Research Journal of Applied Sciences, Engineering and Technology 5(2): 579-584, 2013
ISSN: 2040-7459; E-ISSN: 2040-7467

Submitted: May 19, 2012 Accepted: July 18, 2012 Published: January 11, 2013

Research and Development on the Photoelectric Detection Technology of Microfluidic Chip

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Abstract: The microfluidic chip has been widely applied to areas such as medicine, bio-detection. Photoelectric detection technology is one of the most common method used in microfluidic chip detection, this study summarizes the development and application of the microfluidic chip photoelectric detection technology in recent years and analyses of the photoelectric detection of the microfluidic chip in key technologies and summarized the advantages and disadvantages of different microfluidic chip photoelectric detection technology. Photoelectric detection technology developed for high sensitivity and accuracy of professional microfluidic chip to provide a reference.

Keywords: Accuracy, microfluidic chip, photoelectric detection, sensitivity

INTRODUCTION

Widmer *et al*. (1990) from Switzerland invented the first Micro-flow control chip, also known as lab-on-a-chip (lab on a chip) in the 1990s. Their goal is to integrate the functionality of the analytical laboratory on the portable devices or even on the small square chip. Since its inception, due to the small size, rapid analysis, low cost, high integration, high degree of automation, portable, easy-to-commercialization and other characteristics, micro-flow control chip is more closely watched and it has been widely used in environmental protection, biomedical engineering life science and other fields (Yin *et al*., 2003). The detector of Microfluidic chip control system is used to determine the analysis of the composition and content of microchip separation or processing material composition. Its overall performance will affect the detection limit of the entire microfluidic chip analysis systems, test speed, scope of application as well as volume and other indicators, which is a key part of the microfluidic chip system. Therefore, the research on detection methods and detector is one of the main directions in the micro-flow control chip area (Schwarz and Hauser, 2001). Photoelectric detection technology is one of the mostly used technologies in the micro-flow detection equipment. According to different theory, it can be divided into the laser-induced fluorescence detection, absorbance detection and chemiluminescent detection.

This study summarizes the development and application of the micro fluidic chip photoelectric detection technology in recent years and analysis of the photoelectric detection of the micro fluidic chip in key technologies and summarized the advantages and disadvantages of different micro fluidic chip photoelectric detection technology. Photoelectric detection technology developed for high sensitivity and accuracy of professional micro fluidic chip to provide a reference.

LASER INDUCED FLUORESCENCE DETECTION

Laser Induced Fluorescence (a laser induced fluorescence, LIF), is a highly sensitive detection method, whose detection limit usually ranging from 10^{-9}~10^{-13} mol/L. Laser Induced Fluorescence together with the use of photon counting, two-photon excitation and other technology can even improve the detection accuracy to a single molecule level, when deal with the fluorescence efficient biochemical substances. Since the microfluidic chip detection of objects with fluorescent functional group or can be derived to produce the fluorescent nucleic acid, protein, amino acids and other chemical. So the laser-induced fluorescence detection is most widely used optical detection means so far. Conventional laser-induced fluorescence detection use orthogonal light path design to reduce background interference, but micro-scale microfluidic chip use laser confocal optical design, shown in Fig. 1, to achieve the same goal. The LIF detection system can be divided into semiconductor diode lasers.

Ordinary laser: Cho *et al*. (2003) carried the study of the LIF detector associated with microfluidic chips. Xiao-Mian *et al*. (2004) reported the use of Nd: YAG (peak wavelength 532 nm) as light source, photoelectric

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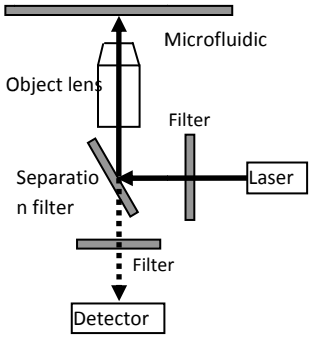

Fig. 1: Structure of fluorescence detection

detection in a homemade glass chip, the results show that the limit of the detection of rhodamine 6G is 1×10^{-10} mol/L. Kong *et al*. (2009) designed a microfluidic chip and linear confocal laser-induced fluorescence detector consisting of microfluidic chip immunoassay device for the Determination of Clenbuterol (Clenbuterol) content. Realized by controlling the microchip integrated micro valves and micro pumps, fluid delivery and testing automation, reducing reagent consumption and analysis time (30 min) is to obtain a good detection performance (linear range is 0~5.0 ng/mL and the detection limit is 0. 088 ng/mL).

Semiconductor diode lasers: The volume of LIF detector is large. The complex optical systems inside are expensive, which is incompatible with the characteristics of the microfluidic chip analysis system. Therefore, people show a strong interest on small size, low-cost semiconductor Light-Emitting Diode (LED), although its luminous intensity, spectral purity and condenser are less than the semiconductor diode laser. Structure of the detection system can be simplified, reduce the manufacturing of microchips costs. Webster *et al*. (2001) designed a LED integrated on-chip fluorescence detection technology. This processing technology etching on silicon making a silicon photodiode and optical interference filter in the above system on a gold electrode and forming a complete chip electrophoresis system, the system of YOYO-1 labeled DNA fragments of the detection limit reached 7.5×10^{-11} g. Chabinyc *et al*. (2001) made a system the upper part of the Polydimethylsiloxane (PDMS) chip to do with the channel and near the edge of the separation channel fixed multimode fiber core diameter of 100 and 80 μm thickness PDMS membrane covering the bottom of the structure, embedded in another PDMS film micro avalanche photodiode covered with a layer of filter membrane to form a chip substructure. The two part structure sealing the complete chip, the fluorescence factors detection limit was 25 nmol/L.

Although the laser-induced fluorescence detection has high sensitivity, its detection system is very complex, high cost and difficult to miniaturization. A lot of material does not have a natural fluorescence properties, which need to use a fluorescent marker, the credibility of many tests can not ensure that the mark on the nature of the dye material changes directly influence the results.

ABSORBANCE DETECTION

The absorption optical detection is a common optical detection method. Due to the small size of microfluidic chip detection, absorption of short optical path, resulting in relatively low sensitivity of detection, its application has been very limited. For this reason, scientists attempt to increase the absorption of the optical path detection cell to improve the detection sensitivity. To sum up, it can be divided into three categories: axial detection, multiple reflections detection and liquid core waveguide detection.

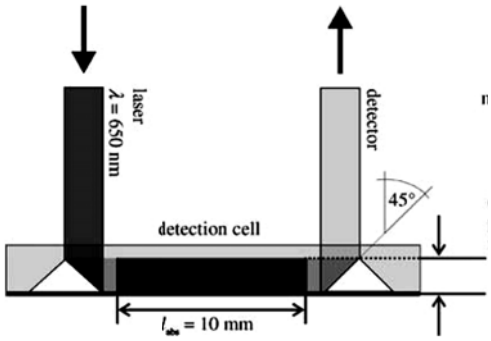

Fig. 2: Transverse axial detection flow cell structure

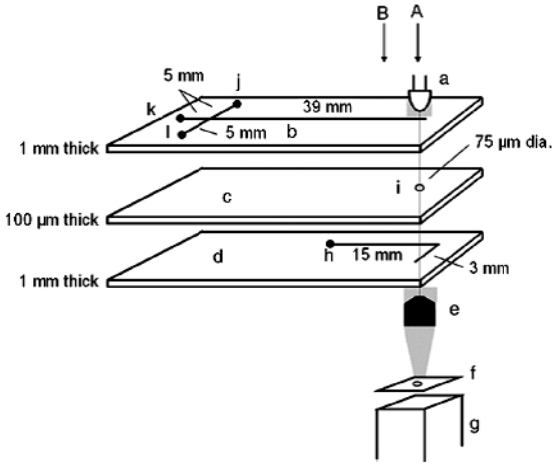

Fig. 3: Longitudinal axial detection flow cell structure

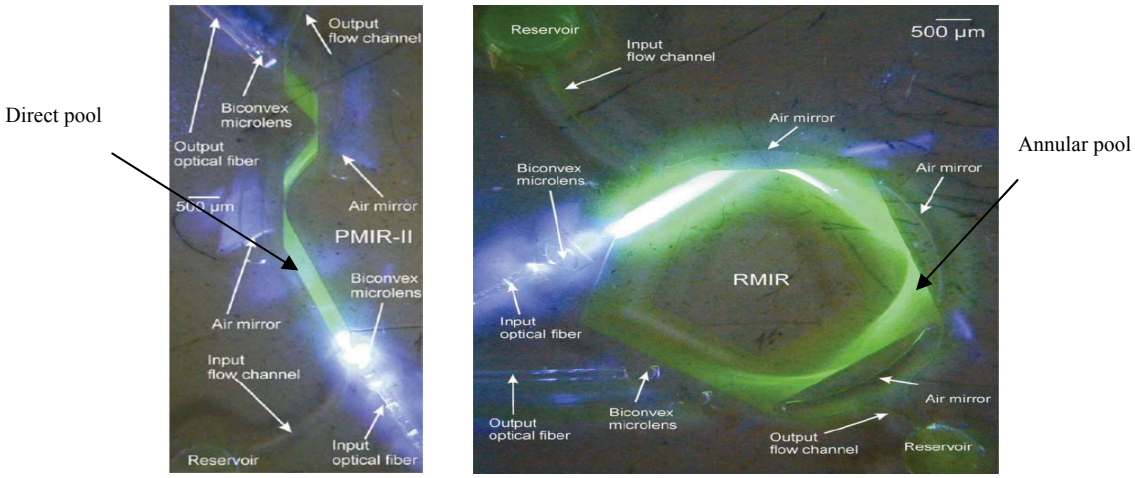

Fig. 4: Chip diagram of the direct and annular pool

Axial detection: Grumann *et al*. (2006) built transverse axial detection flow cell incyclic hydrocarbon copolymer (Cycloolefin, copolymer) centrifugal chip, flow cell structure shown in Fig. 2. An axial length of 10 mm micro-channel processing on the chip, the channel at both ends of the design of two triangular groove, the groove surface and the channel plane angle of 45°. The groove surface reflection along the axial channel through the flow cell to reach the other side of the groove is reflected into the detector to detect. The system is available to the effective optical path 10 mm, but to avoid the laser beam into the sidewall of the flow cell, flow cell width of 20 mm, making the large increase in consumption of sample. Collins *et al*. (2007) invented another longitudinal axial detection for capillary electrophoresis chip absorbance analysis system, the chip architecture shown in Fig. 3. The electrophoretic separation of cross-channel chip for the three-tier structure, the upper layer processing, separation of the end of the channel and the lower chip is connected through a laminated chip 75 µm holes through the laminated chip thickness of 100 µm. LED and PMT are the light source and detector at normal incidence of light above the chip detected by the PMT through the laminated vertical channel. The chip obtained 126 µm, the effective optical path.

Repeatedly reflex: Multiple reflections detection is the specular reflective layer produced within the micro channel, making the detection of light multiple reflections between the mirrors, which extended optical path. Specular reflection from the surface to provide smooth chip material, the refractive index difference between the transparent materials formed by total internal reflection interface can be used to apply.

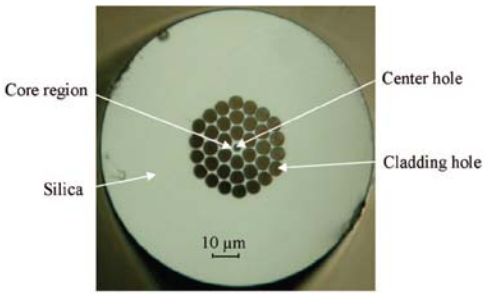

Fig. 5: Cross-section of the photonic crystal fiber

Llobera *et al*. (2007) invent a chip multiple reflection long-path absorbance detection system based on Polydimethylsiloxane (Poly (dimethylsiloxane), PDMS), its principle is shown in Fig. 4. Air reflectors are made on both sides of the fluid channel of the PDMS chip. The system uses the direct and annular pool to obtain the effective optical path of 8 and 14 mm. The system processing and optical tuning is relatively simple, air-focusing lens, air-mirror and micro-channel through soft lithography technology, without post adjustment. However, the enhancement of the optical path depends largely on the diameter and length of the channel to obtain higher optical path reagent cost inevitably increases. Sun find pores arranged in a circle based on multiple cross-section of the PCF (Photonic the Crystal Fiber PCF) contain the scale of the wavelength. These pores are roughly the same order of magnitude and throughout the entire length of the fiber. The light waves are limited to propagation in the fiber core area. The middle of the pores were used as a flow cell to detect the light focused by the lens port incident from the PCF, trapped in the fibers within the heart region spread along the

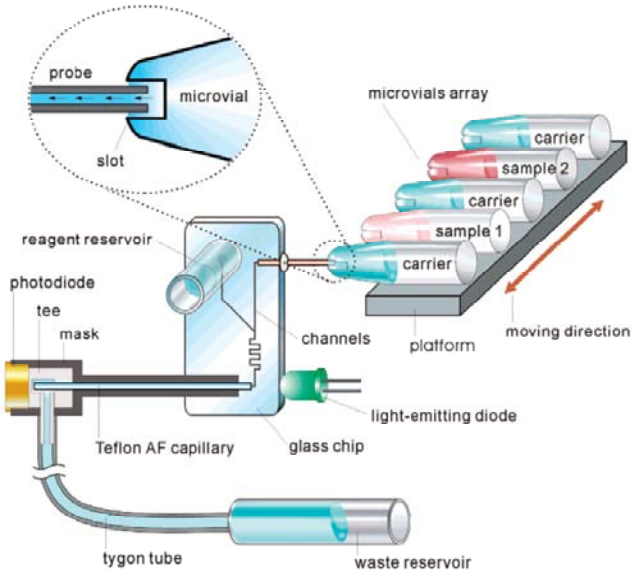

Fig. 6: Teflon AF2400 absorption spectrophotometry

PCF. The system reaches the 50 mm length of PCF with a 9.3 mm effective optical path (Sun *et al*., 2008). Figure 4 shows the chip diagram of the direct and annular pool. Figure 5 shows the Cross-section of the photonic crystal fiber.

The liquid core waveguide to detect: Du, etc., use liquid core waveguide tube glass chip to build a long optical path flow cell, the system structure shown in Fig. 6. Flow cell is made up by a long 2 cm of Teflon AF2400 liquid core waveguide composition. Waveguide connect to the inlet of the reaction channel outlet end. It mixed reaction produced a colored solution through the flow cell, which can be detected in the Y-shaped channel of the solution on the chip. The effective optical path is 17 mm and the detection volume is only 40 nL (Du *et al*., 2005).

CHEMILUMINESCENCE DETECTOR

Chemiluminescence is the emission of energy with limited emission of heat (luminescence), as the result of a chemical reaction. Chemiluminescence is one of the ideal detection methods in microfluidic chip system. It has the advantage of high sensitivity, easy integration and not require light source.

Ordinary chemiluminescence detector: Huang *et al*. (2001) use the H-type channel electrophoresis chip with flow injection chemiluminescence reagents (luminol-hydrogen peroxide) by detection of the bottom of the pool into the encounter and migrated from the separation channel samples (metal ions), light-emitting reactionthe light emitted by the optical fiber to collect and pass to the photomultiplier tube, the Co (II) and Cu (II) detection limits were 1.25×10^{-8} and 2.3×10^{-6} mol/L, respectively. Zhao *et al*. (2009) use other chemiluminescent detection for microfluidic chip determination to a single individual red blood cells glutathione. The determination of glutathione in human red blood cells is 64.9 mol/cell.

ELECTRO CHEMILUMINESCENCE DETECTOR

Electro Chemiluminescence (ECL) is a chemical reaction and the energy released in the form of light caused by the power. ECL detection device is simple, sensitive and controlled the degree of response. ECL reaction use more terpyridine ruthenium Ru (bpy) 32+ reaction system. The reaction system for a wide detector into the micro fluidic chip. They placed U-range can be applied to the analysis of a variety of substances. Arora *et al*. (2001) firstly integrated ECL shaped suspended platinum electrodes in separation channel. The potential of the electrochemical reaction required to rely on electrophoresis separation channel electric field in the U-shaped electrodes at both ends. Two-foot U-shaped electrode as the electrochemical reaction electrode and the counter electrode, determination of amino acid sample confirmed the initial electrophoresis chip feasibility of ECL determination. Qiu *et al*. (2003) use the lithography to make Indium-Tin Oxide (ITO) electrode, integrated ECL detector. The chip determination of proline detection limit was 1.2 μmol/L.

Table 1: Comparison of a variety of optical detections

The main testing methods	Detection limit (mol/L)	Advantage	Disadvantage
Laser induced fluorescence detection	10^{-9}~10^{-12}	High sensitivity, up to single molecule detection	Analyte fluorescence characteristics; fluorescently labeled substance chemical activity may result in changes
Absorbance detection	10^{-7}	Versatility, analysis of material need not be derived or mark	Sensitivity is low, the chip material and structural requirements
Chemiluminescence detection	10^{-8}	Without light, simple equipment, easy to implement integrated	Chemiluminescence reagents and test substance and efficient mixing, the composition of the reaction
Electro chemiluminescence detector	5×10^{-13}	High sensitivity and selectivity	Detection of substances have electrochemical activity, poor reproducibility

CONCLUSION

The characteristics of the various detection methods are shown in Table 1. With the development of MEMS technology, a variety of micro scale electronic components, optical devices are able to more easily be created before processing and more broadly applied to the chip-level detector. In order to further improve the efficiency, speed of detection and the scope of application of the device, detector integrated on a chip multi-channel parallel detection and integration on a single chip in different ways will become the future direction of development.

ACKNOWLEDGMENT

This study was supported the Priority Academic Program Development of Jiangsu Higher Education Institutions (PAPD).

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