Paper-Based Microfluidic Chips

Subjects: Others

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Traditional detectors mostly consist of complex structures that are difficult to use. However, paper-based microfluidic chips combine the advantages of small size, high efficiency, easy processing and environmental protection. Paper-based microfluidic chips for biomedical applications focus on efficiency, accuracy, integration and innovation. As a result, continuous progress has been observed in the transition from single-channel to multi-channel detection and from qualitative to quantitative detection. These developments have improved the efficiency and accuracy of single cells and biochemical markers detection. Paper-based microfluidic chips can provide insights into multiple fields, including biomedicine and other related fields.

paper-based microfluidics chips biomedicine biomarker clinical detection

1. Introduction

The perfect integration of medicine and engineering has led to the development of many biotechnologies, such as marker detection, gene amplification, cell culture, etc. In professional laboratories, however, professional instruments are used, which raises costs, makes relevant experiments more difficult, and restricts discipline development. So, biomedical research has slowly moved toward making new devices that are economical, easy to use, environmentally friendly, and yield great results.

In 1990, microfluidics was first proposed for microfluidic control in microelectromechanical systems (MEMS) [1]. Microfluidic chips were initially applied for chemical analysis [2]. Among different types of microfluidic chips, paper-based microfluidic chips have recently gained attention in the biomedical field because of their potential for developing into ideal biomedical devices [3][4].

2. Overview of Paper-Based Microfluidic Chips

2.1. Characteristics of Paper-Based Microfluidic Chips

Microfluidic chips are small and lightweight devices with highly integrated detection. It integrates sample preparation, reaction, separation, detection, and other components at the micron scale level with fine processing technology. As a result, it can carry out complex physical and chemical processes as well as complete the whole experimental analysis, from adding samples to reading results. Therefore, it is also called “lab on chip” [5][6][7]. Whitesides’ research group at Harvard University in the United States proposed the concept of paper-based

microfluidic analytical devices (μPADs) in 2007 [8]. For "lab on papers", filter paper is used as a substrate for microfluidic chips instead of inorganic or polymeric materials. There are several advantages to using paper-based microfluidic chips: the paper itself has a capillary effect, which can guide reagent flow without requiring additional power sources. Paper is relatively inexpensive, easy to obtain and process, so chip preparation cost is reduced. Similarly, the size is small and the volume is light, making it easy to transport and store. As it degrades more easily than other synthetic materials, it reduces the environmental restrictions on chips' use and is more environmentally friendly. Thus, μPADs are more economical, safer, and easier to use and transport than other microfluidic chips [9][10][11].

2.2. Materials of Paper-Based Microfluidic Chips

The design and preparation of a paper-based material plays a decisive role in determining how well the μPADs will perform. There are currently three paper-based materials widely used for the production of paper chips: filter paper [12], nitrocellulose paper [13], and glass fiber paper [14]. All of them have their own characteristics and applications (described in **Table 1**), and can also be used alone or combined with each other to achieve the overall function. Furthermore, parameters such as the thickness of the paper and the porosity of the paper also affect fluid velocity. These parameters should be taken into consideration when performing more detailed fluid control calculations [15].

Table 1. Materials of paper-based microfluidic chips [12][13][14].

Material	Characteristics	Applications
Filter paper	**Suitable water absorption, easy to obtain, low cost, poor strength**	**Suitable for all kinds of paper chips, the most widely used paper-based materials**
Nitrocellulose paper	**It can bind and fix protein, and high cost**	**Detection based on Western blot reaction, colloidal gold test paper reaction zone**
Glass fiber paper	**Stable properties, not easy to break, high temperature resistance, corrosion resistance**	**Detection based on chemical reactions**

4. Analysis Method of Paper-Based Microfluidic Chip

The paper-based microfluidic chip focuses on the results being presented in a visual way. Using colorimetry, electrochemistry, and fluorescence, the paper chip can find out both qualitative and quantitative information about different substances based on their physical, biological, and chemical properties [44][45][46] (described in **Table 3**).

3. Preparation Method of Paper-Based Microfluidic Chip

3.1. Two-Dimensional Paper Chip Preparation

Table 3. Analysis method of paper-based microfluidic chips.

Methods	Advantages	Disadvantages
Colorimetric method	Intuitive results, easy to read with the naked eye, low cost [47][48]	Unable to achieve accurate quantitative detection [49]
Electrochemical method	Quantitatively accurate, fast reading [50][51]	Rely on electrochemical workstation, increase cost and reduce flexibility [52]
Fluorescence method	Low detection limit, very sensitive [53][54]	Relying on fluorescence detection equipment, easily affected by the signal of paper fluorescent agent [55]
United electronics	Combining the aforementioned methods enables non-professionals to obtain accurate results [56][57]	Need to install a mobile APP or even larger devices, reducing flexibility [4]
Plasma treatment technology	More suitable for mass production and have low cost [21]	Depends on templates, reducing flexibility [22]
Wax printing	Simple processing, environmentally friendly materials [23][24]	Rely on wax spray printers, heating-induced horizontal diffusion reduces structure accuracy [25]
Inkjet method	Simple processing can be drawn with ink pen, no heating diffusion, more precise structure [26][27]	Hydrophobic inks can be toxic, ink pens are inaccurate for hand drawing, still rely on inkjet printers [28]
Screen printing	Ideal for mass production, simple process, and low cost [29][30]	Rely on templates, greatly reducing flexibility during research [31]
Laser processing technology	Very precise structures can be prepared [32]	Rely on expensive laser equipment and difficult to popularize [33]
3D origami method	3D structure has more functions, direct registration of each layer [34][35]	Means of fixing are required between layers, only single material can be used [36]
3D lamination method	3D structure has more functions, can use a variety of materials [37]	Fixed means are required between layers, registration methods are required [38]
Other 3D methods	Highly innovative and has huge development potential [39]	Special uses, difficult to promote [40]

Paper-based chips differ from glass, plastic, or other materials-based chips. For example, the hydrophilic channels flanked by hydrophobic barriers in paper-based microfluidic devices guide liquid flow and the reaction is etched on paper in a materials. ethods for

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s to 016; pp.

257–297.

7. Lisowski, P.; Zarzycki, P.K. Microfluidic Paper-Based Analytical Devices (μPADs) and Micro Total Analysis Systems (μTAS): Development, Applications and Future Trends. Chromatographia 2013, 76, 1201–1214.
8. Martinez, A.W.; Phillips, S.T.; Butte, M.J.; Whitesides, G.M. Patterned Paper as a Platform for Inexpensive, Low-Volume, Portable Bioassays. Angew. Chem. Int. Ed. 2007, 46, 1318–1320.

3.2. Three-Dimensional Paper Chips Preparation

In fact, three-dimensional paper chips are just a superposition of two-dimensional paper chips, but they achieve the goal of "1 + 1 > 2". By providing a multilayer structure and vertical flow channels, the flux of the paper chip is increased and the layers of the paper chip are enriched, allowing for a more controlled detection reaction in time and space, one of the new directions for paper chip development [41][42]. In comparison to 2D paper chips, 3D

9. Almeida, M.I.G.S.; Jayawardane, B.M.; Kolev, S.D.; McKelvie, I.D. Developments of microfluidic paper-based analytical devices (μPADs) for water analysis: A review. Talanta 2018, 177, 176–190. [43].

10. Dou, M.; Sanjay, S.T.; Benhabib, M.; Xu, F.; Li, X. Low-cost bioanalysis on paper-based and its hybrid microfluidic platforms. Talanta 2015, 145, 43–54.

11. Mabbott, S.; Fernandes, S.C.; Schechinger, M.; Cote, G.L.; Faulds, K.; Mace, C.R.; Graham, D. Detection of cardiovascular disease associated miR-29a using paper-based microfluidics and surface enhanced Raman scattering. Analyst 2020, 145, 983–991.

12. Zeng, Y.; Liang, D.; Zheng, P.; Zhang, Y.; Wang, Z.; Mari, G.M.; Jiang, H. A simple and rapid immunochromatography test based on readily available filter paper modified with chitosan to screen for 13 sulfonamides in milk. J. Dairy Sci. 2021, 104, 126–133.

13. Wang, C.-H.; Wu, J.-J.; Lee, G.-B. Screening of highly-specific aptamers and their applications in paper-based microfluidic chips for rapid diagnosis of multiple bacteria. Sens. Actuators B Chem. 2019, 284, 395–402.

14. Deng, D.; Lin, Q.; Li, H.; Huang, Z.; Kuang, Y.; Chen, H.; Kong, J. Rapid detection of malachite green residues in fish using a surface-enhanced Raman scattering-active glass fiber paper prepared by in situ reduction method. Talanta 2019, 200, 272–278.

15. Evans, E.; Gabriel, E.F.M.; Coltro, W.K.T.; Garcia, C.D. Rational selection of substrates to improve color intensity and uniformity on microfluidic paper-based analytical devices. Analyst 2014, 139, 2127–2132.

16. Noviana, E.; Ozer, T.; Carrell, C.S.; Link, J.S.; McMahon, C.; Jang, I.; Henry, C.S. Microfluidic Paper-Based Analytical Devices: From Design to Applications. Chem. Rev. 2021, 121, 11835–11885.

17. Brooks, J.C.; Mace, C.R. Scalable Methods for Device Patterning as an Outstanding Challenge in Translating Paper-Based Microfluidics from the Academic Benchtop to the Point-of-Care. J. Anal. Test. 2019, 3, 50–60.

18. Mahato, K.; Purohit, B.; Kumar, A.; Srivastava, A.; Chandra, P. Next-Generation Immunosensing Technologies Based on Nano-Bio-Engineered Paper Matrices. In Immunodiagnostic Technologies from Laboratory to Point-of-Care Testing; Suman, P., Chandra, P., Eds.; Springer: Singapore, 2021; pp. 93–110.

19. Wang, C.-M.; Chen, C.-Y.; Liao, W.-S. Enclosed paper-based analytical devices: Concept, variety, and outlook. Anal. Chim. Acta 2021, 1144, 158–174.

20. Busa, L.S.A.; Maeki, M.; Ishida, A.; Tani, H.; Tokeshi, M. Simple and sensitive colorimetric assay system for horseradish peroxidase using microfluidic paper-based devices. Sens. Actuators B Chem. 2016, 236, 433–441.

21. Li, X.; Tian, J.; Garnier, G.; Shen, W. Fabrication of paper-based microfluidic sensors by printing. Colloids Surf. B Biointerfaces 2010, 76, 564–570.
22. Hecht, L.; Philipp, J.; Mattern, K.; Dietzel, A.; Klages, C.-P. Controlling wettability in paper by atmospheric-pressure microplasma processes to be used in µPAD fabrication. Microfluid. Nanofluidics 2016, 20, 25.
23. Li, H.; Cui, J.; Yan, Z.; Jin, M.; Zheng, Y.; Zhou, G.; Shui, L. Paper-based electrowetting devices fabricated with cellulose paper and paraffin wax. Results Phys. 2021, 31, 105042.
24. Martins, G.V.; Marques, A.C.; Fortunato, E.; Sales, M.G.F. Wax-printed paper-based device for direct electrochemical detection of 3-nitrotyrosine. Electrochim. Acta 2018, 284, 60–68.
25. Lu, Y.; Shi, W.; Jiang, L.; Qin, J.; Lin, B. Rapid prototyping of paper-based microfluidics with wax for low-cost, portable bioassay. Electrophoresis 2009, 30, 1497–1500.
26. Lv, P.; Song, L.; Li, Y.; Pang, H.; Liu, W. Hybrid ternary rice paper/polypyrrole ink/pen ink nanocomposites as components of flexible supercapacitors. Int. J. Hydrog. Energy 2021, 46, 13219–13229.
27. Shen, W.; Filonanko, Y.; Truong, Y.; Parker, I.H.; Brack, N.; Pigram, P.; Liesegang, J. Contact angle measurement and surface energetics of sized and unsized paper. Colloids Surfaces. A Physicochem. Eng. Asp. 2000, 173, 117–126.
28. Rahbar, M.; Nesterenko, P.N.; Paull, B.; Macka, M. High-throughput deposition of chemical reagents via pen-plotting technique for microfluidic paper-based analytical devices. Anal. Chim. Acta 2019, 1047, 115–123.
29. Sitanurak, J.; Fukana, N.; Wongpakdee, T.; Thepchuay, Y.; Ratanawimarnwong, N.; Amornsakchai, T.; Nacapricha, D. T-shirt ink for one-step screen-printing of hydrophobic barriers for 2D- and 3D-microfluidic paper-based analytical devices. Talanta 2019, 205, 120113.
30. Yao, Y.; Zhang, C. A novel screen-printed microfluidic paper-based electrochemical device for detection of glucose and uric acid in urine. Biomed. Microdevices 2016, 18, 92.
31. Dungchai, W.; Chailapakul, O.; Henry, C.S. A low-cost, simple, and rapid fabrication method for paper-based microfluidics using wax screen-printing. Analyst 2010, 136, 77–82.
32. Mahmud, M.A.; Blondeel, E.J.M.; Kaddoura, M.; MacDonald, B.D. Creating compact and microscale features in paper-based devices by laser cutting. Analyst 2016, 141, 6449–6454.
33. Ghosh, R.; Gopalakrishnan, S.; Savitha, R.; Renganathan, T.; Pushpavanam, S. Fabrication of laser printed microfluidic paper-based analytical devices (LP-µPADs) for point-of-care applications. Sci. Rep. 2019, 9, 7896.
34. Sharifi, H.; Tashkhourian, J.; Hemmateenejad, B. A 3D origami paper-based analytical device combined with PVC membrane for colorimetric assay of heavy metal ions: Application to

determination of Cu(II) in water samples. Anal. Chim. Acta 2020, 1126, 114–123.

35. Cai, X.; Zhang, H.; Yu, X.; Wang, W. A microfluidic paper-based laser-induced fluorescence sensor based on duplex-specific nuclease amplification for selective and sensitive detection of miRNAs in cancer cells. Talanta 2020, 216, 120996.
36. Xiao, W.; Gao, Y.; Zhang, Y.; Li, J.; Liu, Z.; Nie, J.; Li, J. Enhanced 3D paper-based devices with a personal glucose meter for highly sensitive and portable biosensing of silver ion. Biosens. Bioelectron. 2019, 137, 154–160.
37. Park, J.; Park, J.-K. Pressed region integrated 3D paper-based microfluidic device that enables vertical flow multistep assays for the detection of C-reactive protein based on programmed reagent loading. Sens. Actuators B Chem. 2017, 246, 1049–1055.
38. Hao, G.; Zhang, Z.; Ma, X.; Zhang, R.; Qin, X.; Sun, H.; Yang, X.; Rong, J. A versatile microfluidic paper chip platform based on MIPs for rapid ratiometric sensing of dual fluorescence signals. Microchem. J. 2020, 157, 105050.
39. Jeong, S.-G.; Lee, S.-H.; Choi, C.-H.; Kim, J.; Lee, C.-S. Toward instrument-free digital measurements: A three-dimensional microfluidic device fabricated in a single sheet of paper by double-sided printing and lamination. Lab Chip 2015, 15, 1188–1194.
40. Wang, M.; Song, Z.; Jiang, Y.; Zhang, X.; Wang, L.; Zhao, H.; Cui, Y.; Gu, F.; Wang, Y.; Zheng, G. A three-dimensional pinwheel-shaped paper-based microfluidic analytical device for fluorescence detection of multiple heavy metals in coastal waters by rational device design. Anal. Bioanal. Chem. 2021, 413, 3299–3313.
41. Cao, L.; Han, G.-C.; Xiao, H.; Chen, Z.; Fang, C. A novel 3D paper-based microfluidic electrochemical glucose biosensor based on rGO-TEPA/PB sensitive film. Anal. Chim. Acta 2020, 1096, 34–43.
42. Yukird, J.; Soum, V.; Kwon, O.-S.; Shin, K.; Chailapakul, O.; Rodthongkum, N. 3D paper-based microfluidic device: A novel dual-detection platform of bisphenol A. Analyst 2020, 145, 1491–1498.
43. Yang, N.; Chen, C.; Wang, P.; Sun, J.; Mao, H. Structure optimization method of microfluidic paper chip based on image grey-level statistics for chromogenic reaction. Chem. Eng. Process. 2019, 143, 107627.
44. Ruecha, N.; Yamada, K.; Suzuki, K.; Citterio, D. (Bio)Chemical Sensors Based on Paper. In Materials for Chemical Sensing; Cesar Paixão, T.R.L., Reddy, S.M., Eds.; Springer International Publishing: Cham, Switzerland, 2017; pp. 29–74.
45. Zheng, W.; Wang, K.; Xu, H.; Zheng, C.; Cao, B.; Qin, Q.; Jin, Q.; Cui, D. Strategies for the detection of target analytes using microfluidic paper-based analytical devices. Anal. Bioanal. Chem. 2021, 413, 2429–2445.

46. Fu, L.-M.; Wang, Y.-N. Detection methods and applications of microfluidic paper-based analytical devices. TrAC Trends Anal. Chem. 2018, 107, 196–211.
47. Anderson, C.E.; Shah, K.G.; Yager, P. Sensitive Protein Detection and Quantification in Paper-Based Microfluidics for the Point of Care. Methods Enzymol. 2017, 589, 383.
48. Wei, S.; Li, J.; He, J.; Zhao, W.; Wang, F.; Song, X.; Xu, K.; Wang, J.; Zhao, C. Paper chip-based colorimetric assay for detection of Salmonella typhimurium by combining aptamer-modified nanoprobes and urease activity inhibition. Mikrochim. Acta 2020, 187, 554.
49. Calabria, D.; Caliceti, C.; Zangheri, M.; Mirasoli, M.; Simoni, P.; Roda, A. Smartphone–based enzymatic biosensor for oral fluid L-lactate detection in one minute using confined multilayer paper reflectometry. Biosens. Bioelectron. 2017, 94, 124–130.
50. Jemmeli, D.; Marcoccio, E.; Moscone, D.; Dridi, C.; Arduini, F. Highly sensitive paper-based electrochemical sensor for reagent free detection of bisphenol A. Talanta 2020, 216, 120924.
51. Yang, N.; Zhou, X.; Yu, D.; Jiao, S.; Han, X.; Zhang, S.; Yin, H.; Mao, H. Pesticide residues identification by impedance time-sequence spectrum of enzyme inhibition on multilayer paper-based microfluidic chip. J. Food Process Eng. 2020, 43, e13544.
52. Wang, W.; Ding, S.-N.; Chen, F.-F.; Zhang, Q. Electrochemical paper-based analytical device for flow injection analysis based on locally enhanced evaporation. Sens. Actuators B Chem. 2022, 371, 132517.
53. Delaney, J.L.; Hogan, C.F.; Tian, J.; Shen, W. Electrogenerated chemiluminescence detection in paper-based microfluidic sensors.(Author abstract)(Report). Anal. Chem. 2011, 83, 1300.
54. Ulep, T.-H.; Zenhausern, R.; Gonzales, A.; Knoff, D.S.; Lengerke Diaz, P.A.; Castro, J.E.; Yoon, J.-Y. Smartphone based on-chip fluorescence imaging and capillary flow velocity measurement for detecting ROR1+ cancer cells from buffy coat blood samples on dual-layer paper microfluidic chip. Biosens. Bioelectron. 2020, 153, 112042.
55. Yehia, A.M.; Farag, M.A.; Tantawy, M.A. A novel trimodal system on a paper-based microfluidic device for on-site detection of the date rape drug “ketamine”. Anal. Chim. Acta 2020, 1104, 95–104.
56. Lan, T.; Zhang, J.; Lu, Y. Transforming the blood glucose meter into a general healthcare meter for in vitro diagnostics in mobile health. Biotechnol. Adv. 2016, 34, 331–341.
57. Shrivas, K.; Patel, S.; Sinha, D.; Thakur, S.S.; Patle, T.K.; Kant, T.; Dewangan, K.; Satnami, M.L.; Nirmalkar, J.; Kumar, S. Colorimetric and smartphone-integrated paper device for on-site determination of arsenic (III) using sucrose modified gold nanoparticles as a nanoprobe. Microchim. Acta 2020, 187, 173.

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