Self-powered Integrated Microfluidic Blood Analysis System (SIMBAS)

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ABSTRACT

We demonstrate a Self-powered Integrated Microfluidic Blood Analysis System (SIMBAS) that efficiently extracts blood plasma from less than 5 μL of whole blood and performs multiplexed sample-to-answer assay with picomolar sensitivity without any external pumping mechanisms. All components of the device are monolithically integrated and the complete assay is performed in 10 min..

KEYWORDS: Self-Powred, Blood Plasma Extraction, Integarted Analysis, Sample-to-Answer

INTRODUCTION

Every minute, the human body's entire blood volume is recirculated; as a result, blood is a treasure-trove of information about the functioning of the body, particularly at the molecular level. Typically, the most sensitive assays for blood analysis are based on optical measurements. However, blood cells generally interfere with the optical path, reducing assay sensitivity. Thus, separation of pure plasma from whole blood is often required for blood analysis.

Our Self-powered Integrated Microfluidic Blood Analysis System (SIMBAS) aims to replace laborious sample-preparation steps by integrating blood plasma separation and multiplexed assays on the same device. Current existing microfluidic technologies for on-chip plasma extraction require 'umbilical' tubes for flow propulsion and control or use external pumping mechanisms (syringe pumps, compressed air, electro-pneumatic systems, or motors) making device control and operation more complex and expensive. For example, separation of plasma on microfluidic devices has been achieved by flowing blood through microfilter-like parallel arrays of shallow channels [1] or bifurcated channels using the Zweifach-Fung effect [2], and lab-on-a-disk platforms [3]. By using external solenoid-pressure pumping, on-chip plasma separation has been demonstrated with immunoassays as an automated blood analysis chip [4]. Here, we describe a tubeless-SIMBAS for blood-plasma separation and plasma-based analysis (Fig. 1).

RESULTS AND DISCUSSION

The tubeless-SIMBAS uses whole blood samples less than 5 μL (eg. directly from the finger) and flow is propelled with a unique self-priming degassing-driven flow technique (Figs. 2) that causes blood to flow spontaneously into air-filled dead-end

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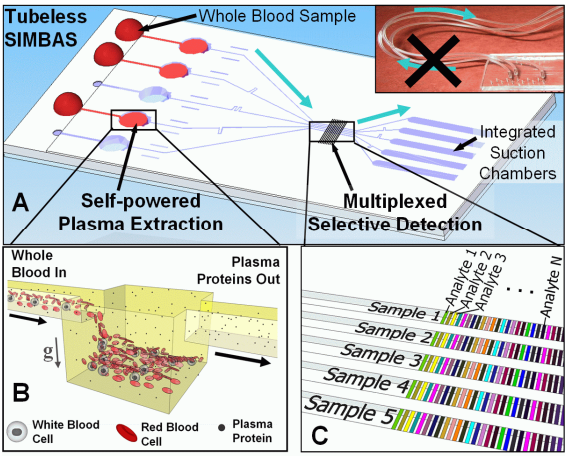

Figure 1. (**A**) Self-priming tubeless-SIMBAS with (i) integrated flow propulsion, (ii) volume metering, and (iii) blood plasma extraction based on a (iv) novel trench filter, (v) a staining-and-mixing region, (vi) a multiplexed bio-recognition matrix, and (vii) waste-suction chambers. Inset: comparison to a conventional microfluidic device that requires 'umbilical' tubes for flow propulsion and control (**B**) Plasma extraction from whole blood using a unique trench filter that sediments and captures blood cells. (**C**) Multiplexed bio-recognition is achieved using bars of immobilized antibodies.

channels without external pumping mechanisms [5] (Fig. 3A-C). The separation of blood cells is achieved using a novel on-chip filter trench where white and red blood cells are sedimented and captured, allowing only cell-free plasma (including platelets) to overflow into the sensing area of the self-priming tubeless-SIMBAS.

Analyte detection was demonstrated using an avidin-biotin assay (Fig. 3D-E). A pattern of 15 µm bars of avidin was immobilized in the sensing area of the chip. Whole-blood samples were spiked with different concentrations of fluorescently-labeled biotin. The results of the tubeless-SIMBAS show that picomolar detection of analytes in whole-blood can be readily achieved (Fig. 3G). Fluorescent readout of the device was performed by inserting its top glass lid into a standard microarray scanner. One of advantage of our device is that it does not require irreversible bonding between the PDMS and glass layers, so it can be easily disassembled, and the glass layers with the captured analytes used for other analysis such as PCR or MS (Fig. 3D). In addition, for multi-analyte detection, each avidin bar could be replaced with a different probe, allowing the detection of several thousand analytes in each blood sample (Fig. 3E).

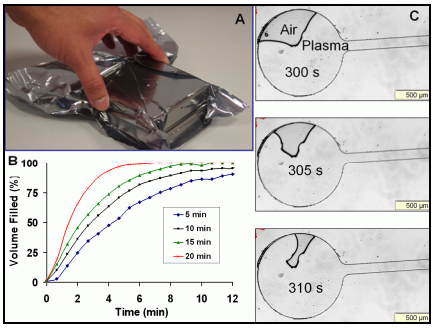

Figure 2. Degassing-driven flow is generated when the SIMBAS device is removed from its vacuum packing (**A**). Flow can still be observed 20 min after unpacking the device (B). The degas-driven flow was characterized using dead-end channels made of PDMS by measuring the filling time after degassing the PDMS channels in a standard vacuum desiccator (C).

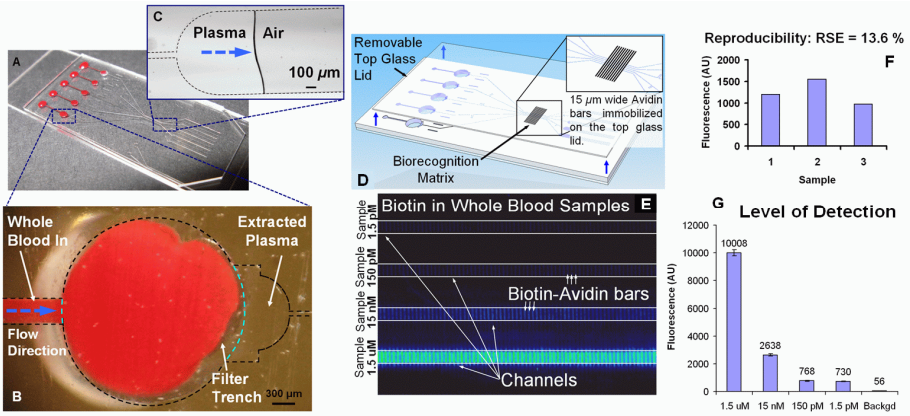

Figure 3. (**A**) Fast and effective plasma separation of 5 distinct whole blood samples by (**B**) filter trench (cylindrical cavity) and gravity-driven blood cell sedimentation in the (**C**) self-priming tubeless-SIMBAS. The device generates results within minutes after placing blood sample droplets on the device inlets. Detection of biotin in whole blood samples with a tubeless-SIMBAS. (**D**) The bio-recognition matrix and (**E**) different sample channels with biotin detection bars. (**F**) Sample-to-sample reproducibility at 150 pM. (**G**) Level of detection of fluorescently labeled biotin in whole blood. By optimizing the probe surface attachment and the channel depths the level of detection could be further improved.

CONCLUSIONS

In summary, we have demonstrated a self-priming tubeless-SIMBAS that efficiently extracts blood plasma from less than 5 μL of whole-blood and performs multiplexed sample-to-answer assay with picomolar sensitivity without any external pumping mechanisms. This sample-to-asnwer monolithic device can be manufactured at low cost and integrated with dense spatial multiplexing to form a "2D-Sample-&-Analyte" result matrix. Our integrated device is well-suited for point-of-care applications because of its self-powering mechanism, disposability, and simplicity of use.

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