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Quantitative Spectroscopic Tomography for Non-invasive Blood Glucose Concentration Measurement

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Abstract—The purpose of this study is to explore the effect of the wavenumber resolution to the prediction accuracy of the glucose concentration. Then, we propose the glucose concentration prediction method by using partial least square (PLS) regression. We measure the interferogram of a glucose solution by using imaging-type 2-dimensional fourier spectroscopy. For increasing wavenumber resolution, zero-filling is applied to measured interferogram. Then, the interferogram is translated into wavenumber domain by discrete fourier transform (DFT). The PLS regression is applied to the spectrum to predict glucose concentration in aqueous solutions. As the experimental results, the error rate of the glucose concentration prediction reduced from xx% to xx% when xxx zeros were added to original interferogram.

1. Introduction

Diabetes is one of the lifestyle diseases and recognized as a serious problem in the world. The patients are required to measure blood glucose concentration several times a day to monitor own conditions. Currently, the patients prick their fingers and obtain small amount of blood for the glucose sensing. However, since pricking fingers is invasive and uncomfortable, this is not kind to patients. Even though most of people don't notice the diabetes because the disease is unseen health problem in the early stage, the bottleneck for the blood glucose sensing prevents people to sense their blood glucose concentration in daily life. In order to maintain patient's health and prevent increasing diabetics, the development of the non-invasive blood glucose sensor is expected.

Near-infrared (NIR) spectroscopy has attracted great interest to achieve non-invasive blood glucose sensing [1]-[3]. NIR is invisible light covers the wavelength range from 750-2500nm, and appropriate to analyze the component in the biological tissues as it can pass through the object. The blood glucose level is measured by analyzing the NIR reflected in the biological tissues. In this study, we use imaging-type 2-dimensional fourier spectroscopy [4] for glucose sensing. The advantage of the imaging-type 2-dimensional fourier spectroscopy is that we can only measure the optical interference limiting the measurement depth into focal plane. Thereby, there is a possibility to measure blood glucose concentration limiting to the layer where blood vessel exists. The other characteristics are the simple structure and robustness for the fluctuation, which enable reasonable product and use at home.

In the glucose sensing, the wavenumber resolution (that is the number of wave cycle proportional to 1cm) is an important factor and needed to be determined to achieve accurate sensing of the glucose concentration. If the wavenumber resolution is low, a peak value will be missed. Moreover, the low wavenumber resolution makes it difficult to analyze the information corresponding to each wavelength light source contains. This problem is discussed in [2]. Therefore, we focus on the wavenumber resolution to improve prediction accuracy of the glucose concentration in aqueous glucose. The characteristic of light source is defined by wavelength, though the data obtained from spectrometer is analyzed in the wavenumber domain. The wavelength (λ) and wavenumber (ν) have non-linear relationship, such as $\lambda = 1/\nu$. Therefore, we need to improve the wavenumber resolution not to miss the information corresponding to each wavelength. In the experiments, we search appropriate wavenumber resolution by using glucose solutions. The glucose concentration of aqueous solution is predicted from the NIR spectrum based on partial least square (PLS) regression.

2. Measurement of NIR Spectrum

2.1. Imaging-type 2-dimensional Fourier Spectroscopy

The overview of the imaging-type 2-dimensional fourier spectroscopy [4] is illustrated in Fig. 1. This spectrum is consisted of objective and imaging lenses, and fixed and movable mirrors. Firstly, the rays from a bright point on the focal plane are paralleled through the objective lens. Secondly, the parallel rays are reflected by the fixed and movable mirrors. The movable mirror moves in the direction of the arrow shown in Fig. 1. As a result, phase difference occurs between the rays reflected by movable and

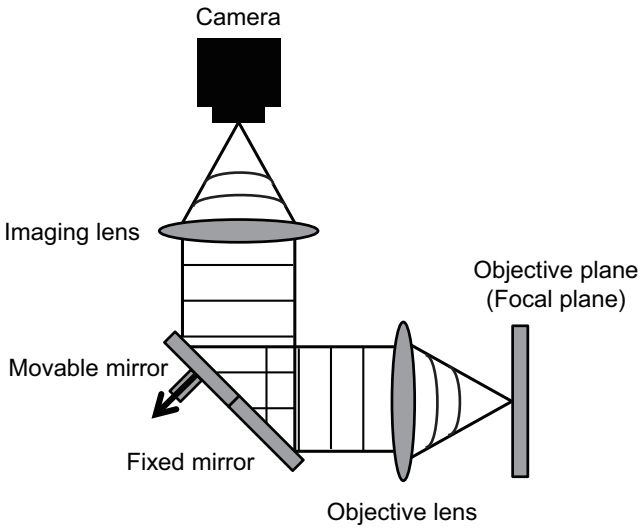


Figure 1: Imaging-type 2-dimensional fourier spectroscopy.

fixed mirrors. Finally, these rays pass through the imaging lens, and form an image on the camera. By recording the optical interference caused on the camera continuously, we can observe interferogram shown in Fig. 2.

2.2. Interferogram

Interferogram which obtained from the spectrometer shown in Fig. 1 is consisted of the superposition of cosine waves with different wavelength. The bandwidth of wavelength is decided by the type of light source. If light source whose bandwidth is between 1500 and 1700[μm] is used, we can observe interferogram as a superposition of cosine waves in that bandwidth. The image of the interferogram is illustrated in Fig. 2. Horizontal axis indicates phase difference changed by movable mirror, and vertical axis indicates amplitude. When the phase difference is zero, the amplitude of the interferogram becomes largest. On the other hand, as the phase difference becomes larger, the amplitude becomes smaller. Measured interferogram is analyzed by discrete fourier transform (DFT) and chemometrics.

3. Proposed Method

Fig. 3 shows the flow of the proposed method. Firstly, we measure interferogram of a glucose solution by using imaging-type 2-dimensional fourier spectroscopy. Secondly, zero is added to measured interferogram to increase wavenumber resolution, and DFT is applied to it to obtain spectral information of interferogram. Finally, the glucose concentration of a solution is estimated from spectral data with PLS regression.

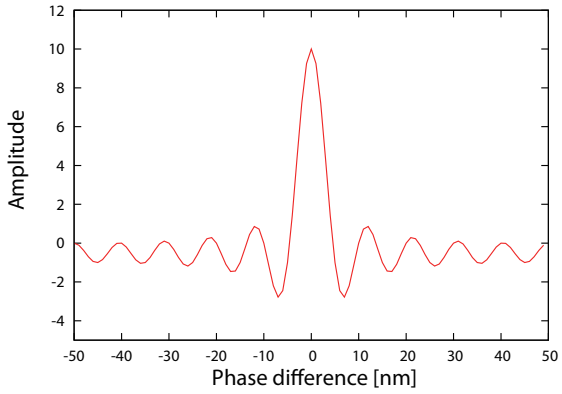


Figure 2: Interferogram.

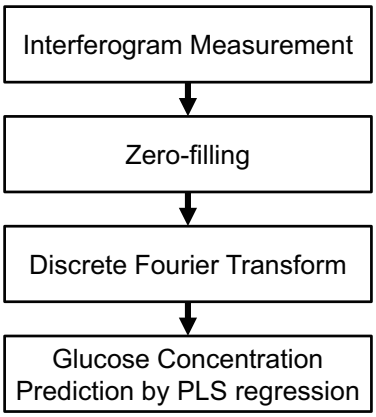


Figure 3: Flow of the proposed method.

3.1. Interferogram Measurement

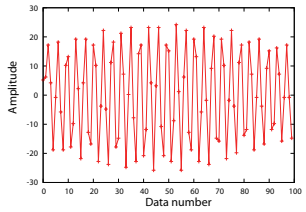
Interferogram of a glucose solution is measured by using imaging-type 2-dimensional fourier spectroscopy. The glucose solution is set on the spectrometer, and the change of the intensity value generated by optical interference is measured to obtain interferogram of the glucose solution.

3.2. Zero-filling

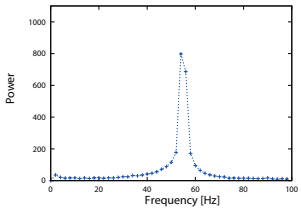
Zero-filling is the up-sampling method, and the wavenumber resolution is interpolated by adding zero to the measured interferogram. The possibility of missing the wavenumber which has peak value will be solved by zero-filling. Fig. 4 and Fig. 5 show the difference of the spectrum with and without zero-filling.

3.3. Partial Least Square (PLS) Regression

PLS regression is one of the statistical methods widely used in the field of chemometrics to predict dependent variables from independent variables. PLS regression is suitable for the condition that the number of independent variables is larger than that of observations. This is because

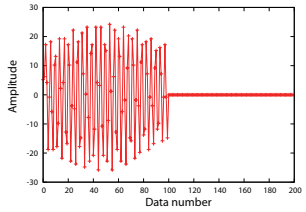


(a)The signal without zero-filling.

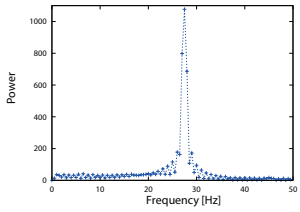


(b)The spectrum of signal without zero-filling.

Figure 4: The spectrum without zero-filling.



(a)The signal with zero-filling.



(b)The spectrum of signal with zero-filling.

Figure 5: The spectrum with zero-filling.

that the multicolinearity can be avoided by projecting dependent and independent variables onto the new spaces, and taking into account the relationship between the projected variables. In this study, we use non-linear iterative partial least squares (NIPLS) algorithm for constructing PLS regression model[5]. Eq.(1)(2) show the dependent variables $\boldsymbol{X}$ and independent variables $\boldsymbol{Y}$ modeled by PLS regression.

$$\boldsymbol{X} = \sum_{i=1}^{N} \boldsymbol{t}_i \boldsymbol{p}_i + \boldsymbol{E}_x = \boldsymbol{T}\boldsymbol{P} + \boldsymbol{E}_x \quad (1)$$

$$\boldsymbol{Y} = \sum_{i=1}^{N} \boldsymbol{u}_i \boldsymbol{q}_i + \boldsymbol{E}_y = \boldsymbol{U}\boldsymbol{Q} + \boldsymbol{E}_y \quad (2)$$

where $\boldsymbol{t}_i$ and $\boldsymbol{u}_i$ are score vectors, $\boldsymbol{p}_i$ and $\boldsymbol{q}_i$ are loading vectors, and $\boldsymbol{E}_x$ and $\boldsymbol{E}_y$ are residuals. The modeling of dependent and independent variables in PLS regression is performed to make the correlation between score vectors max. The regression from score matrix $\boldsymbol{T}$ to score matrix $\boldsymbol{U}$ is expressed in Eq.(3).

$$\boldsymbol{U} = \boldsymbol{B}\boldsymbol{T} \quad (3)$$

where B is a matrix of regression coefficient.

4. Experiments

4.1. Experimental Conditions

The interferogram of a glucose solution is measured by using imaging-type 2-dimensional fourier spectroscopy depicted in Fig. 1. A glucose solution is placed between the phase shifter and objective lens, and the rays which transmitted the solution form an image on the camera. By observing the changes of the intensity on the image continuously, we obtain interferogram of a glucose solution. The sampling distance and total length of the phase shifter are 431[nm] and 42[μm], respectively. We prepare the 6 kinds of glucose solutions, 500[mg/dl], 2000[mg/dl], 2500[mg/dl], 5000[mg/dl], 7500[mg/dl] and 10000[mg/dl]. 5 points are ramdomly selected from the image obtained in a solution. They are used for constructing PLS regression model, and also used for validating the prediction performance of the model.

Before applying the DFT to measured interferogram, zero value is added to the interferogram to increase wavenumber resolution. When the PLS regression model is constructed, the number of loading vector $\boldsymbol{P}$ is determined based on the cumulative contribution rate. In this experiment, the loading vector is selected to the cumulative contribution rate exceeds 0.98.

4.2. Evaluation Criterion

The prediction performance of the PLS regression model in the glucose concentration is evaluated using error rate.

$$\text{Err.} = \frac{1}{N}\sum_{i=1}^{N}\frac{|C_\text{t} - C_{\text{p}i}|}{C_\text{t}} \times 100 \quad [\%] \quad (4)$$

where C_t and C_p are target and predicted values of glucose concentration, respectively. N is the number of data.

4.3. Experimental Results

The error rate of predicted glucose concentration is shown in Fig. 6. The horizontal axis indicates the number of zero added to interferogram, and the vertical axis indicates the error rate between predicted and target values. In Fig. 6, error rate is decreased as the number of zero increases. In particular, when the number of added zero is 300, the lowest error rate is obtained. On the other hand, when zero is not added to measured interferogram, it shows the highest error rate among all of them. Then, we show the error rate of the glucose concentration of dataset with 300 zeros in Fig. 7. The horizontal axis indicates the glucose concentration of the solution, and vertical axis indicates the error rate. The error rates of the all solutions are within the 18%, and varied depending on the glucose concentration of the solutions.

4.4. Discussions

In this experiment, we increased the wavenumber resolution by zero-filling to improve the accuracy of the glucose concentration. From Fig. 6, it was shown that zero-filling is effective to improve the prediction accuracy of the glucose concentration. However, zero-filling only interpolates

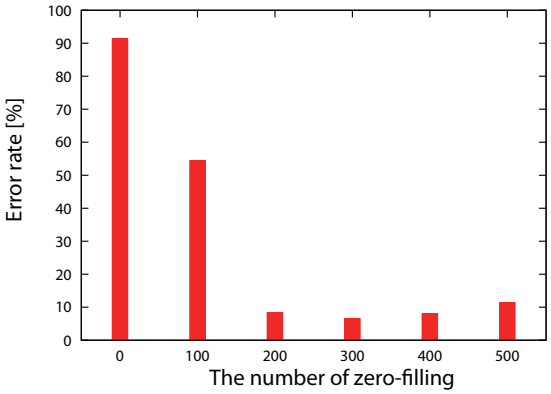


Figure 6: The error rate of glucose concentration.

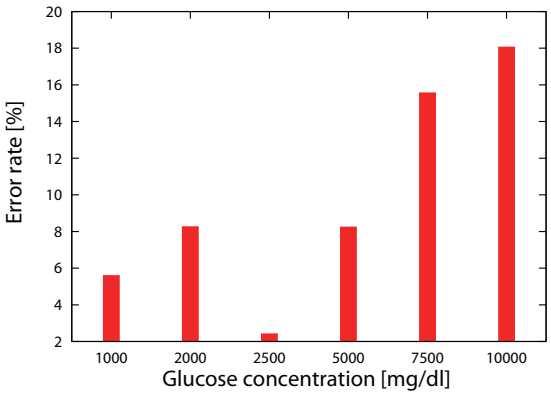


Figure 7: The error rate of glucose concentration with 300 zeros.

data, and can't get the information more than original interferogram containing. In Fig. 7, it was shown that the error rate of the predicting glucose concentration was within 18%. For more precise glucose concentration sensing, we need to observe interferogram in higher sampling rate or longer total shift length of the phase shifter to increase the wavenumber resolution.

5. Conclusions

In this study, we proposed the glucose concentration prediction method by using PLS regression to explore the effect of the wavenumber resolution to the prediction accuracy of the glucose concentration. The interferogram of a glucose solution was obtained by using imaging-type 2-dimensional fourier spectroscopy. The glucose concentration was predicted by applying PLS regression to the spectrum of the interferogram calculated by DFT. From the experiments, it was confirmed that the prediction accuracy of the glucose concentration was improved by adding 300 zeros to the interferogram to increase the wavenumber resolution. In order to achieve more precise prediction, we require to increase the sampling rate of imaging-type 2-dimensional fourier spectroscopy or use longer sample window. the number of samples obtained from imaging-type 2-dimensional fourier spectroscopy. Moreover, we need to implement more experiments to ensure the usefulness of the proposed method.

Acknowledgments

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