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A microfluidic cigarette smoke collecting platform for simultaneous sample extraction and multiplex analysis

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ABSTRACT

In this work, we report a novel microfluidic gas collecting platform aiming at simultaneous sample extraction and multiplex mass spectrometry (MS) analysis. An alveolar-mimicking elastic polydimethylsiloxane (PDMS) structures was designed to move dynamically driven by external pressure. The movement was well tuned both by its amplitude and rhythm following the natural process of human respiration. By integrating the alveolar units into arrays and assembling them to gas channels, a cyclic contraction/expansion system for gas inhale and exhale was successfully constructed. Upon equipping this system with a droplet array on the alveolar array surface, we were able to get information of inhaled smoke in a new strategy. Here, with cigarette smoke as an example, analysis of accumulation for target molecules during passive smoking is taken. Relationships between the breathing times, distances away from smokers and inhaled content of nicotine are clarified. Further, by applying different types of extraction solvent droplets on different locations of the droplet array, simultaneous extraction of nicotine, formaldehyde and caproic acid in sidestream smoke (SS) are realized. Since the extract droplets are spatially separated, they can be directly analyzed by MS which is fast and can rid us of all complex sample separation and purification steps. Combining all these merits, this small, cheap and portable platform might find wide application in inhaled air pollutant analysis both in and outdoors.

1. Introduction

Cigarette smoke is one of the most concerning air pollutants which is closely linked with public health especially with many pulmonary diseases such as chronic obstructive lung disease [1] and cancer [2]. Thus it is important to develop delicate cigarette smoke collecting and analysis platforms to facilitate researches on the relationship between the content and certain diseases. Although many standard analysis methods have been applied for cigarette smoke content analysis like Gas chromatography mass spectrometry (GC–MS) [3,4], liquid chromatography mass spectrometry (LC–MS) [5,6], Matrix-Assisted Laser Desorption/Ionization Time of Flight Mass Spectrometry (MALDI-TOF-MS-MS) [7,8], little has advanced in recent years for sample collection. Smoking machine is typically used in combination with solvent trap, sorbent tube for the collection of cigarette smoke, which is accepted as standard cigarette smoke collection approach [9]. However, the collecting machine is bulky, expensive and complex to operate, which cannot meet the needs for booming researches. Thus a small, cheap and portable collecting platform is preferable.

In recent years, microfluidic is well established in academia and industry as a platform for the development of new methods and products due to its advantages such as small, cheap and with little reagent consumption [10]. Moreover, microfluidic devices which employ microfluidic features like channels, electrodes, reactors and filters are able to manipulate fluid samples with high precision and efficiency [11], and offer the possibility of miniaturization and integration in biochemical assays [12–14]. Microfluidic devices have been applied to gas analysis for many years. To date, microfluidic gas collecting interface can be constructed by four different structures: gas permeable substrate [15–17], microporous structures [18,19], open structure with direct gas bubbling [20–22], and smaller microchannels array [23,24]. Gas permeable membrane can well separate gas from liquid while allows permeable molecules to selectively transfer from gas to liquid [15–17]. Microporous structures is composed of interconnected pores that allows for faster gas diffusion than permeable membrane at a price of less

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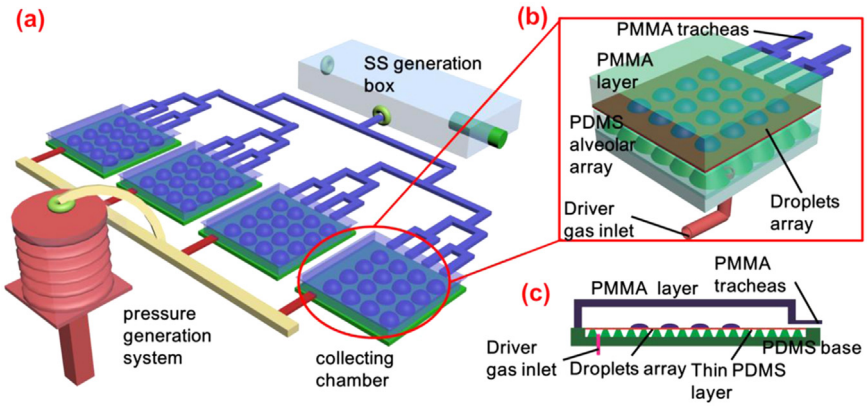

Scheme 1. Schematic representation of the smoke analysis platform. (a) The whole platform. (b) A zoom-in image of the collecting chamber. (c) Sectional view of the collecting chamber.

transparency [18,19]. Open structure with bubbles on chips can help gases such as air [20], CO_2 [21], O_2 [22] mix convectively with their soluble solvent which holds the fastest collection speed. Smaller microchannels array allows for fast gas collection in a more controllable way for its speed and spatial distribution [23,24]. Based on these functional gas collection interface, traditional analysis method such as fluorescence [15,16], surface plasmon resonance-enhanced fluorescence [25,26] and electrochemistry [27] have been successfully coupled on chip. Components such as gaseous trimethylamine [15], gaseous odorant [16], and reactive oxygen species [25–27] are selectively captured by beforehand immobilized probes and enriched for the following high sensitive detection.

However, when it comes to air pollutant such as cigarette smoke, the application of microfluidic platform is still limited. Thus, it is urgent to develop lab-on-a-chip platforms capable of smoke collection and analysis. In one hand, for collecting process, an ideal analysis platform requires a reflection of what has reached the lung exactly, rather than what is out in the air, thus requires modeling close to respiratory movement and capture what has been deeply inhaled. In the other, for the subsequent analysis, considering that most air pollutants are composed of complex and unknown species, it would also be necessary to introduce proper collection mechanisms for multiplex analysis.

Herein, we proposed a microfluidic gas collecting platform aiming at inhaled air pollution analysis. An arrayed alveolar model is built on chip, which could be driven by periodic pressure generation system mimicking the respiratory motion of human. An alveolar array on chip in connection with the SS generation via branched gas channels is able to inhale and exhale gas. A droplet array is mounted on alveolar surface for gas collecting. The content captured was later analyzed by MALDI-TOF-MS-MS or electrospray ionization mass spectrometry (ESI–MS). Taking nicotine in SS as an example, relationship between its accumulation and the breathing time/the distance from the smoker is clarified. Further, by applying different types of extraction solvent droplets, different species inside smoke are captured simultaneously and analyzed by mass spectrometry. To this, an automatic, economical and miniaturized smoking machine is realized and it may be extended to a platform for the analysis of other critical components in cigarettes smoke such as carbon monoxide, as well as many other inhaled air pollutants.

2. Experimental section

2.1. Materials, equipment and apparatus

Sylgard 184 elastomer base and curing agent for PDMS were both purchased from Dow Corning (Midland, MI). PMMA was purchased from Shichengjin (Guangdong, China). 2,5-Dihydroxybenzoic acid (DHB), Trifluoroacetic acid (TFA) and Tetraethylammonium bromide were purchased from Sigma. Standard substances such as nicotine, formaldehyde and caproic acid were obtained from J&K Chemical. 3R4F reference cigarette was provided by Zhengzhou Tobacco Research Institute.

The homemade periodic switch controller for respiration rhythm control is based on atmega128 microcontroller. The pump system is composed of a compressed air source, a SMC air cylinder (Japan) and an SMC SY7120-5G-02 electromagnetic solenoid valve (Japan). Universal Laser Systems VLS 2.30 was applied for PMMA channel laser engraving. Images were monitored by the Leica DMIRE2 microscope fluorescence analyzing system. Data in images were analyzed by Image-Pro Plus (IPP) program. MALDI-TOF-MS tests were conducted on MALDI-TOF-MS 4800 plus of ABSCIEX. ESI–MS was conducted on Agilent 6530 Q-TOF.

2.2. Smoke analysis platform design

The whole setting for this gas collecting platform is demonstrated in Scheme 1. As shown in Scheme 1a, it is mainly composed of three parts: A. the periodic pressure generation system; B. collecting chamber; C. SS generation box. The real setting is detailed in Fig. 1. The pressure generation system is designed to generate periodic pressure to drive the collecting chamber for the inhale and exhale movement. It is composed of an electronic controller for rhythm control and an air cylinder for mechanical periodic pressure generation. The collecting chamber is detailed in Scheme 1b (sectional view in Scheme 1c). An elastic PDMS alveolar array is made from a PDMS substrate with cone shaped array covered with a thin PDMS layer. A droplets array is mounted on the thin PDMS layer for gas absorption. A PMMA cavity (4.0 cm × 4.0 cm × 1.5 mm) is sealed with the top of thin PDMS layer by clamping. And the cavity is linked with PMMA branched gas channels at one end. The alveolar array is linked with the driver gas at the bottom. When positive pressure is added by pressure generator, compressed air is injected into the alveolar array from the driver gas inlet, deforming the alveolar array and thus expelling gas out of the cavity from the PMMA tracheas, and vice versa. PMMA tracheas are connected to SS generation box by a plastic tube, the length of which is changeable to mimic the distance between passive smoker and active smoker.