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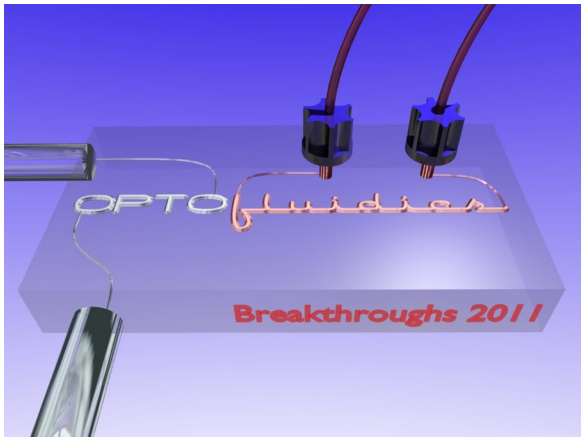

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Optofluidics for Biophotonic Applications

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(Invited Paper)

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Abstract: Optofluidics experienced significant developments in the past few years and is still proving to be a dynamic field of research with a particular focus on biological and chemical sensing applications. This paper reviews a selection of 2011 achievements concerning different aspects of the on-chip integration of photonics and microfluidics and, in particular, highlighting how the versatility and simple reconfigurability of the optofluidic approach can represent an added value in biophotonic applications.

Index Terms: Optofluidics, biophotonics, optofluidic sensor, optofluidic manipulation, lab-on-chip.

1. Introduction

Optofluidics defines a wide research field that is characterized by the synergic combination of optics and microfluidics; hence, the term can be applied either when light senses or modifies a fluid or when a fluid is used to define or tune the properties of a photonic device (e.g., laser activated fluids, liquid lenses or microfluidic microscope) [1], [2]. In biophotonic applications, the combination of microfluidics and optics is typically exploited to further increase the miniaturization of the devices toward an integrated optofluidic platform [3]. Such a platform would benefit from both aspects previously mentioned in the definition of optofluidics; on the one hand, small amounts of fluid can provide unprecedented reconfigurability of the photonic devices; on the other hand, the very high sensitivity of optical detection methods can provide relevant measurements even on small amounts of biological fluid samples (nano/picoliters), down to single molecule detection [4], [5]. Particular attention is dedicated to the integration of different functionalities on a single substrate to obtain a lab-on-chip microsystem that can address biochemical and biomedical assays in a cost-effective, miniaturized, and automated way. Here, we review a selection of results reported in 2011, by classifying them into four main areas of research: 1) lens-free optofluidic microscopes (OFMs); 2) fluidic tuning of photonic devices; 3) on-chip optofluidic sensors; 4) optofluidic micromanipulation of biosamples.

2. Discussion

One interesting research area concerns the development of low-cost lens-free imaging systems to replace the traditional bulky microscopes. The OFM is one such method [6], offering lens-less high-resolution imaging by using a suitable microfluidic flow to scan specimens across submicrometer

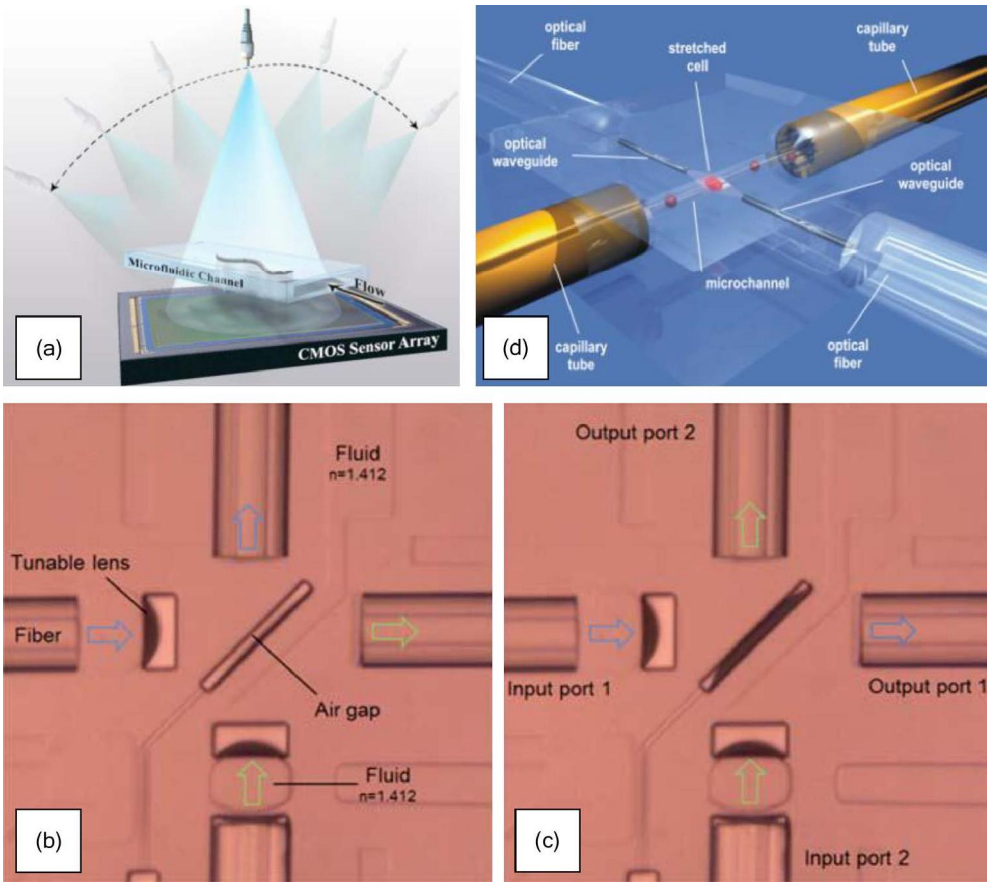

Fig. 1. (a) Schematic diagram of optofluidic tomographic microscopy setup [8] (courtesy of *Applied Physics Letters*). (b)–(c) Microscopy images of the pneumatically tunable 2 × 2 optofluidic switch for on-chip light routing controlled by compressed air, switching between exchange (b) and bypass (c) mode [14] (courtesy of Lab Chip). (d) 3-D rendering of the monolithic optical stretcher fabricated by femtosecond laser micromachining [25], [26] (courtesy of *Optics Express*).

apertures on a complementary metal–oxide–semiconductor (CMOS) image sensor. In 2011, a color imaging of blood samples to detect malaria has been reported [7]. Color illumination in a subpixel resolving OFM device yielded a resolution of 660 nm by using sequential red–green–blue (RGB) illumination to obtain a low-resolution sequence for each color and then combine them into a single high-resolution full-color image. A different approach has been reported in [8], [9] where the demonstration of optofluidic tomographic microscopy is shown. This on-chip tomographic imaging modality would be quite valuable for microfluidic lab-on-a-chip platforms where high-throughput 3-D imaging of the specimen is needed. A partially coherent light source is used to illuminate the objects flowing in a microfluidic channel directly placed on a digital sensor array. As sketched in Fig. 1(a) the light source is rotated to record lens-free holograms of the objects at different viewing directions. By capturing multiple frames at each illumination angle, pixel super-resolution techniques are utilized to reconstruct high-resolution transmission images.

A second important research area is that of fluidic tuning of optical components. In the past few years, there has been tremendous interest in the development of on-chip optical components such as lenses, mirrors, liquid waveguides, and light sources to be integrated with microfluidic components on a chip. As already mentioned, reconfigurability is a major advantage of optofluidics, where the optical properties of the device can be tuned by manipulating fluids. In [10], a novel method for building optofluidic microlenses with excellent flexibility, robustness, and simplicity has been reported. A compound microlens system is constructed with multiple lens elements self-aligned

together inside a monolithic polydimethylsiloxane (PDMS) microchip. The gas permeability of PDMS allows dead-end microchannels and microchambers to be completely filled with liquid, and the elasticity of PDMS ensures the deformation of thin membranes for tuning the lens. The tuning mechanism consists in discretely actuated pneumatic valves, integrated on-chip, which precisely adjusts the shape of the lenses. This method leads to high zoom ratio (7–8×), wide tuning of the angle of view (15°–80°), large range of focal adjustment (from mm to cm), high numerical apertures (up to 0.44), and small lens-size (a few hundreds of micrometers in diameter). Another important component for biophotonic applications, e.g., fluorescence and Raman spectroscopy, is an optical spectral filter. In [11], on-chip optofluidic filters have been reported, where multiple spectral regions with high and low transmissions are achieved by tailoring three bottom layers of a liquid-core antiresonant reflecting optical waveguide (ARROW). High extinction (37 dB) was shown, using 4-mm-long optofluidic filters. In traditional optical systems, a prism is typically used to change the optical path of a collimated light beam or to perform light dispersion. A tunable optofluidic prism, based on two laminar flow streams with different refractive indices in a microfluidic triangular chamber, has been presented in [12]. This optofluidic prism provides new features, as its capability to transform from a symmetric to an asymmetric prism with the assistance of a third flow, and it might be useful in several applications as, for example, the precise deflection of an optical beam inside an integrated lab-on-a-chip system. Active devices have also been reported in 2011, such as an optofluidic modulator [13] and an optofluidic switch [14]. This latter device could play a key role in a reconfigurable optofluidic chip where several photonic circuits and microfluidic networks could be integrated. The authors presented a pneumatically tunable 2 × 2 optofluidic switch for on-chip light routing controlled by compressed air. The optical switching is realized in a PDMS chip with a tunable air-gap mirror that deflects the light, due to total internal reflection, in the exchange mode. When the device is subjected to high pressure, the air gap collapses and hence the light is switched to the bypass mode, as shown in Fig. 1(b) and (c). The device has a switching speed of more than 5 Hz and an extinction ratio of 8 dB. This switch can be integrated with other microfluidic circuits, and the authors demonstrated a simple reconfigurable optical waveguide circuit for dual-channel spectroscopy on a microfluidic chip.

A third area, in which research on optofluidics for biophotonic applications produced fruitful results in 2011, concerns the realization of integrated optofluidic sensors on a chip. Because of the variety of possible sensing techniques in the biological and biochemical field, this area saw achievements both in the exploitation of new technologies to fabricate optofluidic lab-on-chip devices and in the development of improved label-free sensing techniques. As new fabrication techniques are concerned, very interesting results were obtained by femtosecond laser micromachining. This technology allows the fabrication of both optical waveguides and microfluidic channels, and their 3-D integration; it has, therefore, great potential for the realization of optofluidic devices, as demonstrated by several examples reported in this 2011 review [15]. Further results have also been reported in 2011, where this technology has been exploited to fabricate optical waveguides on a commercial lab-on-chip to detect fluorescence from electrophoretically separated DNA molecules with an ultralow limit of detection [16]; this result paves the way to point-of-care, fast, and sensitive bioassays for detection of genetic diseases. A second example is the fabrication of a lab-on-a-chip that works as a compact and robust device for fast screening, real-time monitoring, and initial classification of algae [17], which is of importance when monitoring effects such as eutrophication, but also when assessing the water quality of watersheds. Concerning label-free sensing techniques, in [18], optofluidic intracavity spectroscopy (OFIS) is exploited to distinguish different types of cells by their optical properties. OFIS sensor chip combine microfluidic cell handling and a Fabry–Perot cavity to acquire transmission spectra that are qualitatively and quantitatively different for neoplastic and non-neoplastic cells. Neoplastic cells produce multimode transmission spectra, while non-neoplastic cells create only weak transmission peaks between bare cavity modes. Another spectroscopic label-free technique that is of great interest in this field of research is surface-enhanced Raman scattering (SERS). In [19], the use of a highly sensitive optical imaging technology using SERS-fluorescence in a dual modal nanoprobe is reported. Fluorescence imaging is used as a fast indicator of molecular recognition, while SERS imaging is subsequently used to determine the signature of specific molecular interactions. In this way, they demonstrated the use of fluorescence

and SERS sensing probes for targeting and imaging specific cancer markers in living cells. One of the main limitations in microfluidic platform for SERS detection is that the metal nanoparticles, which work as the Raman enhancers, are dispersed in solution. In [20], a novel active SERS platform based on optoelectrofluidics is presented, in which metal nanoparticles are spontaneously concentrated and assembled within the laser spot by optically induced electrokinetic mechanisms, resulting in the *in situ* enhancement of the SERS signal. What is interesting is that both the metal particle concentration and the Raman signal can be obtained with a single laser beam. A different sensor has been reported in [21], where a new device for measuring on-chip microfluidic pressure and flow rate using integrated optofluidic membrane interferometers (OMIs) is shown. The device is made of two layers of structured PDMS on a glass substrate by multilayer soft lithography. The OMI consists of a flexible air-gap optical cavity which, upon illumination by monochromatic light, generates interference patterns that depend on the pressure. Once the interference patterns are captured with a microscope and computer analyzed on the basis of a pattern recognition algorithm, a dynamic range of 0–10 psi with an accuracy of $\pm 2\%$ is achieved. By exploiting two OMI sensors it is possible to measure the flow rate in a channel. The exploitation of this sensor might be useful when a real time monitor of the flow of biological liquid samples is needed.

Finally, because of the importance that single cell methods are assuming in unraveling biological complexity [22], it is worth mentioning the application of optofluidics to optical manipulation and analysis of single particles/cells dispersed in liquids. In biological research and clinical medicine the possibility of sorting specific target cells from a heterogeneous population is of great importance. Two devices for single cell sorting are presented in [23] and [24], both based on the combination of microfluidics with optical tweezers. In the first paper sorting is conditioned to cell size or fluorescence and performed by means of moving optical tweezers. In the second paper the optical tweezers are exploited to trap and perform Raman spectral analysis on the cell; the outcome of the measurement is used to sort the cell by switching the flow between two outlet channels. Despite the low throughput of the systems both devices proved to be effective in discriminating different types of cells and might be used in the future for sorting rare progenitor cell populations in regenerative biology or to discriminate between normal blood cells and circulating tumor cells. A different approach in handling and analyzing single cells by integrating both fluidics and optics has been recently shown in [25] and [26], where a dual beam laser trap fabricated by means of femtosecond laser micromachining has been successfully used to trap and stretch one single red blood cell at a time to evaluate its mechanical properties. A high-throughput system for single cell manipulation has been presented in [27]. This microfluidic PDMS system is composed of one main channel with cell-trapping pockets and drain channels that also collect the single-cell content. The sequence of single-cell trapping and content extraction has been demonstrated with a 512-pocket device. In the future, this device could be applied to the quantification of the molecular weight variability in organelles like mitochondria. Most of the optofluidic approaches in micromanipulation are based on traditional optical tweezing techniques, which have proven to be inadequate in direct application to the handling of nanoscale materials. To overcome this limitation a relatively new research field is growing concerning nanomanipulation by means of near field photonics. As reviewed in [28], a number of research groups have demonstrated how the evanescent fields surrounding photonic structures like photonic waveguides, optical resonators, and plasmonic nanoparticles can be used to greatly enhance optical forces envisaging the possibility of exploiting these techniques into lab-on-a-chip devices for single molecule analysis, nanoassembly, and optical chromatography.

3. Conclusion

Research in optofluidics saw significant activity in 2011 and a broad variety of biophotonic applications. Integration seems to be the main drive as well as the search for high-performance and cost-effective solutions. This highly interdisciplinary field is continuously growing every year and can help life sciences to have a tangible impact on our everyday life.

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