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Optical Measurement of Blood Hematocrit on Medical Tubing with Dual Wavelength and Detector Model

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Abstract—**Blood hematocrit (Hct) is a clinically important index to detect death-dealing symptoms such as anemia and thrombosis, especially for patients with artificial heart, in dialysis and during open-heart surgery. Optical technology has been applied to monitor hematocrit noninvasively, continuously and conveniently, however, it was not well established for actual use. The purpose of this study is to develop an accurate and stable optical hematocrit measurement without any calibrations for device-mounting errors. To this end, we propose a theoretical method. In this method, disturbances are cancelled by using dual detector and optical path changes are calibrated by dual wavelength so that we can measure hematocrit without calibrations of these. Based on the method, a measurement unit that has two LEDs (805/1300[nm]) and four photo detectors was developed. Then, we performed experiments with 38 blood samples from five bovines' blood (Hct: 19-55%). These blood samples were circulated in a mock-up circuit by a blood pump. During the experiment, we measured hematocrit on medical tubing with the developed measurement system. As a result, we could measure hematocrit within 1.7 Hct% mean errors for 38 blood samples without any calibrations. The result indicates that the proposed method is applicable for hematocrit measurement on medical tube in enough small error. We found this proposed method is effective for developments of clinically workable hematocrit measurement/monitoring system.**

I. Introduction

PERCENTAGE of the whole blood cell, especially red blood cell (RBC) is called blood hematocrit. The normal range of hematocrit in human is around 35-50%. When the level of hematocrit is reduced, symptoms of anemia and bleeding are usually suspected. Particularly, they are death-dealing issues for patients with artificial heart, in dialysis, and during open-heart surgery, who dose antithrombogenic agents [1], [2]. In addition, hematatocrit changes affect the safe control of blood pump [3]. Some researchers also reported that high hematocrit is a factor of thrombus formation and increase a risk for thrombosis [4]. These studies indicate the importance of hematocrit information.

In order to prevent the serious symptoms, it is required to provide hematocrit information with a non-invasive, convenient and continuous way during the treatments. Hence, we employ near-infrared optical techniques to measure hematocrit for this study. With optical technology, we can obtain the information reflecting RBCs' properties of absorption and scattering. Several researches have already reported methodologies to measure hematocrit with optical technology [5]. Measurements in experiments were also performed under several situations (e.g. artificial dialysis, centrifugal pump, etc) [6], [7]. For development of clinically applicable method, however, issues of accuracy and stability uninfluenced by disturbances and device-mounting errors are still remained. Optical measurements still showed around 5 Hct% error even when it was performed *in-vitro*, while invasive measurements requiring a drop of blood yield accuracy within 0.4 Hct% error [8], [9]. Though we can acquire relative hematocrit changes by performing a calibration with invasively measured hematocrit, it is difficult to measure absolute hematocrit without any calibrations of the optical device.

Therefore, the purpose of this study is to develop an accurate and stable optical hematocrit measurement on medical tubing, without requiring calibrations for device-mounting errors. In addition, the proposed method is confirmed in *in-vitro* blood experiment with a developed measurement system.

II. Methods of Hematocrit Measurement

A. Theoretical background

Lambert-beer's law is generally applied for analysis of a density of optical absorber. In the case of whole blood that has particles' optical scattering, however, the limitation of the law has been discussed [10]. To describe both optical absorption and scattering characteristics, Twersky developed a mathematical formula [11]. Twersky's theory describes total optical density ($O.D._{total}$) as a sum of the light absorbance ($O.D._{absorb}$) and light scattering ($O.D._{scatter}$). This theory has been shown to be applicable to whole blood in use of artificial heart blood pump [6]. To deal with the theory easily for practical use (the range between 25-60 Hct%), the formula can be modified as follows [12].

$$\begin{aligned} O.D._{total} &= O.D._{absorb} + O.D._{scatter} \\ &= \log_{10}\left(\frac{I_0}{I}\right) \\ &= k \cdot L \cdot Hct - \log_{10}[(1-q)10^{-a \cdot L \cdot Hct(1-Hct)} + q] \\ &= K \cdot L \cdot Hct + S \end{aligned} \quad (1)$$

where I_0 and I are the incident and transmitted light

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intensities; k is absorption coefficient; Hct is hematocrit [%]; L is optical path length; a is a constant (<1) depending upon particle size, wavelength, refractive index of particles and suspending medium for plasma; q (<1) is a constant depending upon the same as a and photo detector aperture angle. In addition, K and S are considered to be constants, which can be determined empirically by blood experiment. K is related to absorption at the selected wavelength and S is corresponding to light scattering including the parameters of a and q.

B. Modeling

Eq. 1 shows that we can calculate hematocrit from transmitted light intensities in theory. For actual use, however, we have to measure hematocrit in the in-direct (on medical tubing) situation in accurate uninfluenced by disturbances and device-mounting errors. To solve the issues by theoretical way, at first we modeled the aimed measurement on medical tubing based on Eq. 1, Twersky's theory. We employs backward scattered optical measurement model. Backward model has an advantage to measure at less limited location without requirement of transmission. Though Twersky's theory is usually applied to only forward scattered model, we applied it to the aimed backward model because they are essentially the same in thick layer of whole blood, which can be regarded as an isotropic scattered substance.

Figure 1 shows a schematic of our modeling. We assumed that the medical tubing's optical property (P_T) is a constant. In addition, optical property of blood plasma is added to the formula as blood includes Hct [%] of RBC and 1-Hct [%] of plasma (water). These assumptions allow us to transform Twersky theory, Eq. 1, as follows.

$$\log_{10} I = -K_R \cdot Hct \cdot L - K_W \cdot (1 - Hct) \cdot L - P_T - S + \log_{10} I_0 \quad (2)$$

where K_R and K_W are each absorption coefficient of RBC and water.

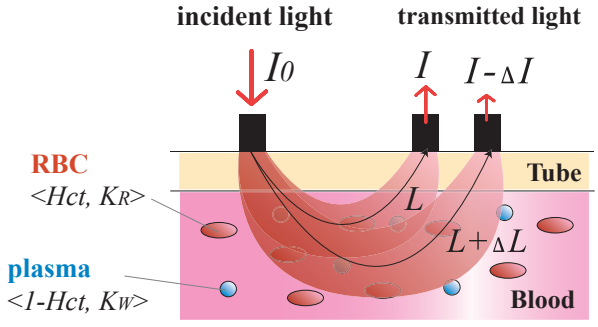

Figure 1: Schematic of the proposed method: I_0 and I are the incident and transmitted light intensities; K_R and K_W are absorption coefficients of RBC and water; Hct is hematocrit [%]; and L is optical path length.

C. Dual Wavelength/Detector Measurement Method

In the modeled formula, Eq. 2, optical path length (L) is changed in each device-mounting time so that we should calibrate the empirical parameters at each mounting time. In addition, fluctuation of linear terms such as $\log_{10} I_0$ cause the errors of disturbances, which affects an accuracy and stability of the measurement. Therefore, we propose a method with dual detector and wavelength to measure absolute hematocrit in accurate uninfluenced by disturbances and mounting errors.

Firstly, we introduce another optical length, ($L+\Delta L$), that indicates optical intensities are measured at two detecting points and lead another equation. By solving simultaneous equations with the led equation and Eq.2, we obtain

$$\log_{10} \frac{I}{I - \Delta I} = \{Ht \cdot (K_R - K_W) + K_W\} \Delta L + \Delta P_T + \Delta S \quad (3)$$

where delta(Δ) indicates the difference between first and second selected detecting point. Since $\log_{10} I_0$ and linear terms are removed here, intensity variability and disturbances would be cancelled out.

Secondly, we employ another absorption coefficients of RBC and water ($K_R+\Delta K_R$, $K_W+\Delta K_W$) that assumes optical intensities are measured with two wavelengths (λ_1, λ_2) at each point. Then, another equation can be acquired. By dividing the acquired equation by Eq.3, we obtain

$$\frac{\log_{10}\left(\frac{I}{I-\Delta I}\right)_{\lambda 1}}{\log_{10}\left(\frac{I}{I-\Delta I}\right)_{\lambda 2}} = \frac{Hct \cdot (K_R - K_W) + K_W}{Hct \cdot \{(K_R + \Delta K_R) - (K_W + \Delta K_W)\} + K_W + (K_W + \Delta K_W)} + \Delta S' \quad (4)$$

where S' is a constant including both ΔS and ΔP_T.

Finally, if $(K_R + \Delta K_R) - (K_W + \Delta K_W) = 0$ that assumes the secondary selected wavelength is isosbestic point of RBC and water can be assumed, the hematocrit measurement method is represented as follows

$$Hct = \alpha \cdot \frac{\log_{10}\left(\frac{I}{I-\Delta I}\right)_{\lambda 1}}{\log_{10}\left(\frac{I}{I-\Delta I}\right)_{\lambda 2}} + \beta \quad (5)$$

where α and β are constants which can be determined empirically by experiment with blood.

α is $(2K_W+\Delta K_W)/(K_R-K_W)$, which depends on wavelength. β is $\{K_W+(2K_W+\Delta K_W)\Delta S'\}/(K_R-K_W)$, which depends on tiny variation of light scattering and tube property in addition to the parameter of α. Since optical path length (L) and intensity light (I_0) are removed in Eq. 5, we can apply this proposed method for accurate and stable hematocrit measurement without calibrations of these parameters.

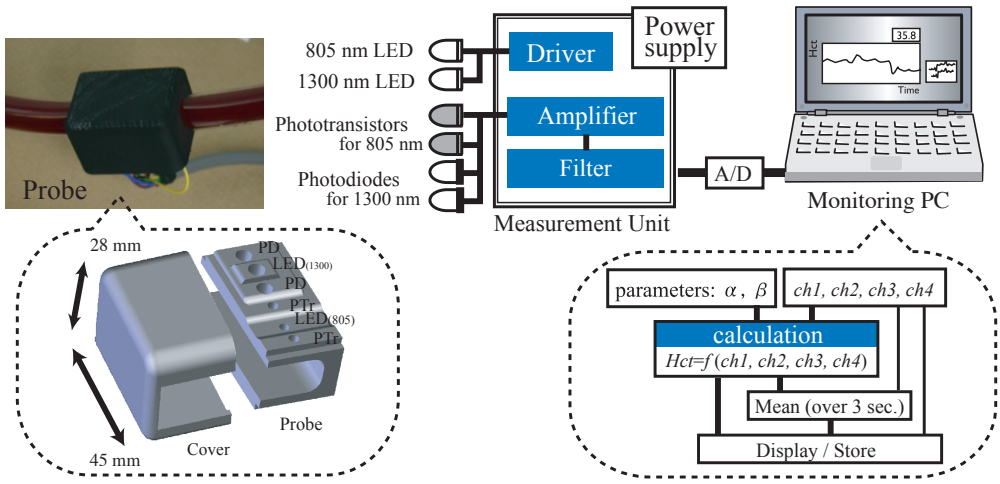

Figure 2: Schematic of a developed measurement system. Two LEDs and four photo detectors were fixed to a sensing probe. The probe can be attached on medical tubing easily. Acquired four signals are sent to a PC through analog amplifier and filter circuit, and A/D convertor. PC displays the calculated hematocrit based on the proposed method.

III. Development of A Measurement System

A. Requirements to apply the method

We summarize the associated specifications as follows, in order to develop a hematocrit measurement system with the proposed method.

1) Absorption coefficient of RBC, K_R, is a constant uninfluenced by oxygen saturation.

2) $(K_R + \Delta K_R) - (K_W + \Delta K_W) = 0$ to fulfill Eq.5.

As for 1), incident light around 800 [nm] and 1200-1400 [nm] of wavelength are met in near-infrared light because these wavelengths are the isosbestic points of oxygenated and deoxygenated hemoglobin in near infrared area. With these light emitters, we need not consider the ratio of oxygen saturation [13]. 2) is also realized by selecting 1200-1400 [nm] wavelength, which is the isosbestic point of hemoglobin (RBC) and water (plasma) [14].

B. Design and Development

We designed and developed a prototype of hematocrit measurement system based on the proposed method and the associated requirements. Figure 2 shows a schematic of the whole system. For two light sources, we select 805 [nm] LED (Alpha-one electronics LTD., Japan) and 1300 [nm] LED (Epitex, Japan) to meet the described requirements of 1) and 2). On the other hand, two photo transistors (Sharp, Japan) and two photo diodes (Epitex, Japan) are employed to detect the 805 [nm] and 1300 [nm] wavelengths' light. They are generally available and not expensive elements. A sensing probe was also developed to measure in convenient. The optical elements are fixed on the probe. Distances between LED and Photo detectors are set to be 6 [mm] and 9 [mm] in both 805 and 1300 [nm] wavelength elements.

Four detected signals (*ch1-ch4*) are sent to a personal computer (PC) through analog amplifiers and filter circuits, and an A/D board with 1 [kHz] sampling frequency.

These signals are analyzed in the PC to calculate hematocrit with proposed method, as follows.

$$Hct = \alpha \cdot \frac{\log_{10}(ch1/ch2)_{805}}{\log_{10}(ch3/ch4)_{1300}} + \beta \qquad (6)$$

Parameters of α and β are preliminary determined by experiments and we can input them on software. The software displays and stores optically calculated hematocrit changes with time. Mean levels of hematocrit over 3 seconds are calculated and also displayed on the PC. In addition, original signals' data from *ch1* to *ch4* are stored to analyze off-line for comparison with the conventional method with single wavelength/detector.

IV. Blood Experiments in Mock-up Circuit

The developed measurement system based on the proposed method was confirmed by *in-vitro* experiments with fresh bovine blood.

Figure 3 shows a schematic of the experiment. An experimental mock-up circuit was constructed with a continuous-flow blood pump, Tygon tubing, and a reservoir. 500ml of the blood was flowed in the tubing and developed instrument was fixed on tube. Pump flow were controlled to be 4.5 [L/min] during the experiment. The blood was included sodium acid citrate to prevent blood's coagulation. Reference hematocrit value was adjusted by adding saline solution and confirmed by using a centrifuge (KUBOTA KH-120MII, Japan).

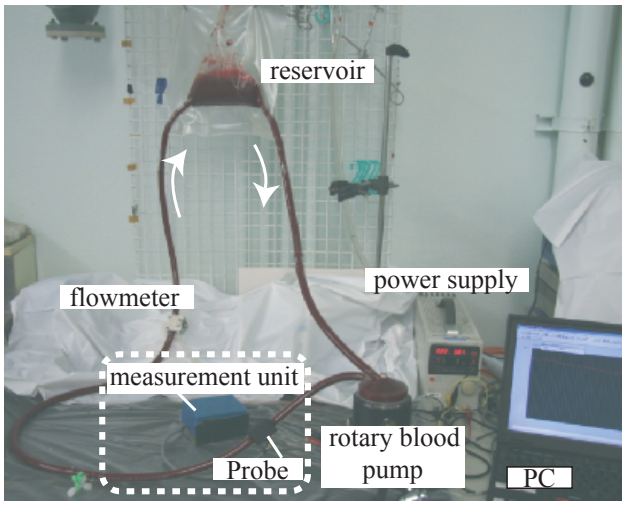

Figure 3: Experimental mock-up circuit constructed with a rotary blood pump, Tygon tubing, and a reservoir; Sensing probe was attached on the tubing and PC displayed the measured data.

A. Validation of the Method (Single Bovine Blood)

Fresh bovine blood (Hct: 55%) was prepared for the experiment. Following three validations were carried out.

1) Applicability of the proposed Method

The theoretically proposed method was confirmed with the blood. Hematocrit was adjusted from 55% to 30% in steps of 5% by adding saline solution. During the experiment, optical intensity was measured with the developed system. At this time, parameters of α and β were unknown so that only signals of optical intensities from *ch1* to *ch4* were stored. The stored data were analyzed off-line to fit the proposed method with dual wavelength/detector (Eq. 5). In addition, parameters of α and β were determined after it was validated that the data could fit the proposed method. For the reference, the data of *ch1* were applied to fit the conventional method with single wavelength/detector (Eq. 1), with determined K and S. This experiment was performed under near ideal circumstance with no re-fixing of the probe.

2) Effectivity for reducing device-mounting errors

The proposed method was composed for reducing device-mounting errors. Effectivity of the method for reducing the mounting errors was validated. During the measurement, the sensing probe was intentionally replaced on medical tubing surface with time. Errors between reference hematocrit and optically measured hematocrit were continuously stored. The errors were calculated by subtracting reference hematocrit from measured hematocrit. Then, the measurement results with the proposed measurement method and the conventional method were compared. Preliminarily determined parameters (α, β) for the proposed method, (K, S) for the conventional method were used to measure hematocrit during this monitoring experiment.

TABLE I
PREPARED BOVINE BLOODS

Bovine ID	Hematocrit changes [%]	Number of Samples
1	55-30	6
2	44-26	9
3	30-19	7
4	29-20	10
5	28-19	6
Sum	55-19	38

3) Stability of the measurement

Stability of the developed measurement system was evaluated by an experiment with long time monitoring. The blood pump circulates the bovine blood for over 2.2 hours. Levels of hematocrit were continuously measured with the developed system. Nothing was added to the blood during the experiment. Reference hematocrit was confirmed by using the centrifuge every 30 minutes. Errors of measured hematocrit were compared with the conventional method.

B. Hematocrit Measurement (Multiple Bovines' Blood)

Applicability of the method to multi blood was demonstrated by using 38 samples acquired from five fresh bovines' blood as shown in Table 1. The optical hematocrit measurement was performed to the 38 samples in the mock-up circuit with the system. Parameters of α and β were set to be constants, $\alpha=\beta=27$. The same parameters were applied for all of the 38 samples. For the reference, measurements based on the conventional method are carried out with data of *ch1* and the same parameters of K and S.

V. RESULT

A. Validation of the Theory (Single Bovine Blood)

1) Applicability of the proposed Method

We confirmed whether the theoretically proposed method is applied to the measurement with blood. Figure 4 shows results of comparison between optically measured data and reference hematocrit in the conventional (Eq.1: single wavelength/detector) and the proposed (Eq.5: dual wavelength/detector) methods. We could obtain high correlations (R=0.99) between reference hematocrit and the theoretical calculations with both measurement methods. It shows theoretically proposed method is enough proper for hematocrit measurement under near ideal circumstance (no re-fixing of the probe).

2) Effectivity for reducing mounting errors

We validated the effectivity of the proposed method for reducing mounting error. During the measurement, sensing probe was intentionally replaced on medical tubing surface with time from 0 to 25 [sec]. Figure 5 shows the errors of hematocrit, which occurred in the continuous hematocrit monitoring. The errors were calculated by subtracting reference hematocrit from measured hematocrit. The result shows that the proposed measurement was not affected by the mounting error, while the conventional model was

clearly influenced. The result shows the effectiveness of the proposed method.

3) Stability of the measurement

Figure 6 shows the comparison result of stability test for 2.2 hours. We confirmed there were no reference hematocrit changes during the experiment by using the centrifuge. We could measure and monitor hematocrit in stable for 2.2 hours with the proposed method.

B. Hematocrit Measurement (Multiple Bovines' Blood)

We applied the proposed method to 38 blood samples acquired from five bovine. Figure 7 shows the results of measured hematocrit at each reference hematocrit of 38 blood samples. Compared with the conventional method, we could measure hematocrit more precisely with the proposed method. Figure 8 shows the mean and maximum errors of the conventional and the proposed method. The proposed method could reduce the measurement errors more than 2-3 times.

VI. Discussion

Blood hematocrit (Hct) is a clinically important index to detect death-dealing symptoms such as bleeding and thrombosis, especially for patients with artificial heart, in dialysis and during open-heart surgery. Though optical technology has been developed to measure hematocrit, accurate and stable hematocrit measurement without calibration is not established [7], [8].

In this paper, we proposed a theoretical method with dual wavelength and detector. Our method provides us an accurate measurement of hematocrit without any calibrations for reducing disturbances and mounting errors.

As a result of first experiment with single bovine blood, we confirmed that the proposed method with dual wavelength/detector was applicable in high correlation for hematocrit measurement. Since absorption of RBC (hemoglobin, K_R) is greater than that of plasma (water, K_W) at 805 [nm] wavelength area, experimentally acquired α and β were positive value.

The experiments with intentionally replacement of the sensing probe and long time measurement clearly indicate the advantage of the proposed method. Though high frequency should be removed in a next system development, the benefit of the proposed method was shown.

Moreover, the proposed method was universally applicable to other individuals' blood without any calibrations. By introducing our proposed method with dual wavelength/detector, we can measure hematocrit with 1.65 Hct% mean errors for 38 blood samples obtained from five bovines' blood. It would be enough accurate for clinical use. The accuracy was 2 to 3 times more improved than the conventional method.

Though we performed the optical measurement in a mock-up circuit with bovine blood, clinical experiments should be performed for the application of hematocrit measurement.

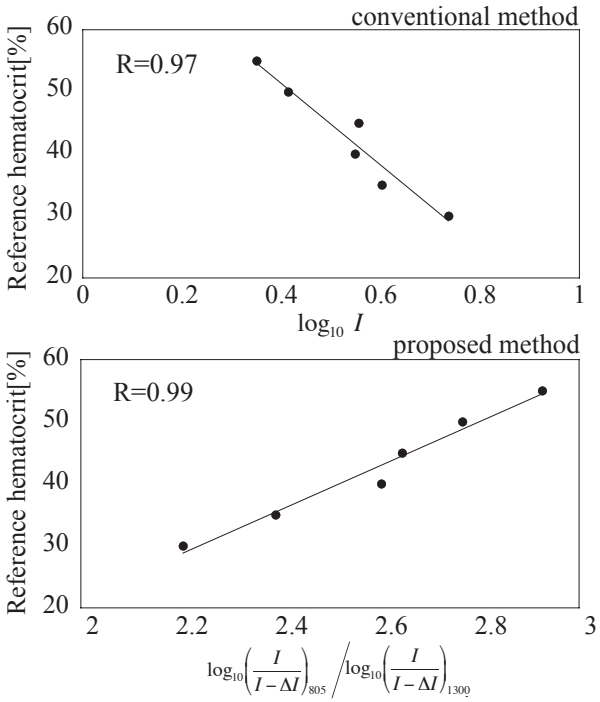

Figure 4: The applicability of the conventional method (Eq. 1: above) and the proposed method (Eq. 5: below) to blood.

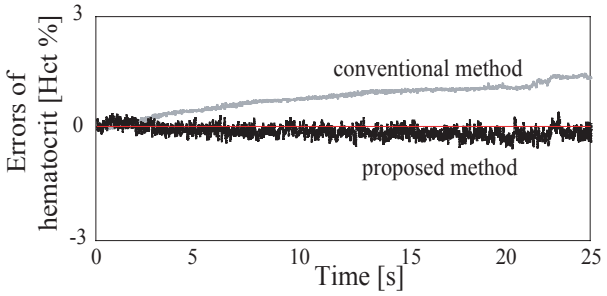

Figure 5: Continuously calculated errors of optically measured hematocrit during 25 seconds experiment; during the experiment, sensing probe was continuously moved on medical tube surface from 0 [sec] to 25 [sec].

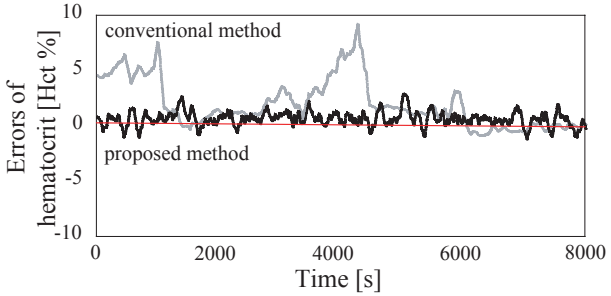

Figure 6: Continuously calculated errors of optically measured hematocrit during 8000 seconds (2.2 hours) experiment; reference hematocrit (red line) was not changed during the experiment.

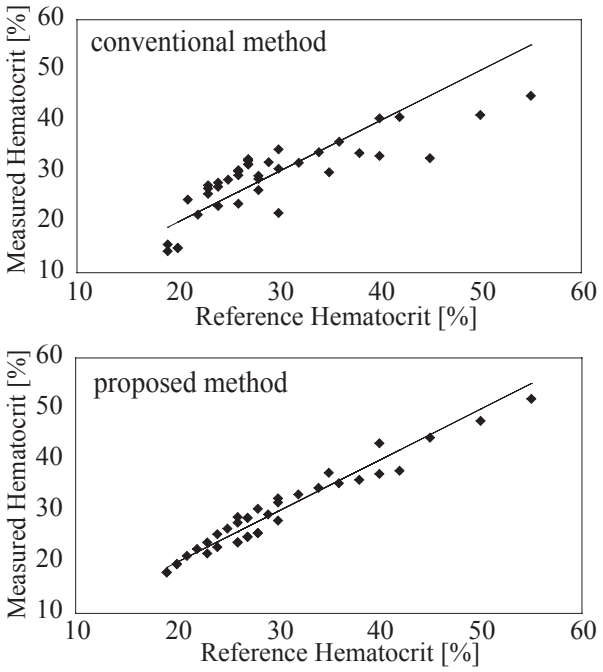

Figure 7: Result of hematocrit measurement with the conventional method (above) and the proposed method (below) for 38 blood samples at various levels of reference hematocrit.

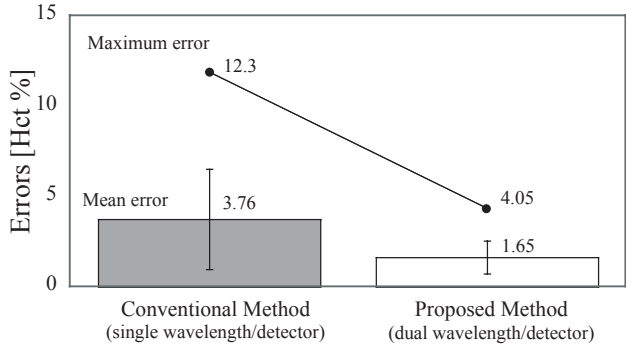

Figure 8: Comparison result of hematocrit measurement errors (mean, maximum) between the conventional and the proposed method.

VII. Conclusion

We developed an accurate and stable optical hematocrit measurement without requiring calibrations for device-mounting errors. To accomplish the hematocrit measurement, we proposed a theoretical method with dual detector and wavelength. A measurement system was developed based on the method. Experimental results with bovine blood showed the applicability, effectivity for reducing device-mounting errors, and stability of the measurement. In the experiments with five bovines' blood, we could measure hematocrit in enough accurate (mean error: 1.65 Hct%) by the developed system without calibration. This hematocrit measurement method would help to detect anemia and thrombosis, which are the serious issues especially for patients with artificial heart, in dialysis and during open-heart surgery.

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