MICRONEEDLE ARRAY INTERFACE TO CE ON CHIP

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Abstract

This paper presents a microneedle array sampler interfaced to a capillary electrophoresis (CE) glass chip with integrated conductivity detection electrodes. A solution of alkali ions was electrokinetically loaded through the microneedles onto the chip and separation was demonstrated compared to a diluted blood sample. This method shows therefore feasibility for clinical relevant analytics.

Keywords: Microneedles, Point-of-care, CE, Conductivity detection, Blood

1. Introduction

Point-of-care testing has a number of advantages, like rapid turn around times, high degree of automation and improved quality of life [1]. Miniaturization strategies allow performing more and faster tests from smaller blood volumes being sampled off-clinic at ever-lower costs. Off-clinical diagnostics also reduces the risk of sample exchange or cross-contamination making a test result more reliable. Therefore, we envision a microneedle array sampler as an interface to diagnostics resulting in high patient's compliance. In this paper, we focus on an analytical device that uses micromachined hollow microneedles in combination with capillary electrophoresis on chip [2]. Out-of-plane needle arrays provide a large needle density, while the fact that the needles are backed witha flat thin plate of a few mm^2 making integration in a small card-type device or a patch possible (Fig.1) [3], [4].

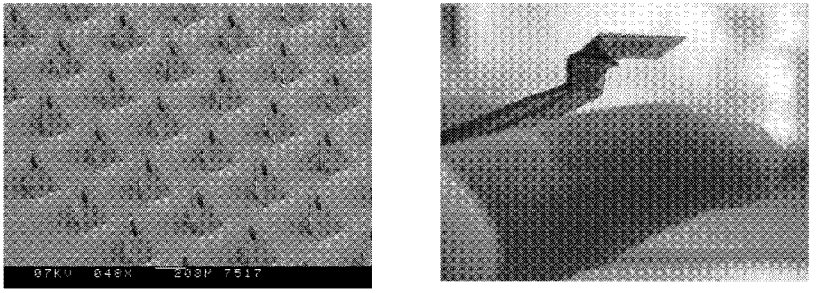

Figure 1. 450 μm high silicon needles with 555 μm pitch (left) [4], needle array approaching finger tip giving an impression of the blood sampler (right).

0-9743611-0-0/μTAS2003/$15.00©2003TRF

The silicon needle array fabrication consists of a sequence of Deep Reactive Ion Etching, anisotropic wet etching and conformal thin film deposition, and allows needle shapes with different, lithography-defined tip curvature [4]. Feasibility of these needles, which were fabricated at MESA$^+$ Research Institute, is presented here for liquid transport and alkali ion diagnostics.

2. Fluidic transport through microneedles

An experiment was performed to characterize the flow of fluorescent dye through the needles. The process of diffusion was captured with a CCD camera at a rate of 1 frame/s. Figure 2 shows the passive flow of the dye diffusing from the needle tips into the buffer at the needle backside, achieved with the set up described in the figure. It was observed that non-uniform fluid flow occurred, although all needles were observed to be open before the test. Partial blockage could have been caused by air bubble or dust particle trapping.

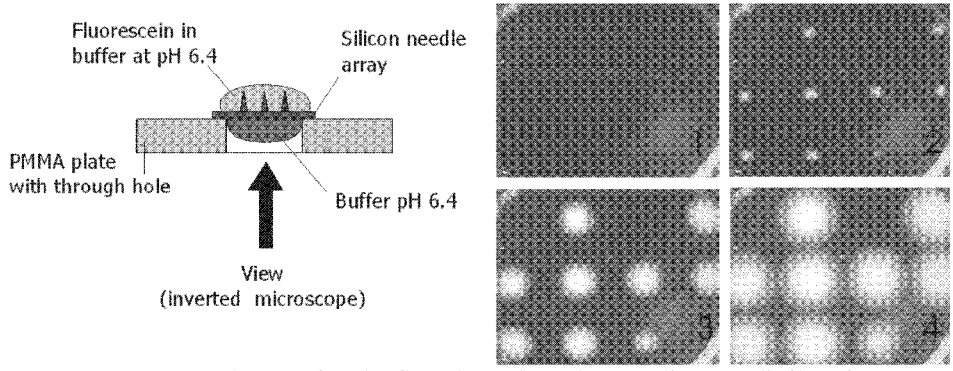

Figure 2. Set-up to characterize the flow through a microneedle array (left). Microscope images of fluorescent dye transported through needles (right).

3. Microneedle sampler for CE

Figure 3 shows a schematic of the set-up as used for interfacing the needle array to a glass CE chip of 2 cm separation length with a channel cross section of 60 µm x 6 µm with end-column integrated electrodes for conductivity detection. The silicon needle chip was clamped onto the CE sample inlet via a PDMS seal. A calibrated solution of alkali ions containing 10 mM K^+, Na^+ and Li^+ and a 10 times diluted blood sample were electrokinetically loaded through the microneedles into the chip. A standard pinching procedure was applied to define and inject a sample plug, which was subsequently separated by Capillary Zone Electrophoresis (CZE). 20 mM MES-His was used as the background electrolyte. Details on the CZE procedure were described earlier [5].

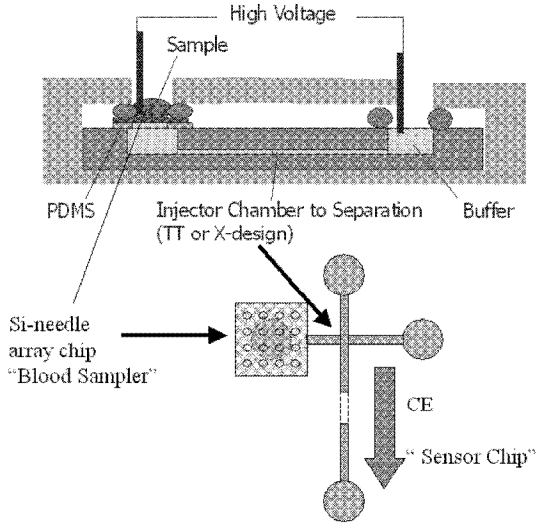

Figure 3. Measurement set-up for silicon microneedle array, coupled to a capillary electrophoresis chip.

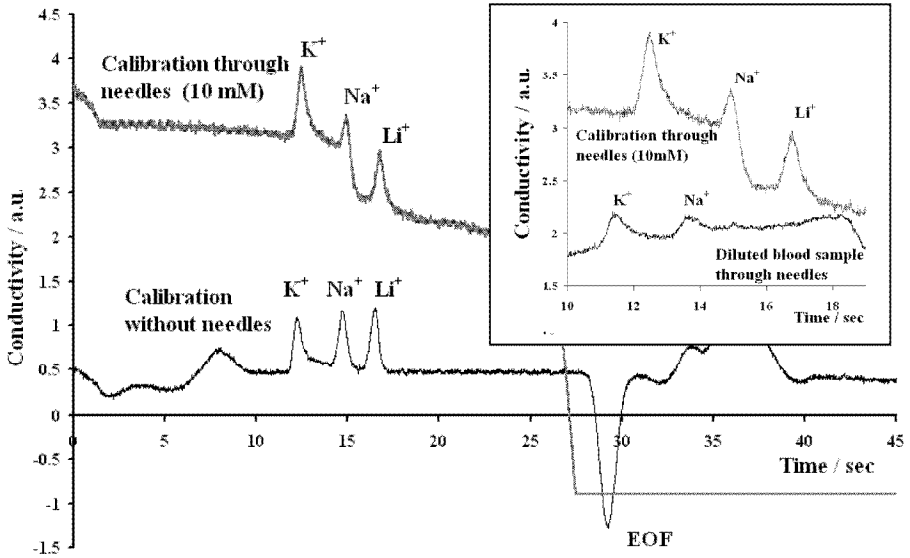

Figure 4. Electropherograms of separation results performed in set-up of Figure 3. Insert shows the same calibration compared to blood being sampled through the needles.

Figure 4 shows resulting electropherograms, which are achieved without and with the microneedle sampler for the 10 mM calibration solution and obtained with identical voltage schemes. In both experiments the concentration (peak area) and migration time of the alkali ions are nearly the same, indicating that no dilution occurs after transport through the needles and confirms that the needle array does not constitute a restriction to ionic transport. The insert shown in Figure 4 compares the same calibration graph for sampling through the needles with a measurement in blood. Here, two peaks were detected and can be identified as potassium and sodium. The ratio of peak areas of K^+ and Na+ in whole blood becomes approximately 1:1 for samples when cell lysis occured during sample preparation.

4. Conclusions

The characterization of the diffusion process through microneedles shows fast passive transport, leading to capillary electrophoresis experiments, in which sampling was achieved through the microneedles without diluting the sample by the loading procedure (note chip inlet and needle volume in Figure 3 not drawn to scale). A calibration solution of 10 mM K^+, Na^+, and Li^+ was successfully sampled by the microneedle method and baseline separated. Performing the sampling method with diluted blood two peaks were identified. It is therefore assumed that due to the fast diffusion the concentration being sampled into the loading channel represents the concentration of the sample positioned onto the needle array.

Acknowledgements

The authors would like to acknowledge the financial support for this research by NanoPass Ltd. and specifically thank Y. Yeshurun and M. Hefetz of NanoPass Ltd. for fruitful discussions.

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