More Accurate Non-invasive Blood Glucose Measurement Based on Dynamic Spectrum and PLS

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Abstract
Non-invasive blood glucose measurement has attracted much attention in recent years. Near-infrared (NIR) spectroscopy is currently used for frequent detection of blood glucose levels. The dynamic spectrum (DS) method, which can eliminate the individual discrepancy, is the development of ordinary NIR spectroscopy. Classic Least Squares (CLS) is usually employed to analyze the spectra. In this work, we apply partial least squares (PLS) regression instead to extract the glucose concentration information from spectra of human blood, which is a mixture of four main ingredients - water, glucose, albumin and hemoglobin. All the calculating work was conducted by Lab VIEW. Comparing to CLS, the PLS algorithm was more precise in extracting the blood glucose concentration from the spectra. The DS method is able to reduce disturbance caused by individual discrepancy. And the PLS algorithm excels in data processing. If PLS is utilized in spectral analysis of DS, non-invasive measurement of blood glucose will surely be much more accurate.

Keywords: PLS, dynamic spectrum, non-invasive, blood glucose, Lab VIEW
1. Introduction

WHO reported that about 1.3 billion people worldwide suffered from diabetes in 1999. At present, diabetes has become a global epidemic of human beings and it is estimated that the number of diabetics will be up to 3.0 billion by 2025 (Ren, 2011). For those diabetics, frequent detection of human blood is often required. To detect the glucose levels, patients’ fingers have to be pricked about 1800 times every year (Zhang, 2011). Thus non-invasive monitoring of diabetes has drawn tremendous attention over the past 30 years.

Several methods are available for the non-invasive monitoring, such as near-infrared (NIR) spectroscopy (Burmeister, 1999), Raman scattering spectroscopy, mid-infrared spectroscopy, fluorescence spectroscopy (Enejder, 2005; Vashist, 2012; Govada, 2014) and so on. NIR spectroscopy offers lots of advantages for quantitative measurements. For instance, it’s non ionizing and demands virtually no sample preparation. Absorptivity of NIR allows detection at higher level of sample thickness. Hence, NIR spectroscopy is widely utilized in a variety of analytical fields. Fundamental of this approach is the absorption of NIR spectrum according to the Beer-Lambert law:

\[ A = - \log \left( \frac{I}{I_0} \right) = \varepsilon \cdot b \cdot c \quad (1) \]

Where \( A \) is the absorbance, \( I \) is the intensity of the incident light, \( I_0 \) is the intensity of transmitted light, \( \varepsilon \) is the wavelength dependent extinction coefficient, \( b \) is the optical path length and \( c \) is the concentration of the analyte.

Generally, “\( A \)” will be made certain if “\( b \)” and “\( c \)” are fixed according to Eq.1. However, the measured value of “\( I \)” is often influenced by lots of disturbances, such as high-frequency noise and individual discrepancy. Under these circumstances, the observed value of absorbance may vary from person to person although their blood glucose levels are the same. Therefore accuracy requirement of clinic application of ordinary NIR spectroscopy may not be satisfied since the exact absorbance of blood is not precisely measured. Besides that, glucose signal is so weak that it will easily be submerged in high-frequency noise, which is another factor that will affect the precision of glucose measurement.

Dynamic spectrum is the advance of ordinary NIR spectroscopy, and it is proved to be able to eliminate the individual discrepancy. To extract the concentration information from the NIR spectra infected by noise, PLS regression was applied in this paper. All the calculations were implemented with Lab VIEW.

2. Methods

2.1 The Dynamic Spectrum Method

The dynamic spectrum method proposed by Y Wang et al (Wang, 2005) is the development of ordinary NIR spectroscopy. Unlike the latter one, dynamic spectrum measures the maximum and minimum values of transmitted light during one period of the pulse in the human tissues regardless of the incident light (Fig. 1). Subsequently, the variation of absorbance, \( \Delta A \), can be figured out by Eq.2:

\[ \Delta A = A_1 - A_2 = \log \left( \frac{I_0}{I_{\text{min}}} \right) - \log \left( \frac{I_0}{I_{\text{max}}} \right) = \log \left( \frac{I_{\text{max}}}{I_{\text{min}}} \right) = \varepsilon \cdot c \cdot L \quad (2) \]

Where \( L \) equals \( b_1-b_2 \), and \( I_{\text{max}} \) and \( I_{\text{min}} \) are merely contributed by the pulsatile component of the artery blood, which will largely eliminate the individual discrepancy contributed by tissues except the pulsatile part. When the wavelength of NIR is changed, we can acquire series of \( \Delta A \) that are the linear combination of concentrations of different analytes:
\[ \Delta A_i = 2.303 \sum_{j=1}^{n} \epsilon_{ij}c_j L + e_j \]  

(3)

Where \( \Delta A_i \) is the variation of absorbance related to the certain wavelength \( i \), \( \epsilon_{ij} \) is the extinction coefficient of \( c_j \), \( c_j \) is the concentration of analyte \( j \), and \( e_j \) is the noise. \( i = 1,2,\ldots,m \), \( j = 1,2,\ldots,n \). However, Y Wang et al didn’t demonstrate the exact way to calculate the concentration of glucose in blood.

![Fig.1 Schematic of DS](image)

Fig.1 Schematic of DS (a) Light source passes through the tissues ; (b) Light intensity and time relationship.
2.2 PLS Algorithm

Some algorithms are available for the data processing of dynamic spectrum. Among all the multivariate calibration methods, classical least-squares regression is the simplest. In this paper, we employ PLS algorithm instead to estimate the concentration of glucose and precision of the two methods is compared.

The PLS algorithm was initially proposed by H. Wold in 1960s and became popular first in chemometrics (Wold, 1989). It allows a sophisticated approach using the full spectral region rather than unique and isolated analytical bands and goes beyond the classic least-squares regression in that it models also the structure of the two matrixes (Gaydou, 2011). Because it takes covariance of both the spectral and concentration matrices into account, which emphasizes the interpretative function of the independent variables to the dependent variables, the noise that is worthless for the regression is removed to some extent.

In this work, we suppose \( X \) as the spectral matrix and \( Y \) the concentration matrix. The PLS regression works as follows (Wold, 2001; Zanon, 2012):

First, compute the maximum eigen value and the corresponding eigenvector \( w_i \) of \( E_{i-1}^T F_{i-1} F_{i-1}^T E_{i-1} \) where \( E_0=X, F_0=Y, i=1,2,\ldots,a, a\leq \text{rank}(E_0) \). The score vector \( t_i \) is computed by Eq.4:

\[
t_i = E_{i-1} w_i / (w_i^T w_i) \quad (4)
\]

The loading vectors \( p_i \) and \( b_i \) are figured out by Eq.5 and Eq.6:

\[
p_i = E_{i-1}^T t_i / (t_i^T t_i) \quad (5)
\]
\[
b_i = F_{i-1}^T t_i / (t_i^T t_i) \quad (6)
\]

The vector \( w_i^* \) is calculated with Eq.7:

\[
w_i^* = (I - w_1 p_1^T)(I - w_2 p_2^T)\ldots(I - w_i-1 p_{i-1}^T)w_i \quad (7)
\]

\( E_i \) and \( F_i \) are worked out by Eq.8 and Eq.9:

\[
E_i = E_{i-1} - t_i p_i^T \quad (8)
\]
\[
F_i = F_{i-1} - t_i b_i^T \quad (9)
\]

Finally, the PLS regression matrix \( B_{PLS} \) is obtained:

\[
B_{PLS} = w_1^* b_1^T + w_2^* b_2^T + \ldots + w_a^* b_a^T \quad (10)
\]

Concentration of interested analytes can then be estimated by:

\[
\hat{Y} = X B_{PLS} \quad (11)
\]

A noise matrix composed of random numbers is added to the spectral matrix \( X \) to simulate the real situation when dynamic spectrum is applied. After \( B_{PLS} \) is solved, we multiply \( X \) by \( B_{PLS} \) to get the estimated concentration matrix \( \hat{Y} \).

2.2 Simulation with LabVIEW

All the calculating work is implemented with LabVIEW. It is a development environment for a graphical language form Nation Instruments. Its extensive support for accessing instrumentation hardware makes LabVIEW standing out from the rest.

The follow chart is shown in Fig.2. Firstly, the concentration matrix \( Y \) and its coefficient matrix \( B \) are created. Each column of the 50x3 matrix \( Y \) is the 50 different values of concentration, which obeys normal distribution, of the three ingredients in human fluid. Following the other steps exhibited in Fig.2, we can acquire the program of computing \( B_{PLS} \).

As we can see from Fig.3, the smaller “for-loop” is designed to build a 160x160 unit matrix \( I \). The boxes marked “1”, “3”, “5” are the 3 sub-VIs whoes block diagrams are also shown in Fig. 3.Sub VI 1 is on the basis
of Eq.(5) and Eq.(8). Its input, $t_1$, is given by sub VI 3 according to Eq.(3), Eq.(4) and Eq.(7). Sub-VI 5 is mainly used to figure out $w_1$, which will enter sub-VI 3.

Fig.2 Procedure follow chart of the PLS algorithm

Fig.3 Block diagram of the PLS algorithm and its sub-VIs
3. Results and Discussion

Absorption spectra of glucose, water, albumin and hemoglobin are presented in Fig.4 where each absorbance value on each curve is related to the corresponding concentration, optical path length as well as wavelength. According to Eq.3, \( \Delta A \) is the linear combination of concentrations of the analytes. The simulative dynamic spectra of 200 different combinations of concentrations of the four main ingredients in blood were generated by adding the curves in Fig.4 and the disturbance. With a 10 nm sampling period, the spectral matrix \( X \) is then generated from the 200 curves. Subsequently, we input \( X \) and the concentration matrix \( Y \), which is known in advance, into the block diagram created by LabVIEW. Once \( B_{PLS} \) was figured out, we estimated the concentration of glucose with the spectral matrix \( X \) according to Eq.11.

Comparing to CLS, we can find that the estimated values are closer to the actual ones when PLS is applied. For example, the absolute error of PLS is -7.02E-06 while the absolute error of CLS is 4.322E-05. The more detailed comparison between PLS and CLS is shown in Tab. 1. Although there is one case where the absolute error of PLS is 6.83E-06 while that of CLS is -2.8E-07, the standard error of CLS is still more than 3.5 times that of PLS. As a whole, PLS performs better in accuracy.

<table>
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<tr>
<th>True Values</th>
<th>PLS</th>
<th>CLS</th>
<th>Absolute Error of PLS</th>
<th>Absolute Error of CLS</th>
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</table>

| Standard Error | 9.17197E-06 | 3.22048E-05 |
4. Conclusion

Dynamic spectrum method is an advance of NIR spectroscopy. It can theoretically eliminate nearly all the influence the individual discrepancy exerts and will certainly improve the accuracy of non-invasive detection of blood glucose. To handle the data generated by dynamic spectrum, we proposed PLS regression and find its great power for the spectral analysis. By combining the two methods together, blood glucose measurement will certainly be much more precise. If the combined methods are successfully applied into practice, the finger prick test for blood glucose levels could eventually become a thing of the past for diabetics.

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References


