Sensors & Transducers, Vol. 166, Issue 3, March 2014, pp. 29-38

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Research Progress of Microfluidic Chips Preparation and its Optical Element

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Received: 28 December 2013 /Accepted: 28 February 2014 /Published: 31 March 2014

Abstract: Microfluidic technology is the emerging technologies in researching fluid channel and related applications in the micro and nano-scale space. Microfluidic chip is a new miniaturized rapid analysis platform by microfluidic technology, it has many characteristics such as liquid flow control, minimal reagent consumption, rapid analysis, which is widely used in physics, chemistry, biology, and engineering science and other fields, it has strong interdisciplinary. This paper mainly discusses research progress of materials used for microfluidic chips and the devices based on microfluidic technology, including microfluidic chip, microfluidic optical devices, microfluidic laser preparation, microfluidic chip applications, focusing on the quasi-molecular laser processing technology and femtosecond laser processing technology in the microfluidic devices preparation, and make development prospects for it. *Copyright © 2014 IFSA Publishing, S. L.*

Keywords: Microfluidic chip, Optical devices, Microfluidic technology.

1. Introduction

In 10~100 μm wide channel systems, the technique manipulating fluids or gases is known as microfluidics technology [1]. Microfluidics form a new functional devices and systems with optics and optoelectronics technology, the main features of microfluidic optical system are adjustable structure, integrated function and miniaturized system. Structural tunability provides a new technical approach for adaptive optics, the integration of optical detection and microfluidic analysis will promote the application and development of micro total analysis system, the integration of optics and microfluidics technology will offer the potential of conventional optical devices are adjustable and miniaturization [2]. This paper describes several kinds of materials for the production of microfluidic chips, points out that because of the polymer's material properties is wide, it do not need coating, ease of mass production, etc., and has broad application prospects.

Then reviewed the applications of microfluidic technology in the preparation of microfluidic chip and microfluidic optical devices, etc., pointed out that with the development of microfluidic optical technology, it will produce more excellent performance microfluidic chips and microfluidic fiber optic devices, and promote the further development of integrated photonics.

2. Research Progress of Materials Used for Microfluidic

The size of microfluidic chip is very small, it is operating in the micrometer space, and thus the materials used in production of microfluidic chips are essential. Generally materials used in the production of microfluidic chip are often divided into rigid materials and elastic materials [3]. Rigid materials are silicon, glass, quartz, and rigid organic polymeric material such as epoxy, polyurea, polyurethane, polystyrene and polymethyl methacrylate, etc.; elastic material dimethylsiloxane (PDMS: poly-dimethylsiloxane) and so on.

2.1. Silicon, Glass, Quartz and Other Materials

In the production of microfluidic chip materials, the application of silicon is very extensive, and has served as the main material used in early microfluidic chip. But it has poor electrical insulation, high price and poor translucency.

Glass and quartz have good optical properties, mechanical properties, electrical infiltration properties and electrical insulation. Its surface adsorption and surface reaction ability are favorable for surface modification, and the production equipment has well compatible with the traditional process equipment, and therefore, in recent years more and more glass and quartz used for microfluidic chips, obtain perfect micro channels [4-9].

The Chinese Academy of Sciences, Shanghai Institute of micro system and information technology such as Chen Jiang [10] put forward the fast, low cost method for fabrication of glass microfluidic chip in 2007. In 2011, Chongqing University, Li Dongling [11] aimed at the problems of glass microfluidic chip fabrication progress is high cost, long processing cycle, presents a low cost and utility method for fabricating based on the wet etching technology.

The materials for microfluidic chips are commercially available microscope slides used as the chip matrix material, only the production process on the mask layer is not the same, but all can get the deepest etch depth – 110 μm. And the whole production process is simple, low cost, good stability, can be widely used in glass microfluidic chip production.

In 2007, Wuhan university of engineering such as Wang Sheng-Gao [12] makes photosensitive microcrystalline glass that has good photochemical processing performance as chip fabrication material. The homogeneous glass raw materials prepared by sol gel method, and used the low temperature melting method, improved the photosensitive glass-ceramic photochemical processing performance; based on high content photosensitizer and the nucleation agent, appropriately extended light irradiation time, shortening the time of heat treatment, reducing the precipitate in the glass crystal granularity, and last improve the quality of photochemical process.

2.2. Polymer Materials

PDMS is present the most widely used polymer materials in the field of microfluidic chip, it is also combination with glass to make microfluidic chips.

For example, in 2012, Shanghai Jiaotong University, Wu Ze-Xi [13], studied and analyzed preparation process of integrated electrodes PDMS-glass microfluidic chip. PDMS-glass chip which has both heating and temperature conductivity electrode, and CE high voltage electrode is mainly adopt the PDMS cover plate which has microfluidic channel prepreg bonding with the electrode substrate. ANSYS simulation analysis shows that the heating chip thermal inertia is small, the temperature distribution effect is good when heating.

Polymethacrylic acid methyl ester (PMMA: polymethylmethacrylate) is a polymer, it has many good properties such as convenient molding and excellent chemical properties, etc., and are widely used as the base material, microfluidic chip can be fabricated by directly processed by the CO2 laser. Cyclic olefin copolymer (COC: cyclo olefin coplymer) with its high chemical stability and transparency was also used for microfluidic chip production [14].

In addition, there are many materials preparation for microfluidic chip, such as nylon. In 2012, Chinese Academy of Sciences Yang Jun [15] produced a new film microfluidic chip, it taked nylon microporous film as base material, used photolithography method to transfer positive ultraviolet photoresist to film to form the target micro-channel graphics. Nylon microporous film chip production process was optimized and improved, so that the production time is within 1h and production steps greatly simplified, and can realize fast, batch production of nylon film chips, it has good application prospects.

2.3. Compared with two Types of Materials

Glass, quartz and other materials are easy to obtain fine channels because of their good electrical permeability, light transmission and surface bio-compatibility, but generally their processing cycle is slightly longer. In comparison, polymer has many advantages used in producing microfluidic chips. Polymer has wide substrate material properties, and substrate can be optimized by surface chemical modification for different applications, there are many suitable micro fabrication technology for polymer microchannel geometry, it also has many characteristics such as no coating, low cost with production of large quantities, easy to copy, so it has broad application prospects.

3. Microfluidic Preparation

Reported in the literature for the production of microfluidic chip lasers are mainly excimer lasers and CO2 lasers.

3.1. Excimer Laser for Microfluidic Chip Preparation

Compared to the lithography chemical etching method which has the complex processing technology, excimer laser processing technology have many advantages, such as great flexibility, high degree of automation. The materials which excimer laser etching can be directly used to produce microfluidic chips commonly include glass, quartz, polymers and so on.

Beijing University, Qi Heng [16] proposed using the excimer laser etched PCR (polymerase chain reaction polymerase chain reaction) microfluidic biochip on the PMMA substrate. In the processing, select a lower laser energy density and higher laser Table speed, can obtain a smoother bottom microchannels. Through thermal bonding method, prepared a complete hermetic PCR microfluidic biochips. Fig. 1 shows the three-dimensional simulation image of the microchannel, the PMMA-based PCR microfluidic biochip is shown in Fig. 2 [16].

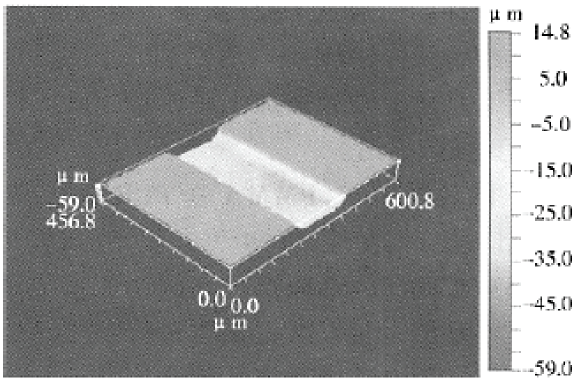

Fig. 1. Microchannel 3D simulation diagram.

In 2011, Beijing University of Technology, Shen Xuefei, et al. [17] use excimer laser micromachining technology and the method of combining molding technology manufacturing microfluidic chip. With the excimer laser etched on the glass substrate layer to obtain high quality microfluidic biochip morphology, by electroforming technique to copy microfluidic chip, get reverse metal dies. Using metal mold by injection molding technology with polycarbonate injection molded microfluidic chip. Through systematic studies have shown that the flow rate is small, with a laser micromachining technology combined with the molding method of processing micro-channel excimer laser direct writing than the processing of micro-channel flow better performance.

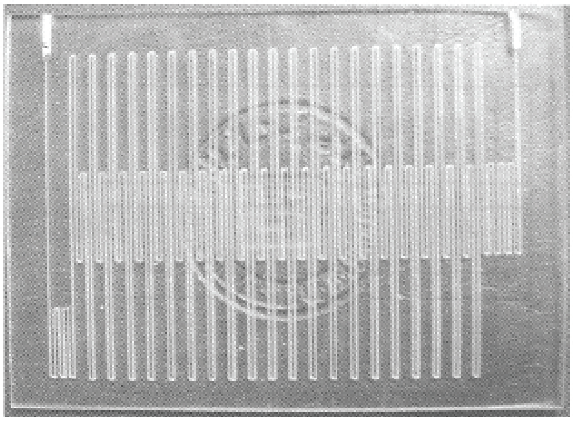

Fig. 2. PMMA-based PCR microfluidic biochip real objects.

3.2. CO2 Laser for Microfluidic Chip Preparation

The basic principle of CO2 laser fabricate microfluidic chip is using high-energy beam of infrared laser directly processing micro-flow channel on the polymer substrate. Compared with the excimer laser, the advantage of this approach is that CO2 laser has much lower price, and does not require special gases; the disadvantage of this approach is that the surface is rough, recasting area is thick, but through annealing and chemical reagents treatment can make the channel surface more smooth. Therefore, the method of using CO2 lasers to achieve microfluidic chip processing is quick and easy, the equipment and operational cost is low, and has good application prospects.

As shown in Fig. 3 [18], in this system, laser is fixing. Through focusing prism, laser focus on chip substrate, transform CAD graphics of the designed micro flow path into the identify instructions of the excimer laser micro machining system. Through the movement of platform to complete the chip processing. However, the material direct used for processing is relatively small, in present, the reported are PMMA, PDMS, polyimide polymer and glass.

Xiamen University, Liu Xiaoqing [19] proposed ordinary nail polish and nail polish/gold/chromium as sacrificial layer, use CO_2 laser ablation to open the window, supplemented by wet etching processing glass microfluidic chip-based method, the method is simple, does not require photolithography expensive equipment and complex step. The results showed that nail polish or nail polish/gold/chromium as sacrificial layer, combined with the CO2 laser machining and wet etching, can remove the lithography expensive equipment and tedious process, a rapid, inexpensive glass substrate microfluidic chip was prepared. Among them, the nail polish/gold/chrome for the sacrificial layer can get great depth, smooth wall of the micro-channel.

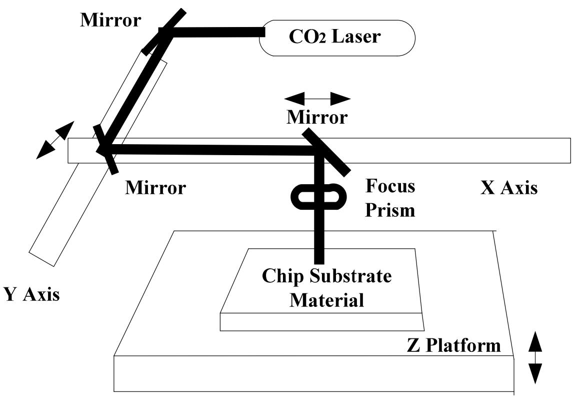

Fig. 3. Laser processing device schematic diagram.

In 2009, Beijing University of Technology, Wang Xiansong [20] using CO2 laser direct writing ablation method for large volume, fast processing of micro channel on the PMMA substrate, one batch processing chip are 125, the process has high stability, and compared with the traditional hot pressing and injection molding process method, it is more simple, and according to the experiment, it can adjust the structure of micro channel and reprocessing at any time.

3.3. Femtosecond Laser for Microfluidic Chip Preparation

This microfluidic device fabrication method is mainly a variety of lithography techniques, they are mainly in the preparation of the two-dimensional surface structure [21].

Femtosecond laser micromachining technology can achieve micron or sub-micron precision machining in the surface of transparent material, and has been widely used in the preparation of a variety of microfluidic devices, for example, through the femtosecond laser ablation in the material surface to obtain micro channel and then be covered with a layer of cover plate [22].

In 2003, Japanese M. Masuda [23] used the femtosecond laser embedded in a 3-D micro flow channel in the photosensitive glass which has good transparency, hardness, chemical properties. The glass has photosensitivity just because it is doped cerium elements. Fig. 4 is Y-branch microfluidic channel structure produced in the photosensitive glass. In the photosensitive glass, vertical direction microfluidic structure has been produced out (Fig. 5) [23].

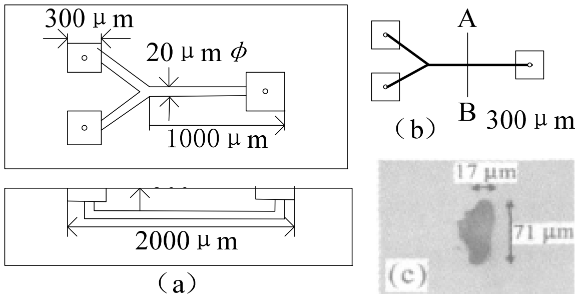

Fig. 4. Horizontal direction Y branch microchannel structure diagram.

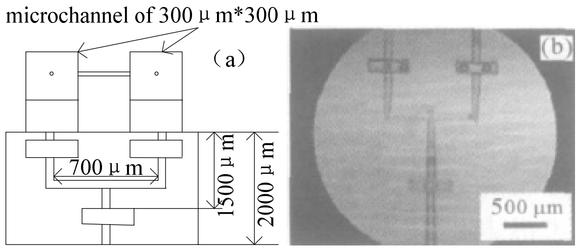

Fig. 5. Vertical microfluidic channel structure.

4. Microfluidic Chip Applications

4.1. Applications of Microfluidic Chip in Food Safety Analysis

Microfluidic chip, also known as lab on a chip is the core of micro total analysis system, it is integrated the sample preparation, reaction, separation, detection, and other basic operating unit which is in chemical and biological areas into a small basic chip (several square centimeters), and the network is formed by the micro-channel, it can control the flow through the system, and last to replace the conventional chemical or biological laboratory of the various functions of a technology platform [24]. In 1999, HP and Caliper company jointly first introduced commercialization of microfluidic devices, it was first used in the field of bio-analytical and clinical analysis. At present the technology is used in drug screening [25], environmental monitoring [26], food safety [27-28] and other areas.

4.1.1. Detection of Food Additives

Studies show that microfluidic chip can be used in the detection of synthetic food colorings, preservatives, bleaches, disinfectants and other food additives [24].

Dosso N., et al. [29] detected Pigment Yellow AB, the new red, sunset yellow, new Carmine and Amaranth these five azo dyes in soft drinks and candy by using chip electrophoresis-electrochemical detection method, the detection limits were 3.8, 3.4, 3.6, 9.1, 15.1 μmol/L, the detection time is less than 300 s. At the same time, he will end the traditional channel electrode adjusted to the channel for the detection of Acid Green S and Patent Blue in soft drinks and candy, detection limits were 17,10 μmol/L, the linear range was 50~2000 μmol/L, detection time is less than 250 s [30]. Lee et al. [31] designed three parallel channels on a chip for detecting juice, fish, pasta, red chili powder, Korean traditional wine pigments (Brilliant Blue FDF, indigo, Fast Green FCF, amaranth, erythritol, Allura Red, Ponceau 4R, tartrazine, sunset yellow FCF), detection limit between 1.0~5.0 nmol/L, the linear range is 1.0~1.0 mmol/L, its sensitivity increased 10,800 times than conventional micellar electrokinetic chromatography-electrochemical detection.

4.1.2. Detection of Heavy Metals

In microfluidic chip, Lu et al. [32] using 4-(2- pyridylazo) resorcinol (PAR) as a metal complexing agent and a chromogenic agent, through diode array absorbed detect Co2 +, V3 +, Ni2 +, Cu2 +, Fe2 +, Mn2 +, Cd2 + and other metal ions, the detection limits were 0.47, 0.97, 0.40, 0.41, 1.00, 1.15, 0.54 μg/mL, the detection time is less than 65 s. Li et al. [33] using single carbon fiber electrode instead of toxic and difficult miniaturized mercury electrode for indirect amperometric detection Pb2 +, Cd2 + and Cu2 +, detection limits were 1.3, 3.3, 7.4 μmol/L. Chailapakul et al. [34] set flat-screen printed carbon electrode in the micro-channel terminal, achieve a direct amperometric detection of heavy metal ions. This method is used to detect Pb2+, Cd2+ and Cu2+ in green vegetable juice, tomato juice, pineapple juice, detection limits were 1.74, 0.73, 0.13 μmol/L. In 2009, Nogami, et al. using chip electrophoretic separation-chemiluminescent detection detect cupric ions of urban water supply, the limit is 7.5 nmol/L [35].

In addition, Liu et al. [36] used chemiluminescence micro-flow injection analysis chip detect different forms of chromium content in the samples water, the detection limit is 2×10^{-8} mol /L (Cr3+) and 4×10^{-8} mol/L ($Cr_2O_7^{2-}$).

4.1.3. Detection of Pesticide Residues

Wang et al. [37] used microfluidic chip on the detection of organophosphorus pesticide residues in water, paraoxon, methyl parathion and fenitrothion detection limits were 0.21, 0.4, 1.06 μg/mL, detection times is less than 140 s; Lee et al. [38] using confocal strengthen Raman spectroscopy to detect methyl parathion, the detection limit was 0.1 μg/mL. Smirnova, et al. [39] integrated hydrolysis, azo derivatives, liquid-liquid extraction, micellar electrokinetic chromatography, thermal lens detection of four kinds of carbamate pesticides (carbaryl, carbofuran, propoxur and evil insects K), the detection limit (0.5 μmol/L) was significantly lower than conventional electrophoresis – UV absorption detector (10 μmol/L).

4.1.4. Detection of Antibiotic Residues

Carcia, et al. [40] using pulsed chip electrophoresis pulse amperometric detection sulfur antibiotics, penicillin and ampicillin, the detection limit is 5 μmol/L. Liu Wei, et al. [36] using online solid-phase extraction chemiluminescence micro-flow injection analysis chip on milk β-lactam antibiotics, the determination of penicillin, cephradine, cefadroxil, cephalexin detection limits were 0.5, 0.04, 0.08, 0.1 μg/mL. Pei Chui Kam, et al. [41] using micro-flow injection chemiluminescence determination of fish and chips in the tetracycline, the linear range is 0.2~10 μg/mL, the detection limit was 0.017 μg/mL. Lee et al. [42] integrated on the chip enrichment, separation and electrochemical detection of tetracycline family of antibiotics, and beef samples for analysis and found that: tetracycline, oxytetracycline, chlortetracycline, doxycycline detection limit is 1.5~4.3 nmol/L. Compared to conventional micellar electrokinetic chromatography-electrochemical detection, the sensitivity increased 10900-fold.

4.2. The Applications of Microfluidic Chip in Cell Biology Research

Unlike static affinity and hybridization-based traditional biochips, microfluidic chip adopt microfluidic control technology, provides a new technology platform bio-dynamic analysis. The applications of microfluidic chip in the biological field can be divided into the molecular level and cellular levels. Cells are the basic unit of structure and function of organisms, all organisms (except viruses) consists of cells, in-depth study on cell is the key uncovering the mysteries of life and treatment of diseases. Although cell analysis instrument which is the representative of capillary electrophoresis and flow cytometry is widely used, but the function is single, and also has its own defects. For example, capillary electrophoresis is not easy for cell manipulation and processing, flow cytometry to consume a large amount of samples [43]. Microfluidic chip has the following advantages in cytological research: 1) microfluidic channel size (10-100 μm), has the similar size with a single cell diameter (10-20 μm) [44], facilitate manipulation of the cells; 2) micro-fluidic chip multidimensional network structure closer to the physiological state of cells in the living environment relatively to closed environment; 3) microfluidic chip to meet the needs of high-throughput cell analysis, which can get a lot of biological information [45]; 4) a flexible combination of multiple operating units on microfluidic chip, making the cell injection, training, capture, cracking and separation detection process can be completed in one chip; 5) microfluidic chips is flat geometry, more convenient were observed [46]; 6) chip upload fast heat and mass transfer, is conducive to the spread of heat and substance. Since microfluidic chip under test conditions can be simulated physiological conditions, as in single-and multi-cellular level to better study the cells to provide a new technology platform [47].

5. A Typical Method of Making Optical Microfluidic Devices

5.1. Femtosecond Laser used in the Production of Microfluidic Optical Devices

Femtosecond laser micromachining technology has many advantage, such as high precision machining, little thermal effects, low damage threshold, ability to achieve true three-dimensional microstructure processing, etc. All these properties do not be replaced by other traditional laser processing technologies [48]. Femtosecond laser pulses can produce microfluidic optical devices in ordinary single-mode fiber and photonic crystal fiber. For example, the advanced microfluidic device was integrated into the fiber, combined with fiber operating advantages together, constitute microfluidic optical devices. Another method is: put the cladding etched fiber or fiber grating immersed into the planar bulk fluid channel. Some techniques are coupling optical fiber with the optical hollow planar waveguide [49]. In order to improve channel integration, reliability, and easier to produce, a better approach is to directly produce the micro-channels in optical fibers. In this integrated structure, the optical waveguide is become the main input/output optical transmission channel. As femtosecond laser pulses has very short pulse width and high peak power, in recent years, it has been successfully used to produce microfluidic optical devices in glass, silicon and other bulk materials [50, 51], used for the production of micro- lasers, sensors, integrated optical waveguide, etc. [52].

In 2006, Y. Lai, et al. [53] first made the micro-channels in ordinary single-mode fiber by using femtosecond laser processing and chemical etching method. The microfluidic optical device made by Y. Lai is consists of 4 μm wide microchannel, it is transected fiber core, and it can be used to produce "Refractive Index Sensor".

In 2007, C. J. Hensley, et al. [54] first use femtosecond laser pulses drilled microchannel in the side of the photonic crystal fiber.

In 2013, Wuhan University of Technology, Zhou Guangfu, et al. [55] discussed femtosecond laser in the preparation of three-dimensional microstructures in the quartz fiber materials. The experimental results show that the ablation threshold of the fiber is approximately 1.5 J/cm^2, the ablation hole depth is substantially in line with the log of the energy. Under certain conditions, an appropriate increase of the laser energy will help to improve the verticality of micropores. By using appropriate processing technology, they try to made three-dimensional micro structure such as fiber FP cavity, fiber end cantilever, it is shown in Fig. 6.

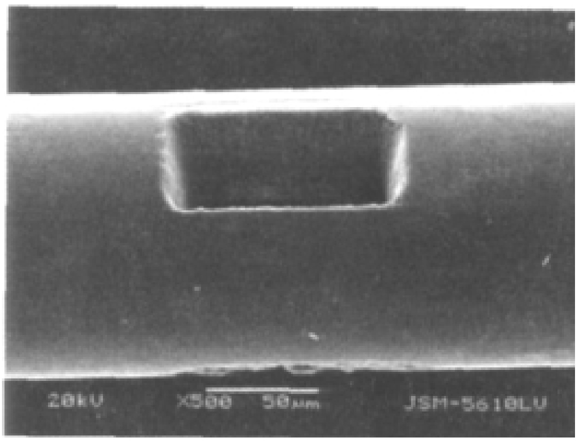

Fig. 6. Femtosecond laser etching fiber F-P cavity.

5.2. Excimer Laser used in the Production of Microfluidic Optical Devices

In 2008, Southeast University, Jin Yonglong, et al. [56] proposes an embedded fiber-type microfluidic chip preparation in order to test sample convenience, fast, low-cost. Using 248 nm KrF excimer laser on PMMA substrate micro-machining, the chip structure constructed and embedded etched single mode fiber which the diameter is 35 μm, thereby forming an embedded optical fiber chip. The analysis shows that with the excimer laser processing chip, it is good controllability, easy and reliable, the process can achieve unmanned. Embedded optical fiber aligned with each other and well aligned with the optical fiber and the center of the flow channel, can sensitive obtain samples of the optical signal. Fig. 7 shows the optical fiber embedding and the sealing of the chip diagram.

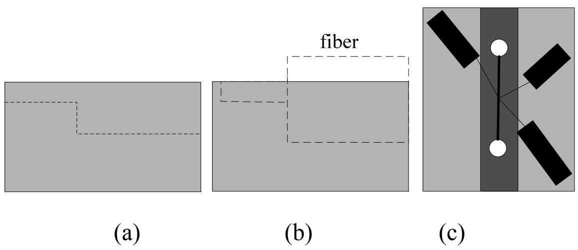

Fig. 7. Optical fiber embedding and the step of the chip closing step: (a) etching chip; (b) embedded fiber and fixed; (c) hot pressing sealing chip.

6. Research Progress of the Microfluidic Microlaser

6.1. Femtosecond Laser used in the Production of Microfluidic Optical Devices

In order to achieve the integrated of the light source and microfluidic chip, several research groups have proposed and demonstrated several structures microfluidic chip lasers based on different materials [57-60].

In 2007, the Chinese Academy of Sciences, He Fei, et al. [61] manufactured various microfluidic devices in photosensitive glass. In the experiment, the hollow microspheres structure is formed inside the glass, which is widely used in the micro total analysis system and the chip lab. Microfluidic laser microscopic image and the optical path diagram are shown in Fig. 8. Four 45° micro mirrors were vertically embedded in the glass to constitute the micro-optical cavity, prepared a microfluidic chamber under 400 μm of the glass surface, the laser dyes may flow through the central cavity of the micro-channel to the micro-channel cavity, the average diameter of the micro-channel is 80 μm, the width of the micro cavity is 800 μm; When injected into the cavity with Rh6G laser dye, and with 532 nm wavelength Nd: YAG laser pumped, there are laser-produced, the beam is surrounded by the beam angle of total reflection mirror spread back and forth to form resonance. As the processing precision is limited, a micro mirror surface is not machined absolutely smooth, the angle between the two mirrors can not be absolutely accurate, so the beam after multiple reflections in the annular cavity, there will be a small portion of the light from the reflecting mirrors tangentially to the output surface.

In 2011, Nankai University, Zhang Weigang, et al. [52] found out that two reflective wall of the femtosecond laser etching fiber micro cavity with one step, is not completely vertical with the fiber core axis, the shape of the micro cavity is relative to the position between the fiber and the focus that femtosecond laser through the microobjective focused.

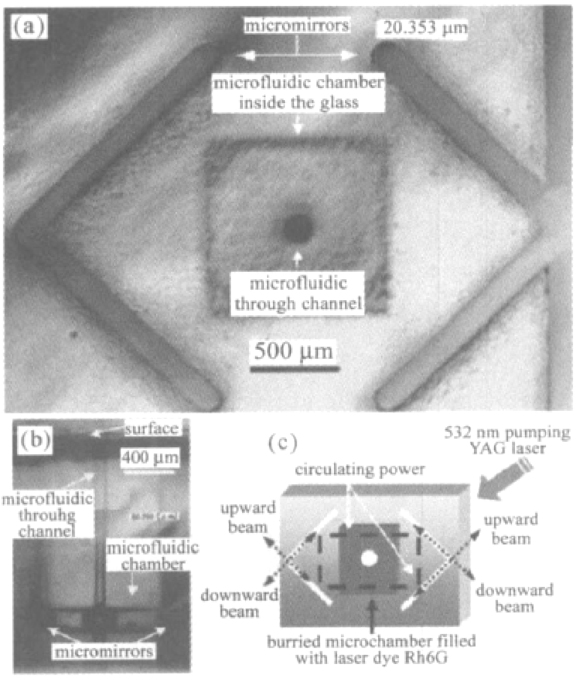

Fig. 8. (a) Microfluidic lasers; (b) Microfluidic cavity and microchannel; (c) Microfluidic laser optical path diagram.

When the laser fiber through the microscope objective to focus on the side surface, the etching micro cavity is approximate V-shaped cavity. Compared with conventional fiber Fabry-Perot (FP) cavity, V-type optical micro-cavity interference spectrum appeared free spectral range, micro-cavity optical loss and interference fringe contrast is related to the wavelength and other anomalies contrast. By introducing the concept of tilt factor to build a V-type optical micro-cavity model, derived V-type F-P cavity interference formula, initially established a V-shaped optical microcavities interference theory. Fig. 9 is a femtosecond laser etching optical microcavity experimental setup.

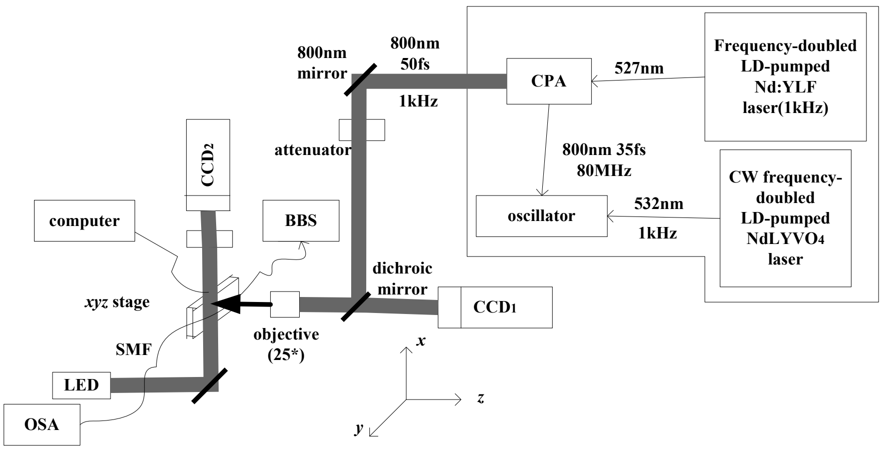

Fig. 9. Femtosecond laser etching optical microcavity experimental setup.

7. Outlook

Microfluidic Optics which is microfluidic technology combined with modern optics, optoelectronics, is a new type cross-frontier Frontier Discipline. Microfluidic chip is a miniaturized, integrated, portable, automated, low-cost and low loss analysis system. Microfluidic optical devices is an excellent, widely used integrated photonic devices, can be widely used in modern biomedicine, chemistry, sensor technology and other aspects. This article discusses the microfluidic technology, preparation materials used for microfluidic devices, and research microfluidic technology in the production of microfluidic devices, microfluidic optical devices, microfluidic lasers. Microfluidics is a new field, theories and a concept is still under development. Nevertheless, the advantages of microfluidic tunable optical systems, such as adjustability, integration and miniaturization, etc. will widely available in adaptive optics, microfluidic optical detection and optical integrated device.

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