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Evaluation of stationarity of laser Doppler signal in the pulse-based synchronized-averaging analysis

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Abstract—**Pulse parameters calculated from the LDF waveform based on time-domain synchronized averaging analysis were shown to be able to discriminate the difference in microvascular resistance, however its applicability depends seriously on the assumption of signal stationarity. In this study, our aim is to investigate the effect of pulse number, which may destroy the signal stationarity, on the pulse LDF parameters. The study presented here has established the criteria for pulse number to achieve the signal stationarity so that the microcirculatory discriminability of the pulse-based time-averaging analysis on LDF signal can be improved. The proposed quantitative method to verify the assumption of signal stationarity when utilizing time-averaging can also be applied to analysis of other bio-signals.**

I. Introduction

Laser Doppler flowmetry (LDF) is a popular method for monitoring the microcirculation. It has clinical advantages such as noninvasive measurement and rapid response. It has been widely used to monitor the microcirculatory condition in patients with various diseases, such as essential hypertension, chronic renal failure, or diabetes [1-3].

However LDF suffers from its main drawback of providing only a relative quantitative measurement index and thus restricts its practical application [4]. Trying to avoid the drawback of LDF signal stated above, Chao et al. focused on the near-HR (heart rate) band, calculated parameters from the LDF waveform based on a pulse-based time-domain synchronized averaging analysis using heartbeat as a self-trigger, and revealed that these parameters can discriminate the difference in renal microvascular resistance between normal and spontaneously hypertensive rats [1]. In this previous work of Chao et al, the differences of the pulse parameters obtained on the renal cortex between normal rats and SHR are all smaller than 20%.

Although synchronizing averaging can separate a repetitive signal from noise without distorting the signal, its performance depends seriously on the assumption of signal stationarity, which implies that a short data sequence can represent the signal properties for an infinite long signal sequence. Therefore it suffers from many potential factors that may distort the averaged waveform. For example, a pulse number that is not sufficiently large may also lead to deviation of pulse parameters from its actual value, and hence decreased the physiological discriminability of these LDF pulse parameters.

Stability of the LDF signal is suggested to be limited since it is generated from multi-scattering of laser light from red blood cell in a random-motion model. In this study, our aim is to investigate the effect of pulse number on the LDF pulse waveform parameters calculated by time-averaging analysis. By analyzing the data sequence acquired from experiments in healthy volunteers, we try to determine the appropriate range of pulse number to guarantee stability of calculated parameters of pulse LDF waveform so that the microcirculatory discriminability of the pulse-based time-averaging analysis on LDF signal can be improved.

II. Methods and Materials

1. Experimental setup and data acquisition

Analysis was made on 40 5-minute data series measured on 4 healthy volunteers (2 males and 2 females) aged 22 to 23 years old (mean ± SD); Informed consent was obtained from all subjects.

ECG signal were measured by surface electrodes, and acquired by a bio-electrical signal pre-amplifier (lead II, RA-LL; 6600-series, Gould, USA). LDF (MBF3, Moor Instruments, UK) was used for the microcirculatory flux measurement with a sampling frequency of 40 Hz. Both ECG and LDF signals were recorded and sampled simultaneously and synchronously. Both signals were connected to an analog-to-digital converter card (PCI-9111DG, Adlink Technology, Taiwan) at a sampling rate of 1024 Hz to get enough information for the profile of each pulse. Typical ECG and LDF waveforms are shown in Fig.1.

The environmental temperature was kept at 23.0-25.0 ℃. Before and after the LDF measurement, we measured HR, SBP (systolic blood pressure) and DBP (diastolic blood pressure) of the subject to monitor the fundamental physiological condition. After a 10-minute rest for the subject, we began the experiment. The measurement site was on the back of the left hand and between the thumb and the index

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finger (see Fig.2. For each experiment, we recorded a 5-minute data sequence.

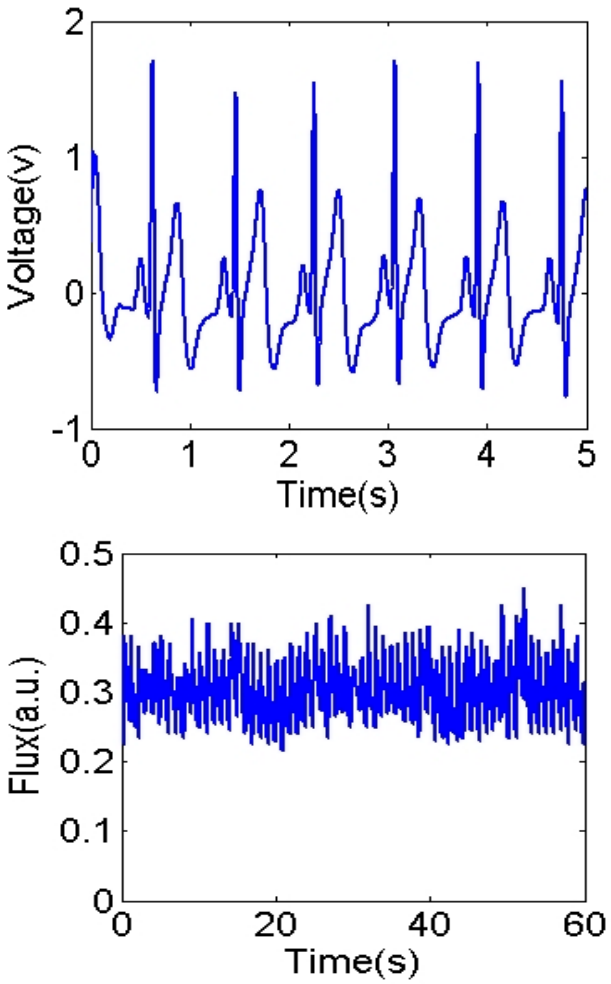

Figure 1: Typical time-domain waveforms. Upper panel: ECG; lower panel: laser Doppler flux signal. There were no obvious fluctuations in the recorded signals.

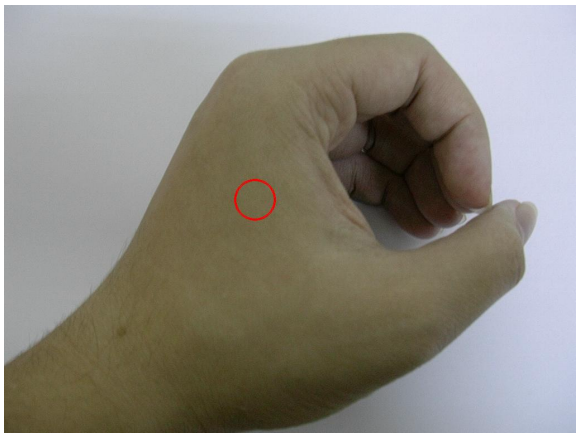

Figure 2: Illustration of measurement site.

2. Signal processing of pulsatile component

Data files with obvious motion artifacts were discarded. The mean, standard deviation (SD) and coefficient of variation (CV; SD/mean) of the HR in each sequence were calculated. In order to be sure that subjects were physiologically stable, chosen data sequences had to satisfy the following criteria: (1) DBP was higher than 60 mmHg; (2) SBP was lower than 130 mmHg; (3) changes of SBP and DBP were smaller than 10 mm-Hg before and after the 5-minute recording; (4) variations of LDF flux signal was smaller than 30%.

In the time-domain synchronized averaging analysis on pulsatile component of the LDF flux, we used the ECG waveform to determine each pulse. The LDF flux signal was filtered by a digital high-pass filter with a cut-off frequency of 0.01 Hz to eliminate the baseline drift. We identified the cardiac component according to the neighboring two R-peaks, and then we cut the LDF flux wave at the same cut point. The cut segments of these signals can be synchronously averaged into one averaged segment (typical LDF waveform can be found in Fig.4) [1].

The pulsatile component of LDF flux signals were acquired and then normalized to the same scale. The following pulsatile time-domain indices were selected as exampled parameters to evaluate the effect on the LDF time-domain averaging analysis:

1. Foot delay time (FDT): time difference between R-peak of the ECG and foot of LDF flux.
2. Peak delay time (PDT): time difference between R-peak of the ECG and maximal points of LDF flux.

Table 1: Physiological parameters in the experiment. Parameters are presented as mean ± SD.

	HR	SBP	DBP
Before	71.79±6.98	111.11±8.94	72.11±6.88
After	70.26±7.63	113.47±8.75	74.05±6.37
p value	0.178	0.132	0.100

Table 2: Average amount of deviation from standard values and numbers of error happening of FDT. STD means standard deviation of FDT deviation. The bottom three rows list numbers of error happening in each percentage range of FDT deviation.

Pulse number	210	180	150	120	90	60
AVERAGE	1.29	2.87	3.28	3.53	4.08	5.17
STD	2.95	8.33	9.95	10.29	8.30	10.81
5-10%	1	2	0	1	3	3
10-20%	2	2	2	1	3	2
>20%	0	1	1	2	2	3

To elucidate the effect on pulsatile LDF parameters, pulse numbers were set at 60, 90, 120, 150, 180, 210 and 240 to compare the different effects on pulse parameters. Within a 5-minute sequence, first we excluded those pulses with a heartbeat length deviated from the average HR for more than 6%, and then we picked the first 240 pulses from these pulses to form a 240-pulse sequence. Pulse parameters calculated from the averaged waveform from these 240 pulses are regards as the standard of comparison. For each 240-pulse data sequence we picked uniformly with equal distance to

form the other pulse sequences. For example, every four pulses in a 240-pulse data sequence, we picked the first pulses to form the 60-pulse sequence.

In the analysis, when one pulse parameter is deviated from the standard value for more than 5%, 10% or 20%, it was regarded as happening of different extent of error. Error percentage (EP) was then defined as the occurring probability of error, that is the number of errors divided by the pulse number. All signal processing was performed with MATLAB (MathWorks, Natick, MA). Two-tailed paired t-test was used to compare the parameters with different pulse numbers, with differences considered as significant when $p < 0.05$.

Table 3: Average amount of deviation from standard values and numbers of error happening of PDT. STD means standard deviation of PDT deviation. The bottom three rows list numbers of error happening in each percentage range of PDT deviation.

Pulse number	210	180	150	120	90	60
AVERAGE	0.49	0.95	1.00	2.47	3.92	4.22
STD	0.87	1.96	2.34	5.97	7.89	10.52
5-10%	0	0	1	1	3	4
10-20%	0	1	1	1	3	1
>20%	0	0	0	2	1	2

III. Results

The basic physiological parameters of HR, SBP and DBP of the experiment are listed in Table 1. There were no significant changes in them before and after the LDF measurement (p all >0.1 by two-tailed paired t-test), which ensures stability of the physiological condition throughout the whole experiment process.

The values and EPs of the pulsatile parameters are listed in Tables 2 and 3, in which we can see that the EPs for all parameters decrease with the pulse number.

When the pulse number is no less than 150, PDT has an EP of 5%. Not until the pulse number is no less than 210, FDT has an EP of no less than 10%. In some cases for both pulse parameters, the calculated value deviated from its standard value for more than 30%.

IV. Discussion

Ideally, if the hemodynamic conditions were all the same and the signal stationary is met throughout the whole measurement process, we only need one pulse to get all these pulse parameters. However we can see from the result in this study that much more pulses is needed to get accurate pulse parameters.

In the analysis, it was revealed that the EP decreases with the increasing pulse number. If we set the acceptable criteria for the EP as 10%, there should be at least 150 pulses for PDT, and 210 pulses for FDT to minimize the possibility of parameter deviations from the actual values.

From Fig.3 we can see the main reason of the parameter deviation. We can see that there are two local minimums near the foot region such that the distortion can therefore take place. It illustrates that determination of the foot point can be seriously distorted by an un-sufficient pulse number.

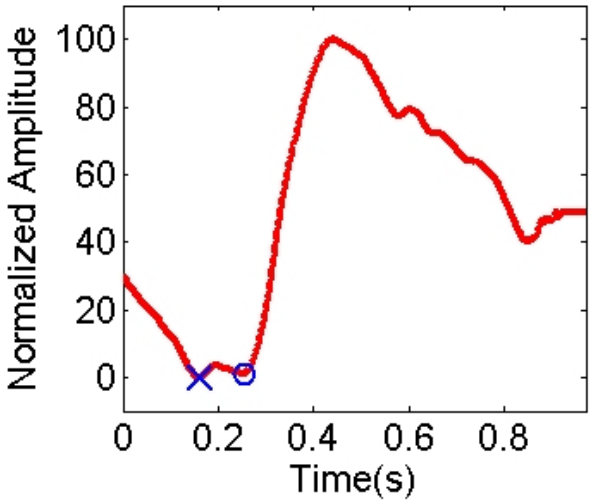

Figure 3: Illustration of waveform distortion caused by un-sufficient pulse number. "x" denotes the estimated location of the foot of the waveform; "o" denotes the accurate location of the foot.

Due to the application advantages including easy implementation, faster calculation, and no requirement for spectral characterization of signal, time-averaging analysis is widely used in analysis on various biomedical signals, such as evoke potential in EEG, heart sound or action potential. Here we propose a quantitative and systematic method to verify the assumption of signal stationarity and to evaluate the effect of potential factors when utilizing time-averaging analysis. This method can be applied to analysis of other bio-signals.

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