DOI: 10.20472/IAC.2019.049.033

KEITA NISHIO
Aoyama Gakuin University, Japan

TAKASHI KABURAGI
International Christian University, Japan

SATOSHI KUMAGAI
Aoyama Gakuin University, Japan

TOSHIYUKI MATSUMOTO
Aoyama Gakuin University, Japan

YOSUKE KURIHARA
Aoyama Gakuin University, Japan

NON-INVASIVE METHOD FOR ESTIMATING BLOOD GLUCOSE LEVEL UTILIZING HARMONIC DISTORTION OF PULSE PRESSURE

Abstract:

In this paper, a non-invasive method for estimating blood glucose level is proposed. We investigate blood viscosity and harmonic distortion using a model with the assumption that high blood viscosity caused by high blood glucose level generates turbulence in blood flow. This consequently leads to the distortion of fundamental frequency of pulsation. Therefore, the harmonic components appear owing to the pressure on the vascular wall. Using the proposed non-invasive method, we calculate the amplitude of the harmonic components. The blood glucose level is estimated with a single regression model whose explanatory variable is the calculated harmonic component. Through validation experiment with 33 measured data, the third harmonic component achieved the highest estimation accuracy with 60% of the data meeting the ISO criteria.

Keywords:

non-invasive, blood glucose level, regression model, diabetes, harmonic distortion, blood pressure monitor, Fast Fourier transform

JEL Classification: I19

1 Introduction

According to the World Health Organization (WHO), the number of diabetes patients is assumed to be over 422 million [1]. Moreover, the International Diabetes Federation reports the prevalence of diabetes is 8.8% and will reach 9.9% by 2045 [2]. The current method for controlling blood glucose level is through insulin injection. Before injecting insulin, a patient needs to take a blood sample to measure their blood glucose level. To do so, a puncture needle is typically used. However, blood withdrawal with a puncture needle is accompanied by some problems, such as scars left by the puncture needle, stress owing to the pain and a risk of infection. Therefore, a non-invasive method for measuring the blood glucose level is required.

Non-invasive methods for estimating blood glucose level have been previously proposed in the literatures [3]-[5]. In the literatures [3], [4], the property of absorbance of blood under the skin is utilized for estimating. This method achieves high-precision estimation; however, they are not suitable for day-to-day monitoring because the measurement instruments are huge and costly. In the literature [5], the blood glucose level is estimated by analyzing a teardrop. Although the teardrop analyzing does not cost too much, the estimation precision is relatively low.

In this paper, we propose a non-invasive blood glucose level estimation method, which uses an arm-cuff blood pressure monitor.

2 Proposed Method

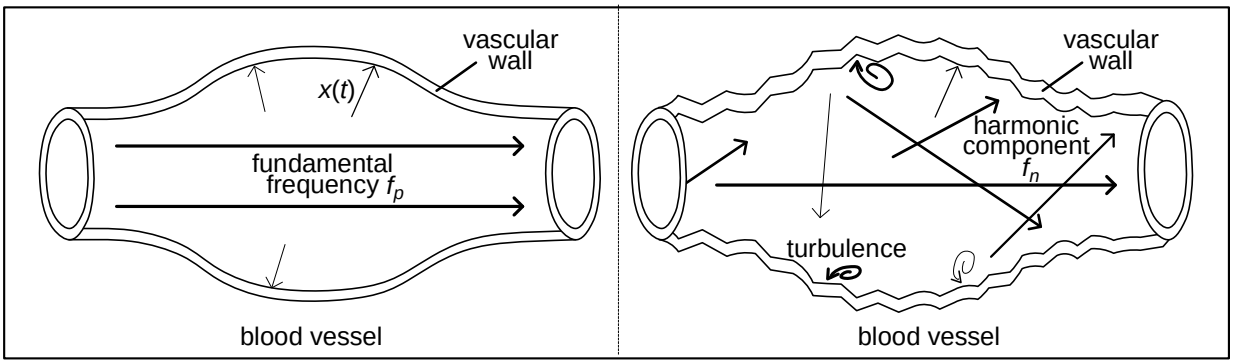
The proposed method consists of two parts: the model part and the signal processing part. The model part represents a diabetes patient's blood flow when they are measuring their blood pressure using an arm-cuff blood pressure monitor. In the other part, blood glucose level is estimated using signal processing based on the model.

A. Modelling of blood viscosity and harmonic distortion

First, the blood viscosity is assumed to be low if the blood glucose level is low. Conversely, the blood viscosity is assumed to be high if the blood glucose level is high.

When a patient measures the blood pressure using an arm-cuff blood pressure monitor, the cuff shrinks and compresses the blood vessel, thereby stopping the blood flow of the arm. When the cuff loosens and the blood vessel expands, blood starts to flow again. The blood flow after the cuff loosens is influenced by blood viscosity. Figure 1 shows the modelling of blood viscosity and harmonic distortion. If the blood viscosity is low, the blood flows smoothly when the cuff loosens. If the blood viscosity is high, the blood flows less smoothly compared to the case of low blood viscosity. Here, we consider the pressure on the vascular wall due to a single pulsation. In the case of low blood viscosity, pressure fluctuation with the fundamental frequency of pulsation occurs on the vascular wall. Whereas, in the case of high blood viscosity, turbulence occurs, leading to vibrations on the vascular wall. Subsequently, the fundamental frequency of pulsation is distorted, and the harmonic components appear. The proportion of the harmonic components

to the fundamental frequency is related to the blood viscosity. This leads to large harmonic components of the pressure on the vascular wall.



(a)Low blood viscosity (b)High blood viscosity

Fig.1 Modelling of blood viscosity and harmonic distortion of pressure on vascular wall

Given that the fundamental frequency of the pulse pressure component is f_p, the nth harmonic component appears at frequency f_n (n=1, 2, …), as shown in Eq.(1). Furthermore, if a_{fn} is the spectrum of the nth harmonic component, then

$$f_n=(n+1)f_p \#(1)$$

Here, $x(t)$ is the pressure on vascular wall, where t is the continuous time. $x(t)$ is expressed as the summation of several harmonic components, as shown in Eq.(2).

$$x(t)=\sum_{n=0}^{\infty}\sin\left[2\pi(n+1)f_p t\right] \#(2)$$

Because a_{fn} is related to a blood glucose level, the estimated blood glucose level $\widehat{B}$ is expressed as a function of a_{fn} as shown in Eq.(3).

$$\widehat{B} = f\left\{a_{2f_p}, a_{3f_p}, a_{4f_p}, \ldots\right\} \#(3)$$

B. Signal Processing

Let us take $y(t)$ as the output signal from the pressure sensor. It is the sum of the noise components and the pressure on vascular wall $x(t)$. This output signal $y(t)$ is A/D converted with a sampling frequency f_s and transferred to a computer as a digital signal $y(k)$ (k=1, 2, …, N), where k is the discrete time step with sampling frequency f_s, and N is the number of data points. N is different for each data because the measurement time varies for each measurement. However, each data needs to have the same number of data points such that all data have the same frequency resolution. Accordingly, data with fixed N_e data points is extracted from each $y(k)$. Fast Fourier transform (FFT) is applied to the extracted data and an amplitude spectrum a_f (f=0, Δf,

$2\Delta f, \ldots, f_s$) is obtained, where the frequency resolution Δf is $\Delta f = f_s/N_e$. Here, the fundamental frequency f_p is determined as the discrete frequency having the largest spectrum in the range of 0.8–6.4 Hz. Next, the discrete frequency that corresponds to the nth harmonic component is calculated based on Eq.(2). To evaluate the size of nth harmonic component, a difference between the spectra around the nth harmonic component is calculated. However, these spectra can be affected by the presence of noise components. Moreover, as the frequency is discrete, f_n is not representative of the exact integer multiple frequency of the nth harmonic component. For these reasons, we calculate the differences between two adjacent spectra for m discrete frequencies above and below f_n. To evaluate the magnitude of the differences, the differences are converted into their absolute values. We consider S_n to be the sum of the absolute values around f_n. It can be calculated using Eq.(4) and represents the amount by which the nth harmonic component influences $y(t)$. In the case of low blood glucose level, S_n is expected to be small. By contrast, in the case of high blood glucose level, S_n is expected to be large.

$$S_n = \sum_{i=-(m-1)}^{m} \left| a_{f_n+i\Delta f} - a_{f_n+(i-1)\Delta f} \right| \quad \#(4)$$

Finally, the function in Eq.(3) is determined by a single regression model whose explanatory variable is S_n.

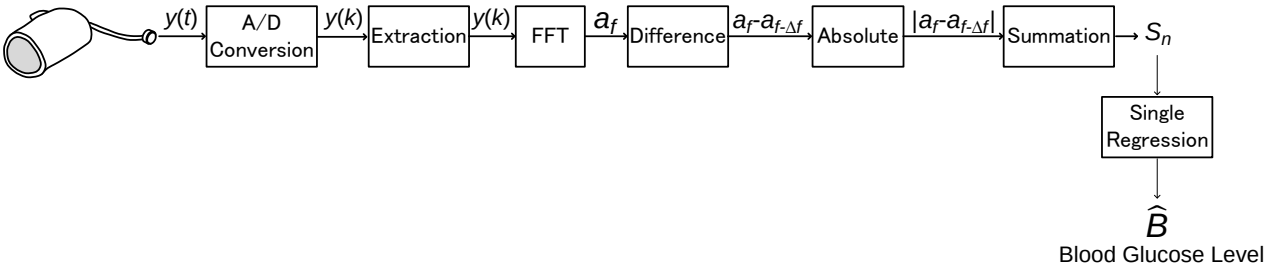


Fig.2 Signal processing for estimating blood glucose level.

3 Experiment

To evaluate the efficiency of the proposed method, we conducted the validation experiment. This section describes the experimental system, experimental procedure, and evaluation criteria.

A. Experimental System

As the sensing device to measure the pulse pressure, the arm-cuff blood pressure monitor HME-7120 (OMRON HEALTHCARE Co., Ltd.) was used. The tube connecting the cuff to the monitor was bifurcated and Electret Condenser Microphone EM114(PRIMO CO., LTD) was attached to one of the bifurcated tubes. The output signal from EM114 was amplified by a low-frequency amplifier MX4836 (PRIMO., Co. Ltd) with a maximum gain of 40.4dB. The amplified signal was A/D converted with AIO-160802AY-USB (Contec Co., Ltd.) with the sampling frequency f_s

=1000Hz and transmitted into a computer. The imported data $y(k)$ were then inputted. Accu- Chek® Mobile (F. Hoffmann-La Roche, Ltd.) was used to measure the true blood glucose level.

B. Experimental Procedure

The participants for the experiment were two males, one in his thirties and the other in his forties. The total number of obtained measurements was 33. Before the measurement, each participant was asked to measure their true blood glucose level using Accu- Chek® Mobile. Next, they were asked to wear the arm-cuff blood pressure monitor HME-7120 on their arms and measure the pressure change $y(t)$. The digital signal $y(k)$ was then obtained in parallel with the measurement. $y(k)$ is analyzed by the proposed method, where m=3 and N_e=10000. Here, we validate the following four patterns as the extracted interval with N_e points: the first 10 s (k=1, 2, …, 10000), the intermediate 10 s (k=10001, 10002, …, 20000), the last 10 s (k=N-9999, N-9998, …, N) and the overall data (k=1, 2, …, N).

C. Evaluation Criteria

To evaluate if the estimated glucose level is valid, we use the criteria established by the International Organization for Standardization (ISO). We consider e to be the error between true blood glucose level B and estimated blood glucose level $\hat{B}$. The ISO criteria are shown in Eq.(5). We applied leave-one-data-out cross validation to the measured data. A portion of the data was selected as test data. The remaining was used as training data to train a single regression model. Applying the test data to the trained regression model, the blood glucose levels of the test data was estimated. The proposed method was evaluated using the *Accuracy* defined in Eq.(6), where *num* is the total number of all data points and *num'* is the number of datapoints that meet the ISO criteria. *Accuracy* was calculated for 40 combinations because the validation was done up to the tenth harmonic component and the four patterns of the extracted interval.

$$\begin{cases} e \leq \pm 15\text{mg/dL} & (B<75\text{mg/dL}) \\ \dfrac{e}{B} \times 100 \leq \pm 20\% & (B \geq 75\text{mg/dL}) \end{cases} \#(5)$$

$$Accuracy = \frac{num'}{num} \#(6)$$

4 Results

This section illustrates the typical measured spectra and an estimation result.

A. Typical measured spectra

Figure 3 shows the typical spectra obtained by the FFT of the overall data in a (a) low blood glucose level, (b) moderate blood glucose level, and (c) high blood glucose level. The true blood glucose level of (a) low blood glucose level is 93 mg/dL. The spectra of the harmonic components

are not so large, although the second harmonic has a little larger spectrum than the other harmonics in this data. Concerning the data of (b) moderate blood glucose level, the true blood glucose level is 110 mg/dL. The spectra of the harmonic components are not significantly large, but slightly larger than those of a (a) low blood glucose level. Concerning the data of (c) high blood glucose level, the true blood glucose level was 160 mg/dL. The spectra of the harmonic components were the largest among the three patterns of glucose levels.

These results indicate that a_{fn} of the harmonic components are large, owing to the high blood glucose level.

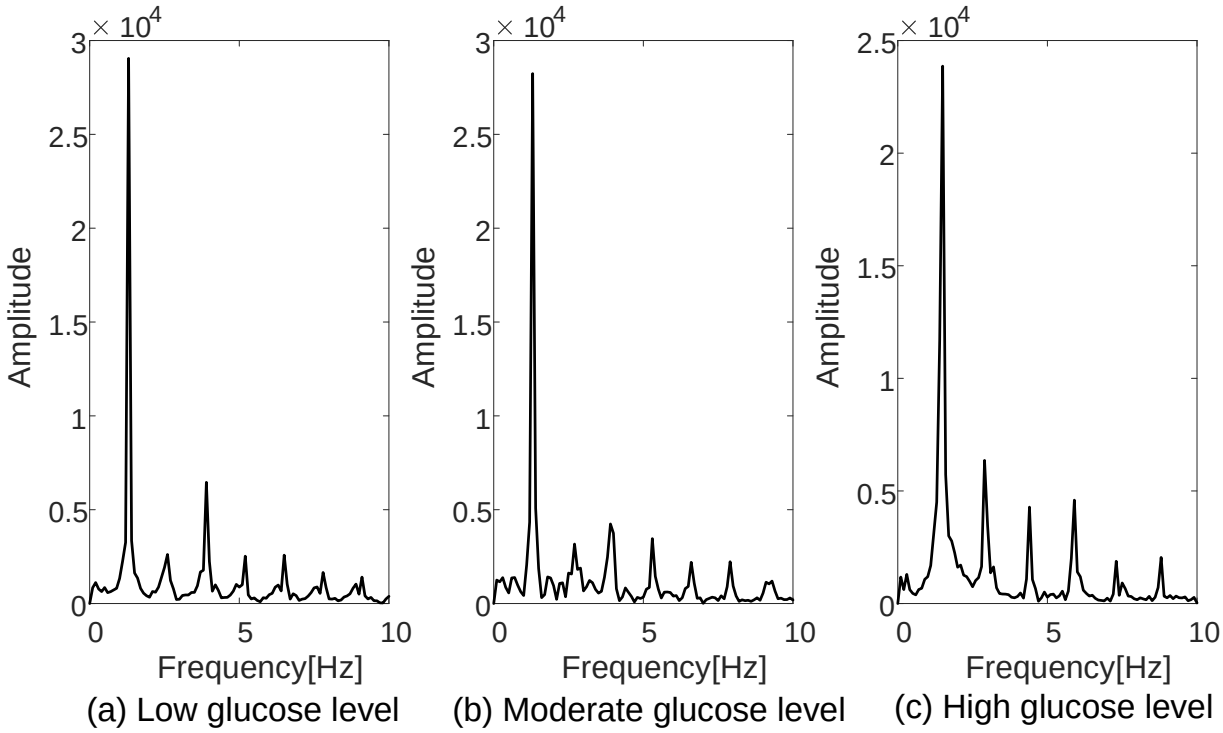


Fig.3 Typical spectra of (a) Low glucose level, (b) Moderate glucose level and (c) High glucose level.

B. Estimation Results

Table.1 shows the *Accuracy* for each combination of harmonic components and extracted intervals. Out of all the combinations, the third harmonic component of the last 10 s achieved the highest *Accuracy* of 0.60. In terms of an average of each harmonic component among all the extracted intervals, the third and the fifth harmonic components together yielded the highest *Accuracy* of 0.47.

Table.1 *Accuracy* of 40 combinations of harmonic components and extracted intervals

	*n*th harmonic component										
	1	2	3	4	5	6	7	8	9	10	Average
First	0.42	0.39	0.36	0.42	0.45	0.51	0.45	0.45	0.42	0.36	0.42
Middle	0.45	0.54	0.48	0.42	0.54	0.42	0.39	0.42	0.42	0.45	0.45
Last	0.45	0.42	**0.60**	0.45	0.48	0.39	0.45	0.45	0.45	0.39	0.45
Overall	0.39	0.42	0.45	0.39	0.39	0.48	0.45	0.39	0.39	0.45	0.42
Average	0.43	0.44	0.47	0.42	0.47	0.45	0.44	0.43	0.42	0.41	

5 Discussion

As stated in the previous section, a_{fn} of the harmonic components are large in the case of high blood glucose level, which validates the model of blood viscosity and harmonic distortion. However, the estimation of blood glucose level was done using a single regression model whose explanatory variable was S_n. As future work, we plan to consider multiple regression analysis for the estimation of blood glucose level.

References

[1] Diabetes Fact Sheet, World Health Organization (WHO), Oct. 2018. (https://www.who.int/news-room/fact-sheets/detail/diabetes)

[2] IDF Diabetes Atlas Eighth Edition 2017, International Diabetes Federation (IDF), 2017. (https://diabetesatlas.org/IDF_Diabetes_Atlas_8e_interactive_EN/)

[3] Andrew J. Berger, T. Koo and I. Itzkan, G. Horowitz, M. Feld, “Multicomponent blood analysis by near-infrared Raman spectroscopy,” *APPLIED OPTICS*, Vol.38, No.13, pp.2916-2926, 1999.

[4] Andrew J. Berger, I. Itzkan and M. Feld, “Feasibility of measuring blood glucose concentration by near-infrared Raman spectroscopy,” *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*, vol.53, issue.2, pp.287-292, Feb.1997.

[5] Ming Xing Chu, K. Miyajima, D. Takahashi, T. Arakawa, K. Sano, S. Sawada, H. Kudo, Y. Iwasaki, K. Akiyoshi, M. Mochizuki and Kohji Mitsubayashi, “Soft contact lens biosensor for in situ monitoring of tear glucose as non-invasive blood sugar assessment,” *Talanta*, vol.83, no.3, pp.960-965, 2