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**One-Touch-Activated Blood Multidiagnostic System** is involving the synergistic integration of a hollow microneedle and paper-based sensor, thus, offers a new approach in future real-time healthcare monitoring devices.

Hollow microneedle, Paper sensor, One-touch-activated, Blood extraction, Blood diagnostic

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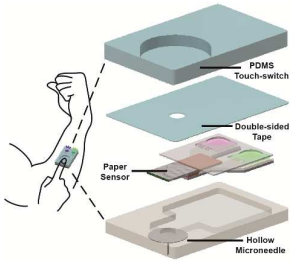

Cite this: DOI: 10.1039/c0xx00000x

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ARTICLE TYPE

# One-Touch-Activated Blood Multidiagnostic System using a Minimally Invasive Hollow Microneedle Integrated with a Paper-Based Sensor

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***Received (in XXX, XXX) Xth XXXXXXXXX 20XX, Accepted Xth XXXXXXXXX 20XX***
**DOI: 10.1039/b000000x**

The development of real-time innocuous blood diagnosis has been a longstanding goal in healthcare; an improved, miniature all-in-one point-of-care testing (POCT) system with low-cost and simplified operation is highly desired. Here, we present a one-touch-activated blood multidiagnostic system (OBMS) involving the synergistic integration of a hollow microneedle and paper-based sensor, providing a number of unique characteristics for simplifying the design of microsystems and enhancing user performance. In this OBMS, all functions of blood collection, serum separation, and detection were sequentially automated in one single device that only required one-touch activation by finger-power without additional operations. For the first time, we successfully demonstrated the operation of this system *in vivo* in glucose and cholesterol diagnosis, showing great possibility for human clinical application and commercialization. Additionally, this novel system offers a new approach to the use of microneedles and paper-sensors as promising intelligent elements in future real-time healthcare monitoring devices.

## Introduction

Point-of-care testing (POCT) represents a system whereby simple, rapid, and low-cost medical diagnostic tools are used at the patient care sites,[1] and has progressed dramatically in the last few years with advances in biomedical microelectromechanical systems, lab-on-a-chip devices, and micro total analysis systems.[2, 3] Blood, a rich source of human biological information,[4] is used as the target diagnostic sample in various POCT biosensors such as glucose meters, lateral flow assay strips, and cholesterol meters.[5] However, the separation of blood collection and sample injection in commercially available POCT devices have been shown to negatively influence the performance of biosensors.[6, 7] In addition to this, the use of hypodermic needles or finger pricking for blood collection and use of pipettes or disposable droppers for sample injection limit the miniaturization of the POCT system, resulting in patient inconvenience.[2] Although the creation of an all-in-one POCT system by combining blood collection with biosensor components has been a longstanding goal for complete, real-time blood diagnosis, such a system has not yet been developed.

The application of microneedles in diagnostic POCT has generated significant interest, owing to the great potential of the needles for minimally invasive pain-free transdermal sensing in micron-size devices.[8-10] Surface-modified microneedle biosensors have been developed to directly capture target samples from the interstitial fluid.[11-14] Nevertheless, it has not been possible to apply them in a blood-sampling diagnostic tool. Alternatively, hollow microneedles have also been introduced for use as blood collection devices,[15-18] however, a method to integrate these needles with biosensor components for on-site detection within the bloodstream has not been proposed. Despite these pioneering works suggesting the potential use of microneedles in diagnostic POCT, currently, offline analysis using lab scale instruments after sample capture or collection is still required, and this makes it difficult to implement real-time diagnostic POCT using the blood. To become a useful tool in an all-in-one POCT blood diagnostic system, an improved miniature system must reduce the actuator complexity while simultaneously simplifying the operation process. Currently, paper-based biosensor technology has been recognized as a future alternative for POCT biosensors for detection and quantification of a broad variety of analytes due to the high specificity and sensitivity of these biosensors as well as their simple and cost-effective fabrication process.[19-20] Various paper-based POCT biosensors such as rapid kits, dip sticks, and glucose meters are already commercialized and allow portable, on-site detection based on colorimetric methods, however, almost all of them are separated from the crucial sample collection process.

Here, we demonstrate a novel one-touch-activated blood multidiagnostic system (OBMS) that consists of a biocompatible minimally invasive hollow microneedle and paper-based multiplex biosensor. We took advantage of microneedle technology for pain-free blood sampling with minimal tissue damage and inflammation, and paper-based sensors that have a simple and cost-effective fabrication process. The OBMS integrated and automated all functions of blood collection, separation, and detection, sequentially, in a single device that only required one-touch activation by finger-power without additional operations. In an *in vivo* experiment, using a rabbit model we demonstrated that the OBMS could perform blood sampling and multidetection of glucose and cholesterol levels in a fully automated manner. This new integrated microneedle and paper-sensor based blood diagnostic platform shows great promise for future POCT and disposable biomedical applications.

## Results and discussion

### One-touch-activated blood diagnosis

The proposed OBMS consists of three major components: (i) a polydimethylsiloxane (PDMS) touch-switch, (ii) a paper-based multiplex sensor, and (iii) a biocompatible hollow microneedle (Fig. 1a). This PDMS touch-switch can be pushed using one finger to generate sufficient pressure to facilitate microneedle insertion into the blood vessel. When the finger is released, the deformable chamber reverts to its original shape, generating a negative pressure to extract a blood sample into the sensor-chamber through the hollow structure of the microneedle. The paper-based multiplex sensor was placed between the touch-switch and hollow microneedle for direct blood analysis. As shown in Fig. 1b, the sensor was composed of a sample pad, asymmetric polysulfone membrane (ASPM), Y-shaped patterned nitrocellulose (NC) membrane, and reaction membrane. The basic operating concept of the paper-based sensor for blood multidiagnostic testing is schematically depicted in Fig. 1c. The extracted blood sample was absorbed by the sample pad and introduced to the ASPM, where blood cells from the whole-blood were separated based on size exclusion. The separated serum was transported to the reaction membrane via the NC membrane, and biomarkers were detected by colorimetric assay. In this paper-based multiplex sensor, an external propulsion or control mechanism was not required; instead, capillary action was enough to separate and transport the serum after the whole-blood sample was introduced into the sample pad. In its current format, this blood diagnostic system can simultaneously analyze glucose and cholesterol in a two-channel unit from whole-blood samples.

Cite this: DOI: 10.1039/c0xx00000x

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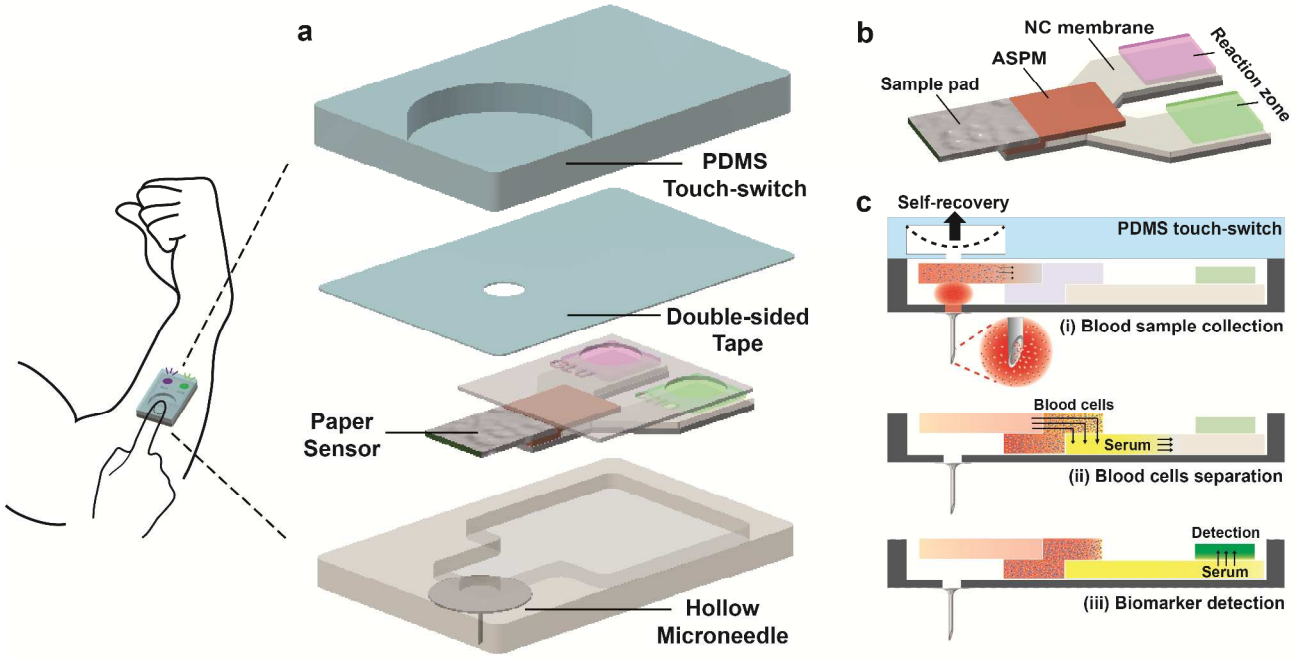


**Fig. 1** Schematic representation of the one-touch-activated blood multidiagnostic system (OBMS). (a) Structure of the OBMS; (b) Diagram of the paper-based multiplex sensor consisting of the sample pad, asymmetric polysulfone membrane (ASPM), nitrocellulose (NC) membrane, and reaction zones; (c) Operating principle of the paper-based sensor for blood sample multidiagnosis: (i) blood sample collection: removing the applied finger force causes the self-recovery of the polydimethylsiloxane (PDMS) touch-switch, inducing a negative pressure to collect a blood sample and induce its absorption by the sample pad; (ii) blood cell separation: filtering of the blood cells based on size exclusion by the ASPM; (iii) biomarker detection: detection of the multiplex biomarkers by colorimetric assay.

### Optimization of the OBMS

As shown in Fig. 2a, the hollow microneedle was fabricated with an optimized structure of 60 μm inner diameter, 120 μm outer diameter, and 15° bevel angle for minimally invasive blood collection by drawing lithography technology.[21, 22] Moreover, to enhance biomedical compatibility, a 1-μm thick biocompatible parylene film was deposited onto the inner and outer surface of the hollow microneedle (Supplementary Fig. S1). The touch-switch was fabricated using the traditional soft lithography method with PDMS as the main material, and was designed as a 20 × 13 × 3 $mm^3$ cube containing a cylindrical chamber. As the blood sample was collected as a result of the negative pressure produced by self-recovery of the deformable PDMS cylindrical chamber, the chamber volume was optimized to have a diameter of 9 mm and a height of 2 mm (127 μL) to collect blood samples of approximately 30 ± 5 μL (Fig. 2b). Through this method, an integrated one-touch-activated blood diagnostic system was accomplished by placing the paper sensor inside the sensor-chamber, which adhered to the upper PDMS touch-switch by double-sided tape in a concentric shaft to form a reversible seal (Fig. 2c). The components of this optimized paper-based sensor, with the corresponding dimensions, are also illustrated (Fig. 2d and Supplementary Fig. S2).

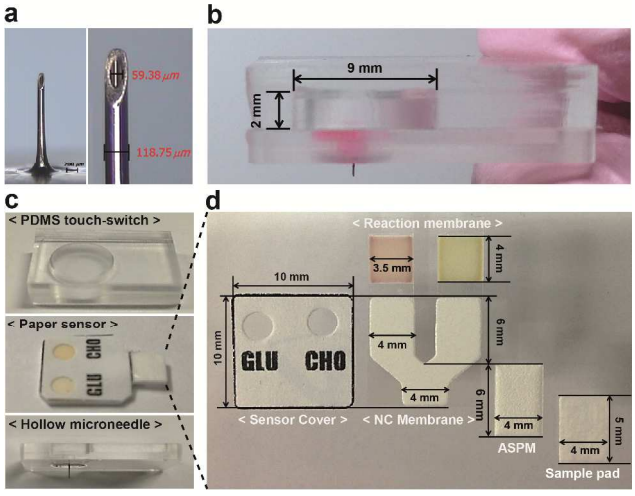


**Fig. 2** Components of the one-touch-activated blood multidiagnostic system (OBMS). (a) Image of the biocompatible minimally invasive hollow microneedle (60 μm inner diameter, 120 μm outer diameter, 15° bevel angle) contained within the OBMS; (b) Chamber volume (127 μL) of the polydimethylsiloxane (PDMS) touch-switch containing the collected blood sample; (c) Stereo structure of the OBMS: the PDMS touch-switch, paper-based sensor, and hollow microneedle with sensor-chamber; (d) Components of the paper-based sensor: sensor cover, reaction membrane, nitrocellulose (NC) membrane, asymmetric

polysulfone membrane (ASPM), and sample pad, with corresponding dimensions.

**Paper-based sensor optimization and performance**

As the blood cell separation capability of a paper sensor in whole-blood samples is often critical to decrease the cell interference in the optical sensor, the efficacy of the ASPM, which was designed to trap the blood cells (normally 6-8 μm in diameter), was analyzed. No red blood cell (RBC) separation was observed when only the sample pad was contained within the paper-based sensor (Supplementary Fig. S3d). RBC separation was achieved by incorporation of ASPM (Supplementary Fig. S3e), and the pretreatment with biofriendly surfactant (surfactant 10G) in the Y-shape NC membrane facilitated complete saturation of the reaction zone with the separated serum (Supplementary Fig. S3f).

As the OBMS was designed to collect approximately 30 ± 5 μL blood samples through the touch-switch, the size of the ASPM was optimized to specifically handle this volume range. Any excess sample volume would induce blood cell overflow in the reaction zone, and too little sample volume would lead to insufficient serum flow in this zone, resulting in the erroneous deviation of any measurements. Three types of paper sensor were designed with different ASPM sizes (0.14 $cm^2$ for type A, 0.26 $cm^2$ for type B, and 0.65 $cm^2$ for type C), and a volume range of 15-40 μL of level-1 blood sample with a hematocrit level of 40% was dropped onto the sensor to evaluate the deviation of colorimetric measurements (Fig. 3a). In type A ASPM, blood cells were observed in the reaction zone at sample volumes of over 25 μL, indicating leakage in this membrane. Moreover, inadequate serum in the reaction zones was observed when the sample volume was less than 25 μL in type C ASPM (data not shown). These results are in accordance with the glucose and cholesterol colorimetric assays (Fig. 3b and c). Although type A and C ASPM showed deviations in the colorimetric assays at the tested sample volumes, type B demonstrated the lowest levels of deviation, indicating it to be the most suitable sensor structure for the suggested sample volume range.

The optimized type B paper sensor was assembled onto the OBMS, and the 40% hematocrit blood samples that had concentration ranges of 0-270 mg $dL^{-1}$ glucose and 0-320 mg $dL^{-1}$ cholesterol were used for calibration. As illustrated in Fig. 3d, blood samples were collected by the hollow microneedle and the separated serum flowed to the reaction zones via the NC membrane, resulting in a color change within 3 min, from colorless to deep purple and green for glucose and cholesterol, respectively (Supplementary Video 1). In this assay, the serum glucose and cholesterol were oxidized by enzymes to induce a dramatic color change in the reaction zone using N-ethyl-N-sulfopropyl-m-toluidine (TOPS) purple and N,N-bis(4-sulfobutyl)-3,5-dimethylaniline, disodium salt (MADB) green colorimetric assays, respectively. Images of the reaction zones were obtained via microscopy. The results of the color intensity analysis showed linear calibration curves with correlation coefficients (R2) of 0.99 and 0.98 for glucose and cholesterol, respectively (Fig. 3e). Furthermore, the performance of the OBMS was compared to that of the traditional lab scale analyzer (FUJI DRI-CHEM 4000 Chemistry Analyzer, Fujifilm Corp., Tokyo, Japan) using rabbit whole-blood samples. No significant differences were observed in the results for glucose and cholesterol concentrations between the two methods, confirming the effective performance of OBMS in simultaneous sample collection and quantitative analysis of whole-blood samples in a single-step process (Supplementary Table S1).

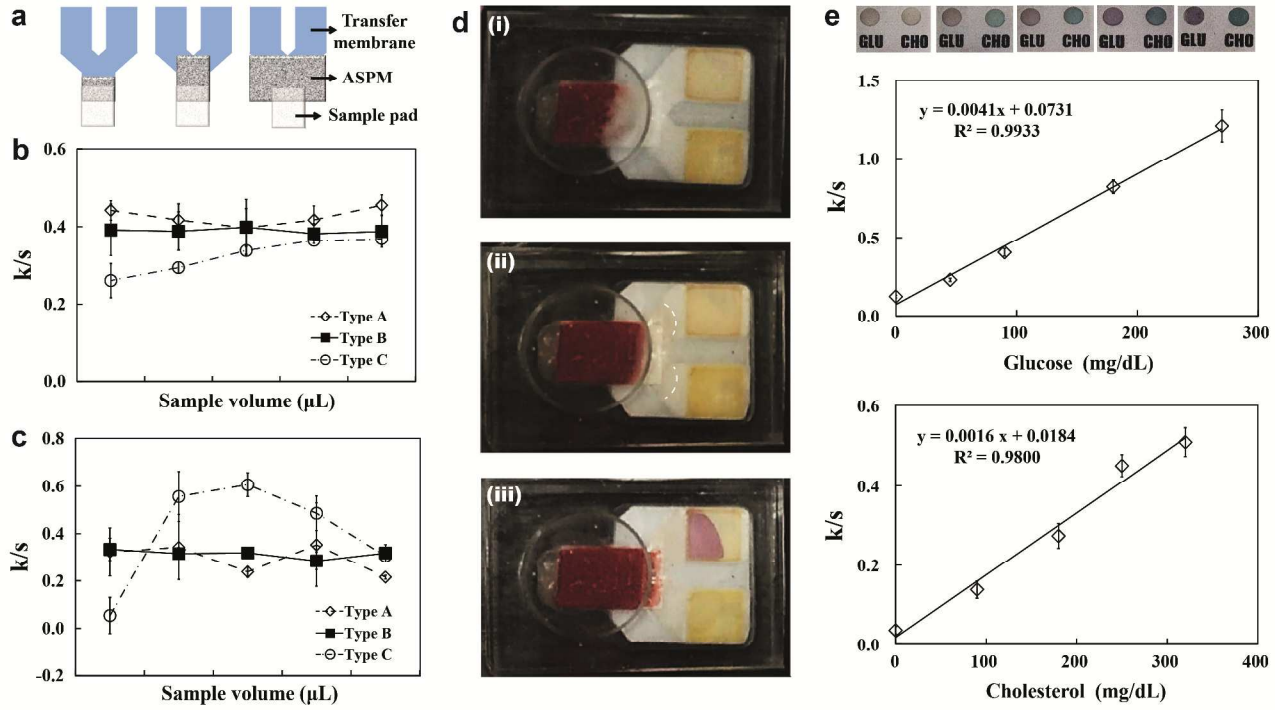


**Fig. 3** Paper-based sensor optimization and performance. (a) Schematic diagram of three types of paper sensor with different asymmetrical polysulfone membrane (ASPM) sizes (0.14 $cm^2$ for type A, 0.26 $cm^2$ for type B, 0.65 $cm^2$ for type C); The correlation between the ASPM size and blood sample

volume effect in (b) glucose and (c) cholesterol colorimetric measurements (◊: Type A, ■: Type B, o: Type C); (d) *In vitro* testing of the one-touch-activated blood multidiagnostic system (OBMS) for multidetection of glucose and cholesterol: (i) collect blood sample and induce its absorption by sample pad; (ii) filter blood cells based on size exclusion by the ASPM; (iii) separated serum flowed to the reaction zones, resulting in purple and green color change for glucose and cholesterol detection, respectively. (e) Calibration curves for glucose and cholesterol in the OBMS (upper panel: images of the OBMS reaction zones with different concentrations of standard blood samples). k/s: k, absorption coefficient; s, scattering coefficient of the membrane.

### *In vivo* operation of OBMS

*In vivo* blood multiplex diagnosis was performed using the OBMS in a rabbit model (New Zealand White, DooYeol Biotech, Inc., Seoul, Korea). By one-touch finger activation, the microneedle was inserted into the ear artery of the rabbit and a blood sample was collected within 10 s. The process of blood sampling, RBC separation, serum transportation, and detection was spontaneously and sequentially performed in the OBMS within 3 min, indicating its successful operation in living organisms as proof-of-concept (Fig. 4). The entire process of this blood multidiagnosis was recorded on video and can be viewed in Supplementary Video 2.

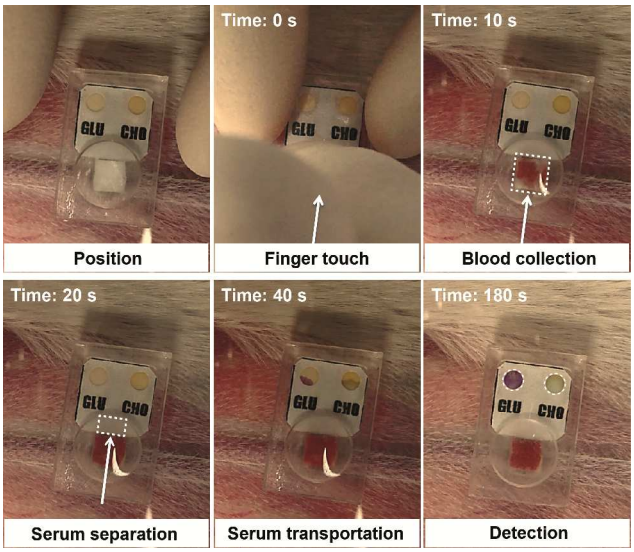


**Fig. 4** *In vivo* one-touch-activated blood diagnosis of glucose and cholesterol. Application of the one-touch-activated blood multidiagnostic system (OBMS) in a rabbit ear artery, initiated by a one-touch finger press, the blood sample was collected into the sensor-chamber and then reached the sample pad. Next, the serum was separated from the collected blood sample by the asymmetrical polysulfone membrane (dashed-line rectangle) and transported into the reaction zones. After 5 min the final image showing the color change was obtained.

## Experimental

### Reagents

Cholesterol esterase (COE-311), cholesterol oxidase (COO-311), glucose oxidase (GLO-201), and peroxidase (PEO-301) were obtained from Toyobo Co., Ltd. (OSK, Japan). N-ethyl-N-sulfopropyl-m-toluidine (TOPS) (OC14-10) and N,N-bis(4-sulfobutyl)-3,5-dimethylaniline, disodium salt (MADB) (OC21-10) were obtained from Dojindo Molecular Technologies, Inc. (Tokyo, Japan). Surfactant 10G (95R-103) was purchased from Fitzgerald Industries International (Acton, MA, USA). Standard serum (Liquichek™ Lipids Control Level-1 and Level-2) was obtained from Bio-Rad Laboratories, Inc. (Hercules, CA, USA). 4-aminoantipyrine (A4382), 3-(N-Morpholino)propanesulfonic acid sodium salt (MOPS; M9381), D-glucose (D7528), and other chemicals were obtained from Sigma-Aldrich (St. Louis, MO, USA). Nitrocellulose (NC) membrane (HF07502XSS) was obtained from Merck Millipore (Darmstadt, Germany). Asymmetric polysulfone membrane (ASPM, Vivid plasma separation) was purchased from Pall Corp. (Port Washington, NY, USA). Sample pad (fusion 5 8151-6621) was obtained from Whatman plc (Buckinghamshire, England).

### Paper-based sensor fabrication

All enzymes and peroxidase substrate stock solutions were adjusted to 10 KU $mL^{-1}$ and 0.5 M, respectively. MOPS buffer (50 mM, pH 5.0) was used for preparation of all stock solutions. Equal volumes of the stock solutions of cholesterol esterase, cholesterol oxidase, peroxidase, 4-aminoantipyrine, MADB, and 10% surfactant 10G solution were mixed for cholesterol measurement. The same volume of the stock solutions of glucose oxidase, peroxidase, 4-aminoantipyrine, and TOPS solution were mixed for glucose measurement. The two prepared mixtures (40 µL) were loaded on to 3.5 × 50 mm asymmetric super micron polysulfone (MMM) 0.8 membranes and then dried for 15 min at 37 °C in an oven. The dried MMM membranes were attached side-by-side to double sided tape and were cut with a craft cutter to a size of 4 mm. The paper-based multiplex sensor was composed of a sample pad (fusion 5), transfer membrane (Y-shape NC membrane), separation membrane (ASPM), reaction membrane, and labeled cover (GLU for glucose and GHO for cholesterol). First, the reaction membrane and separation membrane were placed on the transfer membrane, and the sample pad was located on the separation membrane. Finally, the double-sided tape was attached to the assembled sensor. The Y-shape transfer membrane was fabricated using the tear-off patterning method.

### Test sample preparation

Whole-blood samples were collected from the leg artery of the rabbits (4 kg, New Zealand White) in a volume of 1 mL using a hypodermic needle. The collected blood samples were transferred to an EDTA-treated blood collector (BD Vacutainer, Becton, Dickinson and Company, Franklin Lakes, NJ, USA) immediately, and then the collector was shaken in an orbital shaker for 10 min. Whole-blood samples were used in the analysis within 30 min of sample collection. Blood samples were centrifuged for 15 min at 2,000 g in order to collect the red blood cells (RBCs). After removing the serum, a 90 mM saline solution was made up to 1 mL in order to wash the RBCs. Then, after shaking smoothly, this same procedure was repeated twice. Finally, 60 µL of the standard serum (Level-1 or Level-2) was mixed with 40 µL washed RBCs in order to prepare the standard blood sample. Before mixing, the D-glucose solution (20 × in distilled water) was spiked to levels in standard human serum. The zero concentration blood samples were prepared by mixing the separated RBCs and saline solution. In order to obtain the calibration curve, the zero concentration, a 1:1 mixture of zero concentration and level-1, level-1 only, a 1:1 mixture of level-1

and level-2, level-2 samples were used.

**Paper-based sensor optimization**

The 40% haematocrit-adjusted blood sample was used for optimization of blood separation efficiency. The three different sensor compositions: sample pad only, sample pad and blood separation membrane, and 0.5% surfactant 10G treated NC membrane with sample pad and separation membrane, were tested. Twenty-five microliter blood samples were loaded onto the end of sample pad, and then the separation and transfer efficiency were observed by microscopy. After that, the correlation of ASPM size and blood sample volume was studied. Three types of paper sensor were prepared with different ASPM sizes (0.14 $cm^2$ for type A, 0.26 $cm^2$ for type B, and 0.65 $cm^2$ for type C) for the same reaction membrane. Then a 15-40 μL volume range of level-1 blood sample was dropped onto the sample pad, and images of the constructions were obtained after 5 min.

**One-touch-activated blood multi-diagnostic system (OBMS) fabrication**

The biocompatible minimally invasive hollow microneedle for blood collection was fabricated by the drawing lithography technique described in our previous work. The microneedle was assembled onto the bottom of sensor chamber, which was made of mechanically processed acrylic. The polydimethylsiloxane (PDMS) touch-switch was fabricated using standard soft lithography replica molding techniques. Briefly, the PDMS prepolymer solution was prepared by mixing the silicone elastomer (Sylgard 184A, Dow Corning, Midland, MI, USA) and curing agent (Sylgard 184B, Dow Corning) in a weight ratio of 10:1. After removing the air bubbles inside the PDMS solution by incubation in a vacuum chamber for 30 min, the PDMS was poured onto the cylindrical aluminum master mold (9 mm × 2 mm) and placed in an oven at 80 ºC for 1 h to cure the mixed PDMS prepolymer. Finally, the cured PDMS mold was carefully peeled from the master to form the PDMS touch-switch with a volume of 127 μL. Double-sided polyvinylchloride tape (DTS-310, Ducksunghitech, Korea) was prepared by punching 1 mm diameter circular holes using a flat-tip needle (Technical Innovations, Brazoria, TX, USA) for connecting the touch-switch and sensor chamber. Totally, the production of a single OBMS required three steps: (i) assembling the microneedle onto the bottom of the sensor chamber; (ii) casting and curing the PDMS touch-switch on the aluminum master mold; (iii) placing the paper-sensor inside the sensor chamber and adhering it to the upper PDMS touch-switch by double sided tape in a concentric shaft.

***In vitro* OBMS measurement**

The hollow microneedle from the OBMS was inserted into the sample container, and finger-power was used to control the process for one-touch-activated sample collection and detection. A single finger precisely pressed the PDMS touch-switch until touch to the sensor-chamber. After removing the finger-force, the blood sample was collected into the chamber and came directly in contact with the sample pad of the paper sensor for blood analysis. Then, the system was removed from the sample container, and the photographic images of the reaction zones in the paper sensor were obtained before collection of sample and after detection (5 min) by bright field microscope (Sam Won Scientific Ind. Co, Ltd., Seoul, Korea).

***In vivo* experiment**

A hollow microneedle with an inner diameter of 60 μm and a 15° bevel angle was integrated into the blood diagnostic system. An individual rabbit (4 kg, New Zealand White) was fixed in a restrainer and then the blood diagnostic system was one-touch-activated by finger-power to induce insertion of the microneedle into the ear artery. After finger-power removal, the induced negative pressure of the PDMS touch-switch prompted extraction of a blood sample into the sensor chamber and contact of this sample with the paper-based sensor. Photographs of the reaction zone in the paper-based sensor were taken after 5 min, as in the *in vitro* method. All experimental procedures were approved by the Department of Laboratory Animal Medicine of Yonsei University College of Medicine and the Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC), and were performed in accordance with the Animal Research Committee Guidelines at Yonsei University College of Medicine.

**Image analysis**

In order to analyse the color intensity change output of the OBMS, photographic images were obtained before and after the reactions as described above, and the signal zone pixel intensity was determined using Image J software (Image J 1.48). Initially, the color image was split into red, green, and blue images, and then reaction zone intensities were obtained from each before and after image. The red image was used for cholesterol measurement and green image was used for glucose measurement. After that, the diffuse reflectance (R) was obtained from the intensity ratio between the before and after reaction images. Finally, the k/s value was obtained using modified Kubelka-Munk theory (equation 1).[23]

$$k/s = (1-R)^2/2\times R \quad (1)$$

Where, k represents an absorption coefficient, s is the scattering coefficient, and R is diffuse reflectance.

## Conclusions

The entire blood diagnosis process of the OBMS was activated by a single finger-press without any additional energy supply, and blood sampling, RBC separation, serum transportation, and multidiagnostic detection were spontaneously and sequentially performed within 3 min of initiation. Blood sample collection was the critical step for OBMS initiation and was successfully performed by an optimized hollow microneedle. The structure of the microneedle, with a 120 μm outer diameter and 15° bevel angle, was demonstrated in our previous study on minimally invasive blood sampling.[24] There were no crooked or broken microneedles observed during repeated *in vivo* experiments due to the choice of nickel as the microneedle material, which has good mechanical strength and ductility. Meanwhile, in order to fulfill its potential for clinical applications, surface modification of the needle was performed by coating with parylene, a biocompatible material widely used in the medical device industry.[25]

From the OBMS optimization results, we confirmed that the

operating blood sample volume could be easily controlled by the deformable PDMS touch-switch volume and ASPM size. Further, control of the sample flow rate was possible by raw material selection and pattern design of the paper sensor. Blood-sample separation was considered a significant challenge for accurate and reliable detection in POCT systems, since the presence of blood cells can interfere with the results. In the OBMS presented here, serum from unprocessed whole-blood samples was successfully isolated by the ASPM based on size exclusion without using external complex microfluidic devices, allowing for a simple and miniaturized diagnostic system. In addition, this system could be applied to a variety of POCT biosensor platforms depending on the purpose and the target molecules by redesigning the paper-based sensor only. For example, a lateral flow assay could be easily introduced to the transfer membrane, as after RBC separation the serum samples flow laterally to the NC membrane. Furthermore, all sensor components in the OBMS have already been used in the conventional POCT biosensor, indicating potentially easy commercialization.

In this study, we performed *in vivo* blood diagnosis in a rabbit model to demonstrate the practical use of our OBMS. Employing our system in humans is the ultimate goal, which includes the conduction of a human clinical trial. Future development of the OBMS will aim to improve the system by using more economical and biocompatible alternative materials to nickel for microneedle fabrication, and to achieve higher mechanical strength allowing safe usage for patients. The pressure relief valve technology which was proposed by our previous work,[17] could be used to restructure OBMS for prevention of the inadvertently gas bubbles injection by PDMS touch-switch. In addition to, a vacuum sealed packing (such as vacuum pouch or container) could be used to solve the storage/contamination avoidance problem to achieve higher performance results with the paper-based sensor for innocuous clinical POCT applications.

In conclusion, the OBMS, containing an integrated microneedle and paper-based sensor, provides a powerful strategy for the development of low-cost multidiagnostic POCT biosensors. Notably, this is the first time that successful operation of the system has been demonstrated in living organisms and our results show great potential for human clinical applications and commercialization. This novel system also offers a new approach to the use of microneedles and paper-based sensors as promising intelligent elements in future real-time healthcare monitoring devices.

## Acknowledgements

This work was supported by the Public Welfare & Safety Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education, Science and Technology (2010-0020772). We thank Jae-Chul Pyun Professor from the Department of Materials Science and Engineering, Yonsei University for use of the parylene position system in his lab.

## Notes and references

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† Electronic Supplementary Information (ESI) available: Videos of OBMS system for *in vitro* and *in vivo* one-touch-activated blood diagnosis. See DOI: 10.1039/b000000x/

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