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Sensing and Bio-Sensing Research 3 (2015) 59–64

Contents lists available at ScienceDirect

Sensing and Bio-Sensing Research

journal homepage: www.elsevier.com/locate/sbsr

Hemagglutination detection for blood typing based on waveguide-mode sensors

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ARTICLE INFO

Keywords:
Blood typing
Immunoassay
Hemagglutination
Waveguide-mode sensor

ABSTRACT

ABO and Rh(D) blood typing is one of the most important tests performed prior to blood transfusion. Although on-site blood testing is desirable for expedient blood transfusion procedure, most conventional methods and instruments lack the required usability or portability. Here, we describe a novel method, based on the detection of hemagglutination using an optical waveguide-mode sensor, for on-site use. The reflectance spectrum of blood alone and that of blood mixed with antibody reagents was measured using the waveguide-mode sensor. Differences in reflectance by agglutinated and non-agglutinated blood samples were observed at the bottom of the spectral dips; due to differences in the manner in which red blood cells interacted with the surface of the sensor chip. Following the addition of the antibody, blood types A, B, O, and AB were clearly distinguishable and Rh(D) typing was also possible using the waveguide-mode sensor. Furthermore, the waveguide-mode-based measurement exhibited the potential to detect weak agglutination, which is difficult for human eyes to distinguish. Thus, this method holds great promise for application in novel on-site test instruments.
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1. Introduction

Blood type, represented by the ABO and Rh(D) systems, is an immunoreactive feature of red blood cells (RBCs) that is determined by the antigenic moieties of sugar chains on the RBC surface. Determination of the blood type is especially important before blood transfusion, because transfusion of mismatched blood types can lead to hemolysis within patient's blood vessels, which mediated by antibodies to the RBCs in blood plasma. Blood typing tests have traditionally been conducted manually, using techniques such as slide and tube agglutination tests. In the last 20–30 years, fully automated blood testing instruments have been developed and these are operational at blood centers and major hospitals. These instruments have advantages such as high throughput and high sensitivity. However, these advantages are somewhat offset by the large size and high cost of the instruments. These are major drawbacks, especially because on-site blood testing is an important requirement during an emergency or natural calamity. Development of a portable, low-cost, and sufficiently sensitive instrument for blood typing is therefore required to make on-site blood testing feasible.

Agglutination of RBCs (hemagglutination) is caused by an immune reaction between the RBCs and antibodies against the corresponding blood type. In conventional blood typing methods, hemagglutination caused by antibodies is detected by human eyes or by imaging techniques. Alternate methods of blood typing using optical techniques have also been reported. Quinn et al. first reported the use of a surface plasmon resonance (SPR) sensor for blood typing [1]. The SPR sensor is a sensitive biosensing instrument based on electrical field enhancement by SPR excitation [2–4]. SPR-based blood typing has been previously performed using the Biacore system [1,5,6] or an SPR imaging technique [7]. Narayanan et al. have reported a technique for absorbance measurement-based blood typing [8]. This group reported the detection of a weak agglutination reaction of A_2 subtype and weak-D. Robb et al. demonstrated fluorescence-based blood typing on a planar microarray

Abbreviations: RBCs, red blood cells; SPR, surface plasmon resonance; PBS, phosphate-buffered saline; LED, light-emitting device.

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http://dx.doi.org/10.1016/j.sbsr.2014.12.003
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platform [6]. In another approaches, blood typing have been performed using a microchannel [9–11] or paper [12,13].

In this study, we propose a blood typing method using an optical waveguide-mode sensor that detects changes in absorbance properties of the blood sample. The waveguide-mode sensor utilizes electric field enhancement in the sensor chip, similar to the SPR sensor, and is, therefore, more sensitive than a reflectance absorption spectrometer. The waveguide-mode sensor-based method provides a simple and sensitive blood typing technique, and utilizes a portable, small-sized instrument. Hemagglutination detection using the waveguide-mode sensor in this study was examined both theoretically and experimentally, using human blood and blood typing antibody reagents. ABO and Rh(D) blood typing was conducted using the waveguide-mode sensor-based hemagglutination detection method.

2. Materials and methods

2.1. Materials

Reagents were used as received with no further purification. Human whole blood containing the anticoagulant ethylenediaminetetraacetic acid dipotassium salt (EDTA 2K) was purchased from Tennessee Blood Service. Tubes containing fresh blood samples were shipped by air and used within 2 weeks. Before using the sample, we checked for hemolysis and used only non-hemolyzed samples. Blood types were confirmed by the supplier. Monoclonal anti-A and anti-B reagents (Neo Kokusai) were purchased from Sysmex Corporation. Monoclonal anti-D reagent (Monoclonal Anti-D Wako), Rh control reagent, and phosphate-buffered saline (PBS) was purchased from Wako Pure Chemical Industries, Ltd. Refractive index matching liquid for fused silica (Fused Silica Matching Liquids 50350) was purchased from Cargille Laboratories. Waveguide-mode sensor chips were supplied from Shin-Etsu Chemical Co., Ltd.

2.2. Experimental details

Hemagglutination was detected using a spectral readout-type waveguide-mode sensor [14]. Fig. 1(a) shows a schematic drawing of the experimental setup. The waveguide-mode sensor is based on the Kretschmann configuration containing a white light-emitting device (LED), collimator lens, polarizer, trapezoidal prism, sensor chip, and spectrometer. All the components of the waveguide-mode sensor are enclosed within a $30 \times 20 \times 15$ cm^3 box, making the device portable. The sensor chip consists of a surface SiO_2 glass waveguide layer and an embedded silicon reflectance layer on silica glass [15]. The chips are placed on the prism at base angle 38°, which corresponds to an incident angle of 70.6° and the index matching liquid is introduced in between. S-polarized incident light from the LED is irradiated onto the chip from the bottom, and the spectrum of the reflected light is measured by the spectrometer. Dips in reflectance were observed because of excitation of waveguide-mode propagation. By monitoring alteration in the dips, changes in the complex refractive index in the vicinity of the sensor chip surface can be detected. The wavelength of the spectral dip is controlled by adjusting the thickness of the SiO_2 waveguide layer and the silicon reflectance layer. In this study, the thickness of the waveguide layer and reflectance layer of the chips were approximately 360 and 45 nm, respectively. Those chips exhibited spectral dip around 540 nm during blood measurements, which were calibrated as per the peak wavelength for the RBC absorbance spectrum. For the hemagglutination detection measurements, a drop of the blood sample was directly placed onto the calibrated chip without surface modifications.

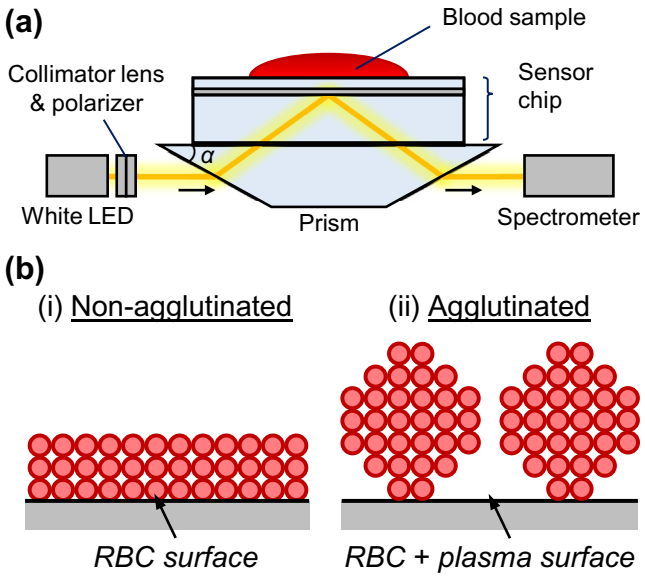

Fig. 1. (a) A schematic diagram of the experimental setup to detect hemagglutination. α represents base angle of the trapezoidal prism. (b) Schematic diagrams of the sensor chip surface with blood samples containing (i) non-agglutinated and (ii) agglutinated RBCs. Red circles represent individual RBCs.

Fig. 1(b) shows a schematic diagram of the sensor chip surface during analysis of blood samples. In case of non-agglutinated blood samples, RBCs will sediment uniformly and form a dense layer on the chip surface. By contrast, agglutinated RBCs (e.g., blood A mixed with anti-A) will sediment discretely onto the chip surface. Consequently, according to the ratio of contact area of RBCs to the surface, the complex refractive indices of the chip surface differ between the agglutinated and non-agglutinated blood samples. Since RBCs exhibit absorption around 540 nm while plasma does not, we focused on the change in extinction coefficient due to hemagglutination. The spectral response of the waveguide-mode sensor to hemagglutination was calculated using the transfer matrix method. To represent hemagglutination in the calculation, we assumed uniformly mixed layers that contained RBCs and plasma in various ratios. The extinction coefficient k of both RBCs and plasma, was calculated from the absorbance A as follows:

$$k = \ln 10 \frac{A\lambda}{4\pi d} \quad (1)$$

where λ is the wavelength and d is the optical path length. The absorbance was measured using NanoDrop 2000c (Thermo Fisher Scientific Inc.). The values of k of RBCs and plasma derived using the measured absorbance and Eq. (1) are shown in Supplementary Fig. S1. The k value of the mixed layer was derived from the weighted average k of RBCs and plasma according to the composition ratio. For the refractive index, n, a previously reported value for RBCs, $n = 1.40$, was used [16].

For detection of hemagglutination using the waveguide-mode sensors, samples of human whole blood were diluted with PBS to 5% of the RBC volume. First, the spectral responses for agglutinated and non-agglutinated blood samples were examined using the diluted blood and blood-antibody mixture in a 1:1 ratio by volume. Second, ABO forward blood typing was conducted using blood types A, B, O, and AB. Diluted blood was placed onto the sensor chip surface, antibody reagents were added and mixed gently by pipetting. The spectra of the blood and blood-antibody mixture were measured and compared to identify any antibody-dependent change. Rh(D) blood typing was also performed. All reactions and measurements were conducted at room temperature.

3. Results and discussion

3.1. Hemagglutination detection

The calculated spectral responses of waveguide-mode sensor measurements of blood samples are shown in Fig. 2. The reflectance spectrum for the composition ratio of RBCs from 0% to 100% is presented. In the calculation, S-polarized light was set at an incident angle of 70.6°. Calculation layers were set, from the bottom to the top, as silica glass, 45-nm single crystalline silicon, 360-nm SiO_2 glass, blood sample, and ambient blood plasma. The blood sample layer consists of a mixture of RBCs and blood plasma in various ratios. The optical property of the blood sample layer was set to reflect the composition ratio as described in Subsection 2.2. The thickness of the blood sample layer was assumed to be 35 nm, derived as a fitting parameter to reproduce a dip in the calculated reflectance spectrum at the wavelength of 540 nm. In other words, the assumed sample layer thickness was chosen to reflect the contribution of RBCs to the optical response in this model. Under these conditions, as the proportion of RBCs in the sample decreased, the reflectance at the bottom of the spectral dip (bottom reflectance) increased. This implies that hemagglutination can be detected by an increase in the bottom reflectance. Of note, the calculation relies on the assumption that blood samples form a physical "layer", although this may not always apply in experimental conditions, since the boundary between blood inside the detection range (several hundred nanometers from the surface of the sensor chip) and that outside should be ambiguous. The assumed 35-nm thickness of the blood sample layer was miniscule, as compared to the thickness of an individual RBC (approximately 2-μm), and we deduce this was due to the assumption of the "layer". Quantitative discussions using our model would be inadequate. However, our results are sufficient to derive qualitative information. Clearly, for a more quantitative method, an advanced calculation model is desirable.

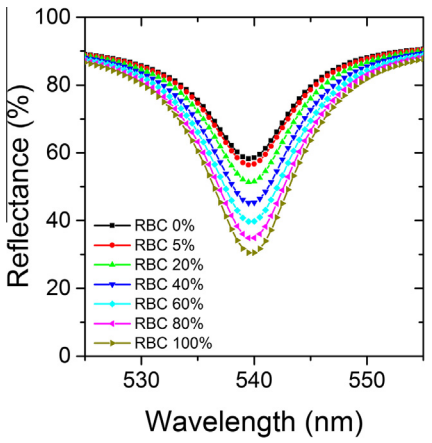

Fig. 2. Simulated spectral response of a waveguide-mode sensor analyzing blood samples containing RBCs in various proportions.

Fig. 3 shows the spectral responses derived from blood samples in the waveguide-mode sensor. A 50-μL droplet of plain blood, blood mixed with anti-A, or blood mixed with anti-B was placed on the waveguide-mode sensor chips using a micropipette. Since type A blood was used in this measurement, the blood mixed with anti-A should agglutinate, whereas that with anti-B did not. In Fig. 3, the spectrum just after the sample drop ("0 min" curves) was similar in all 3 samples. As time progressed from placing the sample drop, the dips in the spectrum were deeper because of the gravitational sedimentation of RBCs onto the chip surface. After 10 min, the dips reached a plateau. In this state, the spectrum of the non-agglutinated samples ("Blood A" and "Blood A + anti-B") and the agglutinated sample ("Blood A + anti-A") were clearly different: the dip of the agglutinated sample elicited higher bottom reflectance than that of the non-agglutinated samples. This trend is consistent with the calculated result (Fig. 2). Observation of the samples using an optical microscope (BX51, Olympus Corporation) supported the hemagglutination state of the samples. Thus, hemagglutination detection using the waveguide-mode sensors can be conducted by comparing the bottom reflectance of the dip at or near the plateau. The spectra in Fig. 3 show that measurements made at 5–10 min after placing the drop are appropriate for the bottom reflectance comparison to detect hemagglutination when the spectral response approaches a plateau. This timeframe was employed in the tests that followed.

3.2. ABO and Rh(D) blood typing

The waveguide-mode sensor-based ABO blood typing test was conducted using A, B, O, and AB blood types. To observe changes in the bottom reflectance of the dips caused by addition of anti-A and anti-B antibodies, the spectra of blood and blood-antibody mixture were serially measured (Fig. 4(a)). Samples used were of 50 μL each. Spectra of blood-only samples were obtained 10 min after the sample was placed and those of blood-antibody mixture

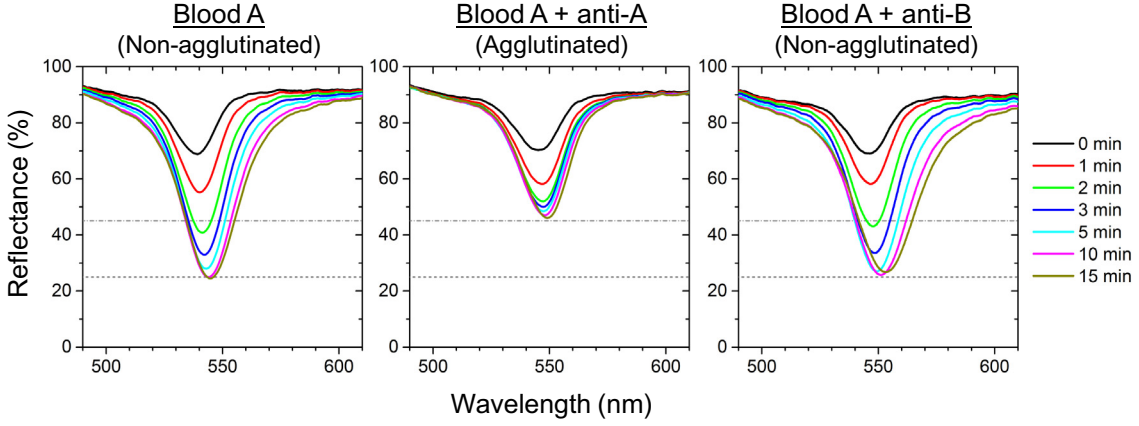

Fig. 3. Reflectance spectra of type A blood samples measured using a waveguide-mode sensor. Spectra measured at 0, 1, 2, 3, 5, 10, and 15 min after placing the drop of sample are shown in colored, solid lines. Gray dotted and dashed lines represent dip reflectance levels of the non-agglutinated ("Blood A" and "Blood A + anti-B") and the agglutinated samples ("Blood A + anti-A"), respectively. The agglutinated sample elicits a higher dip reflectance than the non-agglutinated samples.

were obtained 5 min after addition of the antibody. Clear difference in the response to addition of the antibody was observed for each of the blood types: agglutinated samples increased the bottom reflectance, while non-agglutinated samples produced no significant changes. Differences in values of the bottom reflectance between the spectra of blood and blood-antibody mixture are summarized in Fig. 4(b). Types A, B O, and AB were obviously distinguishable in the graph. Compared with types A and B, type AB blood induced a slightly smaller bottom reflectance change. This is likely due to the number of blood type antigens (sugar chains) on the RBC surface: the total number of these antigens on RBC is almost the same, and therefore RBCs of type AB have smaller numbers of both, type A and B antigens as compared to type A and B RBCs that possess only A or only B antigens, respectively. In the waveguide-mode sensor-based hemagglutination detection method, we infer that the intensity of agglutination can be estimated by the magnitude of change of the bottom reflectance.

Fig. 4(c) shows photographs of the sensor chips that were used to analyze blood-antibody mixture. The photographs were taken at the same time as the spectrum measurements shown in Fig. 4(a). In some cases, visual judgment of agglutination was difficult; e.g., the difference between "Blood B + anti-A" (non-agglutinated) and "Blood B + anti-B" (agglutinated) in Fig. 4(c) is not clearly discernible. However, even in these cases, the difference in spectra measured using the waveguide-mode sensors was very clear, as shown in Fig. 4(a). We therefore consider that waveguide-mode sensor-based hemagglutination detection is more sensitive and accurate than a visual test. Weak agglutination reactions, such as a reaction between weak-A RBC antigen and anti-A, sometimes appear as false negative during the blood testing. Our hemagglutination

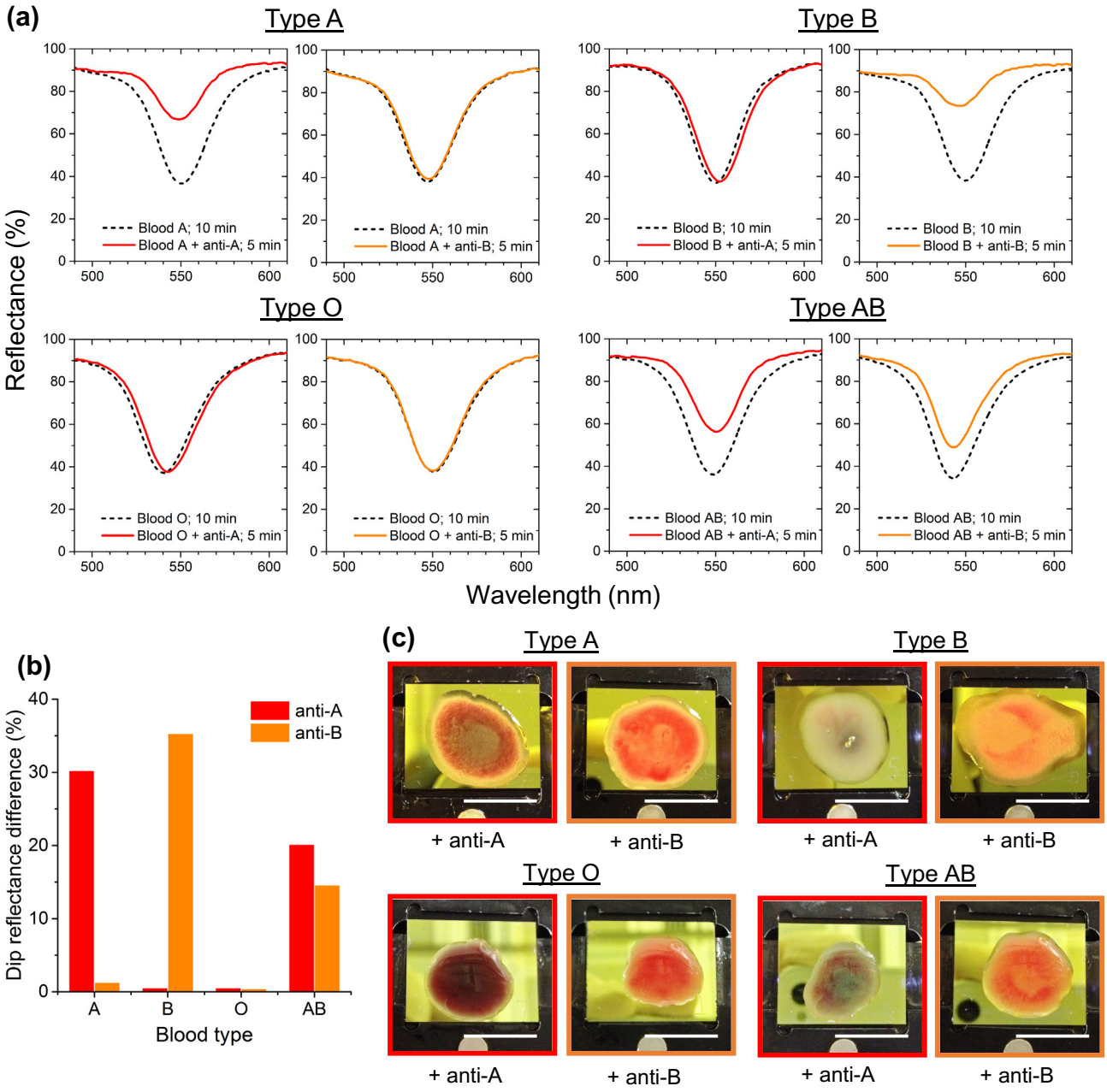

Fig. 4. (a) ABO blood typing using a waveguide-mode sensor. After measuring the reflectance spectra of blood samples (dashed lines), antibody reagents were added to the samples and the spectra of the blood-antibody mixture (solid lines) were measured. Spectra were measured 10 min after the sample drop was placed and that of the blood-antibody mixture were measured 5 min after addition of antibody. (b) Bottom reflectance change between spectra of blood and blood-antibody mixture shown in (a). (c) Photographs of sensor chips analyzing the blood-antibody mixture. Each photograph corresponds to the spectra shown in (a). Scale bars in the figure indicate 10 mm.

detection method demonstrated the potential to deal with such challenging cases.

It should be noted that the anti-A and anti-B reagents used in this study were colored, in the same manner as general diagnostic reagents used for manual ABO blood typing. The anti-A reagent was blue and the anti-B reagent was yellow in color, and these colors could possibly affect the reflectance spectra of the blood samples. We checked the effect of the colors by placing a drop of the antibody reagents alone on the sensor chip. The difference in the value of the bottom reflectance between the spectra of the anti-A and anti-B reagents was approximately 2%. The effect of the colors was small as compared to the spectral change caused by hemagglutination as shown in Fig. 4(b). In addition, since the effect of the colors should be constant if the experimental conditions such as the sample volume and mixture ratio were the same, the effect can be removed during the analysis. Thus, the colors do not affect the blood typing using the waveguide-mode sensor.

Our method is not limited to ABO typing, but also applicable to another tests that use hemagglutination, such as the Rh(D) blood typing and ABO reverse typing. The reflectance spectra of demonstrated for Rh(D) blood typing is shown in Fig. 5. The anti-D and Rh control reagents were mixed with Rh+ and Rh− blood in equal volumes and the reflectance spectra were measured 5 min after placing a 50-μL droplet of the samples. Rh+ and Rh− blood samples were distinguished by comparing the bottom reflectance of the respective samples, as done for ABO blood typing. The difference in bottom reflectance of the agglutinated Rh+ sample (approximately 10%) was smaller than that of the agglutinated samples from the ABO typing tests (15–35%). Agglutination produced by the anti-D reagent is generally weaker than that by anti-A and anti-B reagents, and the smaller magnitude of difference in reflectance is considered to reflect the intensity of the agglutination reaction, as previously mentioned regarding ABO blood typing. Thus, using adequate samples and reagents, our method can be used in various tests utilizing hemagglutination.

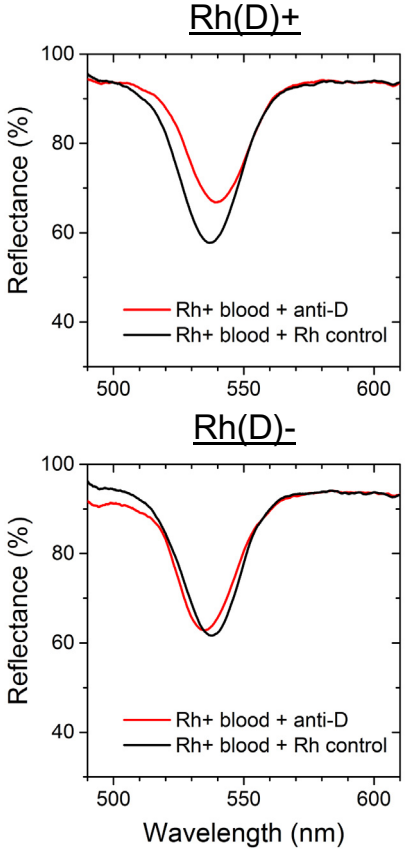

Fig. 5. Rh(D) blood typing using a waveguide-mode sensor. Spectra measured at 5 min after placing the drop of sample are shown in red (blood and anti-D reagent mixture) and black (blood and Rh control reagent mixture) solid lines. Rh(D)+ blood mixed with anti-D reagent showed agglutination and the other samples did not. Difference in bottom reflectance of the spectra of agglutinated Rh(D)+ sample was observed similar to that obtained with ABO blood typing.

3.3. Tolerance for hematocrit variation

Considering on-site blood typing, the volume ratio of RBCs in blood (hematocrit) of tested samples is usually unknown, and this can influence the results. Thus, the method should account for variable values of hematocrit. To this end, the tolerance of the waveguide-mode sensor for hematocrit variations was tested. Type A and B blood samples were diluted with PBS to 2.5%, 5%, 7.5%, and 10% of RBC volume, and measured using the waveguide-mode sensor. The procedure described in Section 3.2 was followed, except that spectra of the blood-antibody mixture were measured 10 min after the addition of antibody. The difference in the values of the bottom reflectance between the spectra of blood and that of blood-antibody mixture are shown in Fig. 6. Clear differences between agglutinated and non-agglutinated samples were observed for the values of the proportion of RBCs ranging from 5% to 10%. This shows that if a 6-fold dilution of the blood sample is used, samples that contain between 30% and 60% proportion of RBCs in the sample volume can be effectively tested. This range covers the variation in hematocrit of healthy individuals, which is between 35% and 55%. Thus, the waveguide-mode sensor-based blood typing test is sufficiently tolerant for on-site use. The samples of 2.5% proportion of RBCs showed relatively shallow dips of spectra (i.e., the bottom reflectance of the dips was high) compared with those containing a larger proportion of RBCs. We infer that this is since RBCs would cover the entire surface of the sensor chip if present at proportions above 5% of the total volume, while RBCs that constitute less than 2.5% would not. The threshold proportion of RBCs for adequate coverage of the chip surface is related to the sample volume per unit area (equal to average height), since the total number of RBCs sinking onto a unit area of the chip surface is a product of the blood volume and the proportion of RBCs. We used 50-μL samples with a diameter of approximately 10 mm in this study. When using samples of different volumes, the

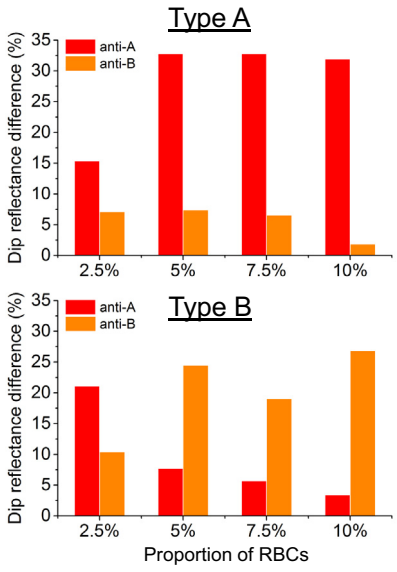

Fig. 6. Bottom reflectance changes between spectra of blood and blood-antibody mixture in samples with varying proportion of RBCs.

appropriate range of the proportion of RBCs would change. For example, in order to decrease the sample volume required for blood typing, the sample height is often reduced by the use of a cover glass or a microchannel. In that case, it should be noted that the proportion of RBCs in the sample that would be required to cover the entire chip would increase because of the decreased sample volume per unit area.

3.4. Comparison with conventional methods and measurement time considerations

Our method of hemagglutination detection provides a simple way of optical-sensor-based blood typing using a portable instrument. The method is as simple as that for manual testing by the glass slide method, with potentially superior sensitivity. Compared with the conventional SPR-based blood typing methods [1,5–7] that require surface modifications to capture RBCs on the sensor chips, our method requires no such surface modification. This reduces the sensor chip preparation time. In addition, our method allows repeat-use of the sensor chips by simply washing trace of blood and is, therefore, cost-effective. The microchannel-based blood typing methods [9–11] have reported much smaller amount of blood sample consumption (generally below 1 μL) than our method. By introducing microchannels in the sensor system, our method could also decrease the amount of sample required. The paper-based blood typing methods [12,13] are considered to be most easy-to-use and cost-effective, albeit at the cost of accuracy. We consider our method lies between the paper-based method and the fully automated blood testing instruments in terms of the device size and cost, whereas the accuracy can be comparable with the automated instruments.

The current procedure to obtain bottom reflectance differences shown in Fig. 4(b) took 15 min, which is not considered ideal for on-site blood testing. One way to shorten the measurement time is to include multiple-channel optical system into the waveguide-mode sensor device. If we used a three-channel waveguide-mode sensor, the spectra required for ABO blood typing (plain blood, blood and anti-A mixture, and blood anti-B mixture) can be obtained simultaneously. This would reduce the time to 5 min for ABO blood typing, as per the time course spectra shown in Fig. 3, since the spectral responses approach a plateau within this timeframe. Further reduction could be achieved by exploiting the velocity of gravitational sedimentation of RBCs. For example, RBC sedimentation can be enhanced by applying an electric field [17]. Introducing such systems to the sensor will dramatically reduce the time required for blood typing using our approach.

4. Conclusion

Here, we have described a novel method for hemagglutination detection for on-site blood testing that is based on a waveguide-mode sensor. The difference of the bottom reflectance between dips of spectra of agglutinated and non-agglutinated blood samples was derived from calculations based on the transfer matrix method, and which account for a change in the contact area ratio of RBCs at the sensor chip surface. This difference in bottom reflectance was also obtained experimentally using diluted human whole blood and the waveguide-mode sensor. The agglutinated samples elicited changes between 10% and 35% in the bottom reflectance, while the non-agglutinated samples induced a maximum change of 7.5%. Blood types A, B, O, and AB can be clearly distinguished by measuring the bottom reflectance difference caused by addition of anti-A and anti-B reagents to the samples. Although the agglutination reaction is sometimes difficult to visually discern, our method did not encounter such issues. In addition, it was demonstrated that our method is applicable to not only ABO forward typing but also Rh(D) typing. Thus, the waveguide-mode sensor-based blood typing is a promising candidate for on-site blood testing. Here, we have presented the prototypic version of the system. By employing advanced optical configurations and fluidic systems in the sensor, we hypothesize improvements such as multiple channel waveguide-mode sensors integrating microchannels, which would save time and reduce the volume of sample required. Furthermore, the system provides the added benefits of automation and increased sensitivity.

Conflict of interest

There is no conflict of interest.

Acknowledgements

This study was supported by SENTAN, Japan Science and Technology Agency (JST). Original wafers of the waveguide-mode sensor chips were supplied by Advanced Functional Materials Research Center of Shin-Etsu Chemical Co., Ltd.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.sbsr.2014.12.003.

References

[1] J.G. Quinn, R. O'Kennedy, M. Smyth, J. Moulds, T. Frame, Detection of blood group antigens utilising immobilised antibodies and surface plasmon resonance, J. Immunol. Methods 206 (1997) 87–96.
[2] J. Homola, S.S. Yee, G. Gauglitz, Surface plasmon resonance sensors: review, Sens. Actuators, B 54 (1999) 3–15.
[3] C. Nylander, B. Liedberg, T. Lind, Gas detection by means of surface plasmon resonance, Sens. Actuators 3 (1982–1983) 79–88.
[4] B. Liedberg, C. Nylander, I. Lunström, Surface plasmon resonance for gas detection and biosensing, Sens. Actuators 4 (1983) 299–304.
[5] J.G. Quinn, S. O'Neill, A. Doyle, C. McAtamney, D. Diamond, B.D. MacCraith, R. O'Kennedy, Development and application of surface plasmon resonance-based biosensors for the detection of cell-ligand interactions, Anal. Biochem. 281 (2000) 135–143.
[6] J.S. Robb, D.J. Roy, P. Ghazal, J. Allan, J. Petrik, Development of non-agglutination microarray blood grouping, Transfus. Med. 16 (2006) 119–129.
[7] N. Houngkamhang, A. Vongsakulyanon, P. Peungthum, K. Sudprasert, P. Kitpoka, M. Kunakorn, B. Sutapun, R. Amarit, A. Somboonkaew, T. Srikhirin, ABO blood-typing using an antibody array technique based on surface plasmon resonance imaging, Sensors 13 (2013) 11913–11922.
[8] S. Narayanan, L. Galloway, A. Nonoyama, G.F. Leparc, L.H. Garcia-Rubio, R.L. Potter, UV-visible spectrophotometric approach to blood typing II: phenotyping of subtype A_2 and weak D and whole blood analysis, Transfusion 42 (2002) 619–626.
[9] D.S. Kim, S.H. Lee, C.H. Ahn, J.Y. Lee, T.H. Kwon, Disposable integrated microfluidic biochip for blood typing by plastic microinjection moulding, Lab Chip 6 (2006) 794–802.
[10] T.R. Kline, M.K. Runyon, M. Pothiawala, R.F. Ismagilov, ABO, D blood typing and subtyping using plug-based microfluidics, Anal. Chem. 80 (2008) 6190–6197.
[11] S. Makulska, S. Jakiela, P. Garstecki, A micro-rheological method for determination of blood type, Lab Chip 13 (2013) 2796–2801.
[12] M.S. Khan, G. Thouas, W. Shen, G. Whyte, G. Garnier, Paper diagnostic for instantaneous blood typing, Anal. Chem. 82 (2010) 4158–4164.
[13] J. Noiphung, K. Talalak, I. Hongwarittorrn, N. Pupinyo, P. Thirabowonkitphithan, W. Laiwattanapaisal, A novel paper-based assay for the simultaneous determination of Rh typing and forward and reverse ABO blood groups, Biosens. Bioelectron. (2014) http://dx.doi.org/10.1016/j.bios.2014.09.011i.
[14] X. Wang, M. Fujimaki, T. Kato, K. Nomura, K. Awazu, Y. Ohki, Optimal design of a spectral readout type planar waveguide-mode sensor with a monolithic structure, Opt. Express 19 (2011) 20205–20213.
[15] M. Fujimaki, C. Rockstuhl, X. Wang, K. Awazu, J. Tominaga, Y. Koganezawa, Y. Ohki, T. Komatsubara, Silica-based monolithic sensing plates for waveguide-mode sensors, Opt. Express 16 (2008) 6408–6416.
[16] D.H. Tycko, M.H. Metz, E.A. Epstein, A. Grinbaum, Flow-cytometric light scattering measurement of red blood cell volume and hemoglobin concentration, Appl. Opt. 24 (1985) 1355–1365.
[17] M. Long, Y. Toyama, T. Dobashi, A. Sakanishi, Y.P. Wu, S. Oka, Effect of electric field on erythrocyte sedimentation rate. II. Dependence on electric current, Biorheology 27 (1990) 769–777.