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Spectrum Correction Considering Light Source Fluctuation for Non-invasive Blood Glucose Sensing

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ABSTRACT

The purpose of this study is to correct baseline shift in absorbance spectrums caused by light source fluctuation. To improve quantitative evaluation performance of blood glucose level, baseline shift is corrected by multiple scatter correction (MSC). Moreover, to increase the effect of the MSC, water vapor absorbance is subtracted, and relative glucose absorbance are calculated by dividing with hemoglobin absorbance at 1544 [cm-1]. In order to verify the effectiveness of the proposed spectrum correction method, light source fluctuation is simulated on the Fourier transform infrared spectroscopy (FT-IR), and we apply the proposed method to the spectrums measured by FT-IR. From the simulation results, the baseline shift was successfully reduced by proposed method.

Keywords: Spectrum correction, light source fluctuation, non-invasive blood glucose measurement

1. INTRODUCTION

Diabetes is a disease that blood glucose level becomes high level. Diabetic patients require to measure their blood glucose level several times per day for monitoring their health conditions. As usual method for measuring blood glucose level, the patients need to prick their finger to obtain blood, and blood glucose level is calculated by sensing the obtained blood sample with special sensor. Although the present measurement method is useful for controlling patient's blood glucose level, it is painful, uncomfortable, risk for infection, and not very acceptable to the patients. To overcome the above problems, we are developing non-invasive blood glucose sensor utilizing optical technologies.[1,2] The glucose sensing in our method is implemented by measuring the light reflected in the biological tissue and analyze it, and doesn't damage patients at all.

We have developed one-shot Fourier spectroscopy which enables line-spectroscopic imaging of target substances with high time resolution nearly the same as frame rate.[2] However, spectrums measured by one-shot Fourier spectroscopy suffers from light source fluctuation, which leads to baseline shift in the spectrums and complicates quantitative evaluation of blood samples. In this study, we propose the method of correcting baseline shift in the spectrums caused by light source fluctuation to improve the quantitative evaluation performance of blood glucose level.

2. ONE-SHOT FOURIER SPECTROSCOPY

The optical setup of one-shot Fourier spectroscopy is shown in Fig.1. The beams from a bright point on the objective plane are transformed to parallel beams through the objective lens. The parallel beams pass through the phase shifter called relative-inclined phase shifter to cause phase difference to them. Then, the beams pass through the imaging lens and focus on the imaging plane. On the imaging plane, interference of beams can be observed as line-imaging. Since one-shot Fourier spectroscopy has the phase difference spatially on the beams, we can measure interferogram with high time resolution nearly the same as frame rate. Therefore, one-shot Fourier spectroscpy is robust for the movement of target.

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3. LIGHT SOURCE FLUCTUATION

Light source fluctuation is the phenomenon that an intensity of light source varies over time. Fig.2 depicts a time-series change of the intensity of light source (black body) directly recorded by IR camera. The intensity of light source is not stable and changes irregularly from 135 to 142 over time. The light source fluctuation can be cause of baseline shift in the absorbance spectrums. Fig.3 shows an example of baseline shift caused by light source fluctuation. Two absorbance spectrums in Fig.3 are measured from exactly the same solution mixed with glucose and hemoglobin, and only the intensity of light source is different. Dashed and solid lines are the absorbance spectrums measured at lower and higher intensity level in the light source, respectively.

Baseline shift involves mainly two problems in terms of accurately sensing blood glucose level. The first is that blood glucose level can be incorrectly measured. Since an absorbance spectrum with baseline shift reflects both blood glucose level and baseline shift, we can't measure actual blood glucose level from the spectrums. The second is that the degradation of the effect of noise reduction by averaging. Mostly, absorbance spectrums are measured many times from same solution, and they are averaged to improve S/N ratio. However, we can't expect the effect of averaging because of the baseline shift. Therefore, we have to correct baseline shift caused by light source fluctuation to successfully measure blood glucose level with one-shot Fourier spectroscopy.

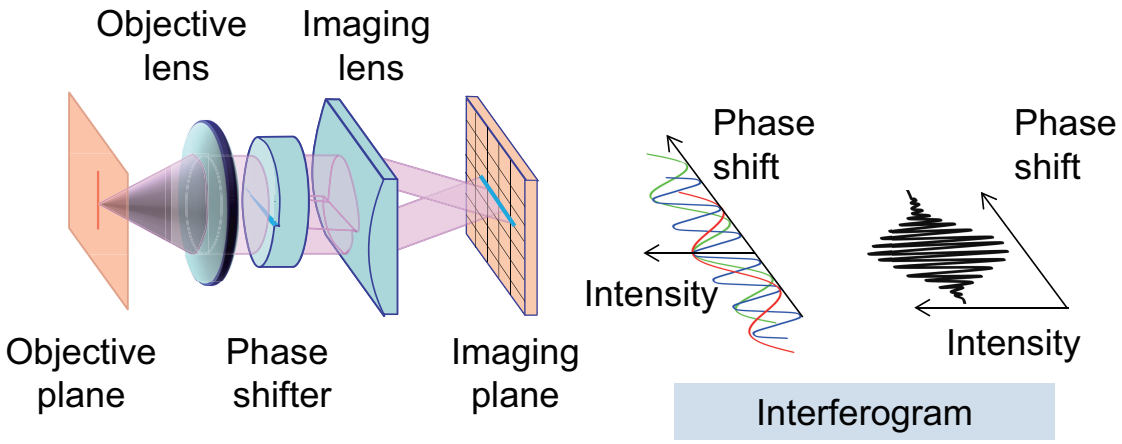

Figure 1. One-shot Fourier spectroscopy

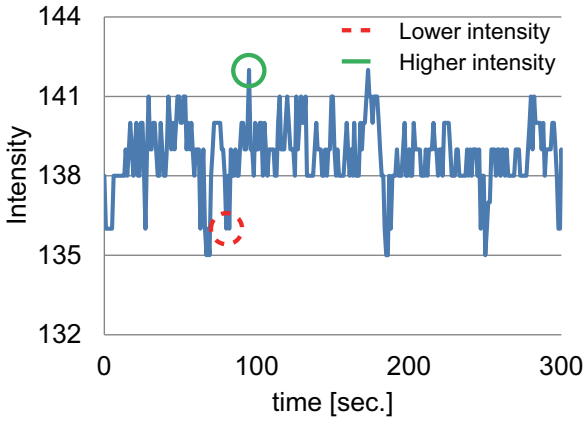

Figure 2. Light source fluctuation

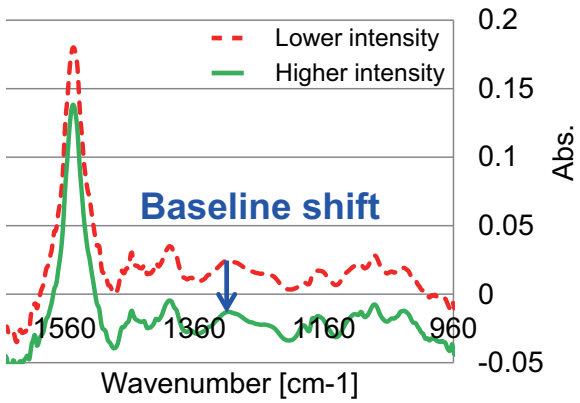

Figure 3. Baseline shift

4. CORRECTION OF LIGHT SOURCE FLUCTUATIONS

Although light source fluctuation only causes baseline shift in absorbance spectrums, it is not simple to correct the spectrums. When we measure an absorbance spectrum of a sample, the absorption of water vapor always observed. The amount of water vapor largely depends on the experimental environments, such as weather conditions, season, indoor or outdoor. Since the amount of water vapor is not stable and may degrade the performance of baseline shift correction, water vapor absorption should be removed in advance. Moreover, the wavenumber of water vapor absorption overlaps with that of hemoglobin, which is used to calculate relative absorbance of glucose to suppress the effects of measurement conditions. Therefore, removing water vapor absorption is highly important for accurate glucose sensing.

Considering above situations, we propose the spectrum correction method to remove the effect of light source fluctuations. The flow of the proposed spectrum correction method is shown in Fig.4. Firstly, we measure absorbance spectrum of aqueous solutions mixed with glucose and hemoglobin. Secondly, the absorbance of water vapor is subtracted from measured spectrums. Thirdly, baseline shifts in absorbance spectrums are corrected by using multiple scatter correction (MSC). Finally, relative glucose absorbance is calculated based on hemoglobin absorbance.

4.1 Measuring absorbance spectrum of aqueous solutions

We measure absorbance spectrums of aqueous solutions by Fourier transform infrared spectroscopy (FT-IR). To simulate the behavior of light source fluctuation, we intentionally increase the amount of light source power in FT-IR when we measure some of sample solutions. As a reference, pure water is measured in the fixed amount of light source power. In other word, we change the amount of light source power only when measuring sample solutions. The absorbance spectrum of a sample is calculated based on Beer-Lambert law.

$$A(\lambda) = -\log\left(\frac{I_{sam.}(\lambda)}{I_{ref.}(\lambda)}\right) \tag{1}$$

where A is an absorbance, $I_{sam.}$ is an intensity of a sample, $I_{ref.}$ is an intensity of reference, and λ is a wavenumber.

4.2 Water vapor subtraction

Water vapor absorbance is firstly subtracted from measured absorbance spectrums to improve the effect of baseline shift correction and calculating relative absorbance spectrums. The amount of water vapor in the environment is evaluated by humidity, and the difference of humidity in each measurement produces water vapor absorption. We show an example of water vapor absorbance in Fig.5. Water vapor absorbance is mainly observed from 1500 to 1300 [cm-1] and overlaps with hemoglobin absorption peak. We subtract water vapor absorption from measured spectrum as follows.[3]

1. Collecting reference water vapor spectrum

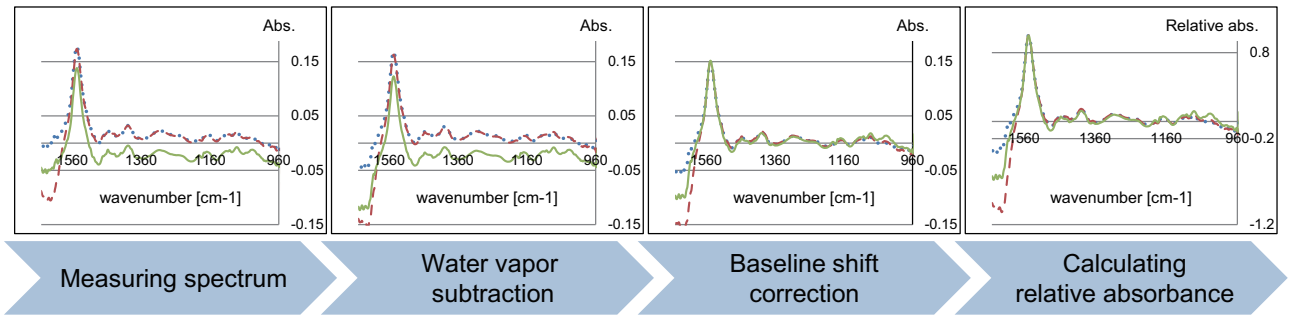

Figure 4. Flow of the proposed method

2. Computing the subtraction coefficient α as the ratio of the water vapor band from 1562 to 1555 [cm-1] on the sample spectrum and water vapor spectrum

3. Subtracting water vapor spectrum from sample spectrum

Water vapor subtraction is formulated as follows.

$$A_{out}(\lambda) = A_{sam.}(\lambda) - \alpha A_{vapor}(\lambda) \tag{2}$$

where A_{out} is a water vapor subtracted spectrum, A_{vapor} is a water vapor spectrum and α is a subtraction coefficient.

4.3 Baseline shift correction

Baseline shift in the spectrums is corrected by using MSC. MSC is often used to correct the absorbance variations caused by optical pass difference when measuring samples, and can remove additive and multiplicative effect in the spectrums. Assuming the intensity of sample changes by c times due to the light source fluctuation, the sample absorbance is computed as follows.

$$A(\lambda) = -\log\left(\frac{cI_{sam.}(\lambda)}{I_{ref.}(\lambda)}\right) \tag{3}$$

$$= \log\left(I_{ref.}(\lambda)\right) - \log\left(I_{sam.}(\lambda)\right) - \log c \tag{4}$$

From Eq.(4), it is clear that baseline shift caused by light source fluctuation has additive effect on the spectrums. To correct baseline shift, regression analysis is applied to the spectrums. By regressing each spectrum to average spectrum calculated from the entire spectrum, baseline shift is corrected. In this study, we apply MSC to the absorption band between 1580 and 960 [cm-1].

4.4 Calculating relative absorbance specturm

Internal standard method (ISM) is one of the spectrum correction method used for quantitative evaluation. The condition of internal standard substance is that the amount of a substance is stable, its absorption peaks don't overlap with sample absorption ones, and showing similar behaviors as sample. Originally, as internal standard, the fixed amount of a substance is poured to sample solution. In this study, we choose hemoglobin as internal standard substance since the amount of hemoglobin in the blood is almost constant. Relative glucose absorbance is calculated by dividing glucose absorbance with hemoglobin absorbance at 1544 [cm-1], which called amid II. Fig.6 shows glucose absorbance spectrums which include baseline shift caused by light source fluctuation. By proposed method, the measured spectrums are corrected shown in Fig.7. The solid line, dashed line and dotted line show glucose absorbance at level of 200, 150 and 100mg/dl, respectively.

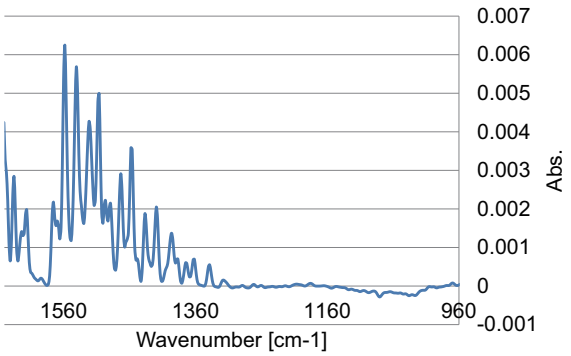

Figure 5. Water vapor absorbance

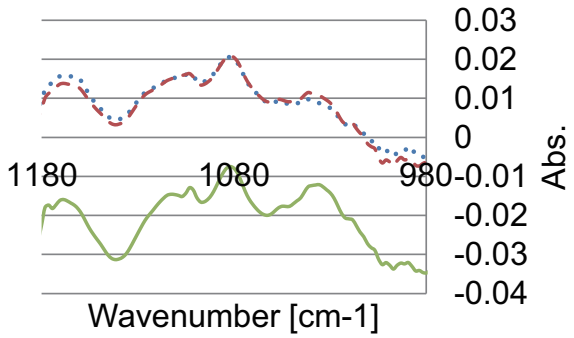

Figure 6. Glucose absorbance with light source fluctuation

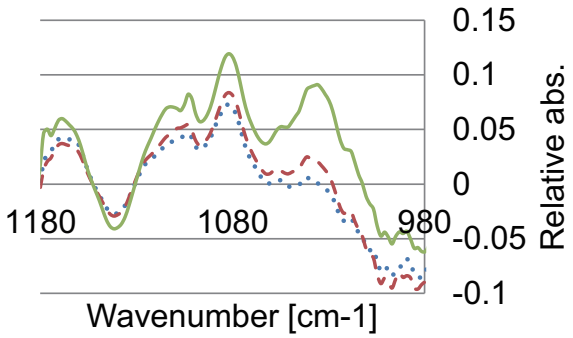

Figure 7. Corrected glucose absorbance

5. SIMULATIONS

5.1 Simulation conditions

In order to verify the effectiveness of the proposed method, we implement simulations. Table 1 indicates measurement conditions of absorbance spectrums. As sample solutions, three kinds of solutions mixed with different glucose level and the same hemoglobin level are prepared. In this simulations, the amount of light source power is increased only when measuring sample(3) to simulate light source fluctuation. From preliminary experiments, the number of accumulation of spectrum is determined as 128, and the wavenumber range is determined as from 1650 to 990 [cm-1] to cover hemoglobin and glucose absorption. Moreover, since higher wavenumber resolution is preferable to reduce water vapor absorption successfully, wavenumber resolution is determined as 4 [cm-1]. We evaluate the effectiveness of the method of correcting the spectrums by comparing the determination coefficient before and after spectrum correction.

5.2 Simulation results of spectrum correction

We show the relationship between glucose level and the absorbance at 1081 [cm-1] before spectrum correction in Fig.8. In Fig.8, the glucose absorption of 200mg/dl becomes smaller than others due to light source fluctuation. From the result, it is difficult to estimate glucose level from the spectrum with light source fluctuations. On the other hand, when the effect of light source fluctuation is removed from the spectrum by proposed method, the relationship between glucose level and relative absorbance is improved shown in Fig.9. Moreover, determination coefficient is also increased. From the simulation results, it is shown that proposed method can be useful for reducing the effect of light source fluctuations.

Table 1. Measurement conditions

Reference	Pure water
Sample	(1)Hemoglobin:2g/dl + Glucose:100mg/dl (2)Hemoglobin:2g/dl + Glucose:150mg/dl (3)Hemoglobin:2g/dl + Glucose:200mg/dl
Measurement equipment	Agilent FT-IR
Measurement method	Transmittance
Accumulation	128
Wavenumber range	1,650∼990 [cm-1]
Wavenumber resolution	4 [cm-1]

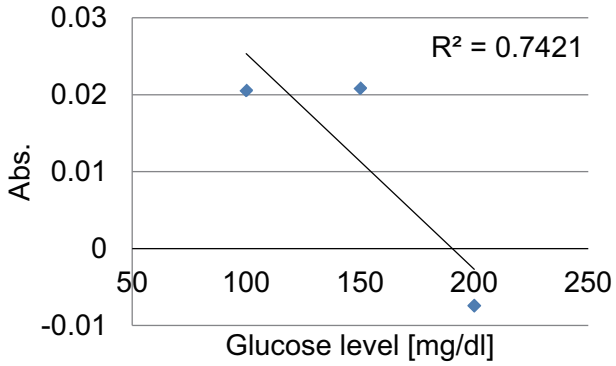

Figure 8. Relationship between glucose level and the absorbance at 1081 [cm-1] (before spectrum correction)

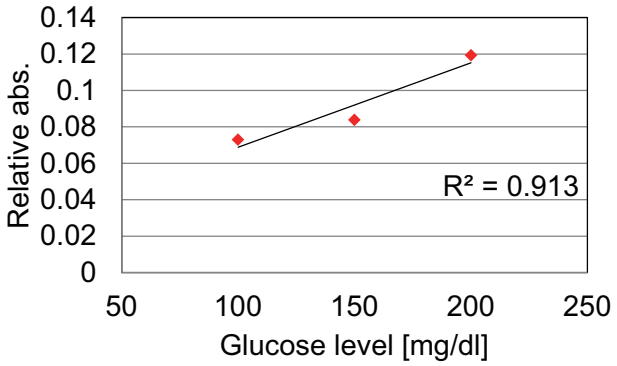

Figure 9. Relationship between glucose level and the absorbance at 1081 [cm-1] (after spectrum correction)

6. CONCLUSIONS

In this study, we proposed spectrum correction method for light source fluctuations. From the simulation results, it was shown that proposed method was useful for reducing baseline shift caused by light source fluctuation.

As future works, we will increase the number of kinds of samples to discuss the spectrum correction performance in detail. Our method was only evaluated by using FT-IR and simulating light source fluctuation intentionally. Then, we will to apply proposed method to spectrums measured by using one-shot Fourier spectroscopy.

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