Biophotonics and Optofluidics Technology – Technical Analysis and Qualitative Review of the Novel Applications*

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Abstract

The subject of Biophotonics and Optofluidics has recently gained importance among the researchers working in modern optics. This paper presents the detailed technical analysis of the instruments based on the phenomena related with these interesting topics, besides discussing some important breakthroughs in the subject like – Uses in the Medical Field, and the Novel Energy generation Devices. The Mathematical Analysis of the Optical traps, and the image enhancement technique useful in in biophotonics and optofluidics has been discussed. Some of the recent novel investigations from the applications point of view, have also been qualitatively reviewed.

Keywords: Biophotonics, Optofluidics, Microfluidic Flow-Scanning Optical Tomography, Optofluidic Switch, Microfluidic Cytometry, Optofluidic Sensors, Subpixel Resolving Optofluidic Microscope.

Resumen

El tema de Biofotónica y Optofluidos recientemente han ganado importancia entre los investigadores que trabajan en la óptica moderna. Este artículo presenta un análisis técnico de los instrumentos basados en fenómenos relacionados con estos temas interesantes, además de discutir algunos avances importantes en el tema como - Uso en el campo de la medicina, y los dispositivos de generación de nuevas energías. Se ha discutido el análisis matemático de las trampas ópticas y la técnica útil de mejora de imagen en Biofotónica y optofluidos. También han sido revisadas cualitativamente desde el punto de vista de la aplicación, algunas de las recientes investigaciones.

Palabras clave: Biofotónica, Optofluidos, Tomografía óptica de digitalización de microfluidos, Switch optofluídico, citometría de microfluidos, Sensores optofluídicos, Resolución de microscopio de subpixel optofluídico.

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I. INTRODUCTION

Topics of Biophotonics and Optofluidics include among others the biomedical optics, laser medical diagnostics optical biopsy, and therapeutics. The optofluidics is mainly concerned with the bioanalytics and other photonic applications, biosensing and other related applications, including spectroscopic optical diagnostics like - diffuse optical imaging, steady-state and time-resolved fluorescence techniques. Fainman *et al*. [1] have written a detailed book on this subject because of the importance of the various related topics. In fact, Optofluidics [2, 3] refers to a research and technology area based on combining the advantages of microfluidics and optics, and has various applications including the displays, biosensors, lab-on-chip devices, lenses, molecular imaging tools and energy. Important sub topics of Optofluidics are: Waveguide and fiber opto-fluidics, Fluid and dynamics, Optical lab-on-a-chip and Flow measurement. In the same way, the Nano-biophotonics has subtopics like Bio-nanotechnologies, Plasmonics, Modelling of nanoscale structures, and Nanoparticles. Optofluidics: Fusion of Optics and Microfluidics. The Schematic of the Optofluidics Technology has been illustrated in the following figure:

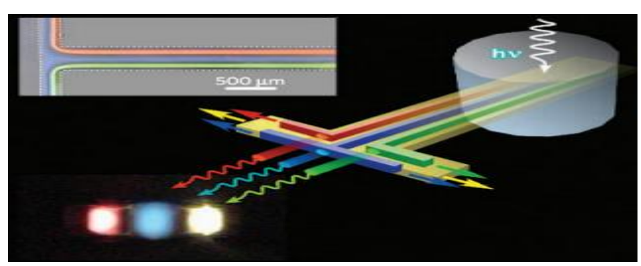

FIGURE 1. Schematic of the Optofluidics Technology (based on combining the advantages of microfluidics and optics), Figure courtesy Biophotonics Review.
http://biophotonicsreview.blogspot.in/2012/07/optofluidics-fusion-of-optics-and.html

Optofluidics is a technology area which combines the advantages of microfluidics, which is a multidisciplinary field combining engineering, physics, chemistry, biochemistry, nanotechnology, and biotechnology, with practical applications in designing of systems based on handling small volumes of fluids. This technology is used in the development of DNA chips, lab-on-a-chip technology, micro-propulsion, and micro-thermal technologies, and deals with the behavior, precise control and manipulation of fluids, which are geometrically constrained to a small, typically sub-millimeter scale. The systems in this technology have various characteristics like - small volumes (nL, pL, fL), small size, low energy consumption, and the effects of the micro domain. The subject of Biophotonics is mainly related with the topics - DNA chips, similar to a DNA microarray, in which a multitude of different capture agents, mostly monoclonal antibodies, are deposited on a chip surface; for determining the presence and/or amount of proteins in biological samples, e.g., blood. The technology is also used to study the Microbial behavior, because the ability to create precise and carefully controlled chemo attractant gradients, qualifies it as the ideal tool to study the motility, the ability to evolve and develop resistance to antibiotics in small populations of microorganisms, and in a short period of time. Another useful topic of this technology's applications is - Evolutionary biology, based on combining microfluidics with landscape ecology and nanofluidics, by which a nano/micro fabricated fluidic landscape can be constructed by building local patches of bacterial hábitat and connecting them by dispersal corridors, thereby studying the evolutionary ecology of the bacterial systems in the synthetic ecosystems, and thus resulting in using biophysics to get useful idea about the evolutionary biology. Another interesting topic of the application of this fast evolving technology is - Cellular biophysics, based on rectifying the motion of individual swimming bacteria, and using microfluidic structures to extract the mechanical motion from a population of motile bacterial cells.

Biophotonics deals with the study of the biological materials and is based on its relations and associations with various forms of radiant energy, including light (especially from lasers). The understanding of biophotonics is helping to create new medical tools e/g. medical imaging, and vitriol diagnostics. Its applications are so important, that huge developments are taking place in this technology. Its various applications in medical field are: (i) Development of the optical characterisation of diseases, by analyzing healthy and diseased samples, and also enabling the effect of the treatment in improving the diseases; (ii) Viewing and detecting the infectious diseases like – HIV (Human Immunodeficiency Virus) transmission; and (iii) Development of devices to diagnose and treat cancer related diseases, by using optical imaging and spectroscopy. Some of the Light Sources used in Biophotonics are: includes: Lasers and gas lasers, Fiber Lasers, Ultra-fast Lasers, Solid State Lasers, ps Lasers, Diode Lasers, Ultrachrome Lasers, Argon Ion Lasers, and Krypton Ion Lasers.

The applications of this evolving technology are in widely different areas like - bio-photonic fluorescence materials and techniques; optical coherence tomography; advanced biological endoscopy and microscopy; molecular imaging, photochemistry and photobiology; multi- and hyperspectral imaging; laser tissue interactions; laser surgery; optics in biotechnology; minimally invasive optical diagnostics; image reconstruction and processing; optical-system engineering for medicine; optical and photonic biosensors; photodynamic therapy; photoacoustic techniques; pathogen detection; optical tweezing and manipulation in biological or medical applications; optogenetics; lab-on-chip devices; on-chip imaging techniques; microfluidically tunable or reconfigurable optical and photonic systems; photonic crystals; optofluidic assembly and lithographic techniques; on-chip light and laser sources. This range of applications of the technology is drawing the interest of many researchers in this field.

II MASTHEMATICAL ANALYSIS

Some very important studies in biophotonics are based on Optical traps, which have become an important tool in the biological sciences because of their ability to manipulate microscopic particles. The various forms of optical traps, single-beam, two-beam, and levitating, have been used to manipulate objects such as viruses and bacteria, cells, chromosomes and DNA. Optical traps are formed because of the fact that each photon of light possesses momentum. The linear momentum flux of a photon is given by p= $\hbar\omega/c$, where $\hbar$ is the reduced Planck's constant, ω is the angular frequency of the light, and c is the speed of light. The total momentum flux of a laser beam with power P is p_z = P/c. Torques are applied by using light's angular momentum. Birefringent materials have a crystalline structure, and therefore, an anisotropic refractive index, which results in two different orthogonal indices of refraction and a polarization dependent phase delay, which is dependent on the wavelength of the light (wavenumber, kr), the ordinary and extraordinary indices of refraction, no and ne, and the thickness of the birefringent particle, d; and is obviously given by:

$$\Gamma = k_r d(n_0 - n_e). \quad (1)$$

A laser beam passing through a birefringent material of constant thickness experiences a torque due to the spin angular momentum, which is shown to be given by:

$$\tau = -\frac{\varepsilon}{2\omega}E_0^{\,2}\sin\Gamma\cos 2\phi\sin 2\theta + \frac{\varepsilon}{2\omega}E_0^{\,2}\{1-\cos\Gamma\}\sin 2\phi, \quad (2)$$

Where ε is the permittivity, E_0 is the electric field amplitude, ϕ is the ellipticity of the light, and θ is the angle between the fast axis of the quarter wave plate and the optic axis of the birefringent particle, with the assumption that the birefringent particles are of the uniform thickness. It has to be understood that the first term of Eq. (2) represents the torque applied to a particle by the linearly polarized portion of the light; and the second term the torque due to the circularly polarized portion of the light. Clearly, the particle undergoes a rotation only when the circularly polarized portion is larger than the linearly polarized portion, the maximum rotational rates occurring when the incoming laser is circularly polarized, i.e. $\phi=\pi/4$.

In practice, the trapped sphere (a) is << the wavelength of the trapping laser (λ), ands thus the conditions for Raleigh scattering are satisfied, and therefore the optical forces can be computed by treating the particle as a point dipole. In this case, the scattering force (F_{scatt}), which is due to the absorption and reradiation of light by the dipole; and the gradient force components are readily separated. For a sphere of radius a, F_{scatt} is given by:

$$F_{scatt.} = \frac{I_o \sigma n_m}{c}, \qquad (3)$$

where I_0 is the intensity of the incident light, n_m is the index of refraction of the medium, c is the speed of light in vacuum, m is the ratio of the index of refraction of the particle to the index of the medium (n_p/n_m), λ is the wavelength of the trapping laser, and σ is the scattering cross section of the sphere, given by:

$$\sigma = \frac{128\pi^5 a^6}{3\lambda^4}\{\frac{(m^2-1)}{(m^2+2)}\}^2. \qquad (4)$$

The gradient force is due to the interaction of the induced dipole with the inhomogeneous field, and its time-averaged value is given by:

$$F_{grad} = \frac{2\pi\alpha}{cn^2 m}\nabla I_o, \qquad (5)$$

where α is the polarizability of the sphere, given by:

$$\alpha = n^2 m a^3\{\frac{(m^2-1)}{(m^2+2)}\}. \qquad (6)$$

It has to be noted that the gradient force is proportional to the intensity gradient, and points up the gradient when m>1. An optical trap consists of a trapping laser, beam expansion and steering optics, an objective with high numerical aperture, a trapping chamber holder, and an arrangement for observing the trapped specimen. This is the reason that mostly, the optical traps are built by modifying an inverted microscope, which facilitates the introduction of a laser beam into the optical path before the objective. The working is quite simple - the microscope provides the imaging, trapping chamber does the manipulation, and objective is used for focusing.

The degree of the enhancement in the single molecule imaging in optofluidics can be calculated on the basis of the Fresnel equations, which describe the behaviour of light when moving between media of different refractive indices. The predicted reflection of light is called as Fresnel reflection.

An incident light striking the interface (at an angle θ_i, with the normal) between two media of refractive índices n_1 and n_2 at is split into two parts, the reflected ray and transmitted ray, making respectively the angles θ_r and θ_t, with the normal.

As the media under consideration are nonmagnetic, the reflectance R and transmittance T depend on the state of polarisation of light, which for the s-polarised light (light polarized with its electric field perpendicular to the plane containing the incident, reflected, and refracted rays) and p-polarised (light polarized with its electric field parallel to the plane containing the incident, reflected, and refracted rays) are given by the well known Fresnel Equations:

$$R_s = \left|\frac{n_1\cos\theta_i - n_2\cos\theta_t}{n_1\cos\theta_i + n_2\cos\theta_t}\right|^2 = \left|\frac{n_1\cos\theta_i - n_2\sqrt{1-\left(\frac{n_1}{n_2}\sin\theta_i\right)^2}}{n_1\cos\theta_i + n_2\sqrt{1-\left(\frac{n_1}{n_2}\sin\theta_i\right)^2}}\right|^2, \qquad (7)$$

and

$$R_p = \left|\frac{n_1\cos\theta_t - n_2\cos\theta_i}{n_1\cos\theta_t + n_2\cos\theta_i}\right|^2 = \left|\frac{n_1\sqrt{1-\left(\frac{n_1}{n_2}\sin\theta_i\right)^2} - n_2\cos\theta_i}{n_1\sqrt{1-\left(\frac{n_1}{n_2}\sin\theta_i\right)^2} + n_2\cos\theta_i}\right|^2, \qquad (8)$$

Where R_S and R_P are the reflectances respectively for the S-polarized light and P-polarised light. As a result of the conservation of energy, the respective transmission coefficients (T_S and T_P) are given by

$$T_s = 1 - R_s, \qquad (9)$$

and

$$T_p = 1 - R_p. \qquad (10)$$

However, in case of the unpolarised (containing equal amounts of the of *s*- and *p*-polarisations) light, the reflection coefficient is just equal to the mean of R_S and R_P.

III QUALITATIVE REVIEW OF THE RECENT IMPORTANT INVESTIGATIONS ON THE BIOPHOTONI|CS AND OPTOFLUIDICS AND THE CONCLUDING REMARKS

The importance of this fast evolving field can be judged from the fact that during the last five years or so, a number of good books [4, 5, 6] and chapters [7, 8] have been written covering the various aspects of the technology. Srinivasan [4] has brought out a very useful book on the latest advances in vibrational spectroscopic biomedical imaging, which includes chapters written by expert spectroscopists. This book discusses recent progress in the field in areas such as instrumentation, detector technology, novel modes of data collection, data analysis, and various biomedical applications, besides describing the IR imaging techniques, including transmission reflection, transflection, and attenuated total reflection (ATR) imaging, and Raman imaging. The efficient use of vibrational spectroscopy in clinical applications has also been emphasized in this state-of-the-art guide. In addition, this book gives useful information about the Automated breast histopathology using mid-IR spectroscopic imaging, Synchrotron-based FTIR spectromicroscopy and imaging of single algai cells and cartilage, Preparation of tissues and cells for infrared and Raman spectroscopy and imaging Evanescent wave imaging, FTIR, Raman, and surface-enhanced Raman spectroscopic imaging of fungal cells, Widefield Raman imaging of cells and tissues Resonance Raman imaging, and quantification of carotenoid antioxidants in the human retina and skin Raman microscopy for biomedical applications-efficient diagnosis of tissues, cells, and bacteria.

Yang *et al*. [5] have written E-book, which is a book to help the librarians for sorting out some of the issues surrounding this technology. The book - Optofluidics: Fundamentals, Devices, and. Applications, has assembled a group of contributors to offer a comprehensive introduction. The book has important chapters on school, public, and academic libraries; and e-book acquisitions and management. One chapter explores the various standards that now exist and what changes need to be made, and the final chapter is on the future of Academic Book Publishing. Lee [6] has emphasized that Biofliudics has gained in importance in recent years, forcing engineers to redefine mechanical engineering theories and apply them to biological functions. This book is one of the first books to take an interdisciplinary approach to the subject, combines engineering principles with human biology to deliver a text specifically designed for biomedical engineering professionals and students.

Wu and Jamshidi [7] have discussed that Optofluidics is the integration of optical and microfluidic systems to achieve novel functionalities.like - the manipulation, assembly, and patterning of objects of interest in a microfluidic environment. They have also emphasized that the recent advances in nanophotonics have introduced exciting methods for biological and chemical sensing with single molecule sensitivities, and have therefore, suggested that the integration of nanophotonic sensors with optofluidic manipulation platforms is essential for sensing and monitoring of single cells and other biomaterials. Mönch and Zappe [8] have written a chapter, which covers the use of microsystems in biophotonics applications., and also includes a brief overview of the most relevant interactions between light and biological samples, followed by the consideration of the biophotonics areas, such as microimaging, sensors, flow cytometry, and microfluidic biochips, in which microsystems play a significant or increasing role.

The fields of Microfluidics and Lab-on-a-Chip Technology: Fabrication and Microfluidics have also been discussed and described in detail in the books [9, 10] The recently increasing interest in the medical applications of the field has resulted in the publication of important review papers [11, 12], which cover the drug research and diagnostic devices. The application of various branches of physics in medical field has recently been increasing. Chopra [13, 14, 15, 16] has discussed in detail the Biomedical Applications based on Spintronics; the Plasma Treatment for Biomedical Applications and use of lasers in surgery. In this direction, some important studies [17, 18, 19, 20, 21, 22, 23] on the use of this technology in medical field have recently been made. A Photonics Global Conference [24] with emphasis on the research papers connected with the topical areas including Optofluidics and Biophotonics, was recently held, in which the biophysical, biochemical and biomedical applications were considered and discussed in detail by various researchers.

It is well understood that the development of the Optofluidic devices is very important, from the point of view of drawing the benefit from other techniques, including liquid crystals in microfluidic channels. It is expected that the optofluidics should have far-reaching consequences like – (i) the on-chip nanofabrication factory taking advantage of the various control techniques as the optical tweezers to build molecular constructions in a fluid environment; and (ii) the photonic integrated circuit, for reconfiguring the optical components with on-chip fluidics. It is clearly understood that such multitasking devices might become possible through a combination of optical devices, which are based on the use of the fluidics for the reconfigurability purpose. In this direction, mention can be made of the optofluidic microscope, which shows promise as a single-task device, but it is necessary to combinine it with other devices to draw maximum potential. Efforts are in progress to combine optics and fluidics with other lab on chip techniques like - electric, mechanical, and thermal. The integration of optics and fluidics on-chip is expected to be developed as a technique for creating new possibilities for tunable microscale devices.

A very novel application of optofluidics is for the possible solution of the challenge of the energy problem. Efforts are being made to use Optofluidics, for the delivery of fluids through extremely small channels or tubes. It is believed that with precision design and nano- and microtechnology – optofluidics can be used very efficiently for providing the solutions for the solar fuel generation. It has to be noted that the term solar fuel refers not just to the photovoltaics, but in addition to the conversion of energy from the sun into fuel to power the systems requiring electricity e.g. the conversion of water and carbon dioxide into methane in large industrial biofuel plants. The solar fuels are generated by the mechanisms including photocatalysis and biofuels, the former being the interaction of light with nanoparticles or materials deposited on the surface of a reactor, resulting in encouraging the chemical reaction for the generation of the fuel. It has been established by Erickson *et al*. [25] that by directing light and concentrating it where it can be most efficiently used, can greatly increase the efficiency of the existing energy-producing systems, and also lead to the innovation of some new forms of energy production, They have been designing and fabricating the systems , which use solar radiation for water purification and for indoor lighting during the daytime, in which case, a Fresnel lens-type solar collector array is used to collect and focus sunlight directly into the optical fibers. In this way, by coupling sunlight to a guiding element, the light is channeled to otherwise inaccessible areas, especially for the indoor illumination. After channeling the sunlight inside, it is directed to the ceilings of office spaces, and the indoor solar panels, and in this way by using the sunlight to drive an indoor solar panel leads to the panel being protected from the elements and thus lasting last longer. Already, some success has been achieved by the group, in the development of a tunable optofluidic solar concentrator and optofluidic switch, which are the core parts of an optofluidic solar lighting system. The schematic of the concentration of the sunlight and then it's coupling into the fibers by the optofluidic solar concentrator panel installed on the roof of the building and adaptable to the position of the sun, is shown below:

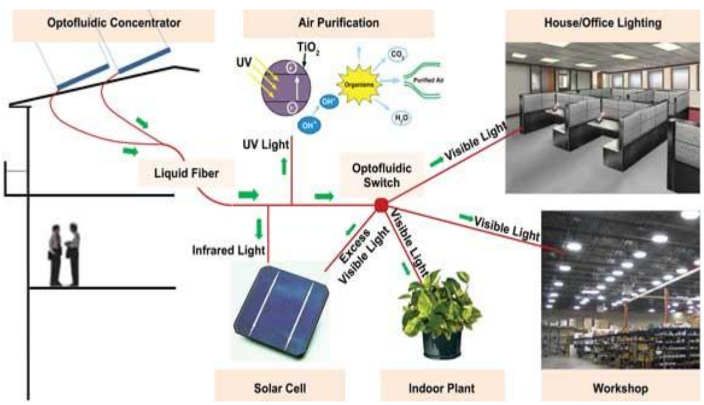

FIGURE 2. Novel proposal of the solar lighting system, composed of an optofluidic solar concentrator, optical fibers in the form of polymer core or liquid core, an optofluidic switch, and the optical lighting terminals. Figure courtesy EPFL.

It is clear that these components constitute a reconfigurable optofluidic illumination network. Another point to be noted is that in this arrangement, the infrared portion of light is separated and directed into the infrared photovoltaic solar cell, while the ultraviolet portion is extracted and used in place of the UV lamp for air purification during the daytime. The residual visible part of the sunlight is finally directed into each room for interior illumination. In this system, the light flow is dynamically controlled by the tunable optofluidic switch, and so the excess visible light can be used to generate electricity by the photovoltaic solar cells. Thus, it is clear that the directltransportation of the sunlight for indoor lighting is a unique and efficient way to conserve energy, and could be much more effective than photovoltaic technology.

Another good effort in this direction is that of the researchers of Cinninati University, who have been able to convert solar energy into biofuels. By performing tests on semitropical frogs, and by using the solar energy and carbon from air, they have been able to make sugar, and it has been emphasized that these sugars can be further transformed into new biofuels, in the direction of fulfilling the promise of nanotechnology. The principle of conversion of solar energy into biofuels has been shown below:

FIGURE 3. Illustration of the principle of conversion of solar energy into biofuels. Figure courtesy University of Cinninati. USA.

Thus, it is a novel way to use solar energy to supplement non-renewable resources. However, in such a system, it is necessary to deviate from the secondary devices like the air filtrage and solar panels so that a comfortable constant light source is maintained for ceiling lighting, so that it is not affected by the flickering of the light source due to a temporary factor, e.g. the cloud passing over the system. These different channels can be modulated to maintain a constant light source, a system using electrowetting can be employed to deviate light from one channel into another quite easily. If a droplet of water is made to sit on the outer surface of light tube, a small current excites the ions in the water, and pushes them to the edge of the droplet, and leads to its expansion just enough for it to touch the surface of another tube. Clearly, this expanded droplet then creates a light bridge between the two parallel light tubes, and thus effectively moderates the amount of light streaming through each. However, as explained by David Erickson, professor at Cornell University and visiting professor at EPFL, there is a real challenge before this technology can be used on a larger scale, as the problem to be encountered is to maintain the precision of nano and micro light and fluid manipulation, while creating the industrial sized installations large enough to meet the population's energyrequirement," explains David Erickson, professor at Cornell University and visiting professor at EPFL. The up-scaling optofluidic technology requires the integration of many liquid chips to create a super-reactor, on the lines of the building of a super computer by small small elements, which is really a tough problem. Another point to be taken care of while designing such reactors is that the most reactions in liquid channels take place at just the point of contact between the liquid and the catalyst-lined tubes, and hence the efficiency of a system depends on the availability of the surface area for the reactions.The real advantage of the technology is that Scaling down the size of the channels to the micro and nano level implies that thousands more channels can be arranged in the same available space, and thus greatly increasing the overall surface area, and consequently leading to a radical reduction of the size needed for catalytic and other chemical reactions, while finally reducing the cost. In this way, by adding a light source as a catalyst to the directed flow of individual molecules in nanotubes, we can have extreme control and high efficiency. It has been suggested that there are many possibilities for up-scaling the optofluidics, including the use of the optical fibers for transporting sunlight into large indoor biofuel reactors with mass-produced nanotubes. Also, it has been emphasized that the use of smaller spaces increases the power density, and reduces the operating costs; and at the same time offering the flexibility when concentrating and directing sunlight for solar collection and photovoltaic panels; and increasing surface area, and consequently, the reducing the use of surface catalysts, which are the most expensive element in such systems.

Optofluidics is quite a newly evolving field, though growing rapidly to prove useful for the applications from analysis of biomolecules and cells to creation of novel optical switches and lasers. Most of the progress made in this field, has been during the last decade, after the two related fields – microfluidics and nanophotonics – have reached the peak of their technology development. Many new technologies are quite mature at the lab scale, and the next step is obviously to develop them for practical large-scale applications. At Cornell, the researchers have designed and developed [26] a microscale optofluidic device which can measure the optical absorption in color-producing enzymatic reactions for biochemical analysis. It has been reported that this device employs cavity-enhanced laser spectrophotometry to probe analytes in a microfluidic channel with silicon nitride microring resonators. It has been discussed that the device has been used by many researchers as the refractive index sensors for measuring the binding events on the surface of a waveguide, and that these devices are based on measuring the shift in resonance wavelength of a microcavity, though this shift can result by the nonspecific binding or even by the thermal fluctuations. This device is capable of performing the cavity-enhanced on analytes in a microfluidic channel with microring resonators. The device consists of an array of such resonators within a microfluidic channel, and the rings, which are sensitive to the colour changes produced in the microchannel by the enzymes being tested.

It is of great significance to know that the researchers have shown that the unique spectral signature of the analyte can be measured, thus eliminating the need to alter the surface of the ring to facilitate the binding of specific biological targets. They have achieved this by using high-quality factor microcavities with high-index contrast materials. It has been explained that the Low losses in the cavities allow the light to propagate many times around the circumference of the ring, and thereby increasing the effective optical path length of the device. The researchers in the University of Alberta in Edmonton, Canada are engaged in using the optofluidic technology for developing the next generation portable cytometers for point-of-care and other applications. Presently available flow cytometers are in the form of the complex systems based on using multiple lasers and detectors, which are not only expensive but also quite bulky. The emphasis is on compressing the light excitement and detection system in the existing cytometers. This microscope-based label-free microfluidic cytometer is capable of differentiating the normal cells from cancerous cells, through analysis of the 2-D light-scattering patterns.

Another important research work reported [27] is that a microscope-based label-free microfluidic cytometer can serve as a prototype for point-of-care clinical applications. It has been discussed that the system allows the non-imaging observation of single cells, and enables the differentiation of normal cells from the cancerous cells, on the basis of analyzing the 2-D light-scattering patterns, made possible by incorporating a microscope objective into the cytometer which, in defocusing mode, functions in a way, that is contrary to how these objectives are normally used. It has been emphasized that the numerical aperture of the optical objective improves the signal-to-noise ratio of the light-scattering detection, and hence enables the system to obtain the patterns from platelets, the smallest mature human blood cells.

It is now understood that the Optofluidic technology is believed to provide a breakthrough for the currently underlying problems in microfluidics and photonics/optics by complementary integration of fluidics and photonics, and the key aspect of the optofluidics technology is based on the use of fluidics for tuning the optical properties and addressing various functional materials inside of the microfluidic channels, which have built-in photonic structures. It is also clear that through the optofluidic integrations, fluidics technology enhances the controllability and tunability of the optical systems. In particular, the colloidal dispersion gives novel properties such as photonic band-gaps and enhanced Raman spectrum that conventional optofluidic devices cannot exhibit. Lee *et al*. [28] have reviewed the state of the art of the colloidal dispersions, especially for the optofluidic applications. It has been discussed that from isolated singlet colloidal particles to colloidal clusters, their self-organized assemblies lead to optical manipulation of the photonic/optical properties and responses. Also, the prospects of the integrated optofluidics technology based on colloidal systems have been highlighted.

Recently, a high level conference [29] was held, which featured advances in biophotonics and medical technology, especially useful for quicker diagnosis and more efficient therapies. Microfluidics and optofluidics have revolutionized high-throughput analysis and chemical synthesis during the last decade. The Single molecule imaging has also progressed a lot, because of its capacity to reveal heterogeneities at high spatial and temporal resolutions, which, however, are dependent on the signal to noise ratio (SNR) of the image. Vasdekis and Laporte [30] have reviewed how the SNR can be enhanced in optofluidics and microfluidics, and have outlined the integrated photonic structures, which increase the signal emitted by single chromophores, and minimize the excitation volume. They have also reviewed the compatible functionalization strategies that reduce noise stemming from non-specific interactions and architectures which minimize bleaching and blinking. For the development of the nanophotonic devices for spectroscopy applications, the optofluidic technologists are engaged in trying to integrate more functionality (electrical, pneumatic, etc.) needs and thus develop stand-alone devices. Such work has progressed in the Shandong University, Jinan, China. Many important diagnosis and detection tests can be performed by using the optofluidic microscope developed by Zheng and his colleagues, shown below:

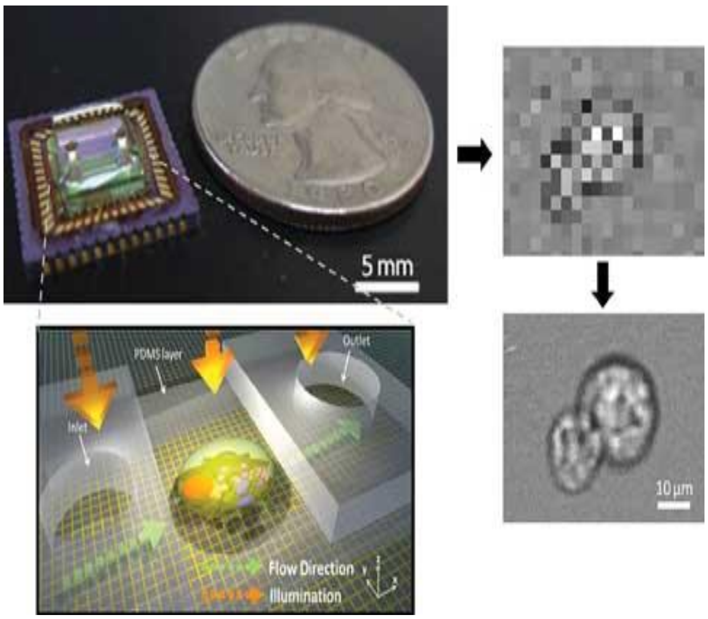

FIGURE 4. The subpixel resolving optofluidic microscope designed by Zheng Guoan, Figure courtesy Zheng Guoan, California Institute of Technology in Pasadena, USA.

The microscope is based on using the oversampling in the time domain to compensate for undersampling in the spatial domain; made possible by applying a superresolution algorithm, the basic principle of this image-enhancement technique being getting one high-resolution image from several low-resolution images. Also, the work is progressing on implementing a new, more robust version using glass-based microfluidic channels integrated at the wafer level. The research groups are trying to incorporate additional imaging modalities onto the current platform, including dark-field and phase imaging capabilities. Use can also be made of the transmission increasing thin films [31] coated by dual ion beam sputtering unit for increasing the image contrast. The subpixel resolving optofluidic microscope microscope has the potential of contributing to a number of point-of-care applications, including improved diagnosis of malaria and detection of blood-borne and water-borne parasites. On the basis of all these very important novel investigations, it can be safely concluded that the Biophotonics and Optofluidics Technology is progressing and evolving fast, and is also on a firm footing.

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