Abstract  True three-dimensionally (3D) integrated biochips are crucial for realizing high performance biochemical analysis and cell engineering, which remain ultimate challenges. In this paper, a new method termed hybrid femtosecond laser microfabrication which consists of successive subtractive (femtosecond laser-assisted wet etching of glass) and additive (two-photon polymerization of polymer) 3D microprocessing was proposed for realizing 3D “ship-in-a-bottle” microchip. Such novel microchips were fabricated by integrating various 3D polymer micro/nanostructures into flexible 3D glass microfluidic channels. The high quality of microchips was ensured by quantitatively investigating the experimental processes containing “line-to-line” scanning mode, improved annealing temperature \(645^\circ \text{C}\), increased prebaking time (18 h for 1mm-length channel), optimal laser power (1.9 times larger than that on the surface) and longer developing time (6 times larger). The ship-in-a-bottle biochips show high capabilities to provide simultaneous filtering and mixing with 87% efficiency in a shorter distance and on-chip synthesis of ZnO microflower particles.

Hybrid femtosecond laser microfabrication to achieve true 3D glass/polymer composite biochips with multiscale features and high performance: the concept of ship-in-a-bottle biochip

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1. Introduction

Biochips are microchips with sizes of just millimeters to centimeters, within which chemical [1] and biological [2,3] laboratories are miniaturized. Compared with conventional macroscopic laboratory equipment such as test tubes and beakers, biochips exhibit many distinct advantages including low material consumption, low cost, and compactness. Additionally, they can perform reaction, detection, analysis [4], separation, and synthesis of biochemical materials [5] with high efficiency [6], high speed, and high sensitivity [7,8]. These specific features are a strong motivation for the development of microfabrication techniques for biochips. A variety of methods such as photolithography [9], soft lithography [10,11], and nanoimprint lithography [12] have been used to fabricate biochips in which two-dimensional (2D) planar microfluidic channels are the main component and other functional components are integrated afterwards depending on the application. These biochips are useful for a wide range of applications in chemistry, physics, biology and medicine, but their 2D feature limits their capabilities. Compared with 2D devices, 3D microfluidic structures can clearly exhibit more advanced functions and thereby provide higher performance [13–15]. For example, 3D microvascular networks were fabricated by direct write assembly of a fugitive organic ink for improved chaotic mixing [15]. 3D microfluidic devices fabricated with layered paper and tape succeeded in testing 4 different samples for up to four different analyses, displaying the results of the assays in a side-by-side configuration [16]. However, their poorly controlled channel shape and big difficulty in integrating functional devices into the microchannels seriously hindered their performance and applications.

It is well known that 3D micro/nanostructure can yield new or high functionalities, such as photonic crystals [17], mechanical microturbines [18], and cell scaffolds [19]. Integration of such 3D micro/nanostructure into microfluidics can further enhance the functionalities of biochips [20,21].

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For example, 3D photonic crystals have been fabricated by laser interference lithography on 2D open channels for refractive index sensing [22]. 3D mechanical rotors were fabricated by multiphoton polymerization of a magnetic photosensitive polymer to achieve stirring in 2D microchannels [23]. However, these 3D micro/nanostructures were fabricated only in 2D planar microfluidic structures due to the inherent limitations of current fabrication methods [21–24], which could not satisfy the requirements for true 3D cell microenvironments in biological engineering [25–27]. Moreover, most of these studies focused only on the integration of a single 3D device with limited functionality. It is therefore crucial to develop a technique to prepare true 3D biochips integrated with multifunctional components for high-performance applications.

In this paper, we solve the fabrication difficulty of true 3D microchip by a new concept that combines 3D glass microfluidics with 3D polymer microcomponents for the first time. The glass/polymer composite microchip is realized by our originally proposed technique consisting of successive subtractive (femtosecond (fs) laser-assisted wet etching of glass (FLAE) [28–30]) and additive (two-photon polymerization (TPP) of polymer [31–35]) 3D microprocessing; we term this new method hybrid fs laser microprocessing. The fabricated microchip is referred to as a "ship-in-a-bottle" biochip, since the polymer 3D microstructure is created in the embedded 3D glass microfluidic structure after the microfluidics fabrication. Substantial improvement of experimental processes (e.g., scanning mode, annealing temperature, prebaking time, optimal laser power, and developing time) ensured the high quality fabrication of true 3D microchips. FLAE can be used to fabricate flexible 3D microfluidic channels with controllable shapes, and TPP can then be used to realize easy integration of a variety of polymer microstructures from 1D to 3D possessing multifunctionalities such as filter-mixer devices.

2. Results and discussions

2.1. Experimental

Fabrication of 3D controllable glass microchannel with high smoothness by FLAE. First, a commercially available photosensitive Foturan glass (Schott Glass Corp.) consisting of lithium aluminoisilicate doped with trace amounts of silver, cerium, sodium and antimony was irradiated with a fs laser focused with an objective lens of 0.46 numerical aperture using a 3D direct-write scheme. In this work, a 522 nm fs laser beam obtained by the second harmonic generation from an amplified fs Er-fiber laser (FCPA μJewel D-400, IMRA America; wavelength: 1045 nm; pulse width: 360 fs; repetition rate: 200 kHz) was used (Supplementary Fig. S1). The fs laser irradiation precipitated silver atoms within the irradiated region by free electrons generated by nonlinear multiphoton absorption. The sample was then annealed in a programmable furnace to form a crystalline phase of lithium metasilicate. The temperature was increased to 500°C at a rate of 5°C/min, held constant for 1 h, then raised to 605°C at a rate of 3°C/min and again held constant for another hour (Fig. 1b). The annealed glass microchip was subjected to chemical etching in an aqueous solution of 10% hydrofluoric acid in an ultrasonic bath to selectively remove the grown crystalline phase area (Fig. 1c). The sample was then treated with the 2nd annealing to produce smooth surfaces. The temperature was increased to 500°C at a 5°C/min rate, raised to 645°C at 3°C/min, and then held constant for 1 h. As a result, 3D microfluidic structures with very smooth surfaces were formed in the glass microchip (Fig. 1d).

Integration of 3D high precision polymer microstructures into 3D glass microchannels. The fabricated microfluidic structures were filled with a commercial epoxy-based negative-type resin SU-8 (2015, MicroChem) widely utilized for TPP fabrication. Before TPP, the sample was pre-baked to evaporate the solvent in the resin. The pre-baking time depends on the channel length, as described above. The temperature was increased to 95°C at 5°C/min and held constant for 18 h (depending on the channel length, see Fig. 3c), then TPP was carried out using the same fs laser used for FLAE and focused by an oil immersion objective lens of 1.4 numerical aperture. After fs laser direct writing, the SU-8 resin was post-baked at a temperature of 95°C for 10 min, and then developed in the SU-8 developer for 3 h (depending on the channel length, Fig. 3d) to remove the unsolidified liquid resin. As a result, 3D polymer microstructures were integrated in the 3D glass microfluidics (Fig. 1e). Again, such an integrated microchip has been termed a ship-in-a-bottle biochip (Supplementary Fig. S2).

Characterization of 3D functional ship-in-a-bottle microchips: A pump-assisted system (Supplementary Fig. S7) built in-house was developed to characterize the functionality of the 3D composite glass/polymer microchips. The system consisted of a pump, a halogen lamp, a CCD, an objective lens (50×) and several plastic tubes. The pump is used to produce a negative pressure in the 3D microchip and suck the solvent from the breaker. Solvents with different particles or cells can be directionally sucked into the microchip. The flow speed can be controlled from 0 to 5 mm/s by negative pressure. The halogen lamp, CCD and objective lens can perform in-situ monitoring of the experimental results.

Fabrication of 3D multifunctional filter-mixer device: Two filters were combined with the inlet and outlet of one passive-type mixer. During the fs direct writing process, the mixer was first scanned layer by layer (Supporting video 1), and then two filters were fabricated. In addition, in order to enable this novel device to be more stable, we designed and fabricated six support pillars (4 μm diameter, 15 μm height) in every layer. This also ensures high quality integration in the microchip and highly functional applications. Because the support pillars are covered inside the device, they could not be observed in the SEM image (Fig. 4b). The optical microscopic image (Top view, Fig. 1e) shows that the support pillars look like black spots in the device.
2.2. Hybrid fs laser microprocessing for 3D ship-in-a-bottle biochip

Figure 1 shows a schematic illustration of the fabrication procedure for a ship-in-a-bottle biochip by hybrid fs laser microprocessing. It involves two main steps. The first is to fabricate 3D hollow microchannels by FLAE of photosensitive Foturan glass (Figs. 1b–c). The surface smoothness is improved by thermal annealing (Fig. 1d). 3D polymer microstructures are then fabricated by TPP for chip functionalization (Fig. 1e). We proposed this hybrid method for fabricating functional glass/polymer composite 3D biochips primarily for the following two reasons. First, FLAE can be used to directly fabricate 3D microfluidic structures...
inside glass and integrate some functional microcomponents [36]. However, the fabrication resolution of FLAE is limited to the order of ∼10 µm, which is mostly determined by the wet etching process. Secondly, TPP can easily be used to fabricate micro/nanocomponents with various functionalities. However, TPP usually employs a negative-tone photore sist for biochip fabrication, so that a lot of labor and time is used to fabricate 3D microfluidics with millimeter lengths due to the bottom-up fabrication (typically a 100–500 nm scanning pitch is employed). For example, in order to create a 1 mm³ volume microfluidic structure, the fabrication time exceeds 104 days even when the scanning pitch is increased to as large as 1 µm. Moreover, the mechanical and chemical properties of the polymer are obviously lower than those of glass, which means glass is a more suitable material as a platform for the biochips.

In order to compensate for each of the weak points (Supplementary Table S1), hybrid fs laser microprocessing which successively performs subtractive and additive 3D microfabrication is proposed to realize 3D glass biochips with integrated high precision 3D polymer microdevices. Compared with other techniques such as the paper-based or assembly methods [15, 16], the hybrid technique provides three advantages. (1) True 3D microfluidic structures can be fabricated in a single glass chip without a complicated procedure of stacking and bonding/sealing of other substrates. (2) The channel cross section can be freely designed and controlled by programming the laser scanning scheme, allowing for a more biomimetic environment for cell culture [25–27] and many other applications [37]. Figure 1f shows 45° (upper) and 0° (lower)—tilted SEM images of cross sections of fabricated microchannels exhibiting rectangular, round, elliptical, pentagram, triangle and hexagon shapes. (3) The most important advantage is that various polymer microstructures can later be integrated at any position in the 3D microfluidics structures for providing a variety of functionalities.

2.3. Systemic optimization of the FLAE process for high smoothness 3D glass microchannels

For realizing ship-in-a-bottle microchips, a key issue is to achieve high surface smoothness for microfluidic structures because they will be used as a platform to integrate high precision 3D polymer devices. An improved scanning mode—line to line with a smaller pitch of 2 µm [Supplementary Figs. S3(a)–(c)]—was adopted to fabricate 3D embedded microchannels. Then, the channel was subjected to post-annealing at an optimized temperature of 645°C [Supplementary Fig. S3(d)] which is somewhat higher than the 570°C used in our previous work [38]. Using these improved protocols, a highly smooth channel was produced. After the post-annealing, the optical transmission at 532 nm fs laser for the glass/air interfaces and the (channel internal surface)/air interface is measured as 95.9% and 95.2%, respectively (Supplementary Fig. S4). This further verifies the high surface quality of the channel realized by the optimized scanning mode and post-annealing. Such a highly smooth surface is not only crucial for subsequent high precision polymer device integration but is also beneficial for many biochip applications, in particular optofluidics [38], since optical loss and light scattering can be minimized.

2.4. Quantitative investigation of TPP parameters for high precision 3D polymer microdevices integration

After optimizing the FLAE process for fabricating high quality 3D glass microchannels, we also need to optimize the TPP process in order to integrate high precision polymer microstructures within the microchannels. The conditions for TPP in a 3D embedded microchannel will be different from those used on the surface, since the fs laser beam propagates through the glass to reach the microchannel. After analyzing the entire process, we found that there were three main factors: laser power, pre-baking time and developing time. First, the optimum laser power on the surface and in the channel was systematically investigated. As shown in the left image in Figs. 2a and b, a series of polymer nanowires were fabricated on the surface and in the channel under different laser powers, from 50 to 250 µW. The linewidths on the surface were subsequently measured to be 180, 570, 980, 1230 and 1450 nm (SEM images in Fig. 2a), while those in the channel were 0, 250, 400, 600 and 750 nm (Optical microscopy images in Fig. 2b), respectively. Generally, the laser power needed in the microchannel was 1.9 ± 0.1 times larger than that on the surface (Fig. 3a). This may be due to reflection/scattering at the channel/polymer interface as well as multiphoton absorption in glass and the polymer in the 60 µm-depth channel, as shown in Fig. 3b. For polymer microfabrication on the surface, optical reflection is caused only by the oil/SU-8 interface (the left image of Fig. 3b). However, for the microchannel, there are three interfaces (oil/SU-8, glass/SU-8, channel/SU-8) generating reflections (the right image of Fig. 3b), so that the laser power needed in the channel should be bigger than that on the surface. In addition, optical loss was also caused by multiphoton absorption of the fs laser during propagation in the glass substrate and the polymer. By optimizing the parameters, a variety of high quality micropatterns, e.g., a 2D metamaterial and an Olympic logo were realized both in the channel and on the surface (Figs. 2a and b). In addition to 2D microstructures, a 3D complex microcage and a woodpile photonic crystal structure were fabricated in Y-shape microchannel and on the surface (Fig. 2c and d), which can be applied for cell capture and refractive index sensing, respectively.

Besides laser power, the pre-baking time and developing time were also quantified, as shown in Figs. 3c and d. Generally, the pre-baking time is about 1 h on the surface, which is sufficiently long to remove the solvent in the resin. However, in 3D embedded channel, evaporation proceeds more slowly so that the pre-baking time needs to be significantly increased to 12, 18, 24 and 36 h for channel
Figure 2  High precision 1D, 2D, 3D polymer microstructures and functional device integration in 3D microchips (a) Optical microscopic images of 1D polymer nanowires and 2D high precision micropatterns in microchannels. The middle image shows metamaterial structures and the right is the Olympic logo “2012 LONDON”. (b) SEM images of the corresponding structures of (a) on a flat surface. (c) Optical microscopic and SEM images of 3D complex cages and woodpile photonic crystals in 3D Y-shape microchannels and glass surface, respectively. (e) SEM image of functional 3D microfilter on a flat surface (left), optical microscopic image of microfilters integrated in embedded microchannels (middle) and demonstration of filtering (right).
Figure 3 Quantitative investigation and comparison of three crucial parameters for TPP: laser power, pre-baked time, and developing time on surface and in channel. (a) The dependence of the polymer linewidths on laser power. Generally, the laser power needed in the microchannel is 1.9 ± 0.1 times larger than that on the surface. (b) Different physical mechanisms of optical loss on the surface and in the channel during the laser writing process. The optical loss may be caused by reflection/scattering at the channel/polymer interface and multiphoton absorption of glass and polymer in the 60-µm-deep channel. (c) Dependence of the prebaked time on the surface and in the channel with different lengths. (d) Comparison of developing time on the surface and in the channel by different solvents. (e) Statistical results of microparticles with sizes of 2–10 µm counted before and after the microfilter. (f) Dependence of the hole size of the filter and particle size that can be filtered on the laser power. The larger the laser power, the smaller the hole size, as shown in the insets (SEM images on a flat surface).

lengths of 500, 1000, 1500 and 2000 µm, respectively. A pre-baking time shorter than 5 h did not allow the resin to be completely removed during the developing process (Supplementary Fig. S5). Similarly, the developing time for a commercial SU-8 developer is as short as 0.5 ± 0.2 h on the surface, whereas it is about 3 ± 0.5 h for a 1000-µm-length channel. Chloroform and acetone can also be used as solvents to remove unpolymerized resin. The developing times for acetone and chloroform are 1 ± 0.2 h and 0.8 ± 0.1 h for the channel, respectively. Obviously, chloroform exhibits the strongest dissolving capability resulting in the shortest developing time; however, such strong dissolving capability
usually leads to floating or deformation of the fabricated microstructures (Supplementary Fig. S6). Therefore, the commercial SU-8 developer was used in the present experiments.

After systematic investigation for determining the optimal experimental parameters for both fabrication of 3D glass microfluidics and integration of 3D polymer microstructures, we attempted to realize functional biochips. As a proof-of-concept, a 3D filter, which is one of the important microcomponents for microfluidic applications to separate different sized biosamples, was integrated into the 3D glass microfluidics (Fig. 2e). The performance of the microfilter with 5 μm-hole was characterized by passing particles with different sizes ranging from 2 to 10 μm through it. We found that 2 and 4 μm microparticles could pass freely through the filter (Supplementary Fig. S8) while the 6, 8 and 10 μm diameter particles were hindered by the filter (Fig. 3e). By adjusting the laser power from 100 to 500 μW, the hole size formed in the filter could be controlled from 6.2 to 0.6 μm (black line in Fig. 3f). These different sized microfilters could be used for flexibly filtering micro and nano particles or bio cells with various sizes (red line in Fig. 3f).

2.5. Design, fabrication, performance and application of a 3D ship-in-a-bottle biochip integrated with a multifunctional microcomponent

Filtering and mixing are key functions for microfluidic applications [15], and have been well studied recently with most efforts concentrated on the fabrication of microcomponents with a single function of either a filter or a mixer [39]. If one microcomponent possesses multifuncions, it will be more useful and attractive. As shown in Fig. 4a, a novel multifunctional filter-mixer device was designed in which two filters were combined with the inlet and outlet of one passive-type mixer. The mixer has a configuration of layered crossing tubes to guide and rearrange fluids effectively and can realize fast mixing in a short channel length [40]. For example, the left-side fluid in the 2nd and 4th layer (indicated by green color numbers and arrows) was realigned from left to right while the right-side fluid in the 1st and 3rd layer (indicated by red color numbers and arrows), was realigned from right to left. Both fluids were rearranged alternately in the vertical direction. In addition to the effect of layer-rearrangement, momentum would also contribute to effective mixing, because the fluids passing inside the tubes have left/right momentum and the fluids discharging to the outside of the tubes have up/down momentum. To realize higher mixing in a shorter distance, the tilted angle was designed as much as 45° (Fig. 4b). Figures 4b-d show SEM images of the fabricated device made of a polymer on a flat glass surface, which agrees well with the designed model (Fig. 4a). The center part of the mixer is sandwiched with two filters with a hole size of 8 μm, as shown in the schematic image of Fig. 4a. The multifunctional device with the same structure was thus integrated in a Y-shaped microchannel embedded in the glass substrate (in Fig. 4g and Fig. 1e). By pouring water and Rhodamine B (dissolved in water, 20–50 ppm, flow speed ~4 mm/s) as two different kinds of solvents, the two were effectively mixed in the microfluidic channel integrated with the microdevice (Fig. 4g). On the other hand, in the simple microfluidic channel without the microdevice (Fig. 4h), no mixing occurred and laminar flow was produced. The device also successfully filtered some dust particles (~10 μm) in the solvents (enlarged inset in Fig. 4i).

We quantitatively investigated the mixing efficiency by extracting the grayscale intensity from the optical microscopic images (insets in Figs. 4g and h). The mixing effect can be quantified by the efficiency ($E_{mixing}$) according to the following formula [41]:

$$E_{mixing} = \frac{\varphi_{out} - \varphi_{in}}{(1 - \varphi_{in})}.$$  

$$\varphi = \frac{2\bar{I}_L}{(\bar{I}_L + \bar{I}_R)}.$$  

Here $\bar{I}_L$ and $\bar{I}_R$ represent the integrated intensities in the left (water) and right (Rhodamine B) half regions of the 270-μm-wide channel, respectively. $\varphi_{out}$ and $\varphi_{in}$ are the relative intensities in the left half regions of the inlet and outlet of the mixer. According to the above formula and the experimental results (Supplementary Table S2), we obtained $E_{mixing} = 87.2\%$. It is worth noting that the distance between A and B is about 270 μm, which is almost same as the channel width. This means that this device can realize high mixing performance even in such a short distance, as compared to conventional passive mixers based on nanopores [39], lamination [42], or helix channels [15, 43] that usually need the channel length to be 20–100 times the channel width.

We also designed a microfluidic system composed of three Y-shaped microchannels connected to two reaction chambers as well as two inlet and one outlet microreservoirs (Figs. 4i and j) to demonstrate application of the system as a microreactor for on-chip synthesis of ZnO flower-like microparticles. For the microchip without the device, the two fluids, water and rhodamine B, could not mix in the first Y channel and were then divided into the second Y channel. The fluids in each reaction chamber are thus pure water and rhodamine B (Fig. 4i), respectively. In the microchip with the device, the two fluids efficiently mixed with each other after passing through the multifunctional device (Fig. 4j). In addition, dust or objects in the fluids were filtered by the device, as shown in the enlarged photograph of Fig. 4j. The integrated biochip was used as a microreactor for synthesis of ZnO flower-like microparticles For this synthesis, zinc nitrate and ammonia water were introduced from the upper and lower inlets respectively (left side of Figs. 4i and j). ZnO flower-like microparticles were thus successfully synthesized in the two reaction chambers (Supplementary Figs. S9–S10), while no ZnO microstructures were observed in the chambers without the microdevice.
3. Conclusions

This work demonstrated glass/polymer composite true 3D biochips by a new method, referred to as hybrid fs laser microprocessing consisting of FLAE and TPP. Such distinct microchips have been termed ship-in-a-bottle biochips. Technically, we have solved two crucial problems: (1) The surface quality of FLAE of glass was significantly improved by optimizing the FLAE process, which is crucial for integration of polymer microstructures by the succeeding TPP. Microchannels with arbitrary cross sectional shapes and very smooth surfaces were created. (2) We experimentally...
demonstrated the feasibility of 3D integration in 3D embedded microchannels by quantitative optimization of three important parameters; however, previous studies performing device integration were based on a 2D planar channel. The true 3D integrated microchip not only provides a more biomimetic environment for 3D cell engineering but also demonstrates the technical possibility of mimicking a 3D biological blood vessel system. As a proof-of-concept of high performance functions and applications, the ship-in-a-bottle biochips were applied to the multifunctionality of filtering and mixing, on-chip synthesis of nanomaterials. (1) Multifunctional biochips with both filtering and mixing were realized by optimal design and integration of a single polymer device. This device achieved mixing efficiency as high as 87.2% within a short distance (only one time of the channel width). (2) The multifunctional device was further integrated into a microfluidic system. This complex 3D ship-in-a-bottle biochip showed its ability as a microreactor for on-chip synthesis of ZnO flower-like microparticles with homogeneous size (6.3 ± 0.4 μm).

Beside fabrication of a true 3D biochip for biochemical applications (Supplementary Fig. S11), including 3D cell/blood vessel engineering, hybrid fs laser microfabrication can also be used to solve the crucial problem of low mechanical strength and easy deformation of 3D polymer devices fabricated by TPP. For example, inspired by safety in cars with a robust frame, 3D polymer functional microstructures or devices designed within a glass frame can realize shock-resistant mechanical micromachines, high quality integrated microoptics etc. Although the cost of glass/polymer composite 3D ship-in-a-bottle microchips is higher than paper-based microchips, they are critical for specific applications such as mechanism investigation of 3D cell/tissue growth and control, fluid physics/chemistry in a true 3D microenvironment, practice of medicine in the military or aerospace regimes with challenging and resource-limited environments requiring robust medical technologies to minimize the burden for people and transport machines.

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References

[1] M. W. Losey, M. A. Schmidt, and K. F. Jensen, Ind. Eng. Chem. Res. 40, 2555–2562 (2001).
[2] M. A. Burns, B. N. Johnson, S. N. Brahmasandra, K. Handique, J. R. Webster, M. Krishnan, T. S. Sammarco, P. M. Man, D. Jones, D. Heldsinger, C. H. Mastrangelo, and D. T. Burke, Science 282, 484–487 (1998).
[3] L. Y. Ye, H. C. Chang, P. P. Y. Chan, and J. R. Friend, Small 7, 12–48 (2011).
[4] E. A. Ottesen, J. W. Hong, S. R. Quake, and J. R. Leadbetter, Science 314, 1464–1467 (2006).
[5] C. C. Lee, G. Sui, A. Elizarov, C. J. Shu, Y. S. Shin, A. N. Dooley, J. Huang, A. Daridon, P. Wyatt, D. Stout, H. C. Kolb, O. N. Witte, N. Satyamurthy, J. R. Heath, M. E. Phelps, S. R. Quake, and H. R. Tseng, Science 310, 1793–1796 (2005).
[6] L. Martin, M. Meier, S. M. Lyons, R. V. Sit, W. F. Marzluff, S. R. Quake, and H. Y. Chang, Nat. Methods 9, 1192–1194 (2012).
[7] D. A. Dunn and I. Feygin, Drug Discovery Today 5, S84-S91 (2000).
[8] H. Craighead, Nature 442, 387–393 (2006).
[9] T. McCready, Trac-Trends Anal. Chem. 19, 396–401 (2000).
[10] D. C. Duffy, J. C. McDonald, J. A. Schueller, and G. M. Whitesides, Anal. Chem. 70, 4974–4984 (1998).
[11] D. Qin, Y. Xia, and G. M. Whitesides, Nat. Protoc. 5, 491–502 (2010).
[12] L. J. Guo, X. Cheng, and C. F. Chou, Nano Lett. 4, 69–73 (2004).
[13] R. Derda, A. Laromaine, A. Mamamoto, S. K. Y. Tang, T. Mamamoto, D. E. Inger, and G. M. Whitesides, PNAS 104, 18457–18462 (2009).
[14] C. L. Randall, Y. V. Kalinin, M. Jamal, T. Manohar, and D. H. Gracias, Lab Chip 11, 127–131 (2011).
[15] D. Therriault, S. R. White, and J. A. Lewis, Nat. Mater. 2, 265–271 (2003).
[16] A. W. Martinez, S. T. Phillips, and G. M. Whitesides, PNAS 105, 19606–19611 (2008).
[17] S. Noda, K. Tomoda, N. Yamamoto, and A. Chutinan, Science 328, 604–606 (2000).
[18] H. Xia, J. Wang, Y. Tian, Q. D. Chen, X. B. Du, Y. L. Zhang, Y. He, and H. B. Sun, Adv. Mater. 22, 3204–3207 (2010).
[19] R. G. Wylie, S. Alhsan, Y. Aizawa, K. L. Maxwell, C. M. Morsch, and M. S. Shoichet, Nat. Mater. 10, 799–806 (2011).
[20] D. Wu, Q. D. Chen, L. G. Niu, J. N. Wang, J. Wang, R. Wang, H. Xia, and H. B. Sun, Lab Chip 9, 2391–2394 (2009).
[21] J. Wang, Y. He, H. Xia, L. G. Niu, R. Zhang, Q. D. Chen, Y. L. Zhang, Y. F. Li, S. J. Zeng, J. H. Qin, B. C. Lin, and H. B. Sun, Lab Chip 10, 1993–1996 (2010).
[22] S. K. Lee, S. G. Park, J. H. Moon, and S. M. Yang, Lab Chip 8, 388–391 (2008).
[23] Y. Tian, Y. L. Zhang, J. F. Ku, Y. He, B. B. Xu, Q. D. Chen, H. Xia, and H. B. Sun, Lab Chip 10, 2902–2905 (2010).
[24] L. Amato, Y. Gu, N. Bellini, S. M. Eaton, G. Cerullo, and R. Osellame, Lab Chip 12, 1135–1142 (2012).
[25] M. Schindler, A. N. E. Kamal, I. Ahmed, J. Kamal, H. Y. Liu, N. Amor, A. S. Ponery, D. P. Crockett, T. H. Grafe, H. Y. Chang, T. Weik, E. Jones, and S. Meiners, Cell Biochem. BioPhy. 45, 215–227 (2006).
[26] D. R. Albrecht, G. H. Underhill, T. B. Wassermann, R. L. Sah, and S. N. Bhatia, Nat. Methods 3, 369–375 (2006).
[27] Y. Luo and M. S. Shoichet, Nat. Mater. 3, 249–253 (2004).
[28] A. Schaap, T. Rohrlick and Y. Bellouard, Lab Chip 1 2, 1527–1532 (2012).
[29] K. Sugioka, Y. Hanada, and K. Midorikawa, Laser Photonics Rev. 4, 386–400 (2010).
[30] R. Osellame, V. Maselli, R. M. Vazquez, R. Ramponi, and G. Cerullo, Appl. Phys. Lett. 90, 231118 (2007).
[31] S. Kawata, H. B. Sun, T. Tanaka, and K. Takada, Nature 412, 697–698 (2001).
[32] S. Maruo, O. Nakamura, and S. Kawata, Opt. Lett. 22, 132–134 (1997).
[33] L. Li, R. R. Gattass, E. Gershgoren, H. Hwang, and J. T. Fourkas, Science 324, 910–913 (2009).
[34] Z. Gan, Y. Cao, R. A. Evans, and M. Gu, Nat. Comm. 4, 2061 (2013).
[35] A. Ledermann, L. Cademartiri, M. Hermatschweiler, C. Toninelli, G. A. Ozin, D. S. Wiersma, M. Wengener, and G. V. Freymann, Nat. Mater. 5, 942–945 (2006).
[36] Y. Cheng, K. Sugioka, and K. Midorikawa, Opt. Express 13, 7225–7232 (2005).
[37] X. Liu, Q. Wang, J. Qin, and B. Lin, Lab Chip 9, 1200–1205 (2009).
[38] Y. Cheng, K. Sugioka, K. Midorikawa, M. Masuda, K. Toyoda, M. Kawachi, and K. Shihoyama, Opt. Lett. 28, 1144–1146 (2003).
[39] S. Jeon, V. Malyarchuk, J. O. White, and J. A. Rogers, Nano Lett. 5, 1351–1356 (2005).
[40] T. W. Lim, Y. Son, Y. J. Jeong, D. Y. Yang, H. J. Kong, K. S. Lee, and D. P. Kim, Lab Chip 11, 100–103 (2011).
[41] Z. Xiao, A. Wang, J. Perumal, and D. P. Kim, Adv. Funct. Mater. 20, 1473–1479 (2010).
[42] A. D. Stroock, S. K. W. Dertinger, A. Ajdari, L. Mezic, H. A. Stone, and G. M. Whitesides, Science 295, 647–651 (2002).
[43] Y. Liao, J. Song, E. Li, Y. Luo, Y. Shen, D. Chen, Y. Cheng, Z. Xu, K. Sugioka, and K. Midorikawa, Lab Chip 12, 746–749 (2012).