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Aerosol sampling using an electrostatic precipitator integrated with a microfluidic interface

Gaspard Pardon[1], Laila Ladhani[1], Niklas Sandström, Maxime Ettori, Gleb Lobov, Wouter van der Wijngaart*

Micro and Nanosystems, KTH Royal Institute of Technology, Osquldas väg 10, 100 44 Stockholm, Sweden

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ABSTRACT

In this work, the development of a point-of-care (PoC) system to capture aerosol from litres of air directly onto a microfluidic lab-on-chip for subsequent analysis is addressed. The system involves an electrostatic precipitator that uses corona charging and electrophoretic transport to capture aerosol droplets onto a microfluidic air-to-liquid interface for downstream analysis. A theoretical study of the governing geometric and operational parameters for optimal electrostatic precipitation is presented. The fabrication of an electrostatic precipitator prototype and its experimental validation using a laboratory-generated aerosolized dye is described. Collection efficiencies were comparable to those of a state-of-the-art Biosampler impinger, with the significant advantage of providing samples that are at least 10 times more concentrated. Finally, we discuss the potential of such a system for breath-based diagnostics.

1. Introduction

The field of in vitro point-of-care (PoC) diagnostic tests has rapidly grown during the past decade. It promises robust systems capable of delivering precise and rapid results about the condition of an individual, which can lead to an improved quality of healthcare at a reduced cost. Urine, blood, and oral or nasal swabs have been extensively investigated as diagnostic samples in the healthcare setting. Here we present a detection method aimed at diagnosis using breath sampling.

Much effort has been made in the past to link volatile organic compounds (VOCs) in exhaled air, to a patient's state of health [1], specifically with respect to identifying biomarkers for cancer [2–6]. Exhaled breath contains both gases, and aerosol droplets, however, the main focus of breath analysis thus far, has been on gas detection, which can contain: inorganic gases, i.e. NO [7] CO [8]; hydrocarbons, i.e. isoprene [9] ethane or pentane [10]; and volatile and non-volatile substances, such as isoprostane, cytokines, leukotrienes [11], proteins, nucleic acids, or polypeptides [12,13], bacteria or viruses. VOCs appear in gaseous form in breath, typically analyzed using ion mobility spectroscopy, chromatographic, or mass spectroscopic techniques, which are reviewed by Buszewski et al. [14]. However, non-volatile substances in breath are transported via aerosol droplets, such as the Torque Teno virus [15], or Influenza [16]. These aerosolized droplets, are thought to be generated from the lung lining fluid via film rupturing following contraction of the bronchioles [17–19]. There has been a lot of emphasis on detection of VOCs using gas analysis or condensates [20–22], however few studies have been aimed at the capture detection of microorganisms in exhaled breath. Specifically, aerosols with droplet size >1 μm are formed through coughing [23–27] and are targeted in our work.

Integrating a capture system for these aerosol droplets in a PoC device could form a completely non-invasive alternative to traditional lung sampling methods, such as the very invasive and uncomfortable bronchoscopy procedure. Nonetheless, there are difficulties that are inherent to sampling breath including: variances in aerosol droplet size, number concentration, composition, and low concentration of analytes present in the sample [24,25,28–31]. Such a complex and diverse aerosol is difficult to simulate in the laboratory, thus a mock breath aerosol of specified composition, droplet size, and concentration is generated and used for characterization. The challenge of the low amount of sample present in breath means it is crucial for a point-of-care test to have both: a high collection efficiency, and the ability to up-concentrate collected samples for very sensitive detection of analytes. There also exists a lack of standard methodology for breath sampling,

* Corresponding author. Tel.: +46 8 7906613; mobile: +46 733 254021.
E-mail address: wouter@kth.se (W. van der Wijngaart).
[1] First authors.

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and appropriate and standardized breathing protocols remain to be established.

Traditionally, sampling of aerosol droplets is achieved using inertial impaction, e.g. using impingers [32–34], which was used for comparison in this work, or via direct impaction [35,36]. In 1955, the use of electrostatic precipitators (ESPs) was introduced as a potential alternative, when Kraemer and Johnstone [37] explained, theoretically, the charging and capture of aerosol droplets in the presence of electrostatic fields. Since then, ESPs have been used extensively by industry, e.g. in air purifiers, but only recently have they been considered as a potential method for the capture of exhaled bioaerosols. Miller et al. [38] demonstrated a hand-held ESP device for breath sampling relying on transmission electron microscopy (TEM) for sample analysis, which is not a suitable detection method for PoC applications. Alternatively, Kettleson et al. [39] demonstrated inactivation of aerosolized viruses using an ESP. Christensen et al. [40] utilized a commercial, chip-based ESP to analyze breath from cattle for detection of foot-and-mouth disease. The drawback with their method is the indirect collection, i.e. not directly from the cattle's mouth but from ambient air in the farmhouse, leading to lower collected amounts of exhaled aerosol when compared with direct breath. Similarly, Han and Mainelis [41] introduced an ESP sampler for bioaerosols, mainly targeting airborne pathogens and microorganisms, by collecting rolling water droplets off the collection electrode. Tan et al. [42] proposed an airborne bacteria sampler using a semi-spherical electrostatic precipitator, and reported varying relative collection efficiencies, $\Upsilon_{\mathrm{ESPon/ESPoff}}$, from 50% to 100%, where the total capture was compared with that when no voltages were applied to the ESP electrodes. The collection was dependent on applied voltages, flow rates, particle sizes and geometrical design parameters. All the above ESP devices, although successful in capturing their target aerosol, are solely focused on capturing airborne droplets from ambient air, and do not provide the possibility for uncomplicated downstream integration of biosensors with the instrument.

For integration of breath aerosol sampling in a PoC diagnostic device, one of the most challenging aspects is the direct interfacing of breath with a lab-on-a-chip (LoC) cartridge [43]. In particular, a robust air–liquid interface is required to allow capture of the aerosol droplets and dispersion of the captured sample in a liquid medium, in which direct initiation of specific ligand–receptor biochemical reactions can occur. We have previously presented microsystem-based components for air–liquid interfacing in combination with downstream analysis, for quartz crystal microbalance (QCM) sensing of airborne narcotics [44,45]. Two examples of such surface tension-based air–liquid interfacing include: pillar forests and perforated diaphragms. They allow for use of a liquid flow in the chip while simultaneously offering a large and robust air–liquid interface area. Moreover, a perforated diaphragm allows for placement of a biosensor in close proximity to the air–liquid interface, which potentially simplifies the overall LoC design and reduce the risk for sample-to-channel surface interactions inherent to fluidic transport in microfluidics.

This paper considers an integrated aerosol sampling and analysis system, designed for future use in point-of-care breath based diagnostics. We first introduce the combination of ESP with lab-on-chip technologies, the former for aerosol collection and the latter for integrated sample handling and biomarker detection. The remainder of the paper details the design, governing parameters and experimental investigation of an aerosol-to-chip ESP based sampler. First we review the major physical phenomena involved in electrostatic aerosol capture and investigate the governing geometric and operational parameters using finite elements (FE) simulations. Thereafter we describe the building and experimental testing of the prototype. We used laboratory generated aerosol to derive the prototype characteristics. Sampling efficiencies of the prototype are reported and compared with those of a commercial Biosampler impinger.

2. PoC concept for integrated aerosol sampling and analysis

The concept of the proposed PoC device arises from the unique combination of two elements: an ESP to capture aerosol droplets, and a microfluidic lab-on-a-chip containing an air–liquid interface and an on-chip biosensor. All of this can potentially be incorporated into one portable instrument with a mouthpiece for sampling patients' breath (Fig. 1).

The aerosol droplets enter the ESP through a mouthpiece, are electrically charged, transported, and captured onto the microfluidic air–liquid interface of the lab-on-a-chip cartridge. In the ESP, a two-electrode multi-point-to-plane corona discharge cell is used to charge and capture aerosol droplets. Metal needles are used as corona discharge electrodes, and the air–liquid interface constitutes the planar capture electrode. The collected sample can then be subsequently analyzed for biomarkers or other biological entities using a relevant assay and on-chip transducer.

Contrary to the analysis of VOCs, which can be performed utilizing optical equipment, the analysis of complex biomolecules such as nucleic acids, proteins or even entire pathogens present in aerosol, requires collection of the dispersed aerosol droplets into a continuous liquid phase suited for subsequent sample preparation and analyte detection. Microfluidic devices are ideal for handling and analysis of such liquid samples [46] and have the advantage of allowing integration with an ESP. A previous

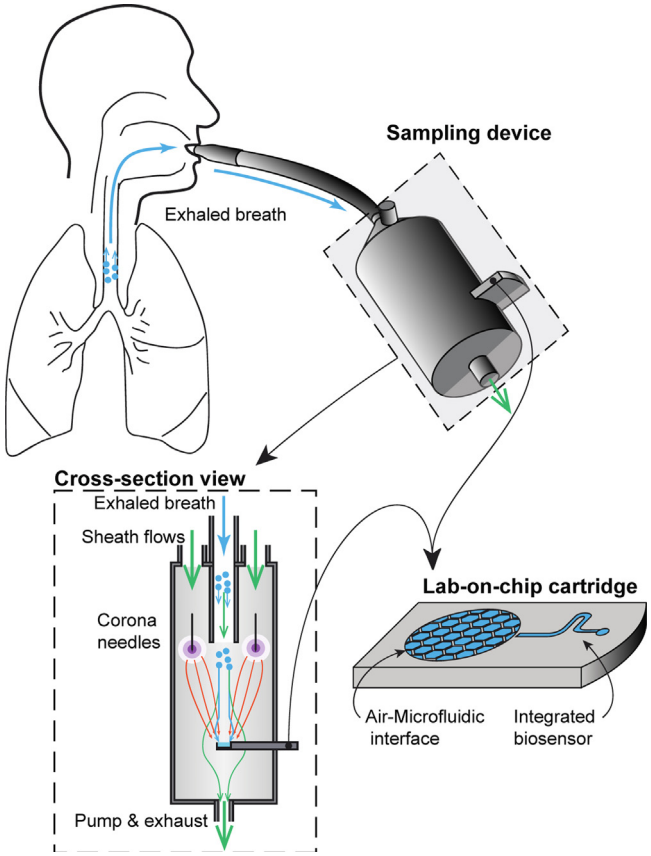

Fig. 1. Conceptual design of the proposed PoC device using exhaled-breath aerosol as diagnostic sample. A cross-section of the PoC ESP sampler shows needles as corona discharge electrodes, while the lab-on-chip cartridge acts as the collection electrode. Exhaled breath aerosol enters in the centre, and a sheath flow is implemented to increase flow control. The lab-on-chip cartridge includes an air–liquid interface, and a biosensor.