

LETTER

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Spontaneous diffusiophoretic separation in paper-based microfluidic device

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Abstract

Microfluidic paper-based analytical devices (μ PADs) for separating particles have been playing a key role for point-of-care diagnostics in the area of remote settings. While splendid separation methods using μ PADs have been extensively developed, they still require external devices inducing external field. In this work, the spontaneous separation method in μ PADs was suggested by leveraging convective flow (the imbibition of paper and nanoporous medium) and diffusiophoresis by ion exchange medium. Especially, the paper's fast imbibition was utilized as driving particles at the first stage, which results in fast overall processing in contrast to the spontaneous separation method of microfluidic chip integrated with only ion exchange medium. Therefore, our novel spontaneous selective preconcentration method based on μ PADs would have key potential to be used in portable point-of-care devices in remote settings.

Keywords: Microfluidic paper-based analytical devices, Spontaneous separation method, Imbibition, Ion exchange medium, Diffusiophoresis

Introduction

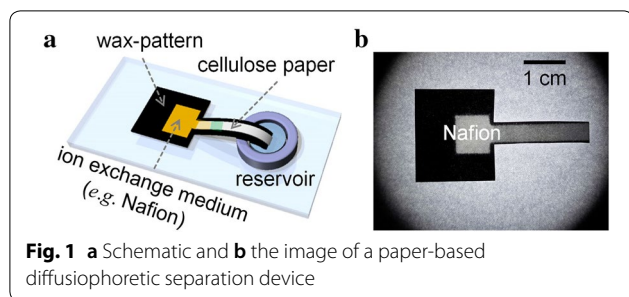
Microfluidic paper-based analytical devices (μ PADs) have received significant attentions in recent years due to the properties of paper such as low cost, portability, bio-degradability, handy portability and simple fabrication [1–3]. These properties make the paper-fluidic device attractive in remote settings and resource limited settings. μ PADs have been studied for point-of-care diagnostics in remote settings, in which diverse methods have been developed for separation and preconcentration of samples [4–7]. Recently, separation and preconcentration of biomolecules has been demonstrated with paper-based ion concentration polarization (ICP) platform. Since conventional ICP preconcentration method has several benefits such as high preconcentration factor and no need of complex buffer exchange, ICP has been extensively studied for the selective preconcentration of biomolecules [8–12]. However, because typical ICP platform required an external electrical field for performing

the separation, paper-based ICP separator also needed an external power source and cause the methods to be against to the original concept of μ PADs.

Our previous work presented the spontaneous preconcentration (or selective preconcentration) method in microfluidic chip with leveraging convective flow through microchannel over diffusiophoresis induced by imbibition and ion exchange of ion exchange medium, respectively [13–18]. Especially, we had demonstrated that the velocity of the convective flow by the imbibition of the medium deviated from original Darcy's law using non-uniformly patterned ion exchange medium, but this work has the limitation of time-consuming and complex process [13]. Therefore, in this work, we would present the spontaneous diffusiophoretic separation of multiple particles using μ PADs. We analyzed the results using the mechanism of previous works such as diffusiophoresis and imbibition, while a part of result was found to be contradictory to such mechanisms so that one need further investigations for the exact fundamentals. However, presenting results can be directly employed for practical μ PAD based selective preconcentration platform.

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Materials and methods

Device fabrication

Paper-based separation device was fabricated by cellulose paper (Whatman grade 1, Sigma Aldrich, USA) with slide glass, as shown in Fig. 1a. The paper has 180 μm of thickness and a mean pore diameter of 11 μm . Using a commercial wax printer (ColorQube 8570, Xerox, USA), the channel was patterned with hydrophobic wax region (black area in Fig. 1b). The printed channel was then baked at 120 $^{\circ}\text{C}$ for 10 min. Then, Nafion was dropped in a broad region of paper for forming ion exchange medium as shown. The Nafion-patterned paper was dried at 95 $^{\circ}\text{C}$ for 10 min. Finally, to avoid sample evaporation, adhesive tapes were attached on both sides of the paper channel.

Chemical preparation

Reservoir was filled with KCl 1 mM solution (Sigma Aldrich, USA) with negatively charged fluorescent carboxylate particles (diameter = 0.2 μm (em. 550 nm, yellow) and 0.04 μm (em. 532 nm, green), Invitrogen, USA).

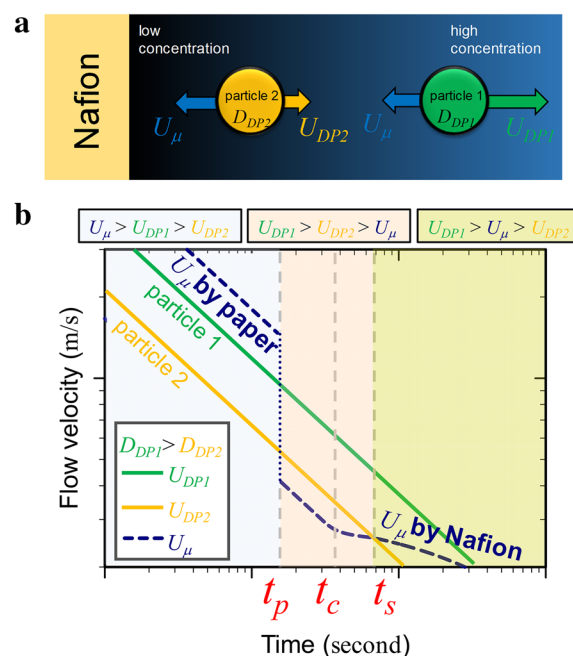
Experimental apparatus

The motions of fluorescent particles were captured by an inverted fluorescence microscope (IX53, Olympus, Japan) and the images were analyzed by CellSens program (Olympus, Japan). The snapshots were captured at every 5 min.

Results and discussions

Mechanism of spontaneous separation method in μPADs

When ion exchange medium (e.g. Nafion) met water containing non-protonic cation, the protons inside the medium were exchanged with other cations, and the concentration gradient was generated due to the different diffusivity of proton and other cations as shown in Fig. 2a. This mechanism is called diffusiophoresis, which spontaneously induces the motion of charged particles under the electrolyte concentration gradient. In this configuration, the particles are affected by diffusiophoretic



velocity (U_{DP}) and also the velocity of convective flow through microchannel (U_{μ}) with the opposite direction to U_{DP} . This convection can be caused by the imbibition of ion exchange medium and paper itself.

Both velocities (U_{DP} and U_{μ}) are proportional to the time^{-1/2} [14]. Thus, they were plotted as a straight line with a negative slope in log scale graph as shown in Fig. 2b. U_{DP} of a particle depends on diffusiophoretic constant (D_{DP}) as a function of zeta potential and radius of particle, etc. However, we used paper-based device to enhance the efficiency of separation time unlike our previous work which has the limitation of slow processing (6–12 h) [13], leading to a complicated behavior of U_{μ} in Fig. 2b. When a paper contacts with water, capillary forces created a fast fluid flow into the paper. Thus, U_{μ} induced by imbibition of paper could be plotted as a straight line above any other U_{DP} s, meaning the fastest velocity (dotted line) before the time of finishing imbibition of paper (t_p) as shown in Fig. 2b. Thus, particle 1 and 2 would move to the Nafion by U_{μ} . After t_p , the imbibition by paper was stopped and the imbibition of Nafion only affected U_{μ} and, as our previous work suggested, U_{μ} was deflected due to the non-uniformly patterned medium at the critical time of convective flow (t_c) [13]. Then, before the time of separating particles (t_s), the particles would move away from Nafion, but each particle

would move as the opposite direction after t_s , which implies that two types of particles with different diffusio-phoresis constant would be separated in μ PADs. Following section will experimentally demonstrate this scenario.

Experimental demonstration of spontaneous separation

As shown in Fig. 3, two particles with different size were spontaneously separated according to the aforementioned mechanism in Fig. 2. Figure 2 showed that the competition between diffusio-phoresis and the imbibition of nanoporous medium lead to spontaneous separation in the paper-based platform. In Fig. 3a, U_{μ} induced by paper's fast imbibition drove multiple particles from reservoir to the region near the Nafion (see green region of image at $t=0$ min). After 2 h, the particles were almost completely separated and preconcentrated. The separation resolution (R_s) calculated by (peak to peak distance)/(average width of bands) under Gaussian distribution assumption [19] led to 1.25 which showed reasonable separation. Compared to our previous work that utilized only microfluidic channel-based device spent 6 h to the completion, we can conclude that the separation in paper-based device was performed faster. Furthermore, the separated particles can be observed with naked eye using fluorescent lamp even after 1 days as shown in Fig. 3b. In this image, soaked water in the paper was completely evaporated. Although the paper has random cellulose network, the fast convective flow induced by imbibition of the paper is obvious in the direction to the nanoporous medium, so that the process time might be

random, but the separation phenomenon would finally occur.

However, previous literature suggested that D_{DP} of larger particle is usually larger than that of small particle. This meant that $0.04\ \mu\text{m}$ particle should be accumulated near Nafion and $0.2\ \mu\text{m}$ particle should be repelled from Nafion. This is contradictory to our present observation [13] and it may come due to the complex geometry of cellulose and interaction of particles with it. In the random (or natural) pore network, various convective flow such as recirculation can be included in the analysis [20–23]. Thus, one need further investigations for the exact fundamentals in paper-based device.

Conclusions

In this work, the spontaneous particle separation method by diffusio-phoresis in μ PAD platform was demonstrated without any external power sources. The separation was leveraged by convective flow induced by imbibition of ion exchange medium over diffusio-phoresis. To overcome the slow processing of our previous work [13], the paper network was designed for utilizing the fast imbibition of paper and, thus, the faster process time was achieved as expected. Although this method has still slow process time to apply in practical cases, this method has an advantage of no need for external power source, so that this method can be useful for separating external power-sensitive bio-samples and a time-insensitive lab on a chip application such as environmental monitoring and food monitoring. While separation order was different from previously reported mechanisms so that one

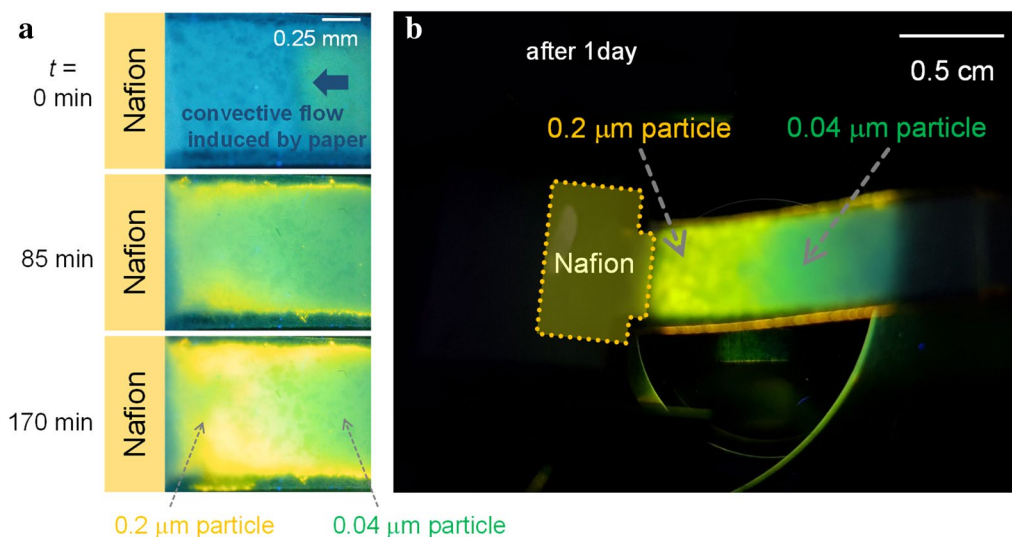


Fig. 3 **a** Time-evolving microscopic images of spontaneous diffusio-phoretic separation and **b** the separated particles captured by regular cellphone camera

need further investigations for the exact fundamentals, presented results can be directly employed for practical μ PAD based selective preconcentration platform and one can expect the applications of this work for the portable diagnosis devices without any external power sources.

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Authors' contributions

DL conducted the main experiment. SJK supervised the project. Both authors wrote the manuscript. Both authors read and approved the final manuscript.

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Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Competing interests

The authors declare no competing interests (both financial and non-financial).

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