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Title	Development of Microfluidic Paper-Based Analytical Devices (μ PADs) for Detection of Biomarkers [an abstract of dissertation and a summary of dissertation review]
Author(s)	Mohammadi, Saeed
Degree Grantor	北海道大学
Degree Name	博士(総合化学)
Dissertation Number	甲第12471号
Issue Date	2016-09-26
Doc URL	https://hdl.handle.net/2115/63395
Rights(URL)	https://creativecommons.org/licenses/by-nc-sa/2.1/jp/
Type	doctoral thesis
File Information	Saeed_Mohammadi_abstract.pdf, 論文内容の要旨



学 位 論 文 内 容 の 要 旨

博士の専攻分野の名称 博士（総合化学） 氏名 サイドモハンマディ

学 位 論 文 題 名

Development of Microfluidic Paper-Based Analytical Devices (μ PADs) for Detection of
Biomarkers

(バイオマーカー検出のためのマイクロ流体ペーパー分析デバイスの開発)

Microfluidic technology has evolved over the past few decades from a molecular analysis endeavour aimed at enhancing separation performance through reduced dimensions, into a diverse field influencing an ever-expanding range of disciplines. Microfluidic techniques are being employed in chemistry, biology, pharmacy medicine, homeland security, and other areas where their inherent advantages trump standard methodologies. Since the last decade, new generation of microfluidic devices which are termed microfluidic paper-based analytical devices (μ PADs) have gained great attention in many fields such as point of care diagnosis, environmental testing, and food analysis. These devices have numerous advantages, including low-cost fabrication, facile application, portability, and environmental compatibility. In this study new techniques have developed to fabricate a μ PAD and to utilize the fabricated μ PAD for detection of biomarkers.

This thesis is results of the author's research for 3 years from October 2013 to September 2016 in Graduate School of Engineering, Hokkaido University.

The thesis includes 5 chapters. First chapter describes the general introduction of what microfluidic technology and μ PADs are and recent development of fabrication methods.

In current chapter advantages and disadvantages of μ PADs have been studied. Second chapter describes a simple and instrument-free screen-printing method to fabricate hydrophilic channels by patterning polydimethylsiloxane (PDMS) onto chromatography paper. First, the minimum width of the printed channel to deliver an aqueous sample was studied. Fabricated μ PADs were tested for several colorimetric assays of pH, glucose, and protein in both buffer and simulated urine samples and results were obtained in less than 30 min. Chapter 3 proposes a novel technique based on spontaneous capillary force of paper substrates for μ PADs to eliminate unbound antigen and antibodies in an enzyme linked immunosorbent assay (ELISA). This study demonstrates that introduction of the washing technique will allow use of the μ PADs as the lowest cost platform of microfluidic devices with high reproducibility and sensitivity. As an assay model, C-reactive protein (CRP), a biomarker of inflammation, was detected with a limit of detection (LOD) of 5 $\mu\text{g mL}^{-1}$. Chapter 4 describes the development of a μ PAD which is a rapid, user friend, cost effective, and portable device to detect cat cystatin C (cCys-C). Since increasing of cystatin C in blood stream leads to irreparable renal disorders in pets, especially in feline, develop a facilitated technique for renal disorder diagnosis is extremely desired. At the first, cCys-C was detected using conventional microtiter plate. Next, we used a new detection system for cCys-C by a microfluidic device that termed immuno-pillar chip. In contrast with conventional 96 microtiter plate, the volume of reagent was significantly decreased from 100 μL to 0.5 μL . In addition, total analysis time was declined from 240 min to 20 min. Then, the background knowledge in this research is used to develop a new system to detect cCys-C using a μ PAD. Finally, chapter 5 summarizes this study.