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Optical biosensors based on microfluidic chip

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Abstract. Microfluidic chips have the advantages of small sample size, low detection cost, and short detection time. Combined with optical sensors, electrochemical sensors, and microwave sensors, they can be used to construct sensitive, repeatable, and portable detection systems. Optical biosensors are powerful analytical instruments that can measure biomolecular interactions in real-time and unlabeled manner. The combination of affinity and kinetics can be measured through high sensitivity. many optical biosensors have microfluidic control, making them extremely sensitive. Combining the concept of microfluidic technology, this article briefly elucidates the various cutting-edge research fields of microfluidic technology combined with optical biosensors, such as optical detection methods suitable for microfluidic chips, microfluidic biological immunofluorescence detection, the application of microfluidic technology in optical detection methods. It also prospects the future development direction and the challenges as well as strategies for addressing the problems in the development of the new generation of biological microfluidic sensors were proposed.

Keywords: optical, microfluidic chip, biosensors.

1. Introduction

With the rapid development of microelectromechanical technology, a wave of miniaturization manufacturing has emerged, and various new technologies characterized by miniaturization, high sensitivity, and intelligence have emerged. Microfluidic chip technology was born in this context. In recent years, microfluidic chip technology has gradually become a research hotspot in the current cutting-edge analysis field due to its miniaturization, low cost, and high sensitivity characteristics. Researchers integrate complex external fluid migration processes into micro chambers with scales ranging from a few micrometers to a few hundred micrometers, and use various microfluidic control technologies such as electrochemical reactions, electrostatic drive, and pneumatic control to achieve precise control of fluid inside pipelines. At present, this technology has been widely applied in various fields such as biochemical analysis, fluid control, and microfluidic optical chips. In recent years, optical analysis and detection systems have been widely used in material detection and analysis due to their integrated, high-precision, and high sensitivity characteristics. However, traditional optical analysis instruments have many defects such as large volume, expensive price, and poor adjustability, which cannot meet the current requirements of micro integration and become a barrier to the further progress of modern micro optical systems. Based on this background, researchers began to apply the concept of microfluidics to miniaturized optical switches, opening a new chapter in the study of miniaturization of optical systems. With the continuous deepening of research on microfluidic optical

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systems, microfluidic chip technology and optical systems have further deepened their connection in various fields, such as detection and analysis, processing and manufacturing, and immunofluorescence analysis. In today's rapidly developing technology, it is believed that in the future, microfluidic technology will also open up a new research approach in optical systems. This article reviews the cutting-edge research fields of microfluidic technology in optical systems in recent years, mainly elaborating on optical detection methods that suit microfluidic chip and representative application fields combined with microfluidic technology such as protein immunoassay and heavy metal fluorescence detection.

2. Optical detection

2.1. Raman spectroscopy detection:

The combination of Surface enhanced Raman spectroscopy (SERS) and microfluidic chips for optofluid detection can achieve fast and non-destructive detection and analysis. Raman spectroscopy can characterize the vibration, rotation, structural characteristics and other spectral fingerprint information of material molecules. Compared to other spectral detection methods such as near-infrared spectroscopy, fluorescence spectroscopy, X-ray spectroscopy, etc., Raman spectroscopy has superior sensitivity and resolution.

Raman spectroscopy can semi-quantitatively represent the content and category of substances based on the Raman shift and intensity information expressed by different structural molecules. It has high detection sensitivity for both polar and non-polar molecules and is currently widely used in the analysis and detection of solid-liquid substances.

Surface enhanced Raman spectroscopy is an emerging advanced trace analysis technique with ultra-high sensitivity and unlabeled fingerprints. Stable, reproducible, high-strength, and highly sensitive SERS signals are the primary conditions for obtaining effective biosensing information.

Numerous studies have shown that controllable metal nanoparticle aggregates or nanoparticle arrays are crucial for generating the aforementioned SERS signals. In clinical immune testing, SERS biosensors can not only quickly detect a single biological protein marker, but also achieve simultaneous detection of sensitive and specific biomarkers based on solid-state SERS active substrates. Portable and intelligent microfluidic SERS biosensor detection equipment will be widely used in fields such as healthcare, environmental monitoring, and food safety.

For example, Castano et al. integrated microfluidic chips, optical tweezers, and Raman detection for real-time detection of the hemoglobin oxygen molecule conversion process of a single red blood cell [1]. Optical tweezers were used to bind a single red blood cell in a microfluidic pipeline, and Raman resonance spectroscopy was used for real-time detection, enabling synchronous changes between intracellular oxygen cooperation and spectral signals for scientific researchers. Huang et al. tested red blood cells and compared them with traditional detection methods, proving that the signal difference between normal and abnormal red blood cells detected through Raman spectroscopy is greater, and the detection sensitivity is higher [2].

Alexandra et al. used SERS to examine and evaluate the number and distribution of Silver Nanoparticles in living cervical cancer cells, combined with cell viability measurements [3]. The system schematic of this chapter is shown in Fig. 1 [3].

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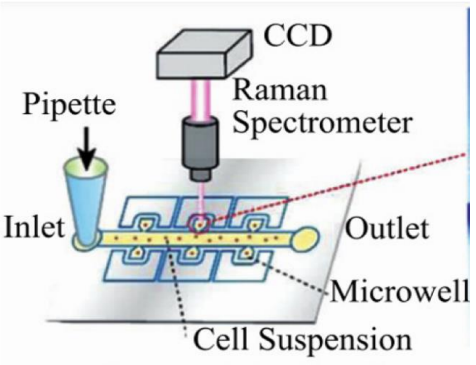

Figure 1. Schematic diagram of single cell SERS system based on microfluidic chips [3].

2.2. Refractive index detection

The refractive index of a material is a physical quantity that measures the speed at which electromagnetic waves propagate within the material. It is defined as the ratio of the propagation speed of electromagnetic waves in vacuum and a certain medium. The combination of microfluidic technology and refractive index detection methods is widely used in biomedical detection. The physical properties of samples are characterized through refractive index detection, which is suitable for certain analytes that cannot be detected by fluorescence spectroscopy, such as sucrose, polyethylene glycol (PEG), and other substances without fluorescence characteristics. The refractive index of cells, as a physical property of the cell itself, varies with the size of the cell volume and the diversity of surface proteins. In addition, the refractive index of cells is closely related to the microenvironment in which they are located, and real-time detection of the current physiological state of cells can be achieved based on changes in the refractive index properties of cells.

For example, Liu's team has established a small refractive index microfluidic detection system. In this study, optical fibers are used to position laser focused targets on the surface of individual cells, thereby achieving refractive index detection of individual cells. This chip system integrates three functions: Bragg grating, cell microenvironment regulation, and droplet separation. It not only achieves non-destructive online refractive index detection of living cells, but also avoids changes in refractive index detection values caused by external uncertain factors that alter cell physiological characteristics [4-6]. The system schematic of this chapter is shown in Fig. 2 [7].

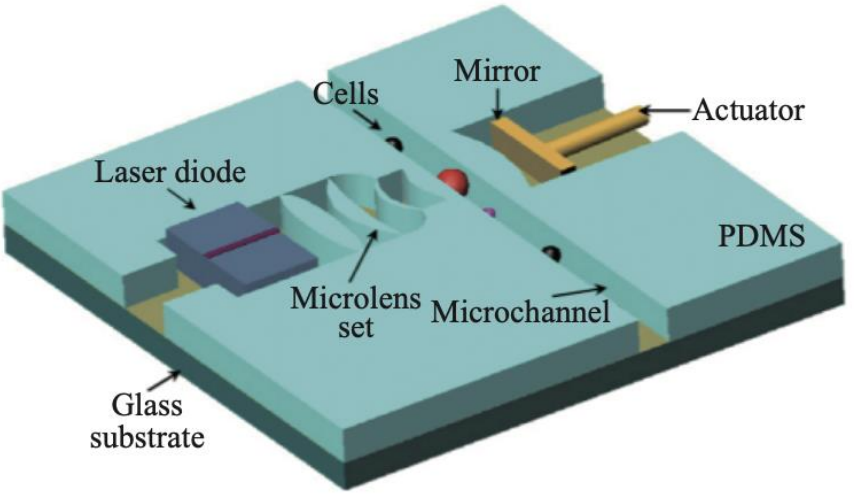

Figure 2. Schematic diagram of microfluidic refractive index detection chip structure [7].

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3. Fluorescence analysis

3.1. Protein immunoassay

Protein immunoassay is based on specific reactions between antigens and antibodies. Conventional immunoassay includes three types: direct competition, indirect competition, and sandwich method. The testing principle is based on the specific adsorption between the antigen or antibody loaded on the solid-phase carrier and the reactant in the sample, thereby achieving the function of capturing the target substance. Then, the dynamic information of the target protein content to be tested can be obtained by comparing it with the linear correlation curve of the standard substance [8-10]. This principle is also widely applied in the field of microfluidic protein detection.

For example, Deng et al. used microfluidic chips to generate micro droplets carrying T cells, and then measured the protein content using immunocapture microspheres and fluorescent secondary antibodies [10]. In addition, immune capture microspheres and fluorescent labeled secondary antibodies can also be directly fixed in microfluidic pipelines using magnetic force or design microfluidic screening structures. By detecting the fluorescence on the surface of the captured microspheres, the content of the target protein in the sample can be obtained. At present, the microfluidic immunofluorescence detection platform designed based on microfluidic technology and combined with immune capture microspheres has been widely used.

3.2. Heavy metal fluorescence detection

Fluorescence detection is also commonly used to detect trace levels of heavy metal ions. For example, Bian et al. used microfluidic chips to measure the concentration of trivalent chromium through online fluorescence derivatization and laser induced fluorescence light, Spectral analysis of Cr (III) [11]. The combination of this self-assembled portable fiber optic fluorescence spectrometer and microfluidic chip enables the detection of Cr (III) concentration in actual water samples. Finally, the chemical sensor exhibits the advantages of high sensitivity, stability, fast response, and low sample consumption. Peng et al. established a simple, portable, and recyclable method for real-time detection of mercury and lead ions by using test paper based on gold (Au) nanoclusters as a fluorescence sensor [12]. This work starts with the structure of microfluidic chip fluorescence detection systems, and elaborates on the development and improvement of microfluidic chip fluorescence detection systems from the aspects of excitation light sources, light transmission assistance methods, and detectors. With the rapid development of life sciences, medicine, and pharmacy, microfluidic chip detection technology is increasingly being applied in various disciplines, and the requirements for its detection performance are also increasing, such as requiring low sample consumption, high analytical flux, fast analysis, high detection sensitivity, and good selectivity.

4. Conclusion

This article starts with the optical detection methods and applications of microfluidic chips, and elaborates on the application and development of microfluidic chip fluorescence detection systems from aspects such as Raman spectroscopy detection, cell refractive index detection and fluorescence analysis of proteins and heavy metals. With the rapid development of life sciences, medicine and pharmacy, microfluidic chip detection technology is increasingly applied in various disciplines, and the requirements for its detection performance are also increasing, such as low sample consumption, fast analysis, high analytical flux, high detection sensitivity, and good selectivity.

With the continuous development of analysis and detection technology, although microfluidic chip detection technology combined with optical biosensors has made certain progress, there is still some development space: for one thing, through integrated microfluidic systems combined with optical tweezers, nanotechnology and other means, the detection process can be more simple and fast. In the future, other detection technologies can be integrated to further improve detection resolution and signal range. And the reagents used for detection, such as enzymes, antigens, antibodies, etc., have high environmental requirements and are difficult to obtain and use immediately, lacking convenience.

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For the other, microfluidic optical detection is also developing towards miniaturization. By miniaturizing the light source, detection module as well as analysis unit, the volume of the microfluidic chip detection system is further reduced, improving convenience.

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