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Sample concentration in a microfluidic paper-based analytical device using ion concentration polarization

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ABSTRACT

We report a low-cost approach for sample concentration in a microfluidic paper-based analytical device using ion concentration polarization. This device platform can attain liquid sample filling by capillary suction through the microporous paper and ion selective transport through a nanoporous polymer matrix under DC electric field. The device demonstrated a fast depletion of fluorescent dye samples and can serve as an effective microfluidic concentrator of fluorescent dye with 60-fold concentration enhancement achieved within 200 s. The device fabrication is simply based on paper cutting and lamination without the need of lithography and printing of hydrophobic material such as wax. The lamination approach presented in this paper has the potential to be transferred to a large-scale production of paper-based analytical devices.

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1. Introduction

Ion concentration polarization (ICP) is an ionic transport phenomenon that occurs near an ion-selective membrane and is included the ion-depletion and ion-enrichment processes [1]. Recently, ICP has attracted a great attention from the microfluidics research community due to its potential applications in sample concentration [2–5], desalination [6,7], mixing [8,9]. Concentrating low-abundance analytes is a critical need for microfluidic point-of-care (POC) portable analytical devices, because subsequent analysis or detection is only possible at a concentration above the limit of detection (LOD) of the analytical device. Several research groups have explored various concentration methods including field amplification stacking [10], isoelectric focusing [11], membrane filtration [12], affinity-based extraction [13], temperature gradient focusing with a combined AC and DC field [14] and electrokinetic trapping based on ion concentration polarization (ICP) [15].

ICP-based electrokinetic trapping method has numerous unique features. Specifically, concentrating molecules using ICP is independent of the hydrophobicity of binding characteristics of the molecules of interest [2]. In addition, an electric field created by simple electrodes can easily manipulate the concentrating process [2]. This allows ICP-based concentrators to be integrated in a wide range of microfluidic platforms for detection of target molecules initially at a low concentration. Conventionally, ICP was observed at the interface of a permselective nanochannel bridging two adjacent microchannels [16]. Once an ICP is established; a depletion zone is formed at one side of the perm-selective nanochannel. In the ion depletion zone, the concentration of both negatively, and positively charged species drops sharply. In contrast, on the other side of the nanochannel, an ion enrichment zone is established with a high concentration of both negatively, and positively charged species [2]. Nanoporous ion-selective materials with non-engineered pores have been used to make ICP-based microfluidic separators and concentrators [2]. Nafion is for instance an ion-selective material with negatively charged sulfonic groups. Kim et al. used a Nafion membrane to generate ICP for continuous seawater desalination. Nafion-based nanojunction was integrated at the bifurcated point of a microchannel where all charged species, particles and microorganisms were repelled into the brine channel and thus pure water was guided to the desalted channel [6]. Kwak et al. adopted a similar approach for continuous-flow concentration of biomolecules, bacteria, and red blood cells [5]. In both designs, the nano junction had to be in contact with an additional buffer channel, which added complexity to the chip design. Ko et al. reported a design improvement in a device for protein preconcentration

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[4]. The Nafion membrane was placed at the bottom of a straight microchannel. In this design, the buffer channel was eliminated, resulting in a simplified fabrication process. Both anode and cathode were located in the same microchannel with one inlet and one outlet. The preconcentrator could enhance the detection sensitivity of the immunoassay for a sample of C-reactive protein by more than 500-fold compared to an immunoassay without preconcentrator.

Over the past few years, paper-based analytical microfluidics for point-of-care applications has also attracted a great attention [17–19]. The low material, fabrication and operation costs of paper-based devices make the applications extremely suitable for resource-limited regions [20]. Passive capillary wetting (suction) through the porous structure of paper makes fluid handling an easy task. In addition, the porous structure of paper provides a suitable matrix for effective immobilization of reagents through physical adsorption [21]. Having such unique properties, various analytical assays have been implemented in the paper-based microfluidic platform; for instance colorimetric detection [22], direct electrochemical detection [19] and electrogenerated chemiluminescence detection [23] are a few to name. The use of a concentrator is inevitable to further improve the detection limit of these analytical methods. Preconcentration process needs flow manipulation, which is challenging since valves should operate without instrumented actuators and controllers [24]. Gong et al. recently integrated a Nafion membrane into a paper strip to make an ICP-based concentrator on paper [25]. The device could concentrate a fluorescent tracer up to 40-fold in a fully wet paper in a stamp-like device with the nanoporous membrane separated from the paper-based assay.

This paper presents the development of a paper-based device platform using simple integration of microporous and nanoporous materials for liquid handling and sample concentration. The device platform functions for liquid sample filling by capillary filling suction through the microporous paper and ion selective transport through the nanoporous polymer matrix under DC electric field. The functionality of this platform is demonstrated by ICP-based microfluidic sample depletion and concentration. This work is distinct from other published works due to the simpler geometry with maintaining functionality, fast fabrication process thus leading to low cost, ease of applicability for practical applications.

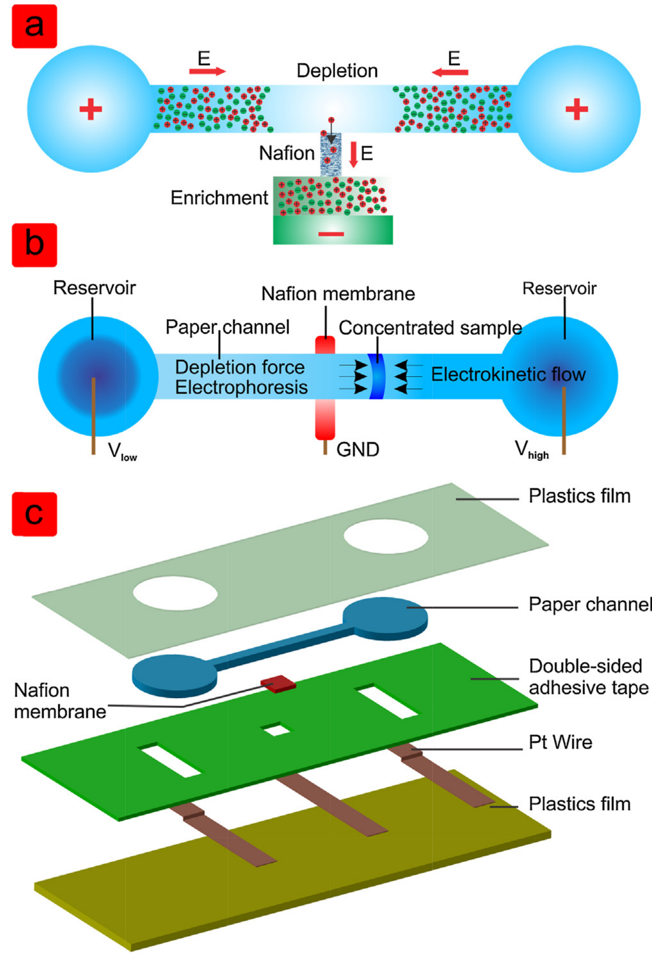

Fig. 1. Paper-based analytical device for sample concentration using ion concentration polarization: (a) ICP phenomenon occurred on a straight paper channel under the influence of an applied electric field across the Nafion junction, which only allows cations to pass through its nanopores. The cathode is acted as an unlimited-anions providing source; (b) working concept showing the combination mechanism of three different forces in the device; (c) device structure containing several layers fabricated with different materials.

2. Material and methods

2.1. Device concept and fabrication

In order to understand the working concept of the proposed device, it is necessary to present a detailed description on ICP occurred in the device. Fig. 1(a) describes the movement of ions when an electric field is applied across the Nafion junction. Due to the permselectivity of the Nafion, only cations can pass through the Nafion membrane, whereas the anions will be stopped right at the Nafion interface with the cathode side. To maintain the local electroneutrality condition, charged molecules are trapped and accumulated on the anodic side of the Nafion membrane to form an ICP boundary. Since our configuration is symmetrical, the depletion zone will develop and expand gradually to two anodic reservoirs over time. On the other hand, on the cathode side, which can be considered as an unlimited-anions source (i.e. connected to GND or a buffer electrode), both ion types are accumulated to form the enrichment region.

Fig. 1(b) shows the concept of the concentration device. A paper strip forms two reservoirs and a main channel for introducing the sample. A thin Nafion membrane is put at the bottom of the paper strip. While the microporous paper represents the microfluidic channels for sample transport, the nanoporous Nafion membrane represents the nano-channels that are ion selective. Two electrodes are placed at the reservoirs at the two ends of the paper strip for producing two different DC voltages. A platinum wire acting as the ground electrode is placed under the Nafion membrane to activate the transport process across the nonporous matrix. This simple device configuration will demonstrate that sample transport and concentration can be implemented on a single paper strip. This platform would allow for the integration of a concentrator with any paper-based microfluidic assay for point-of-care applications.

Fig. 1(c) shows the implementation of the concept depicted in Fig. 1(b) through lamination of multiple layers of the different materials. Each layer of the device was cut in appropriate sizes and dimensions using an electronic craft cutter (Silhouette America, Inc., Silhouette Cameo) [25]. Cellulose filter paper (Whatman) of an average pore size of 11 μm (Grade 1) and an average thickness of 180 μm was used as the substrate for the paper layer with two circular reservoirs of 1-cm diameter. The strip connecting the reservoirs has a width of 1.5 mm and a length of 25 mm. The nanoporous membrane Nafion (NRE-212, DuPont, USA) with an average thickness of 50 μm was cut in to a 1.5 mm × 5 mm piece and placed under the paper strip to create the microporous/nanoporous interface. Platinum electrodes with a diameter of 100 μm (Sigma–Aldrich) were connected to the two reservoirs and the Nafion membrane. A