

New technology and application of microfluidic technology in biological sample analysis

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Abstract: Microfluidic technology has become a revolutionary potential technology in the field of biological sample analysis. This paper summarizes the new technology and application of microfluidic technology in biological sample analysis, emphasizing its key role in high-throughput analysis, single-cell analysis, personalized medicine, environmental monitoring and future development trends. In the new technology and application of microfluidic technology, high throughput analysis is a prominent direction. Microfluidic system can effectively process a large number of biological samples, reducing the time-consuming and cost of experiments. This provides powerful tools in the fields of genomics, protein omics and drug screening, and provides new opportunities for scientific research and clinical diagnosis. Single cell analysis is another remarkable application of microfluidic technology. Microfluidic chip can efficiently analyze a single cell and reveal cell heterogeneity and disease mechanism. This provides a profound insight for cancer research, immunology and neuroscience. In the future, microfluidic technology will continue to promote the development of biological sample analysis. Multifunctional chips, portable applications and the combination with machine learning will provide researchers with more tools and methods to deeply understand the complexity of biology.

1. Introduction

Microfluidic technology is a booming interdisciplinary field, which combines the knowledge of micro-electromechanical systems (MEMS), nanotechnology and biology, aiming at precisely controlling the flow of liquid and gas in micron scale. With the continuous evolution and increasing demand in the field of biological sample analysis, microfluidic technology has become a powerful tool to realize efficient, automated and miniaturized biological analysis [1-2]. In the past decades, microfluidic technology has made remarkable progress in the analysis of biological samples, providing researchers with a unique opportunity to understand the complexity of biological systems more deeply. The development of this technology has created many new opportunities, from basic research to clinical diagnosis, covering a wide range of application fields.

This paper will discuss the new technology and application of microfluidic technology in biological sample analysis. First of all, we will review the basic principles of microfluidic technology, including the characteristics of microfluidic, the design and preparation of microfluidic chips, and the operation and control methods of fluids. Then, we will introduce the latest progress of microfluidic technology in the preparation, separation, detection and analysis of biological

samples, including cell sorting, DNA sequencing, protein analysis and microbial detection. These applications not only have important value in life science research, but also have a far-reaching impact in medical diagnosis and drug research and development [3].

Microfluidic technology provides a new perspective and tool for biological sample analysis, which is expected to play a more important role in future research and clinical practice. By studying the latest progress and application of microfluidic technology, we can better understand the complexity of biological systems and make contributions to the progress in health science and medicine.

2. Basic principles of microfluidic technology

Microfluidic technology is a technology to manipulate liquid flow at micron scale, which combines the knowledge of microfluidic dynamics, MEMS, chemistry and biology. This technology has made remarkable progress in the fields of biological sample analysis, life science research, medical diagnosis and drug research and development [4]. To deeply understand microfluidic technology, we need to master its basic principles, including microfluidic characteristics, microfluidic chip design and preparation, and fluid operation and control methods.

(1) Microfluidic characteristics

Microfluid refers to the fluid that moves on the micron scale. Compared with traditional macrofluids, micro-fluids show some unique characteristics, including:

Capillary phenomenon: Capillary phenomenon plays a leading role in microfluidic system due to the micro-scale of microfluidic channel, which leads to obvious surface tension effect of liquid in the channel.

Low Reynolds number: the liquid in the microchannel usually flows at a low Reynolds number, so there will be no turbulence, but a laminar or steady flow.

Fast mass transfer: due to the small scale of microfluidic channel and fast mass transfer speed, it is helpful for mixing and reaction.

(2) Design and fabrication of microfluidic chip

Microfluidic chip is the core of microfluidic technology. These chips are usually prepared by micromachining technology, including lithography, thin film preparation, three-dimensional printing and so on. The design of microfluidic chip needs to consider the flow channel structure, the layout of components such as valves and pumps, and the interface that interacts with biological samples [5-6]. Chips are usually made of materials such as polydimethylsiloxane (PDMS) or glass to ensure compatibility and transparency. Fig. 1 shows a microfluidic refractive index detection chip structure.

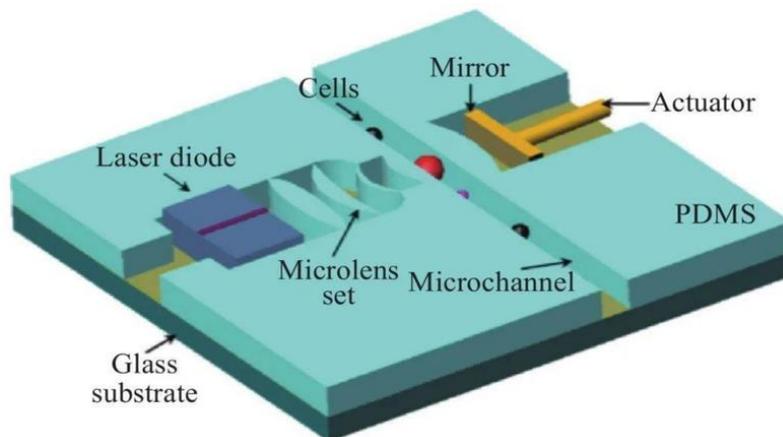


Figure 1: Microfluidic refractive index detection chip structure

(3) Fluid operation and control method

Microfluidic technology uses many methods to control the flow in microfluidic, including:

Valves and pumps: Microfluidic chips usually include micro valves and pumps to control the flow and distribution of liquids.

Electric field control: electrophoresis and electrokinetic flow are commonly used methods in microfluidic systems, which can be used to sort and separate charged particles.

Bubble drive: By introducing bubbles, the liquid can be driven to flow in the microfluidic channel, so as to realize mixing and manipulation.

The basic principle of microfluidic technology allows for highly accurate manipulation of biological samples at the micron scale, realizing automatic and miniaturized analysis. The application of this technology includes cell sorting, DNA sequencing, protein analysis, microbial detection and so on, which is of great significance for life science and medical research. By deeply understanding the basic principle of microfluidic technology, researchers can better apply and develop this field and promote the development of biological sample analysis and medical diagnosis.

3. Application field of microfluidic technology

3.1. Cell sorting and capture

The application of microfluidic technology in the field of cell sorting and capture has made remarkable progress, which provides a powerful tool for biomedical research and clinical application. Microfluidic technology allows the design of highly integrated microfluidic chips, which contain various elements needed for cell sorting and capture, such as microchannels, valves, pumps and detection and analysis devices. This highly integrated design reduces the complexity of laboratory operations, improves the efficiency of experiments, and reduces the potential sample pollution and loss.

It has been studied that the capture of a single slim hug can also be realized quickly by using the size of the slim hug or its electrical, magnetic, acoustic and optical characteristics [7]. Using dielectrophoresis (DEP) force applied to cells, larger podocytes can be captured in each well in a few minutes. As shown in fig. 2, the DEP force exerted on the cells is proportional to the size of the cells, which is in contrast to the smaller normal blood cells, and the larger podocytes will be preferentially trapped in the pores. The device consists of a microporous array chip and a glass plate coated with indium tin hydride (ITO) film. Hundreds of thousands of micropores are patterned on the photoresist (SU8) film, and die electrodes are formed on the glass substrate coated with ITO, so that the ITO electrode is at the bottom of each hole. When an alternating voltage is applied between the electrodes, the frequency is 100 kHz-10 MHz, and the potential is 20-50Vp-p, and a non-uniform electric field with the intensity of 40-100kV/m is generated in each hole, so that cells labeled with magnetic particles will be trapped.

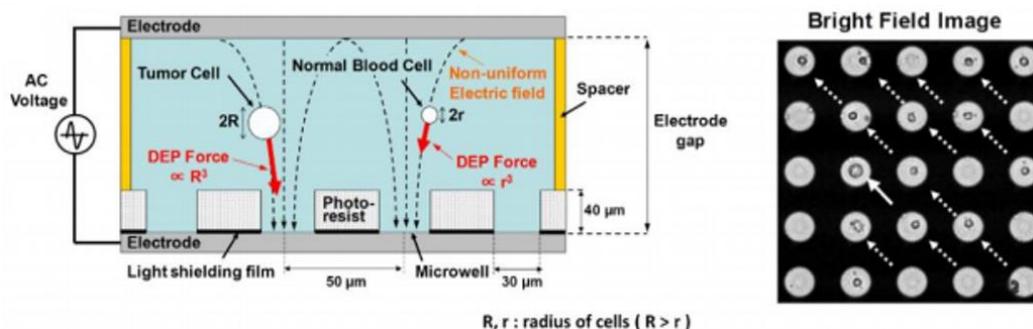


Figure 2: Schematic diagram of capturing cells in micropore array by DEP force

Microfluidic technology usually requires a very small sample size in cell sorting and capture. This is very valuable for restricted biological samples, such as clinical specimens or rare cell subsets. The micro-channel of microfluidic technology allows effective use of limited samples and reduces waste. Microfluidic technology provides high-resolution cell sorting and capture. Through the micro-detection device on the microfluidic chip, the properties of cells, such as size, shape, surface marks and so on, can be monitored and analyzed in real time. This provides a highly sensitive analysis and helps to identify and separate different types of cells.

Microfluidic technology is widely used in many fields, including oncology, immunology, stem cell research and microbiology. In cancer research, microfluidic technology can be used to capture circulating tumor cells, which provides a powerful tool for early cancer diagnosis and disease monitoring. In stem cell research, microfluidic technology is used to sort and capture specific cell subsets, which is helpful to understand the characteristics and functions of stem cells.

3.2. DNA sequencing and gene analysis

Microfluidic technology has been successfully applied to high-throughput DNA sequencing. Through microchannels and micro-reaction chambers on microfluidic chips, multiple DNA samples can be processed in parallel to speed up the sequencing process. This method is of great significance for large-scale genome sequencing projects, such as human genome sequencing and disease gene research. Microfluidic technology reduces the sample size of DNA sequencing and gene analysis, which is very useful for restrictive biological samples. In addition, microfluidic technology usually reduces reagent consumption and analysis cost, which helps to make DNA sequencing and gene analysis more economical. Provides a highly accurate control of the DNA analysis reaction. Rapid DNA amplification, fragment separation and sequencing can be achieved through precise manipulation in the micro-reaction chamber and micro-channel. This ensures the accuracy and reproducibility of the reaction and helps to improve the data quality. The micro-detection device can realize high-sensitivity DNA detection. They can detect the number, sequence, mutation and epigenetic markers of DNA, and provide high-resolution gene analysis. This is of great significance to the study of gene expression, DNA methylation and single nucleotide polymorphism (SNP).

Microfluidic technology is widely used in the field of gene analysis, including clinical diagnosis, genomics research, personalized medicine and drug research and development. In clinical diagnosis, microfluidic technology can be used to detect genetic diseases, cancer markers and infectious pathogens. In genomics research, it is helpful to study the function and evolution of genes. In personalized medicine, microfluidic technology can be used to determine the genotype and drug response of individuals. In drug research and development, it can help to screen candidate drugs and study drug metabolism pathways.

3.3. Protein analysis and protein omics

The application of protein analysis and protein omics in biomedical research and life science is very important, which plays an important role in understanding cell function, disease mechanism and drug research and development. The application of microfluidic technology in these fields provides an efficient, automated and miniaturized solution for protein analysis.

Microfluidic technology can be used for high-throughput protein analysis (Figure 3). Through the micro reaction chamber and detection channel on the microfluidic chip, multiple protein samples can be processed in parallel to realize efficient protein analysis. This is helpful to study the expression level, subcellular localization, structure and function of protein. Protein can be separated and enriched through microchannels and micro adsorption columns on microfluidic chips[8]. This is

very useful for the detection and analysis of low-abundance protein, and is helpful for the in-depth study of protein in complex biological samples. Microfluidic chip integrates many functions, including sample loading, separation, detection and data analysis, which reduces the complexity of laboratory operation. In addition, microfluidic technology usually requires less reagents and samples, which reduces the analysis cost. Micro-detection devices on microfluidic chips can monitor and analyze the properties of protein in real time, such as molecular weight, structure and subcellular localization. This provides a high-resolution protein analysis, which helps to identify different types of protein and their functions.

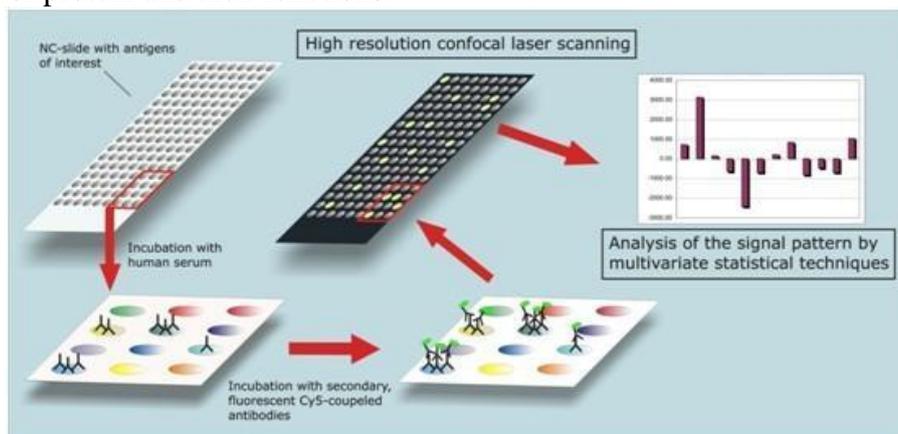


Figure 3: Fully automatic microfluidic protein detection and analysis system

Microfluidic technology is widely used in protein analysis and protein omics, including biomedical research, clinical diagnosis, drug development and food safety. In biomedical research, microfluidic technology is used to study the relationship between protein and diseases, such as the discovery of cancer markers. In clinical diagnosis, it can be used to detect biomarkers and assist disease diagnosis. In drug research and development, microfluidic technology is helpful to screen drug targets and study drug interactions in protein.

3.4. Drug screening and drug delivery system

The application of microfluidic technology in drug screening and drug delivery system has made remarkable progress, providing innovative solutions for drug research and development, personalized therapy and drug delivery. Through the micro-reaction chamber on the microfluidic chip, multiple drug candidate compounds and cell models can be processed in parallel to achieve efficient screening. This helps to reduce the time and cost of drug research and development. By integrating the patient's biological samples (such as blood or tissue samples) with the microfluidic system, the drug sensitivity test can be carried out. This allows doctors to choose the most suitable treatment scheme according to the individual characteristics of patients and improve the treatment effect.

The application of microfluidic technology in drug delivery system is very promising. Microfluidic chips can be used to design and test micro drug delivery systems, such as microneedle arrays, micropumps and nanocarriers. These systems can achieve accurate drug delivery, which is helpful to improve the efficacy of treatment and reduce adverse reactions.

Microfluidic technology allows the establishment of three-dimensional cell culture system in microfluidic chip to simulate the complex cell microenvironment in human body. This is helpful to evaluate the effect of drugs in vivo more truly, thus improving the accuracy of drug screening.

Microfluidic technology creates a micro-laboratory, which reduces the volume and cost of laboratory equipment. This is helpful to carry out rapid preliminary screening experiments and

reduce the waste of time and resources in drug development. Microfluidic technology can also be used to evaluate the safety of drugs. By simulating drug metabolism and toxicity test in microfluidic chip, potential safety problems can be found and solved earlier and the efficiency of drug development can be improved.

3.5. Microbial detection and identification

Microfluidic technology can be used for rapid and efficient microbial detection. Micro-channels and micro-reaction chambers on microfluidic chips allow rapid analysis of microbial samples and reduce detection time. This is of great significance for quickly discovering pathogenic microorganisms, monitoring water quality and food safety.

Microfluidic technology can be used for the separation and enrichment of microorganisms. Through microchannels and micro-filtration devices on microfluidic chips, microorganisms can be separated and enriched, and background interfering substances can be reduced. This is helpful to improve the specificity and sensitivity of detection. There is a paper focusing on the rapid drug sensitivity detection of microorganisms [9]. In this study, a micro-droplet chip based on flow resistance is designed, and the resazurin biological indicator can indicate the growth of microorganisms under different concentrations of antibiotics within 5 hours. The chip has several independent retention chambers, which can automatically generate antibiotic concentration gradient and form independent micro-droplets for detecting bacterial drug sensitivity. The chip simplifies the control operation and equipment integration, shortens the time of drug sensitivity detection compared with the traditional method, and has a good application prospect. Fig. 4 is a schematic diagram of the design and application of concentration gradient microfluidic chip for drug sensitivity detection of bacterial antibiotics: (a) the manufacturing process of the chip; (b) The process of generating gradient concentration in the chip. Among them, the chip mold is made of Mozambican precision nanoArch S140.

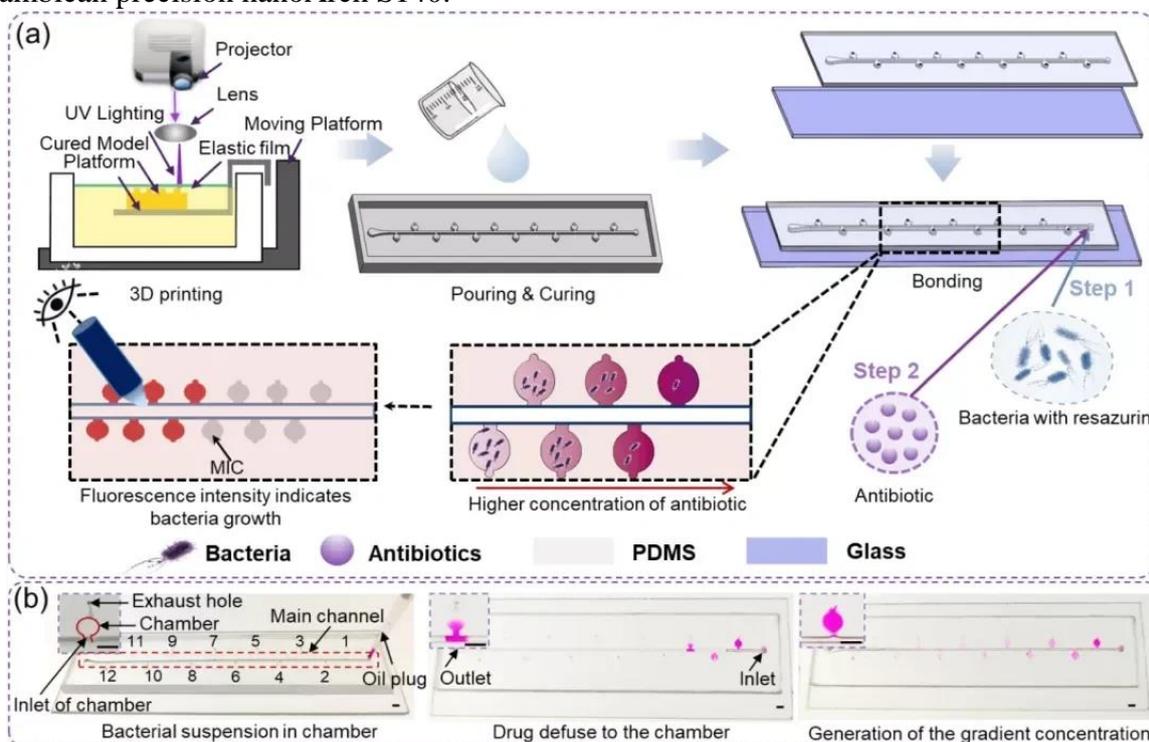


Figure 4: Design and application of concentration gradient microfluidic chip for drug sensitivity detection of bacterial antibiotics

Microfluidic technology realizes the automation and miniaturization of microbial detection. Microfluidic chip integrates many functions, including sample processing, bacterial culture, analysis and data processing, which reduces the complexity of laboratory operation. In addition, microfluidic technology usually requires less reagents and samples, which reduces the detection cost.

Micro-detection device of microfluidic technology can realize high-sensitivity microbial detection. They can detect the number, species, subspecies and antibiotic resistance of microorganisms, and provide high-resolution microbial analysis. This is very useful for monitoring the epidemiology and antibiotic sensitivity of pathogenic microorganisms.

Microfluidic technology is widely used in the field of microbial detection and identification, including medical diagnosis, environmental monitoring, food safety and biological deterioration detection [10]. In medical diagnosis, microfluidic technology can be used to detect pathogenic microorganisms caused by diseases, such as bacteria, viruses and fungi. In environmental monitoring, it is helpful to monitor microbial pollution in water and air. In the field of food safety, microfluidic technology can be used to detect pathogenic microorganisms and food quality in food.

4. Future development trend

Microfluidic technology is a technology for micro-volume droplets or fluid channels, and has made remarkable progress in the field of biological sample analysis. Its future development trend includes the emergence of more new technologies and applications, which will promote the revolutionary changes in biological sample analysis. Microfluidic technology will continue to promote the development of high throughput analysis. Microfluidic chip can process hundreds to thousands of tiny reaction volumes at the same time, thus greatly improving the experimental efficiency and reducing the waste of samples and reagents.

In the future, high-throughput microfluidic systems will be used in single cell analysis, drug screening, gene sequencing and other fields. In the future, microfluidic chips will become more multifunctional. This means that they can perform more kinds of biological sample analysis, such as protein analysis, metabolite detection, cell imaging and so on. Multifunctional chips will reduce the number of devices needed for analysis and improve the convenience of experiments. Microfluidic system will be combined with automation and machine learning technology to realize the automation and data analysis of experiments. This will improve the repeatability of the experiment and help to extract useful information from large-scale data.

5. Conclusions

The continuous development and innovation of microfluidic technology in biological sample analysis has brought many important research conclusions and application prospects to life sciences and medical fields. The new technology and application of microfluidic technology in biological sample analysis have made remarkable achievements and are full of hope. It provides researchers with more tools and methods to deeply understand the fields of biology and medicine and brings more opportunities for health care and environmental protection. In the future, microfluidic technology will continue to promote the innovation and development of biological sample analysis in various fields.

References

[1] Yu Ke. (2013). *Microfluidic-based cell assay for biomedical application. Recent Patents on Biomedical Engineering*, 6(3), 195-202.

- [2] Zhao, X., Wang, G., Shao, S., Meng, Q., & Zhang, C. (2021). Terahertz characteristics of magnetic fluid based on microfluidic technology. *International Journal of Optics*, 2021(8), 1-8.
- [3] Mary, P., Dauphinot, L., Nadège Bois, Potier, M. C., & Tabelaing, P. (2011). Analysis of gene expression at the single-cell level using microdroplet-based microfluidic technology. *Biomicrofluidics*, 5(2), 24109.
- [4] Zhang, J., Sun, J., Li, B., Yang, C., & Liu, K. (2020). Robust biological fibers based on widely available proteins: facile fabrication and suturing application. *Small*, 16(8), 1907598.
- [5] Fan, J. F., Zhu, Y., Shi, X. T., Fang, Q., & Huang, J. (2012). Microfluidic sequential injection analysis system based on polydimethylsiloxane (pdms) chip with integrated pneumatic-actuated valves. *SCIENCE CHINA Chemistry*, 55(4), 531-536.
- [6] Jeremy, Masbou, David, Point, Jeroen, & E., et al. (2013). Application of a selective extraction method for methyl mercury compound specific stable isotope analysis (mehg-csia) in biological materials. *Journal of Analytical Atomic Spectrometry*, 28(10), 1620-1628.
- [7] Watanabe, T., Ono, T., & Kimura, Y. (2011). Continuous fabrication of monodisperse polylactide microspheres by droplet-to-particle technology using microfluidic emulsification and emulsion-solvent diffusion. *Soft Matter*, 7(21), 9894-9897.
- [8] Zhang, A. L., & Zha, Y. (2012). Fabrication of paper-based microfluidic device using printed circuit technology. *Aip Advances*, 2(2), 1.
- [9] Takehara, H., Jiang, C., Uto, K., Ebara, M., & Ichiki, T. (2013). Novel microfluidic valve technology based on shape memory effect of poly (ϵ -caprolactone). *Applied Physics Express*, 6(3), 7201.
- [10] Ainla, A. (2012). Hydrodynamic flow confinement technology in microfluidic perfusion devices. *Micromachines*, 3(2), 442-461.