The optical force could precisely separate peripheral blood mononuclear cells that were similar in shape but different in RI ($n_{lymphocytes}$ =1.39–1.41, $n_{monocytes}$ =1.36–1.37). In this study, the separation accuracy for lymphocytes and monocytes was more than 98%, and 95% for sorting granulocytes. It was useful for the clinical diagnosis and analysis of leukemia.

In addition, the optical resonator has a good performance in biochemical testing⁷¹. The resonators, such as F-P cavity, Bragg grating, whispering gallery mode (WGM), and Mach-Zehnder interferometer can be smoothly integrated on optofluidic chip with high quality factor (Q factor)⁷². In 2006, Song et al. developed a novel RI sensor which depends on F-P cavity for single living cell detection⁷³. Later, Chin et al. improved it to determine the effective RI and thickness of the cell⁷⁴. In his experiments, single Madin-Darby canine kidney (MDCK) cell was captured in the microcavity and the transmission spectrum shifted due to changes in the surrounding buffer (with or without cells) for determining the effective RI and thickness of the cell. Another important application of the interaction between light and flowing liquid is absorption detection. Spectrophotometry on basis of Lambert-Beer law is a standard method for the quantitative analysis of substances associated with absorption. Some portable devices presented low reagents and power consumption, as well as precise measurements of soluble nutrients in the seawater^{75,76}. However, the absorption length of these instruments was up to centimeters to maintain high accuracy. In 2017, Zhu et al. designed a novel resonator device for phosphate detection based on micro F-P cavity⁷⁷. Compared with the previous seawater detection

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technology, this design integrated sample preparation, reaction and detection feedback into one microchip. The high integration level made the detection faster and more accuracy. Shi et al. applied differential colorimetry method to nitrite detection and provided a new idea for the detection of nutrients in water⁷⁸. These unique methods eliminated the requirement of complicated calibration curve measurements, enabling fast sample detection as short as possible and minimal reagent consumption. In 2019, Chauvin et al. proposed an unmarked optofluidic sensor based on microrings to monitor cadmium ions in tap water⁷⁹. The methods with low limit of detection, low consumption and high portability have great potential in biological and chemical examination.

Conclusions

This review reports the recent advances of the optofluidics, a rising interdisciplinary subject combined microfluidics and optics. We summarized the light modulation in heterogeneous media by unique fluid dynamic properties such as mass diffusion, heat conduction, centrifugal effect, the interaction between substances and light in flowing liquids and others. By understanding the guiding light mechanism of optofluidic system, quantities of tunable and reconfigurable optofluidic devices such as waveguides, lenses, and laser are introduced. The applications and mechanisms introduced will help readers know the importance of optofluidics in light detection, and it will promote the development of rapid, precise, low consumed and small size lab-on-chip systems for light detection in biochemical analysis and environment monitoring.

References

- Psaltis D, Quake S R, Yang C. Developing optofluidic technology through the fusion of microfluidics and optics. *Nature* 442, 381–386 (2006).
- Tang S K Y, Stan C A, Whitesides G M. Dynamically reconfigurable liquid-core liquid-cladding lens in a microfluidic channel. *Lab Chip* 8, 395–401 (2008).
- Lim J M, Kim S H, Yang S M. Liquid–liquid fluorescent waveguides using microfluidic-drifting-induced hydrodynamic focusing. *Microfluid Nanofluid* 10, 211–217 (2011).
- Chung A J, Erickson D. Optofluidic waveguides for reconfigurable photonic systems. *Opt Express* 19, 8602–8609 (2011).
- Kiraz A, Chen Q S, Fan X D. Optofluidic lasers with aqueous quantum dots. ACS Photonics 2, 707–713 (2015).
- Chen Q S, Kiraz A, Fan X D. Optofluidic FRET lasers using aqueous quantum dots as donors. *Lab Chip* 16, 353–359 (2016).
- Chen Y C, Chen Q S, Fan X D. Optofluidic chlorophyll lasers. Lab Chip 16, 2228–2235 (2016).
- Dong L, Agarwal A K, Beebe D J, Jiang H R. Adaptive liquid microlenses activated by stimuli-responsive hydrogels. *Nature* 442, 551–554 (2006).
- Seow Y C, Lim S P, Lee H P. Optofluidic variable-focus lenses for light manipulation. *Lab Chip* 12, 3810–3815 (2012).

- Groisman A, Zamek S, Campbell K, Pang L, Levy U et al. Optofluidic 1×4 switch. Opt Express 16, 13499–13508 (2008).
- Yang A H J, Erickson D. Optofluidic ring resonator switch for optical particle transport. *Lab Chip* **10**, 769–774 (2010).
- Song W Z, Psaltis D. Electrically tunable optofluidic light switch for reconfigurable solar lighting. *Lab Chip* **13**, 2708–2713 (2013).
- Seow Y C, Lim S P, Lee H P. Tunable optofluidic switch via hydrodynamic control of laminar flow rate. *Appl Phys Lett* 95, 114105 (2009).
- Zhuang G S, Jensen T G, Kutter J P. Detection of unlabeled particles in the low micrometer size range using light scattering and hydrodynamic 3D focusing in a microfluidic system. *Electrophoresis* 33, 1715-1722 (2012).
- Yang Y, Liu A Q, Lei L, Chin L K, Ohl C D *et al*. A tunable 3D optofluidic waveguide dye laser via two centrifugal dean flow streams. *Lab Chip* **11**, 3182–3187 (2011).
- Fei P, He Z, Zheng C H, Chen T, Men Y F *et al.* Discretely tunable optofluidic compound microlenses. *Lab Chip* **11**, 2835–2841 (2011).
- Zhao H T, Yang Y, Chin L K, Chen H F, Zhu W M et al. Optofluidic lens with low spherical and low field curvature aberrations. *Lab Chip* 16, 1617–1624 (2016).
- Leake K D, Phillips B S, Yuzvinsky T D, Hawkins A R, Schmidt H. Optical particle sorting on an optofluidic chip. *Opt Express* 21, 32605–32610 (2013).
- Kühn S, Measor P, Lunt E J, Phillips B S, Deamer D W et al. Loss-based optical trap for on-chip particle analysis. *Lab Chip* 9, 2212–2216 (2009).
- Shi Y Z, Xiong S, Chin L K, Zhang J B, Ser W *et al.* Nanometer-precision linear sorting with synchronized optofluidic dual barriers. *Sci Adv* 4, eaao0773 (2018).
- Fan X D, White I M, Shopova S I, Zhu H Y, Suter J D *et al.* Sensitive optical biosensors for unlabeled targets: a review. *Anal Chim Acta* 620, 8–26 (2008).
- Perumal M, Raju K G R. Approximate convection-diffusion equations. J Hydrol Eng 4, 160–164 (1999).
- Sudarsan A P, Ugaz V M. Multivortex micromixing. Proc Natl Acad Sci USA 103, 7228–7233 (2006).
- Wolfe D B, Conroy R S, Garstecki P, Mayers B T, Fischbach M A et al. Dynamic control of liquid-core/liquid-cladding optical waveguides. *Proc Natl Acad Sci USA* **101**, 12434–12438 (2004).
- Mayers B T, Vezenov D V, Vullev V I, Whitesides G M. Arrays and cascades of fluorescent liquid-liquid waveguides: broadband light sources for spectroscopy in microchannels. *Anal Chem* 77, 1310–1316 (2005).
- Li X C, Wu J, Liu A Q, Li Z G, Soew Y C *et al*. A liquid waveguide based evanescent wave sensor integrated onto a microfluidic chip. *Appl Phys Lett* **93**, 193901(2008).
- Li L, Zhu X Q, Liang L, Zuo Y F, Xu Y S *et al.* Switchable 3D optofluidic y-branch waveguides tuned by dean flows. *Sci Rep* 6, 38338 (2016).
- Fang C L, Dai B, Xu Q, Zhuo R, Wang Q et al. Hydrodynamically reconfigurable optofluidic microlens with continuous shape tuning from biconvex to biconcave. *Opt Express* 25, 888–897 (2017).
- Mao X L, Waldeisen J R, Juluri B K, Huang T J. Hydrodynamically tunable optofluidic cylindrical microlens. *Lab Chip* 7, 1303–1308 (2007).
- 30. Rosenauer M, Vellekoop M J. 3D fluidic lens shaping-a

multiconvex hydrodynamically adjustable optofluidic microlens. *Lab Chip* **9**, 1040–1042 (2009).

- Liang L, Zhu X Q, Liu H L, Shi Y, Yang Y. A switchable 3D liquid–liquid biconvex lens with enhanced resolution using dean flow. *Lab Chip* 17, 3258–3263 (2017).
- Huang H, Mao X L, Lin S C S, Kiraly B, Huang Y P *et al*. Tunable two-dimensional liquid gradient refractive index (L-GRIN) lens for variable light focusing. *Lab Chip* **10**, 2387–2393 (2010).
- Shi Y, Liang L, Zhu X Q, Zhang X M, Yang Y. Tunable self-imaging effect using hybrid optofluidic waveguides. *Lab Chip* 15, 4398–4403 (2015).
- Zhao H T, Zhang Y, Liu P Y, Yap P H, Ser W *et al.* Chemical reaction monitoring via the light focusing in optofluidic waveguides. Sens Actuators B Chem 280, 16–23 (2019).
- Tang S K Y, Mayers B T, Vezenov D V, Whitesides G M. Optical waveguiding using thermal gradients across homogeneous liquids in microfluidic channels. *Appl Phys Lett* 88, 061112 (2006).
- Chen Q M, Jian A Q, Li Z H, Zhang X M. Optofluidic tunable lenses using laser-induced thermal gradient. *Lab Chip* 16, 104–111 (2016).
- Liu H L, Shi Y, Liang L, Li L, Guo S S et al. A liquid thermal gradient refractive index lens and using it to trap single living cell in flowing environments. *Lab Chip* 17, 1280–1286 (2017).
- Roberts D A, Kundtz N, Smith D R. Optical lens compression via transformation optics. *Opt Express* **17**, 16535–16542 (2009).
- Yang Y, Liu A Q, Chin L K, Zhang X M, Tsai D P et al. Optofluidic waveguide as a transformation optics device for lightwave bending and manipulation. *Nat Commun* 3, 651 (2012).
- Liu H L, Zhu X Q, Liang L, Zhang X M, Yang Y. Tunable transformation optical waveguide bends in liquid. *Optica* 4, 839–846 (2017).
- Zhu X Q, Liang L, Zuo Y F, Zhang X M, Yang Y. Tunable visible cloaking using liquid diffusion. *Laser Photonics Rev* 11, 1700066 (2017).
- Yang Y, Chin L K, Tsai J M, Tsai D P, Zheludev N I *et al.* Transformation optofluidics for large-angle light bending and tuning. *Lab Chip* **12**, 3785–3790 (2012).
- Mao X L, Waldeisen J R, Huang T J. "Microfluidic drifting"—implementing three-dimensional hydrodynamic focusing with a single-layer planar microfluidic device. *Lab Chip* 7, 1260–1262 (2007).
- Wu Z G, Nguyen N T. Hydrodynamic focusing in microchannels under consideration of diffusive dispersion: theories and experiments. Sens Actuators B Chem 107, 965–974 (2005).
- Cho S H, Godin J M, Chen C H, Qiao W, Lee H *et al.* Review article: recent advancements in optofluidic flow cytometer. *Biomicrofluidics* 4, 043001 (2010).
- 46. Mao X L, Nawaz A A, Lin S C S, Lapsley M I, Zhao Y H et al. An integrated, multiparametric flow cytometry chip using "microfluidic drifting" based three-dimensional hydrodynamic focusing. *Biomicrofluidics* 6, 024113 (2012).
- Yu J Q, Huang W, Chin L K, Lei L, Lin Z P *et al.* Droplet optofluidic imaging for λ-bacteriophage detection *via* co-culture with host cell *Escherichia coli. Lab Chip* **14**, 3519–3524 (2014).
- Wang J, Fei B, Geahlen R L, Lu C. Quantitative analysis of protein translocations by microfluidic total internal reflection fluorescence flow cytometry. *Lab Chip* 10, 2673–2679 (2010).
- Liang L, Zuo Y F, Wu W, Zhu X Q, Yang Y. Optofluidic restricted imaging, spectroscopy and counting of nanoparticles by eva-

DOI: 10.29026/oea.2019.190007

nescent wave using immiscible liquids. Lab Chip 16, 3007–3014 (2016).

- Liang L, Jin Y X, Zhu X Q, Zhou F L, Yang Y. Real-time detection and monitoring of the drug resistance of single myeloid leukemia cells by diffused total internal reflection. *Lab Chip* 18, 1422–1429 (2018).
- Lei C, Kobayashi H, Wu Y, Li M, Isozaki A et al. High-throughput imaging flow cytometry by optofluidic time-stretch microscopy. *Nat Protoc* **13**, 1603–1631 (2018).
- Ashkin A, Dziedzic J M, Bjorkholm J E, Chu S. Observation of a single-beam gradient force optical trap for dielectric particles. *Opt Lett* **11**, 288–290 (1986).
- Svoboda K, Block S M. Biological applications of optical forces. *Annu Rev Biophys Biomol Struct* 23, 247–285 (1994).
- Lincoln B, Schinkinger S, Travis K, Wottawah F, Ebert S *et al.* Reconfigurable microfluidic integration of a dual-beam laser trap with biomedical applications. *Biomed Microdevices* 9, 703–710 (2007).
- Ebert S, Travis K, Lincoln B, Guck J. Fluorescence ratio thermometry in a microfluidic dual-beam laser trap. *Opt Express* 15, 15493–15499 (2007).
- 56. Grier D G. A revolution in optical manipulation. *Nature* **424**, 810–816 (2003).
- Moffitt J R, Chemla Y R, Smith S B, Bustamante C. Recent advances in optical tweezers. *Annu Rev Biochem* 77, 205–228 (2008).
- MacDonald M P, Spalding G C, Dholakia K. Microfluidic sorting in an optical lattice. *Nature* 426, 421–424. (2003).
- Hart S J, Terray A V. Refractive-index-driven separation of colloidal polymer particles using optical chromatography. *Appl Phys Lett* 83, 5316–5318 (2003).
- Yang A H J, Moore S D, Schmidt B S, Klug M, Lipson M *et al.* Optical manipulation of nanoparticles and biomolecules in sub-wavelength slot waveguides. *Nature* 457, 71–75 (2009).
- Wu W, Zhu X Q, Zuo Y F, Liang L, Zhang S P *et al*. Precise sorting of gold nanoparticles in a flowing system. *ACS Photonics* 3, 2497–2504 (2016).
- Shi Y Z, Xiong S, Chin L K, Yang Y, Zhang J B et al. High-resolution and multi-range particle separation by microscopic vibration in an optofluidic chip. *Lab Chip* **17**, 2443–2450 (2017).
- Shi Y Z, Xiong S, Zhang Y, Chin L K, Chen Y Y et al. Sculpting nanoparticle dynamics for single-bacteria-level screening and direct binding-efficiency measurement. Nat Commun 9, 815 (2018)
- Li P, Mao Z M, Peng Z L, Zhou L L, Chen Y C *et al.* Acoustic separation of circulating tumor cells. *Proc Natl Acad Sci USA* 112, 4970–4975 (2015).
- Ding X Y, Peng Z L, Lin S C S, Geri M, Li S X *et al.* Cell separation using tilted-angle standing surface acoustic waves. *Proc Natl Acad Sci USA* 111, 12992–12997 (2014).
- Wu M X, Chen K J, Yang S J, Wang Z Y, Huang P H *et al.* High-throughput cell focusing and separation via acoustofluidic tweezers. *Lab Chip* 18, 3003–3010 (2018).
- Shi J J, Ahmed D, Mao X L, Lin S C S, Lawit A *et al.* Acoustic tweezers: patterning cells and microparticles using standing surface acoustic waves (SSAW). *Lab Chip* **9**, 2890–2895 (2009).
- Li S X, Ma F, Bachman H, Cameron C E, Zeng X Q et al. Acoustofluidic bacteria separation. J Micromech Microeng 27, 015031 (2017).

DOI: 10.29026/oea.2019.190007

- Guo F, Mao Z M, Chen Y C, Xie Z W, Lata J P et al. Three-dimensional manipulation of single cells using surface acoustic waves. *Proc Natl Acad Sci USA* **113**, 1522–1527 (2016).
- Hu X J, Liu H L, Jin Y X, Liang L, Zhu D M *et al.* Precise label-free leukocyte subpopulation separation using hybrid acoustic-optical chip. *Lab Chip* 18, 3405–3412 (2018).
- Fan X D, White I M. Optofluidic microsystems for chemical and biological analysis. *Nat Photonics* 5, 591–597 (2011).
- 72. Vahala K J. Optical microcavities. Nature 424, 839-846 (2003).
- Song W Z, Zhang X M, Liu A Q, Lim C S, Yap P H et al. Refractive index measurement of single living cells using on-chip Fabry-Pérot cavity. *Appl Phys Lett* 89, 203901 (2006).
- Chin L K, Liu A Q, Lim C S, Zhang X M, Ng J H *et al*. Differential single living cell refractometry using grating resonant cavity with optical trap. *Appl Phys Lett* **91**, 243901 (2007).
- Legiret F E, Sieben V J, Woodward E M S, Abi Kaed Bey S K, Mowlem M C *et al.* A high performance microfluidic analyser for phosphate measurements in marine waters using the vanadomolybdate method. *Talanta* **116**, 382–387 (2013).
- Beaton A D, Cardwell C L, Thomas R S, Sieben V J, Legiret F E et al. Lab-on-chip measurement of nitrate and nitrite for in situ analysis of natural waters. *Environ Sci Technol* 46, 9548–9556 (2012).
- Zhu J M, Shi Y, Zhu X Q, Yang Y, Jiang F H *et al*. Optofluidic marine phosphate detection with enhanced absorption using a Fabry-Pérot resonator. *Lab Chip* **17**, 4025–4030 (2017).

- Shi Y, Liu H L, Zhu X Q, Zhu J M, Zuo Y F *et al.* Optofluidic differential colorimetry for rapid nitrite determination. *Lab Chip* 18, 2994–3002 (2018).
- Chauvin D, Bell J, Leray I, Ledoux-Rak I, Nguyen C T. Label-free optofluidic sensor based on polymeric microresonator for the detection of cadmium ions in tap water. *Sens Actuators B Chem* 280, 77–85 (2019).

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Author contributions

J. M. Zhu and Y. Yang proposed the original idea. X. Q. Zhu and Y. F. Zuo helped with the text modification. X. J. Hu helped with the image modification. Y. Yang supervised the project. All authors took part in regular discussions and were involved in the completion of the manuscript.

Competing interests

The authors declare no competing financial interests.