

Low-coherence method of hematocrit measurement

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Abstract—During the last thirty years low-coherence measurement methods have gained popularity because of their unique advantages. Low-coherence interferometry, low-coherence reflectometry and low-coherence optical tomography offer resolution and dynamic range of measurement at the range of classical optical techniques. Moreover, they enable measurements of the absolute value of the optical path differences, which is still an unsolved problem in high-coherence interferometry. Furthermore, the use of the spectral signal processing makes this method immune for any change of the optical system transmission.

In this article the low-coherence method of a hematocrit measurement has been presented. Elaborated measurement method has many advantages: relatively simple configuration, potentially low cost and high resolution. Investigation of this method confirms its ability to determine the hematocrit value with appropriate measurement accuracy. Furthermore, results of experimental works have shown that the application of the fiberoptic low-coherent interferometry can become an effective base of method of the *in-vivo* hematocrit measurement in the future.

I. INTRODUCTION

BLOOD analysis is frequently performed for medical diagnosis. One of the important analytes is the blood hematocrit (HCT), defined as the ratio of packed red blood cells volume to whole blood volume. The normal ranges of the hematocrit are 39-50% for male and 35-45% for female respectively. The high level of the hematocrit indicates risk factors for heart and cerebral infarction due to hemoconcentration. Dehydration or cerebral can be also origins of the HCT high level. Therefore, the hematocrit value as well as blood pressure should be controlled during the daily life as the indices of various physiological conditions in order to reduce the cardiovascular disease risk factor. It should be noted that the continuous monitoring of the HCT is also needed to perform appropriate dialysis and blood infusion.

The blood hematocrit is routinely determined in the clinic by analysis of blood samples. There are several methods of measurement of the HCT and hemoglobin. Unfortunately, almost all of them require either blood sampling or catheterization. Repeatable blood sampling during continuous monitoring of the hematocrit value is associated with an increasing

risk of infection (e.g. HIV or hepatitis). Moreover, such way of examination and loss of even small volume of blood required for the HCT measurement can be harmful to the patients (especially for neonates, small children and old peoples). Therefore, there is a need of non-invasive method of the hematocrit measurement, because recently used methods are based on the *in-vitro* measurement.

There is a great interest in optical measurement that would permit simultaneous analysis of multiple components (analytes) in whole blood without the need for conventional sample processing, such as centrifuging and adding reagents. There are few optical methods of the hematocrit measurement. Schmitt et al. [1] uses the dual-wavelength near IR-photoplethysmography. Intensity sensitivity detector working with dual wavelength has been described by Oshima et al. [2]. Xu et al. applied optical coherence tomography for investigating the HCT value [3]. Enejder et al. [4] used Raman spectroscopy and partial least squares (PLS) data analysis for simultaneous measurement of concentrations of multiple analytes in whole blood, including the hematocrit and hemoglobin. There are also works in which authors tried to find correlation between oxygen saturation of whole blood and hematocrit value [5, 6]. However, all of them investigated the HCT value *in-vitro* by using sample of blood. Recently, only one method of non-invasive hematocrit measurement by the use of spectral domain low coherence interferometry has been demonstrated by Iftimia et al. [7]. Unfortunately, until now it is possible to make such a measurement only insight the eye, which is uncomfortable for the patient and difficult because of the eye movement. The light beam interrogating the eye must be stabilized on a fixed location on a specific retinal vessel to collect reproducible depth-reflectivity profiles in the blood. This is possible only by employing the eye motion stabilization technique. The eye motion stabilization can generally be accomplished invasively with suction cups or retrobulbar injections, inaccurately with fixation, more precisely at slower speeds with a passive image processing approach, or at high speeds with active tracking. Fixation requires patient cooperation and is difficult in patients with poor vision. Therefore, at the present state of art *in-vivo* measurement of the HCT is more complex and expensive than laboratory analysis of collected blood samples.

The purpose of our study is to develop an accurate and stable low-coherence optical hematocrit measurement

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method. The preliminary stage of research, which is subject of this paper, includes analysis and selection of sufficient configuration of the low-coherence system for the HCT determination, setting up the low-coherence measurement system and *in-vitro* confirmation whether proposed method has sufficient accuracy to be the base of system which, if manufactured successfully, could have impact to development of the systems for *in-vivo* monitoring of the hematocrit.

II. LOW-COHERENCE MEASUREMENT METHOD

The low-coherence interferometric measurement system consists of a broadband source, a sensing interferometer and an optical processor (see Fig.1).

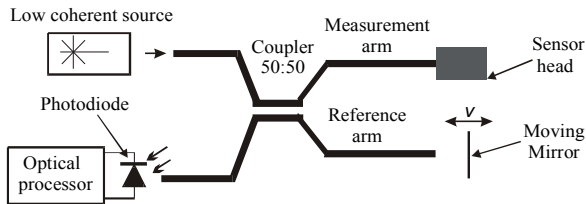


Fig. 1. Basic low-coherence interferometry setup.

The light from the broadband source is transmitted to the sensing interferometer by the coupler and a fiber optic link. At the sensing interferometer the amplitude of light is divided into two components and an optical path difference (OPD), which depends on the instantaneous value of the measurand (mainly its dimension or refractive index), is introduced between them. The sensing interferometer is designed in such a way that a defined relationship exists between the optical path difference and the measurand. The signal from the sensing interferometer is transmitted back by the fiber to the optical processor. The optical processor consists of a second optical system, the output of which is a function of OPD generated at the sensing interferometer. The sensing interferometer is located inside the measurand field whilst the optical processor is placed in a controlled environment far from the field. The optical processor is either a second interferometer (when the phase processing of the measured signal is used) or a spectrometer (when the spectral processing of the measured signal is used). The measurement system with the phase processing of the measured signal has very high measurement sensitivity and resolution, much higher than that of the system with spectral processing. However, the system with spectral processing of the measured signal has two important advantages. It does not need movable mechanical elements for precise adjustment as well as it is immune to any change of the optical system transmission. This is possible because in such a system the information about the measurand is encoded in the spectra of the measurement signal. Optical intensity at the output of such an interferometer can be expressed as [10]:

$$I_{out} = \langle EE^* \rangle \quad (1)$$

where: $E = E_1 + E_2$, E_1 and E_2 – amplitudes of the electric vector of the light wave reflected from the first and the

second reflective surfaces inside the sensing interferometer respectively; brackets $\langle \rangle$ denote time averages, asterisk $*$ denote the complex conjugation.

When the spectral signal processing is used, the recorded signal can be expressed as [11]:

$$I_{out}(\nu) = S(\nu) \left[1 + V_0 \cos(\Delta\phi(\nu)) \right] \quad (2)$$

where: $S(\nu)$ - spectral distribution of the light source; V_0 - visibility of the measured signal, $\Delta\phi(\nu)$ - the phase difference between interfering beams.

The phase difference between interfering beams can be calculated from a following equation [8]:

$$\phi(\nu) = \frac{2\pi \nu \delta}{c} \quad (3)$$

where: δ – optical path difference, c – velocity of the light in vacuum.

If the light source exhibits a Gaussian spectrum, the normalized spectra pattern is predicted to be a cosine function modified by the Gaussian visibility profile. In the spectral domain signal processing the modulation frequency of the measurement signal gives information about the measurand (Equation (2)), as shown in Fig. 2.

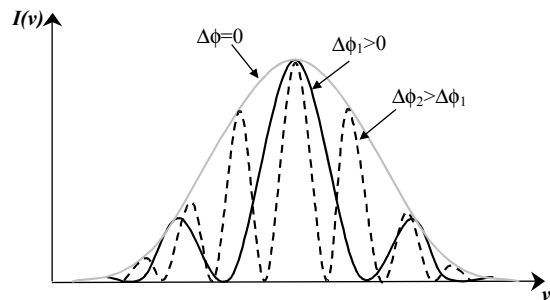


Fig. 2. Calculated measured signal from interferometer with spectral signal processing for different phase differences between interfering beams. ($\Delta\phi$ - phase difference).

It can be noted that for $\Delta\phi = 0$ there is no spectral modulation. If the phase difference between the interfering beams varies from zero, the function takes the form of the cosine curve. The spacing of adjacent transmission peaks is proportional to the inverse of the optical path difference ($1/\delta$) [12].

In this processing, it is necessary to use special measurement equipment and advanced mathematical processing of the measurement signal. However, as it was mentioned earlier, low-coherence measurement system based on the spectral signal processing has significant advantages - there is no need of precise mechanical scanning and no need of use of movable adjusting components. Moreover, the system using the spectral signal processing and Fabry-Perot sensing interferometer is not sensitive for any change of a transmission of the optical system. This is possible because in the system information about the measurand is encoded in the spectra of the measured signal. Therefore such a setup is the most convenient for the low-coherence hematocrit measurement.

III. EXPERIMENTAL

A. Measurement setup

The scheme of the developed low-coherence fiber-optic set-up for hematocrit measurement is shown in Fig.3. The optical spectrum analyzer (Ando AQ6319 or Anritsu MS9740A) was implemented as the optical processor. The superluminescent diode with Gaussian spectral intensity distribution was used as a low-coherence source. The optimal choice of optical source parameters is a very important problem in low-coherence measurement system because they affect the metrological parameters of such a system. Therefore, not only the central wavelength (λ) and optical spectral bandwidth full width at half maximum ($\Delta\lambda$), but the shape of spectral characteristic as well, should be selected very carefully. In presented research work the selection of optical parameters of the source was made to increase visibility of the measured signal. During laboratory tests conducted for a few sources having different parameters, the best results were obtained for superluminescent diode Superlum Broadlighter S1300-G-I-20 having following optical parameters: $\lambda_0 = 1290$ nm, $\Delta\lambda = 50$ nm.

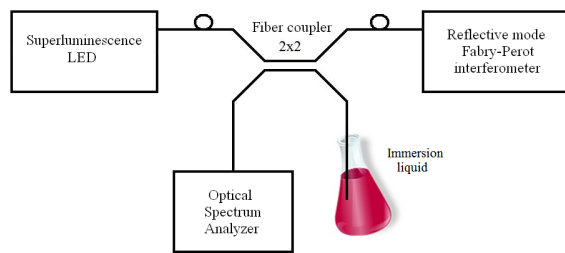


Fig. 3. The experimental setup.

As a sensing interferometer authors implemented a low-finesse fiber-optic Fabry-Perot interferometer, shown in Fig. 4. The theoretical investigation had shown that the use of a single mode optical fiber would be the most convenient. Hence, the Fabry-Perot interferometer was built using the standard single mode telecommunication optical fibers, a fiber coupler, the measurand field and a mirror. The interferometer consists of optic-fiber with uncoated end, which has a reflectance of 0.04. The second reflectance surface is made by the silver mirror with reflectance of 0.99. This configuration provided high visibility value of measured signal.

When the measurand field is filled by the investigated liquid, the reflective surfaces of the Fabry-Perot are made by two boundaries: fiber/liquid and liquid/mirror respectively. In such a setup each change of refractive index of the investigated liquid results in change of the optical path difference of interfering beams and the phase difference of those beams due to Equations 2 and 3.

B. Object of investigation

In order to find out whether proposed method has sufficient accuracy to be base of system for *in-vivo* monitoring of the hematocrit in the future, serie of *in-vitro* measurements

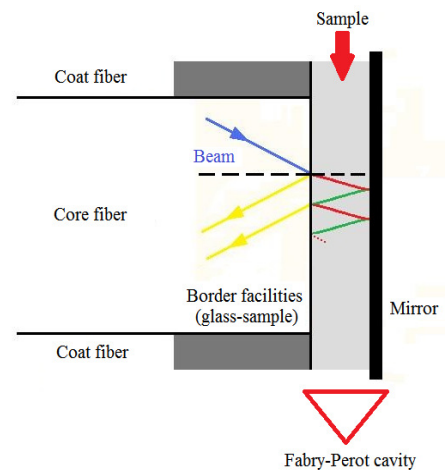


Fig. 4. The experimental setup.

was carried out. During experimental work authors used the whole human blood for tests. Set of 2 ml blood samples with various hematocrit levels were provided by the Gdansk Blood Donor Centre. Such approach has significant advantage, because we were able to use wide representative group of volunteers. It should be noted that samples were get from rather healthy volunteers and therefore our measurement range of the hematocrit measurement was limited to the value of 30 to 50%. However, this range was wide enough to find out the relationship between the HCT and measured optical signal and if resolution of the measurement is sufficient, as well. At this stage we were not measuring blood samples having very extreme HCT values which refers to very sick patients. This will be the object of the future research work. Detailed information the HCT distribution in investigated samples is given in Table 1.

HCT range	Number of samples
32,2 ÷ 33,8	12
34,0 ÷ 35,8	9
36,1 ÷ 37,9	12
38,0 ÷ 39,8	10
40,0 ÷ 41,5	13
42,1 ÷ 43,9	14
44,1 ÷ 45,8	19
46,2 ÷ 47,6	6
48,0 ÷ 49,0	4

Moreover, the hematocrit level of each blood sample was obtained by clinical diagnostics with accuracy ± 0.1 at the Gdansk Blood Donor Centre as reference measurements, as well. Our investigation, as well as clinically research, showed that obtained HCT level of blood probes were stabled for 72 hours. During all part of our measurement

process the temperature of blood probes were restricted controlled.

IV. RESULTS AND DISCUSSION

With the use of elaborated low-coherence system with Fabry-Perot interferometer, the hematocrit value of numerous blood sample was measured. Experimental investigation gave a series of recorded spectra. In Fig. 5 measured reference signal from sensor without any liquid is presented. Measured signals of the blood sample with $HCT = 35.2\%$ and with $HCT = 49.2\%$ are shown in Fig. 6a and 6b respectively.

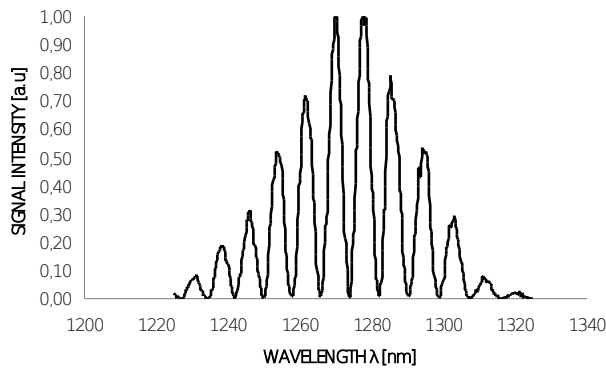
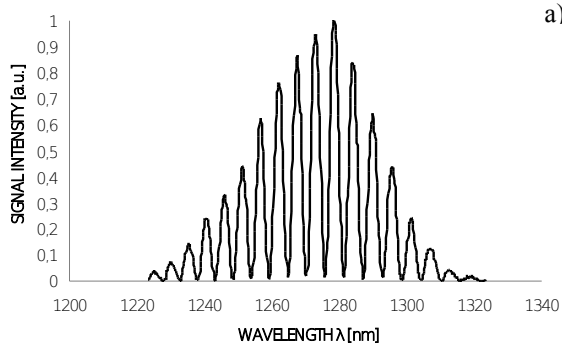
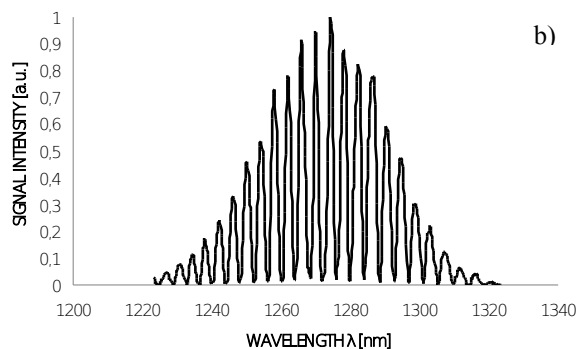


Fig. 5. The reference signal.



a)



b)

Fig. 6. Measured signal of the blood sample with a) $HCT=35.2\%$, b) $HCT=49.2\%$.

It should be noted (Fig.5, Fig.6) that by the use a dedicated sensing interferometer, designed in our laboratory, it was possible to get visibility of the measured signal $V=0.98$, which is really hard to achieve in really optoelectronic low-coherence system.

As there are shown in Fig. 6a and 6b, the change of the hematocrit value changes the refractive index of the blood sample and optical path difference between interfering beams as well. It occurs in phase changes (Equation 2 and 3) and can be detected by the analysis of the measured signal modulation or by counting number of fringes in the measured signal. The change in the number of fringes in the measured signal due to HCT level is shown in Fig. 7. Additionally, the deviation of the number fringes during HCT level measurement is presented in Fig. 8

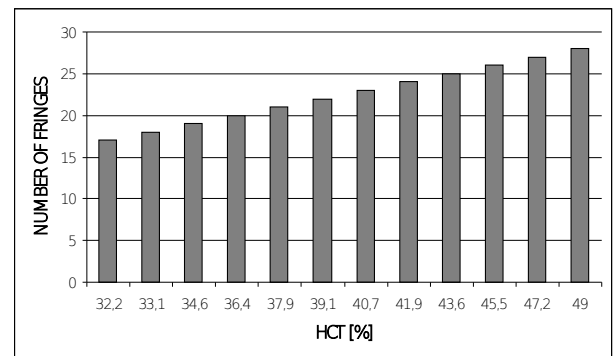


Fig. 7. Number of fringes in the spectra of measured signal vs. HCT level.

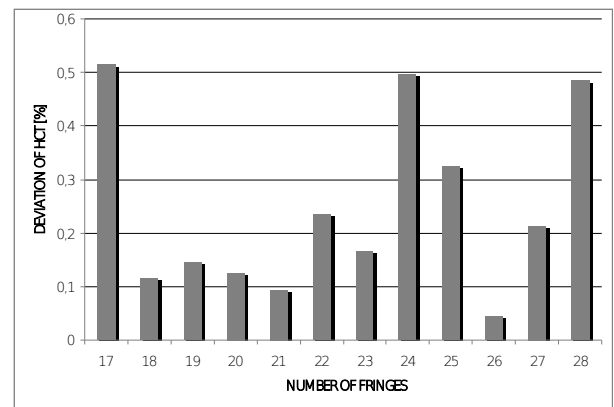


Fig.8. Number of fringes in the spectra of measured signal vs. HCT level.

Mathematical processing of the measured signals provided information about measurand from the spectrum of signal is shown in Fig. 9.

The result of experimental works shows, that can be seen in Fig. 7, that low-coherence method of hematocrit measurement with Fabry-Perot interferometer configuration has proper accuracy to measure the hematocrit value. The method was elaborated in the HCT range extending from 30% to 50%. The output signal was analysed by measurement the change of fringe numbers of the spectra pattern. The change of the number of fringes of investigated spectral pattern equal to 8 was achieved in investigated range, thus obtained sensitivity of the hematocrit measurement can be

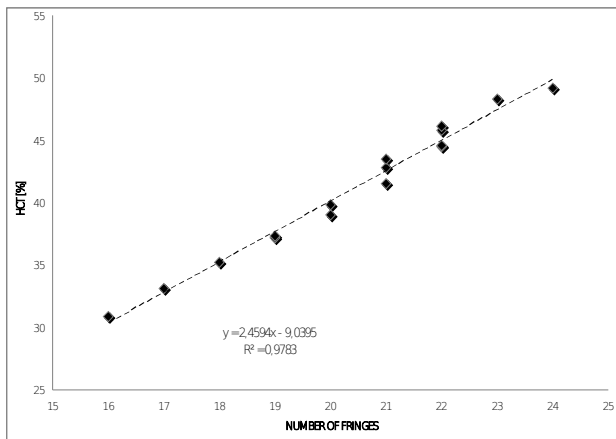


Fig. 9. Experimental results - change of number of signal spectra fringes vs. hematocrit value: dots – measured value, dash line – regression line. (R^2 - determination coefficient of statistical model of HCT vs. number of fringes relationship)

estimated as 0.4 [a.u./%]. Time required for single measurement was in range of 0.8-1.2 s. Experimental configuration had very high the value of visibility of the measured signal (usually 0.98), what always leads to decrease of the value of signal-to-noise ratio of the measured signal. Furthermore, it had very high determination coefficient of statistical model of HCT vs. number of fringes relationship ($R^2=0.978$) as well.

V. CONCLUSIONS

In this paper the low-coherence method of the hematocrit measurement with spectral signal processing has been presented. Elaborated measurement system which used this method has numerous advantages: relatively simple configuration, potentially low cost, high resolution, dielectric construction. Furthermore, it had optical sensor head (Fabry-Perot interferometer) of small size and very low thermal inertia. What is more important, by utilizing spectral signal processing those sensors exhibit immunity of any changes of optical transmission in measurement system.

The results of experimental works showed that implemented experimental set-up provided good quality of the measured optical signals by offering great value of visibility of the measured signal, exhibits immunity for changes of the optical signal polarization and got simple configuration.

The investigation of this method confirms its ability for the hematocrit control with appropriate measurement accuracy. The presented preliminary results can be the base for building sensor ready for practical applications and in the opinion of authors it will be possible to build the low-coherence optical *in-vivo* hematocrit sensor in the future. In the further stage of the research, developed system will be applied for the *in-vivo* measurements carried out through the skin. The best place on the human body for measurement as well as method of preparation patient skin surface will be determined. As during the *in-vivo* measurements results would be probably influenced not only by refractive index of the blood but also by change of Fabry-Perot cavity dimensions caused by a human pulse, we predict that phase-sensitive detection synchronised with the human pulse should be applied.

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