Disposable integrated microfluidics with self-aligned planar microlenses

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Abstract

Design, fabrication, and characterization of the disposable integrated microfluidic devices with self-aligned planar microlenses for the applications of bioanalytical system are described. The development of the polydimethylsiloxane (PDMS)-based disposable integrated microfluidics is realized by the monolithic integration of self-aligned two-dimensional (2D) planar micro-optics with microfluidic chips. The disposable integrated microfluidics with self-aligned planar microlenses allows increasing sensitivity of the device and reducing time-consuming optical alignments. The optical detection of the chips is based on the orthogonal arrangement of excitation light source via integrated 2D planar microlenses onto the microfluidic channel and the collection of fluorescent emission. It provides an effective detection mechanism with increased signal-to-noise ratio and a simple ‘lab-on-a-chip’ platform with light emitting diodes (LEDs) as excitation sources and photodiodes as detectors. The 2D compound microlenses of the disposable integrated microfluidic devices promise minimized optical aberration, amplified fluorescence, and self-alignment of the micro-optical components of the bioanalysis systems. The disposable integrated microfluidic devices with self-aligned planar microlenses can be used effectively as low-cost, rapid, and sensitive diagnostic chips. © 2003 Elsevier B.V. All rights reserved.

Keywords: Integrated biophotonic chips; Integrated microfluidics; Fluorescent biosensor; Planar microlens

1. Introduction

Various miniaturized systems for analytical chemistry have been developed and demonstrated since the concept of micro total analytical systems (μTAS) was proposed [1]. The goal of the μTAS is to create miniaturized lab-on-a-chips with autonomous functions of analysis in genomics, proteomics or other related fields. With the advanced technology of microfabrication, various functional components are integrated into the μTAS. Recently, the integration of micro-optical components has been demonstrated. Microlenses [2–4], waveguides [5,6], and detectors [7,8] are coupled with the microfluidics in order to accomplish laser-induced fluorescence detection (LIF) in the μTAS, which has been preferred because of its sensitivity and simplicity [9–12]. The waveguides that are in plane with microfluidic channels are used to transport excitation light to the microfluidic channels, combined with optical fiber couplings. The microlenses on microfluidic channels were used to focus an excitation light source onto the microfluidic channel [13]. However, they have optical aberration, complex fabrication processes, optical misalignment problems to the microfluidic channels, and low controllability of lens shapes and configurations.

Unlike conventional integrated microlenses, a new integration method using the two-dimensional (2D) planar microlenses is adopted to amplify fluorescent signals in the microfluidic channels by focusing the excitation light through compound microlenses without any additional optical fiber coupling. Since the planar microlenses are fabricated simultaneously with the microfluidic channels and parallel to the plane of the device, it is possible to self-align the microlenses to the channel and to make the compound configurations of the microlenses, which allow less aberration than single microlens. The minimization of optical aberration and the precise self-alignment of the microlenses permit fluorescent amplification with a pre-aligned excitation source and detector. The development of the polydimethylsiloxane (PDMS)-based integrated optical microfluidic devices using a low-cost molding technique also maximizes disposability of the devices.

This paper presents the disposable integrated microfluidic devices with self-aligned planar microlenses for fluorescence amplification by the 2D planar microlenses.
The disposable integrated microfluidic device can be used effectively as low-cost, rapid, and sensitive diagnostic chips utilizing optical functions. The versatile designs of the disposable polymer bio-microelectromechnical system (BioMEMS) will provide a new method of integrating self-aligned optical systems and detecting fluorescent signals for biochemical analysis and point-of-care systems.

2. Design of integrated microfluidics

The disposable integrated microfluidics adopt new features of planar micro-optical components beside the microfluidic channels as shown in Fig. 1a. The planar microlenses are fabricated in the same plane of microfluidic networks. The optical axis of the planar microlenses is parallel to the main plane of the devices. The planar microlenses have several advantages such as minimized optical aberrations, simplified fabrication process, and self-alignments to microfluidic channels. In addition, they can be directly coupled to an excitation source without using any additional optical fiber.

By using optical ray tracing methods for the optical simulation, the single microlens and compound microlenses are compared in Fig. 2. The refractive index of PDMS, 1.38 [14] is used in this optical simulation. The dimensions of the microlenses are shown in Table 1. The simulations show that single spherical microlens has large spherical aberration while compound microlenses have less as expected. However, it is difficult to form the desired compound microlenses with the conventional techniques [2–4] since it requires multi-layer structures of microlenses. Even though a few lenses can be stacked, optical alignment of each lens is another barrier for the integration of the compound microlenses. Lens types, focal length, and distance of each microlens must be also exactly controlled in order to minimize...
Fig. 2. Comparison of optical simulation results for single microlens and compound microlenses: a single microlens (a) shows more spherical aberration than compound microlenses (b). (c) Point spread function of each design at middle point of the channel.

Table 1
Dimensions of the planar microlenses

<table>
<thead>
<tr>
<th></th>
<th>Compound lenses</th>
<th>Spherical lens</th>
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<tbody>
<tr>
<td>First lens</td>
<td></td>
<td></td>
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<tr>
<td>First surface</td>
<td>Curvature</td>
<td>900</td>
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<tr>
<td>Aperture radius</td>
<td>500</td>
<td>500</td>
</tr>
<tr>
<td>Second surface</td>
<td>Curvature</td>
<td>∞</td>
</tr>
<tr>
<td>Aperture radius</td>
<td>500</td>
<td>500</td>
</tr>
<tr>
<td>Thickness at the center axis</td>
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<td>1400</td>
</tr>
<tr>
<td>Distance to second lens</td>
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<td>NA*</td>
</tr>
<tr>
<td>Second lens</td>
<td></td>
<td></td>
</tr>
<tr>
<td>First surface</td>
<td>Curvature</td>
<td>1000</td>
</tr>
<tr>
<td>Aperture radius</td>
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<td></td>
</tr>
<tr>
<td>Second surface</td>
<td>Curvature</td>
<td>∞</td>
</tr>
<tr>
<td>Aperture radius</td>
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<td></td>
</tr>
<tr>
<td>Thickness at the center axis</td>
<td>300</td>
<td></td>
</tr>
<tr>
<td>Distance to third lens</td>
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<td></td>
</tr>
<tr>
<td>Third lens</td>
<td></td>
<td></td>
</tr>
<tr>
<td>First surface</td>
<td>Curvature</td>
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</tr>
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<td>Aperture radius</td>
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<td></td>
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<tr>
<td>Second surface</td>
<td>Curvature</td>
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<tr>
<td>Aperture radius</td>
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<tr>
<td>Thickness at the center axis</td>
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<td></td>
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</table>

* The unit is μm.
* Not applicable.
* Negative curvature means a concave lens while positive curvature means a convex lens.
Fig. 3. Fabrication process of disposable integrated microfluidic optical systems and a fabricated device: (a) Si substrate, (b) photolithography process, (c) deep-reactive ion etching to make a mold, (d) PDMS molding, and (e) O₂ plasma treatment and bonding to a pre-cleaned glass substrate.

Unlike microlenses vertically integrated onto microfluidic devices, the planar microlenses and microfluidic channels, which are self-aligned initially at the design, are fabricated in the same step of the fabrication process. The lens types and dimensions of the planar microlenses are designed and combined together in order to compensate aberration and then the planar microlenses are fabricated as exactly designed using surface micromachining techniques. Since the integration of the planar microlenses does not need multi-layer process, the fabrication steps for the disposable integrated optical microfluidics are simplified and the process cost is minimized. The channels and the planar microlenses are disposable while the LED and detector remain as fixed components in μTAS.

3. Experimental

The disposable integrated microfluidic devices with self-aligned planar microlenses are fabricated by using PDMS (Sylgard 184, Dow Corning) as shown Fig. 3. First, a mold of Si is prepared using a deep reactive ion etching (DRIE) method. A 2 μm thickness photore sist layer is coated and patterned for an etching mask layer. The photo-patterned substrate is etched up to 110 μm depth by DRIE. After the mask layer is removed, liquid PDMS pre-mixed with 10:1 volume ratio of a base and curing agent is evenly coated on the mold. It is cured thermally at 70 °C.

Fig. 4. SEM images of fabricated devices: (a) single-lens type of the 2D planar microlens and (b) compound microlenses.

Fig. 5. Spectra of LED (a) with 0 and 90° angles between the detector and LED and (b) with 0, 1, 2, 3, 5 and 8 mm offset from an optical center axis, the applied voltage to the LED is 2.7 V and the distance from the LED to the spectrometer is 40 mm and the medium between the LED and spectrometer is air.
for 1 h. Each device is detached mechanically and treated by O₂ plasma for hydrophilic surfaces. The treated devices are bonded to pre-cleaned glass substrates. The scanning electron microscopy (SEM) images of fabricated devices are shown in Fig. 4.

After a disposable unit consisting of microfluidic networks and optical components is placed under the detector, the excitation light is introduced to the system from a side of the system and is focused into samples in the channel through the planar optical systems. The emitted fluorescence signal is detected from the top of the channels. This orthogonal arrangement of excitation source and detector is schematically illustrated in Fig. 1b. As an excitation source, a blue light emitting diode (LED) is used (Hosfelt®, peak wavelength 466 nm). The range of the applied voltage is 3.5–3.7 V. An objective lens, a charge-coupled-devices (CCD) camera, and a spectrometer are used in order to analyze the fluorescent signals by two different methods; one is spectrum and the other is optical images. The excitation by the LED is characterized using 40 nm fluorescence nanospheres (Flurosphere®, 505 nm excitation/515 nm emission) in the channel of 150 μm (width) × 110 μm (depth).

The original fluorescent solution of 5% solid concentration is diluted with deionized water. All solutions are kept in the dark at low temperature before experiments.

4. Results and discussion

The spectrum of LED has a wide range of bandwidth as shown in Fig. 5a, which had made lasers the preferred fluorescent excitation source. The intensity at 515 nm, which is close to the wavelength of the fluorescent emission, is 34.5% of that at 505 nm. If the intensity around 515 nm from LED is larger than the intensity of the fluorescent emission, the fluorescent emission signal can not be distinguished. However, by using the orthogonal optical path, the noise from LED can be largely avoided. As shown in Fig. 5a, the spectrum of LED measured with 90° angles to LED does not show any peak since LED excitation light can be minimized to the detector. After exciting the fluorescence, the incident light passes into the other side of the device and then the emitted fluorescent signals are detected with less noise. The intensity of LED also has a spatial distribution as shown in Fig. 5b. With 1 mm offset from an optical axis, the intensity of an excitation light decreases by 8.4%. If the planar microlenses are aligned within 1 mm precision to an optical center axis of LED, the reduction of fluorescent signals will be less than 8.4%. The excitation power of the LED coupled into the compound microlenses is measured with a digital optical power meter (Newport® 1830-C, 818-SL detector). At 40 mm from the LED, the power of excitation light at 466 nm through the compound lens is 4.15 ± 0.0590 μW with 3.7 V of the applied voltage, while the power through the single lens is 2.63 ± 0.0720 μW. With 3.5 V of the applied voltage, the powers through the compound lenses and the single lens decreased to 2.65 ± 0.0277 μW and 1.82 ± 0.0766 μW, respectively.

Fig. 6 shows the spectra of the fluorescent signals captured on the top of the microfluidic channel while the different concentration of fluorescent nanospheres and water in the microfluidic channel are excited by LED light passing through the planar microlenses. The applied voltage to the LED is 3.7 V and 1.5, 0.5, and 0.05% solid...
concentrations of the fluorescent nanosphere are used. Equivalent fluorescein molar concentrations of 1.5, 0.5, and 0.05% solid concentration of the nanosphere samples are $2.39 \times 10^{-4}$ M, $7.98 \times 10^{-5}$ M, and $7.98 \times 10^{-6}$ M, respectively [15]. The spectrum consists of two major peaks at 466 and 515 nm. The first signal with relatively small peak at 466 nm comes from the LED and the second peak at 515 nm from the fluorescent signals. The intensity at 466 nm is around four times less than the intensity at 515 nm in the measurement for 1.5% solid concentration of the fluorescent nanospheres. The intensity of the excitation light should be initially much larger than the intensity of the fluorescence emission. However, the intensity of excitation at the detector is smaller than the intensity of the fluorescence emission in the orthogonal arrangement of the excitation source and detector. Therefore, the S/N ratio is

![Fig. 7. CCD images of fluorescent emission excited through single microlens and compound microlenses: (a) fluorescence excitation through microlenses by LED, (b) intensity profile of focused beam through microlenses, and (c) fluorescence amplification by the NA planar microlenses. (b, s, and c denotes ‘without microlenses’, ‘with single microlens’, and ‘with compound microlenses’, respectively).](image-url)
increased by the orthogonal arrangement. Even though the excitation light does not reach the detector basically, those peaks around 466 nm of each spectrum are the scattered excitation light from the fluorescent nanospheres and the PDMS surface.

The optical fluorescent images are taken by the CCD camera and filter with the same excitation light. The captured images are analyzed using Matlab™ to measure the light intensity of the images. The intensity of light is automatically scaled from 0 (dark) to 255 (bright). The applied voltage to the LED is 3.5 V and 1% solid concentration of the fluorescent dye is used. The fluorescent images are captured with 500 ms of exposure. The microfluidic channels of 110 μm depth are placed 40 mm away from LED. The planar compound microlenses make a focused beam with minimized aberration as expected while the planar single microlens makes a dispersed beam as shown in Fig. 7a and b. As discussed in Fig. 2, the single planar lenses have more spherical aberration than the compound planar microlenses. This spherical aberration causes the dispersed fluorescent beam profile. Fig. 7c shows the amplification of the fluorescent intensity by the planar microlenses by comparing the maximum fluorescent intensity in each condition. Since the compound microlenses effectively collect and focus more excitation light on the channel without optical aberration, the fluorescence intensity increases up to about seven times more than that without microlenses. Compared with single lenses, the design of the compound microlenses increase about four times more because they have less optical aberration as expected. Since higher NA planar lenses can focus more excitation light, more amplification of fluorescent signals is expected.

5. Conclusion

The disposable integrated microfluidic devices with self-aligned planar microlenses are successfully demonstrated for LED-based fluorescence amplification, using new integration methods of the planar micro-optics. The planar lenses are integrated with microfluidic networks and fabricated together so that they enable several advantages such as disposability, controllability of optical characteristics, self-alignment, simplified fabrication process, increased S/N ratio and removal of additional couplings for optical fibers. The fluorescent signal of the planar lenses is amplified about seven times more than that without the lenses. This new approaches to integrating planar optical components with microfluidics will be able to advance the performance of μTAS.

Acknowledgements

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References

[14] Private communication with Dow Corning Corporation.

Biographies

Jongji Seo received his BS and MS in physics at Yonsei University, Korea. He researched thin-film growth in ultra-high vacuum. In 1999, he joined Samsung Electronics Inc. as an engineer of process development.
He has been working towards his PhD degree in Applied Science and Bioengineering, University of California at Berkeley, USA since 2000. His research includes integrated microfluidic optical systems and cell dynamics using the technologies of microelectromechanical systems.

Luke P. Lee is assistant professor in the Department of Bioengineering and Co-Director of Berkeley Sensor and Actuator Center at UC Berkeley. He received both his BA in biophysics and PhD in applied physics (major)/bioengineering (minor) from UC Berkeley. Prof. Lee has more than 10 years of industrial experience in integrated optoelectronics, holographic lithography, high-power surface emitting laser diodes, Superconducting Quantum Interference Devices (SQUIDs), and magnetic biosensors. At Berkeley, he has developed polymer-based BioMEMS. His current research interests are integrated biophotonic devices, bio-polymer-opto-electro-mechanical-systems (BioPOEMS) for lab-on-a-chip, Nano-POEMS for single molecule detection and manipulation, neural interfaces, and nanogap DNA junctions-based bioelectronics. Prof. Lee has authored and co-authored over 60 journal and conference articles on integrated surface emitting laser diodes, SQUIDs, biomagnetic sensors, and nanogap DNA junctions for label free DNA detection.