A NEW ASYMMETRIC CAPILLARY FORCE DRIVEN WHOLE BLOOD/PLASMA SEPARATOR USING SPRAY LAYER-BY-LAYER NANO ASSEMBLY

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ABSTRACT

A new simple polymer microchannel with asymmetric hydrophilic surfaces over the channel inside with a patterned 10 mm hydrophobic patch, as an on-chip whole blood/plasma separator, has been designed, fabricated and characterized for the application toward point-of-care (POC) clinical diagnostics. The asymmetric hydrophilic surfaces in the polymer microchannel are fabricated using a spray layer-by-layer (LbL) nano assembly. Effective plasma separation from whole blood is achieved through the microchannel due to the asymmetric hydrophilic surfaces as well as the patterned hydrophobic patch. The blood cells are continuously accumulated within the hydrophobic patch over the time while the blood plasma is successfully separated from the whole blood throughout the microfilter made of blood cells column, so-called 'self-organized blood cell microfilter'. The separated plasma was approximate 0.102 µL from a single drop of whole blood within 10 minutes.

KEYWORDS

Asymmetric capillary force, Hydrophobic patch, On-chip whole blood/plasma separator, Point-of-care diagnostics, Spray layer-by-layer nano assembly

1. INTRODUCTION

Plasma or serum separated from human whole blood is most widely used in clinical analysis for disease diagnosis and health monitoring because blood contains critical information concerning the function of whole body. Separation of plasma from the whole blood is essential for the general blood analyses based on florescence immunoassays to minimize the noises from blood cells interfered with excitation optics.

Centrifugation technique and membrane filtration are standard methods for the separation of blood plasma. These systems are bulky, expensive, time-consuming, and require a large amount of blood sample. Furthermore, they are unable to fit the on-chip approach, thus creating a large demand for the development of a new blood/plasma separator for the POC clinical diagnosis. Recently, various on-chip blood/plasma separators have been realized and reported [1-3]. Either an external mechanical pumping force or capillary force drives these devices. The externally driving separator is not suitable for on-chip applications. A strong capillary force for better separation is favorable for the on-chip approach.

In this work, we propose a new simple on-chip whole blood/plasma separator by utilizing both the asymmetric capillary force and the patterned hydrophobic patch. The separator operates completely upon asymmetric capillary action without any external power resources and is able to efficiently separate nanoliter volumes of plasma from a single drop of whole blood, a suitable amount for the single-use application of POC clinical diagnostics.

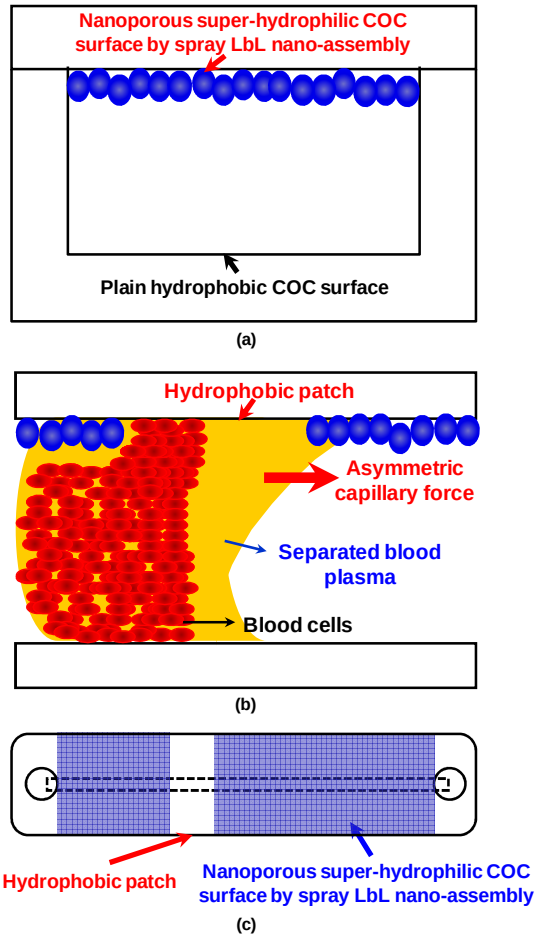

Figure 1. Schematic diagram for the separation principle of whole blood/plasma separator: (a) cut view; (b) side view; and (c) top view.

2. DESIGN AND FABRICATION

The basic principle for the blood plasma separator is based on the asymmetric capillary action and the patterned hydrophobic patch across the microchannel described in Figure 1. The plasma separated from the whole blood in the microchannel was moving faster due to the asymmetric capillary force developed between the nanoporous super-hydrophilic surface and the plain hydrophobic surface. However, the movement of the whole blood was effectively retarded in the microchannel because of the patterned hydrophobic patch, which has no asymmetric

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capillary action in this region. Over the time, this caused continuous accumulation of the blood cells within the hydrophobic patch. The accumulated column of blood cells worked as a naturally organized microfilter, and blood plasma was successfully separated from the whole blood throughout this 'self-organized blood cell microfilter'. The separated blood plasma was flowing across from the hydrophobic patch while moving towards the other super-hydrophilic region, where a strong asymmetric capillary force along the walls was also developed. This force allowed the blood plasma to be separated much faster than in the hydrophobic patch region where the flowing rate of blood cells was relatively slow.

Figure 2 summarizes the fabrication process of the whole blood/plasma separator. An aluminum master mold was fabricated first using a micro-milling machine (Microlution 5100S) for the replica of cyclic olefin copolymer (COC) microchannel. To fabricate the separator, COC chip patterned with microfluidic channels were prepared by the hot embossing technique. The dimension of fabricated microchannel was 100 μm × 100 μm × 50 mm with a 10 mm hydrophobic patch as shown in Figure 2(c). Then, the spray LbL nano-assembly process with silica nanoparticles [4] was done for the asymmetric super-hydrophilic surfaces over the microchannel with 10 mm hydrophobic patch. Finally, two polymer substrates were bonded for a chip using thermal bonding technique.

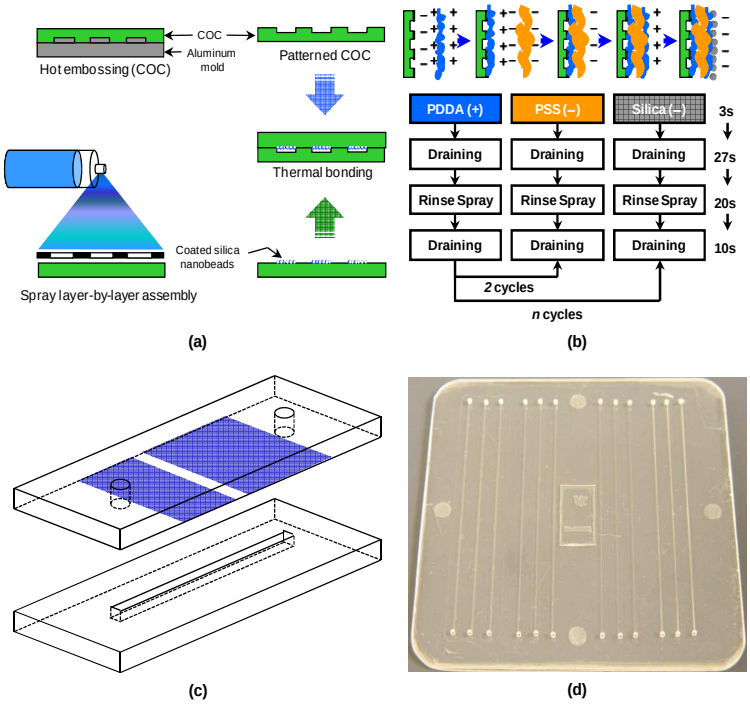

Figure 2. Summary of fabrication process of the whole blood/plasma separator: (a) fabrication methods; (b) spray LbL nano assembly; (c) device design; and (d) fabricated device.

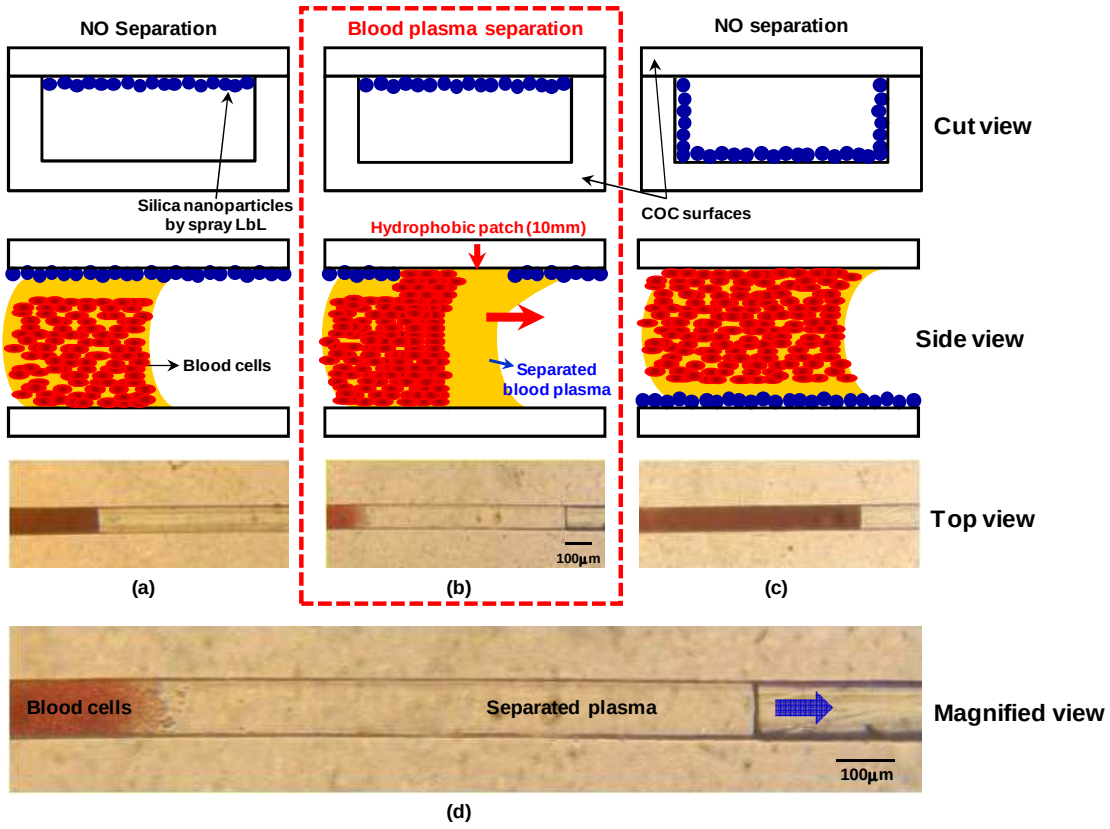

Figure 3. Coating structures: (a) top wall coating only; (b) top wall coating with hydrophobic patch (10 mm); (c) side wall coatings only; and (d) separated plasma.

3. RESULTS AND DISCUSSION

The radical drop in contact angles by the spray LbL nano assembly [4] indicates that the COC surface can be super-hydrophilic (contact angle below 5°) with silica nanoparticles because of the intrinsically high level of wettability of the silica nanoparticles which are coupled with the nanoporous nature of the multilayer surface. Five coatings of (PDDA/silica) bilayers were chosen as the optimum coatings of bilayers in order to obtain the maximum nanoporous capillary pumping effect in this process. 12 nm silica nanoparticles were chosen for the spray LbL nano assembly on the COC microchannels since the lowest contact angle with smallest standard deviation was obtained from the COC surface coated with that size [4].

Figure 3 describes the achievable separations from the various structures with the asymmetric super-hydrophilic surfaces and hydrophobic patch. A single drop (~3.0 µL) of human whole blood was injected into the inlet of the separator. Since only the asymmetric capillary forces along the microchannel surfaces moved the whole blood, and those structures did not provide enough asymmetric capillary force required for the separation of blood plasma, only a fairly small amount of separations were obtained as shown in Figure 3(a) and (c). However, a relatively large amount of blood plasma separation was achieved by utilizing both the asymmetric capillary force and the patterned 10 mm hydrophobic patch as shown in Figure 3(b). This shows that the patterned hydrophobic patch is very desirable for achieving the plasma separation from whole blood as described in Figure 1.

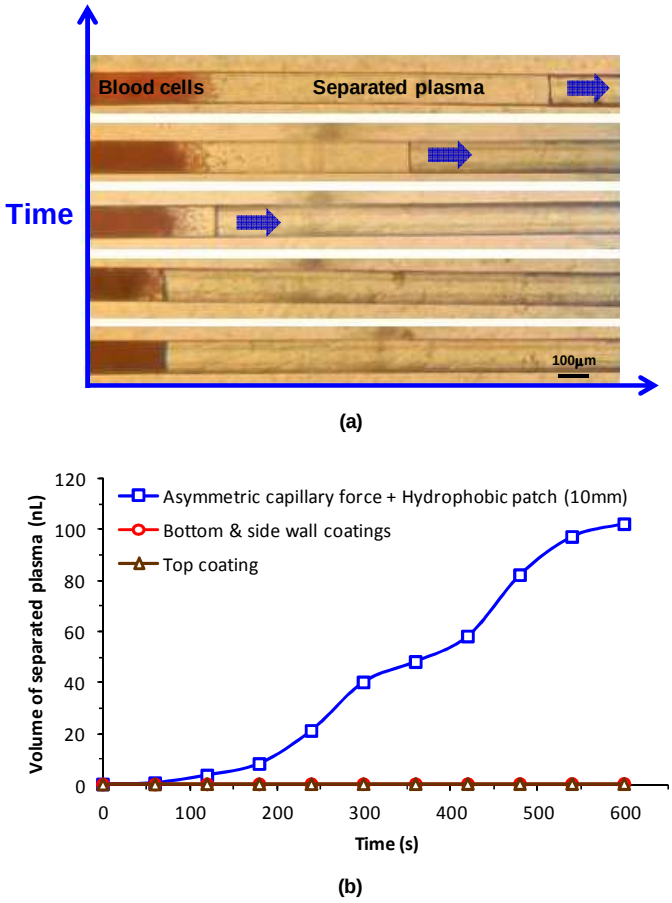

Figure 4. Separation results: (a) separation images and (b) volume changes of the separated plasma as the separation time.

Figure 4(a) shows the separated plasma from the whole blood was increased over the time due to both the strong asymmetric capillary force and the patterned hydrophobic patch, and 0.102 µL of the separated plasma from a drop of whole drop was finally obtained as shown in Figure 4(b). The volume of the separated plasma between 300 and 400 seconds in Figure 4(b) was slightly decreased over the time due to the accumulation of the blood cells over the hydrophobic patch with blood plasma during the separation.

CONCLUSION

A new asymmetric capillary force-based whole blood/plasma separator has been proposed, fabricated and fully characterized in this work. Asymmetric nanoporous super-hydrophilic surfaces and patterned hydrophobic patch were combined to attain an asymmetric capillary force through the microchannel for the separation of plasma from whole blood. The separator developed in this work has successfully separated plasma from whole blood. This separator with a simple micorchannel structure is very suitable for the applications of on-chip blood/plasma separator for POC clinical diagnostics.

REFERENCES

[1] S. Yang, A. Under, J.D. Zahn, *A microfluidic device for continuous, real time blood plasma separation, Lab Chip*, **6**, pp. 871-880, (2006).

[2] M. Amasia, M. Madou, *Large-volume centrifugal microfluidic device for blood plasma separation, Bioanalysis*, **2**, pp.1701-1710, (2010).

[3] J. S. Shim, C. H. Ahn, *An on-chip whole blood/plasma separator using hetero-packed beads at the inlet of a microchannel, Lab Chip*, **12**, pp. 863-866, (2012).

[4] K. K. Lee, C. H. Ahn, *Nanoporous-based hydrophilic polymer µchannel using a spray layer-by-layer electrostatic nano-assembly, Proceedings of the Solid-State Sensors, Actuators, and Microsystems Workshop*, June 3-7, Hilton Head Island, South Carolina, USA, pp. 209-212, (2012).

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