Infrared Physics & Technology 72 (2015) 117–121

Contents lists available at ScienceDirect

Infrared Physics & Technology

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

Research on improving the accuracy of near infrared non-invasive hemoglobin detection

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HIGHLIGHTS

- A high performance near-infrared spectrophotometric system.
- Appropriate prepossessing algorithm has been optimized. DOSC & PLS.
- The detection precision almost reaching the requirements of clinical application.

ARTICLE INFO

Article history:
Received 14 April 2015
Available online 13 July 2015

Keywords:
Near-infrared spectroscopy
Non-invasive detection
Directs orthogonal signal correction
Hemoglobin concentration

ABSTRACT

To optimize the accuracy of near-infrared non-invasive hemoglobin (Hb) clinical detection, high-performance instrument and prepossessing algorithm have been investigated. A near-infrared spectrophotometric system was constructed adopting InGaAs detector array with 16 pixels and plane grating spectrometer to obtain high signal noise ratio (SNR) spectral data. In our experiment, we applied the device independently to collect spectra data from 91 volunteers' fingertips non-invasively. Two prediction tests were conducted to verify the effects of preprocessing algorithms improving the accuracy of near-infrared Hb detection and exclude the occasionality of satisfactory results in a single trial. Our non-invasive Hb detection methods were based on partial least squares (PLS). In each test, PLS, MSC coupled with PLS, DOSC coupled with PLS, three methods for non-invasive Hb detection, were analyzed respectively. The results of two trials showed that only DOSC & PLS performed excellently in both predictive ability and stability, obviously better than other two methods. Relative RMSEP was 6.16% in predicting test 1, 6.08% in predicting test 2, almost reaching the requirements of clinical application. It indicates that our independent-developed high-performance instrument and the method DOSC coupled with PLS are promising in non-invasive Hb detection clinical application.

1. Introduction

Hemoglobin (Hb) concentration is one of the most reliable parameter in anemia diagnosing [1,2], as well as an important monitoring index during peri operation period [3].

As a frequent disease, about 1.6 billion people all over the world are suffering from anemia in varying degrees [4]. Every year, more than tens of millions of people died of various diseases caused by anemia. Particularly for neonates, anemia results in more severe impacts. Statistics manifest that more than 30% of neonates suffer from anemia. Anemia will lead to neonates appear symptoms such as anorexia, picky eaters and weakened immunity, which seriously affects the physical and intellectual development of anemic babies. Therefore, early diagnosis is extremely essential in preventing and curing neonatal anemia.

Hb is also utilized as a parameter routinely being monitored during the treatment of patients with vascular, orthopedic and other deep-invasive abdominal surgeries where a great quantity of blood loss possibly occurs. When the loss reaches the minimum margin of oxygen-carrying function, transfusion therapy should be conducted in time. Increasing evidences demonstrate that anemia during peri operation period will induce more postoperative complications, which is a major cause of death especially for patients with multiple diseases [5,6]. Therefore, anesthetists need to acquire actual situation of blood loss by real-time monitoring of Hb levels, so that they are capable of offering effective guidance to blood transfusion intra-operative. It not only can avoid delaying the opportunity of blood transfusion, but also avoid side effects and high costs generated by unnecessary blood transfusions to patients.

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http://dx.doi.org/10.1016/j.infrared.2015.06.009
1350-4495/

Cyanomethemoglobin (HICN) method is recognized as the standard method for Hb concentration measurement with accurate and stable results. However, disadvantages are unavoidable accompanied with the method. (1) It is an invasive method. Drawing blood increases not only the pain of the patients, but also possibilities for them to acquire diseases infection. Especially for neonates, drawing blood is inconvenient since they possess more narrow blood vessels and a smaller total circulating blood volume than adults. As neonatal immunity is also weak, the risk of diseases infection would be increased by invasive methods. (2) Long detection period. It is difficult for HICN to achieve real-time monitoring since Hb is restricted to be monitored during the process of transfusion. Significant advantage will be attached to measuring Hb in succession especially during surgeries. While in natural disasters or battle grounds, rapid Hb level analysis should be conducted to treat wounded people timely and effectively [7–9]. Therefore, non-invasive Hb concentration measurement technology with the property of fast analysis is in urgent demand, presenting a broad prospect in clinical application.

Near infrared spectroscopy has become one of the focus researches in non-invasive biochemical detection research field ascribed to its non-invasive, fast, multi-component analysis and other advantages [2,10,11]. In 1977, Jobsis first reported Hb absorption characteristics in the near infrared region, which provided theoretical support to near infrared spectroscopy non-invasive Hb detection [12]. In 1995, Kuenstner and Norris put forward "Near infrared hemoglobinometry". Then they measured Hb concentration in vitro based on the hemoglobinometry and got good analysis accuracy [13]. After years of practice and development, non-invasive Hb measurement instruments based on this technology have come out. Radical-7 and Pronto-7 produced by Masimo Corporation could accomplish non-invasive Hb real-time monitoring [14,15]. Though near infrared non-invasive Hb measurement technology has developed tremendously, and numerous researches and practices have been achieved, the not intensely excellent measurement precision and stability are the important obstacles hindering widespread application of this technology in clinic [4].

Now, weak valid spectra signal and strong background interference have become the primary problems which obstacle the development of near infrared non-invasive detection, leading to a difficulty for precision of near infrared non-invasive Hb measurement to meet the requirements of clinical applications. In this paper, to further improve the accuracy of non-invasive detection, high-performance detection system was constructed to obtain spectral data with high signal noise ratio (SNR). Meanwhile, preprocessing algorithms were optimized to filter interference when building non-invasive Hb prediction model. In order to obtain all spectra at the same time and avoid the influence from blood flowing, the 16-pixel InGaAs array detector was adopted. The plane grating was used as a beam-splitting component accordingly. And we also designed 16 independent amplifier circuit cooperated with our detector to obtain higher SNR and sampling rate. Utilizing our near infrared spectrophotometric system, spectra were collected from 91 volunteers in vivo and divided into calibration set, two prediction sets to conduct clinical trials. Having compared results from two predicting tests, we optimized the best method DOSC coupled with PLS, and then discussed the precision and stability of non-invasive Hb concentration detection based on this method.

2. Device

The block diagram of near infrared spectroscopy non-invasive Hb detection system is shown in Fig. 1. This system consists of a light source (75 W tungsten halogen), a beam-splitting system, a detection system and a data acquisition system. The spectral range is from 1100 nm to 1400 nm, spectral sampling rate is 50 spectra per second, the repetitive SNR is better than 15,000:1.

2.1. Detection system

Due to the heartbeat, blood circulation and other physiological phenomenon existing, blood vessel size is varying over time. The variation will result in spectra obtained at different time corresponding to different optical path. G7150 InGaAs array detector produced by Hamamatsu Photonics Co., Ltd is adopted so that all spectra could be obtained at the same time and errors generated by scanning could be avoided. The detector consists of 16 independent InGaAs pixels, so that it could effectively avoid signal crosstalk. High detection sensitivity and frequency response further make it well meet fast and high SNR requirements of non-invasive Hb detection.

2.2. Amplification circuit

To cooperate with array detector for detecting weak signal, system of the whole amplifier circuit adopts 16 independent amplifier circuit schemes, which could effectively avoid inter-pixel crosstalk and reduce noise rather than the single amplifier and multiplex structure. As light intensity will be reduced by more than one order of magnitude after transmission, amplification circuit needs to reach to 10^9 that faint variation of the signal can be detected. To achieve this goal, the first order amplifying circuit with less noise introducing is utilized. Meanwhile, we adopt low-noise amplifier chips, low noise resistors and other precise components in our amplifier circuit and optimize the designs about printed circuit board arrangement and electromagnetic shielding device. Ultimately, we accomplish the high SNR amplification circuit system within 50 Hz bandwidth.

2.3. Beam-splitting system

Reflective plane grating is adopted as the spectral component, which could obtain spectrum with plane surface to match with array detectors well. Our beam-splitting system structure uses cross-asymmetric Czerny–Turner with excellent performance in weak signal detection. This asymmetric structure is compact that avails to control the stray light in system. Meanwhile, it also could control the coma aberration. Beam-splitting system consisted of a slit, a collimating mirror, a granting and focus mirror. The groove density of grating is 300 g/mm, the blaze wavelength is 900 nm.

2.4. Data acquisition system

We selected multi-function data acquisition card (DAQ) 6281 M from National Instruments for the acquisition module and developed data acquisition software for our spectrophotometric system. The relevant parameter settings of DAQ are shown as follows. Sampling rate is 2 k/s, collecting time is 20 s, 20,000 points per channel. When collecting data, the computer displays the measured spectral data onto the software interface synchronously. Then the operator determines whether measured data is ideal. If it is suitable we will end the acquisition process and save data. Otherwise, we will collect data once more.

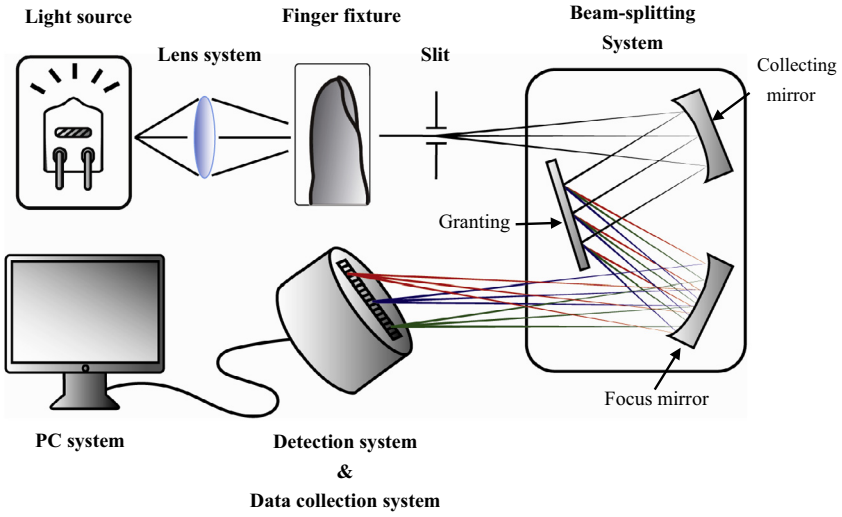

Fig. 1. Block diagram of the near infrared spectrophotometric system.

3. Experiment

3.1. Measurement process

91 volunteers who participate in physical examination were our measurement objects. We collected blood spectral data non-invasively from their right index finger by utilizing our non-invasive Hb spectrophotometric system. The volunteers were asked to fast on the day of the tests. Before measuring, volunteers sat quietly for a little while until they were in placid state. Then put their right finger into the finger fixture, completely covered and gently pressed the aperture that near infrared light through. During the experiment, volunteers should keep their arm relaxed and the pressure stable then we obtained their blood spectra data. Measurement lasts 20 s. After that, to prepare for the modeling work later, the hospital professionals would draw blood from volunteers immediately to obtain the reference Hb clinical concentration correspondingly by an automatic blood analyzer.

3.2. Sample sets

To verify the effects of pretreatment algorithms for improving the accuracy of near infrared non-invasive Hb detection and exclude the occasionality of satisfactory results in single trial, we conducted two prediction tests. Therefore, we divided 91 samples collected previously into three groups, one calibration set and two prediction sets. The samples amount distributed with the ratio of 2:1:1. Firstly, 91 samples were ranked on a basis of the Hb clinical value from low to high. Then each set selected samples according to the amount ratio interval, the ranges of Hb clinical level in each set were almost consistent. According to the above principle, 46 samples was selected for calibration set, 23 samples was selected for prediction set 1, and the rest 22 samples was prediction set 2 (see Table 1).

Table 1
Distribution of HB concentration in sample sets.

	Number of samples	Minimum (g/L)	Maximum (g/L)	Mean (g/L)	Standard deviation (g/L)
Overall	91	113	176	147.94	15.44
Calibration set	46	113	176	148.07	15.72
Prediction set 1	23	118	176	147.39	15.33
Prediction set 2	22	120	174	147.68	15.15

After the completion of the three samples sets partitioning, we began to established calibration model and conducted two prediction tests on the basis of partial least squares (PLS). In each prediction test, we analyzed the results of three different methods contrastively, they are (1) Only PLS (spectra without any preprocessing). (2) Multiplicative scatter correction (MSC) coupled with PLS. (3) Direct orthogonal signal correction (DOSC) coupled with PLS. We named the calibration models built by different methods are PLS, MSC & PLS and DOSC & PLS model respectively. Then forecast the samples Hb level in per prediction set.

4. Results and discussion

When we used calibration set spectra and corresponding Hb clinical values to built non-invasive Hb models by PLS, more principal components would lead in more interference information such as instrument noise, which would lead to over fitting in models as well known. So the al components number of PLS was optimized inside five.

4.1. Predicting test 1

For prediction set 1 sample the best prediction results of each model have been shown in Fig. 2.

For the optimal PLS model without any pretreatment, the root-mean standard error of prediction (RMSEP) was 9.30 g/L, relative RMSEP was 6.31%, the prediction result is satisfactory and almost reach the Hb detection clinical precision requirement.

However, after MSC processing, RMSEP respectively increased to 10.32 g/L, and relative RMSEP were 7.30%, prediction accuracy of MSC & PLS model declined. In some degree, MSC could eliminate scattering influence; further enhance the useful information related to Hb. However, it is an algorithm based on an assumption that scattering influence is irrelevant to concentration variance. So using MSC may lead to some valid information are eliminated as interference, which is related to the concentration matrix in fact. Then impact the robustness of MSC & PLS model. In our non-invasive Hb quantitative study, we need sufficiently consider the relevance between spectra and concentration values, MSC may not suit our study well.

After DOSC processing, RMSEP decreased to 9.07 g/L, relative RMSEP decreased to 6.16%, the prediction accuracy elevated a little than PLS model. Direct orthogonal signal correction (DOSC) [16], which is proposed by Westerhuis. One or more directions in

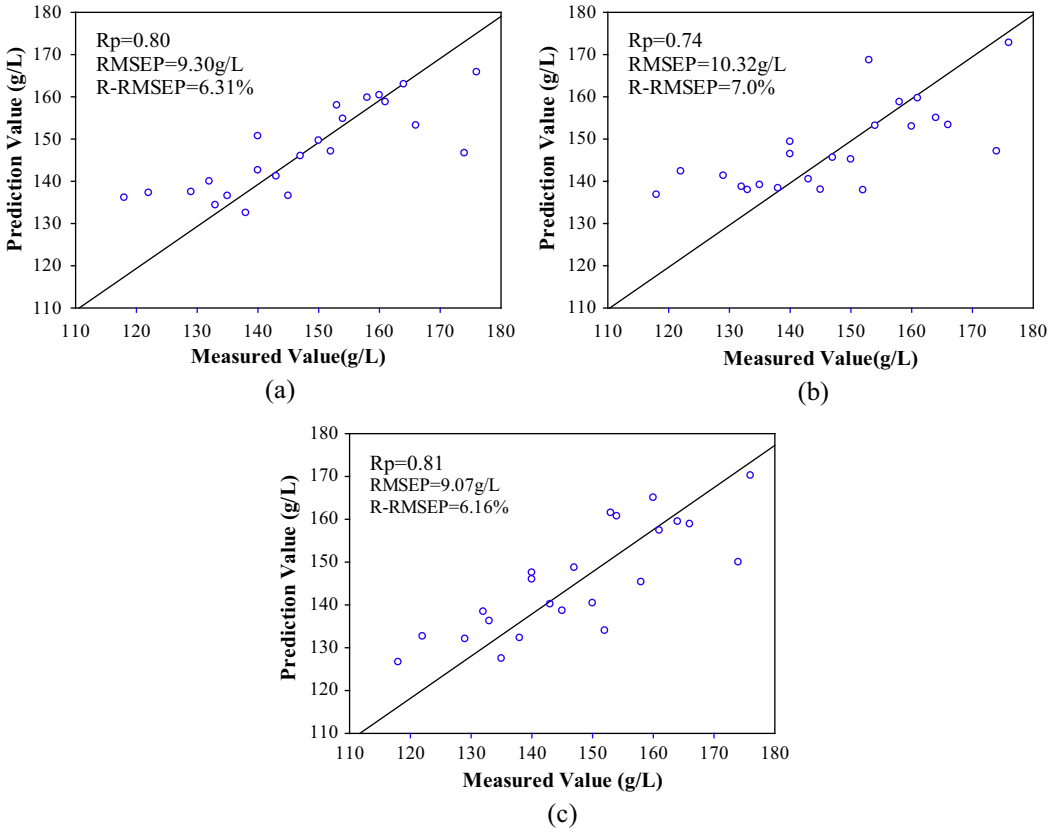

Fig. 2. For predicting test 1, scatter diagrams show comparison of the actual and analysis SpHb values. (a) Without any treatment. (b) After MSC treatment. (c) After DOSC treatment.

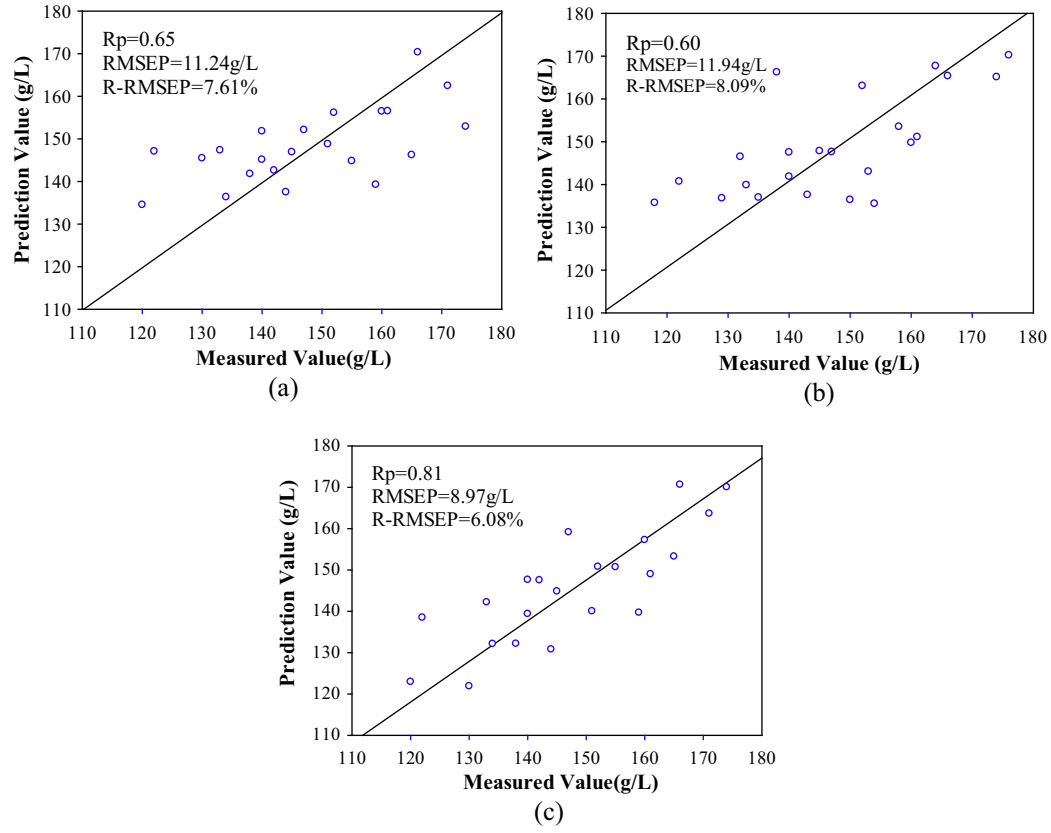

Fig. 3. For predicting test 2, scatter diagrams show comparison of the actual and analysis SpHb values. (a) Without any treatment. (b) After MSC treatment. (c) After DOSC treatment.

spectra matrix *X* orthogonal to concentration matrix *Y* that account for the largest variation in *X*, however, a little low variation of the product quality *Y*. Information contained in these directions is unrelated with concentration matrix actually. It will result in losing some valid information or filtering out noise incompletely if such directions to be without appropriate preprocess, which would impact the quality of near infrared analysis models further. DOSC would be to calculate such directions and eliminate them efficiently. After taking a full consideration of the association between spectra and concentration matrix, DOSC would eliminates the impacts of directions in *X* that orthogonal to *Y*, and then improve the accuracy of near infrared prediction models. In prediction test 1, comparing with MSC, the advantage of DOSC to filter out interference within Hb near infrared spectra is more remarkable.

4.2. Predicating test 2

This test is intended to examine the adaptability of PLS, MSC & PLS DOSC & PLS calibration models. Using the three calibration models we predict Hb level of samples in prediction set 2. The best results were shown in Fig. 3.

For prediction set 2 samples, RMSEP of PLS model was 11.24 g/L and relative RMSEP was 7.61%. The prediction accuracy declined sharply when compared with the result in predicting test 1. It indicated that the predictive ability of PLS calibration model without any preprocessing is not steady. And it is not adaptable in predicting Hb value of some new samples. The main reason was attributed that PLS model was built up with none pretreatment; PLS algorithm is unable to effectively filter our interference information in Hb spectra, which would impact the predictive precision of near infrared calibration model. Meanwhile, as the number of principal components was determined when the best result was obtained in test 1, PLS model accommodated well with the samples in prediction set 1 and performed satisfactory predictive ability. Whereas, for other new samples, the PLS model did not adapted to them, the prediction precision declined sharply.

For MSC & PLS model, RMSEP was 11.94 g/L, relative RMSEP was 8.09%, the result was even worse.

For DOSC & PLS model, RMSEP was 8.97 g/L, relative RMSEP was 6.08%, the results were very close to predicting test 1, which indicated that the adaptability of DOSC & PLS model was satisfactory. Before building model, we have filtered out interference information and remain valid information in maximum degree by utilizing DOSC. So the DOSC & PLS model is more robust.

From results of DOSC & PLS in two predicting trials, we found Hb prediction accuracy were both under 6.2%, almost met the requirement of clinical application. It demonstrated that DOSC could filter out interference information well, and when it coupled with PLS, the predictive ability and adaptability to predict Hb value were remarkable.

5. Conclusion

To optimize the accuracy of non-invasive hemoglobin (Hb) clinical detection by near infrared spectroscopy, high-performance instrument has been designed. A near-infrared spectrophotometric system was constructed adopting InGaAs detector array with 16 pixels and plane grating spectrometer to obtain high signal noise ratio (SNR) spectral data. Prepossessing algorithm has been investigated as well. In this paper, we conducted two tests to predict two different sets samples Hb level so that we could verified the validity and stability of pretreatment algorithms MSC and DOSC. The results of two tests showed that (1) For PLS, the Hb value prediction results are relative RMSEP was 6.31% and 7.61% respectively. Due to the interference information is not filtered out effectively by PLS itself, the predictive ability of PLS is not steady. (2) For MSC coupled with PLS method, the results are relative RMSEP was 7.0% and 8.09% respectively. As MSC do not take a full consideration of the association between spectra and concentration matrix, it contributes much less than DOSC to improve the Hb level prediction precision. (3) For DOSC coupled with PLS method, the results are relative RMSEP was 6.16% and 6.08%. The predictive accuracy is remarkable and almost reaches the requirement of clinical application. Comparing the results of two prediction tests, we confirmed the appropriate preprocessing algorithm is able to improve the predictive precision of near infrared non-invasive Hb detection. And we also confirmed the validity and stability of the DOSC & PLS Hb prediction model. The high-performance instrument developed by ourselves and the method DOSC coupled with PLS will have broad prospects in non-invasive Hb detection clinical application.

Conflict of interest

There is no conflict of interest.

Acknowledgments

We are grateful for continued financial support from the National High Technology Research and Development Program of China (2012AA022602), National Natural Science Foundation of China (61308067, 61475155), Jilin province Science and Technology Development Program item (20140204078GX) and the fund of State Key Laboratory of Applied Optics of China (Y2Q03FQZ01).

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