A new approach of spontaneous baroreflex sensitivity based on detrended fluctuation analysis: methodology and an application

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Abstract—Cardiac baroreflex function may be assessed from spontaneous fluctuation of systolic arterial pressure (SAP) and R-R interval. In previous studies, time-domain sequence and cross-spectral analysis had been applied to present the baroreflex response of cardiac system. Detrended fluctuation analysis (DFA) is also a promising algorithm to evaluate the fluctuations under various timescales. Thus, we proposed a new approach of spontaneous baroreflex sensitivity (SBR) analysis based on the technique of DFA. Meanwhile, the proposed methodology was applied to analyze the blood pressure signal during the surgery of total knee replacement (TKR) in this investigation. Analysis results show significant differences among the values of SBR under various stages of surgical operations.

***Keywords*—**Cardiac baroreflex function, systolic arterial pressure (SAP), detrended fluctuation analysis (DFA), sensitivity of baroreflex (SBR), total knee replacement (TKR).

I. Introduction

Cardiac baroreflex may be assessed from beat-to-beat fluctuations of systolic arterial pressure (SAP) and R-R interval.

Based on the baroreflex mechanism, baroreflex responses can be traced via sequences of three or more consecutive beats in which SAP and R-R interval changed in the same direction [1-3]. As a different approach of baroreflex response, the cross-spectral analysis of SAP and R-R interval had been proposed to derive the HF and MF gains between spectra of SAP and R-R interval [4, 5]. The beat-to-beat SAP and R-R interval data had been re-sampled at a rate of 4Hz. Furthermore, the trend of re-sampled data had been removed by Hanning window before spectral analysis. The analysis result of cross-spectral analysis shows baroreflex response can be observed in HF gains but not significant in MF gains.

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Obviously, both SAP and R-R interval are nonlinear and non-stationary physiological signals [6, 7]. However, Fourier transform applied in cross-spectral analysis is only suitable for linear systems [8]. Thus, in this investigation, we propose a different approach of evaluating the baroreflex mechanism based on an innovative signal analysis algorithm of detrended fluctuation analysis (DFA). DFA is a signal analysis algorithm applied in nonlinear and non-stationary systems [9]. In DFA, the time series of nonlinear and non-stationary signal is detrened by last square lines and the fluctuation is presented using the root-mean-square (RMS) energy of detrended time series. Different from the spectral analysis, DFA presents the relationship between the fluctuations of detrended time series and the timescales of trends. We proposed that the gain values between the detrended fluctuations of SAP and R-R interval are also a promising factor for evaluating the baroreflex response. Whereas this new analysis algorithm is based on DFA, it is named as DFA-based baroreflex sensitivity analysis.

In this study, we present an application of the DFA-based baroreflex sensitivity analysis in three surgical operations of total knee replacement (TKR). TKR is a common surgery for elder patients. During the process of surgical operation, the blood flow is blocked to reduce the leakage of blood. And, the blocking is relaxed after operation. Thus, we divide the process of TKR surgery to three stages (i.e., before operation, during operation, and after operation). It is obvious that a sequence of bio-chemical and physiological reactions happened during the process of TKR surgery. So, the changes of physiological mechanism are complex and unpredictable. Thus, the aim of this investigation is narrowed down to focus on the response of baroreflex mechanism.

According to the analysis results of DFA-based baroreflex sensitivity analysis, there are significant differences among three stages of surgery. However, the number of study cases is too less to derive a medical conclusion. And, the new approach ignores some critical assumption. Thus, the further investigation of both methodology and clinical applications should be conduct in the future works.

II. Methods

2.1 Spontaneous baroreflex sensitivity (SBR)

Spontaneous baroreflex sensitivity is determined by the ratio between the changes of SAP and R-R interval. The calculation of SBR had originally proposed by Bertinieri et al. and further modified. Basically, the change of SAP triggers the change of R-R interval. The modified method traces the sequences with R-R interval lags of 0, 1, and 2. The heart beat in which SAP affects the R-R interval of the same beat is noted as lag 0. The beats in which SAP affects the following and the next following beats of R-R interval are noted as lags 1 and 2. Sequences of three or more beats in which three lags of SAP and R-R interval changed in the same direction (either increasing or decreasing) were identified as baroreflex responses. Then, linear regression was applied to obtain the ratio between the changes of SAP and R-R interval during baroreflex responses. Thus, the ratio of changes is named spontaneous baroreflex sensitivity.

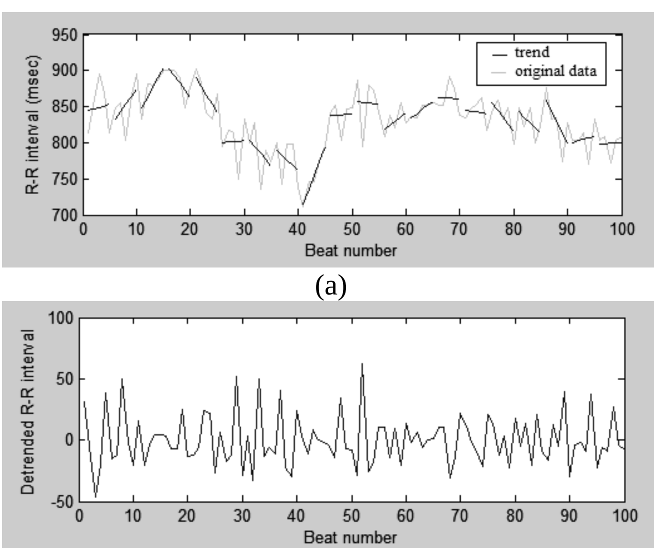
2.2 DFA-based baroreflex sensitivity analysis

The original algorithm of detrended fluctuation analysis (DFA) had been proposed with a simplified detrended operation of using least square lines. In DFA, least square lines are fit to sections of data in the window of the fixed size and present the trend of data. The size of windows is the timescale of detrending operation. Therefore, the trend of data is subtracted from the original data and the rest part of the data is the detrended signal. Furthermore, the fluctuation of detrended signal is calculated using the root-mean-square energy (RMS) and shown as following.

$$F(n) = \sqrt{\frac{1}{N}\sum_{k=1}^{N}\left[y(k) - y_n(k)\right]^2} \quad (1)$$

where $F(n)$ is the fluctuation of an integrated time series for a given window with timescale of n, N is number of heart beats and $y_n(k)$ is the kth point on the trend with a given window with timescale of n.

Fig.1 shows the illustration of a detrending operation. In Fig. 1(a), the straight lines are the least square lines fit to section of the original data. And, Fig. 1(b) shows the detrended data.



(a)

(b)

Fig. 1 The illustration of detrendeing operation. (a) The original data and trend of least square lines. (b) The detrended data.

We can obtain a plot of detrended fluctuation against its corresponding timescale. In Fig. 2, we illustrate an example of the plot of detrended fluctuation against its corresponding timescale. In this plot, we can find that the detrended fluctuation is increasing with timescale.

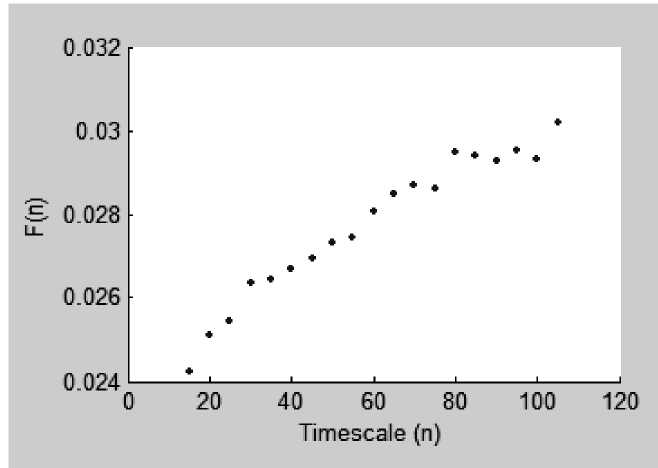
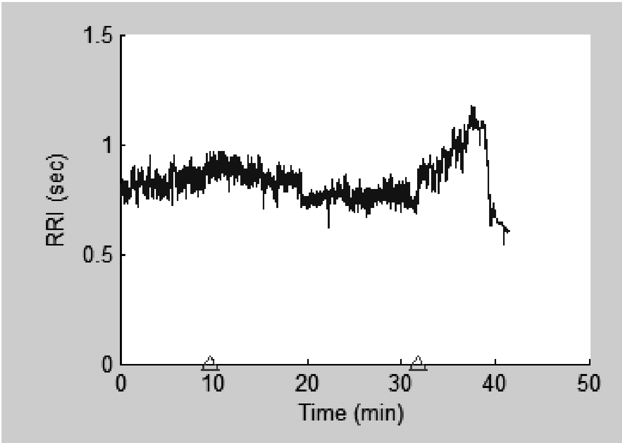


Fig. 2 The plot of detrended fluctuation against its corresponding timescale.

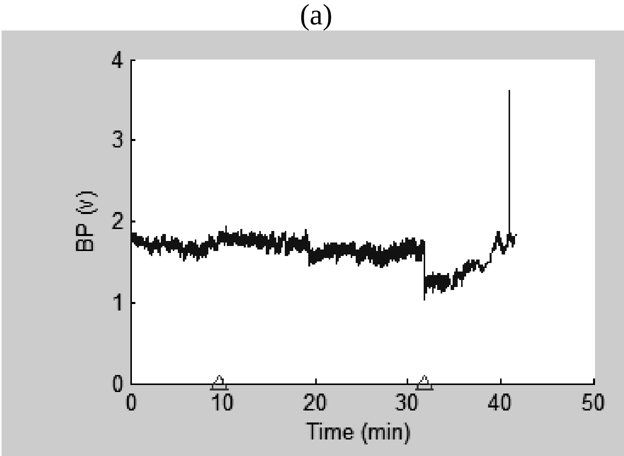
In this investigation, we tried to figure out the baroreflex response according to the detrended fluctuations of SAP and R-R interval. Thus, we conducted the DFA on both time series of SAP and R-R interval. The gain values between detrended fluctuations of SAP and R-R interval on various timescales present the sensitivity of baroreflex response.

III. MATERIAL

In this investigation, the study cases of three total knee replacement (TKR) patients were used as the material for the application of DFA-based baroreflex sensitivity analysis. All of the patients are female and at the age from 61 to 67. Averages and standard deviations of weight and height are 56 ± 5.6 Kg and 142 ± 3 cm. The data of blood pressure was recorded in voltage. And, the data of R-R interval was recorded in second. According to the process of surgery, we divided the recordings of SAP and R-R interval to three stages: they are before-operation (stage 1), during-operation (stage 2), and after- operation (stage 3). We captured a section of recoding under the situation of steady state to present the data of each stage. In Fig.3, the data of SAP and R-R interval for one out of the three patients were shown to present the raw data for our investigation.



(a)



(b)

Fig. 3 The data of SAP and R-R interval for one out of the three patients in this investigation. (a) The R-R interval; (b) The SAP.

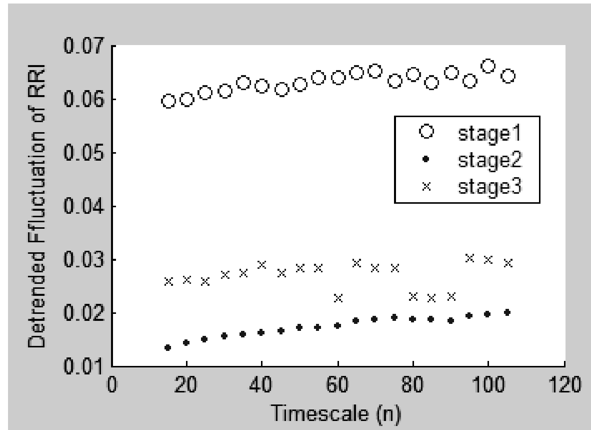
In Fig.3, time is shown in a continuous sequence. However, as mentioned above, we captured a section of recording under a steady state to present the data of each stage and combined to a continuous data. Therefore, the data includes three stages and the boundary between two consecutive stages was marked by triangles. In this case, we can find the SAP at stage 2 is bigger than that at stage 1 and the blood pressure dropped down when the operation was completed and blocking of blood flow was relaxed.

IV. RESULTS

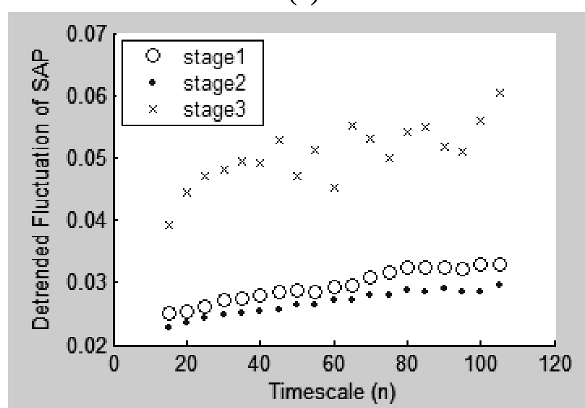
The analysis results were presents in three parts. In the first part, we presented a complete analysis result for one out of the three cases. We also presented the final results of three cases in the second part. Finally, we make a table and take a comparison among the analysis results of three cases.

Fig. 4 shows a complete analysis result for one study case. Fig. 4(a) shows the detrended fluctuations of R-R interval against their corresponding timescale for three stages. The scale of fluctuations of R-R interval at stage 1 is bigger than those at the other two stages. However, Fig. 4(b) shows a different result for SAP. We found the fluctuation of SAP at stage 3 is bigger than those at the other two stages. Moreover, Fig. 4(c) shows the final gain values between SAP and R-R interval. In this case, the fluctuation of R-R interval is strong and the gain value shows a more sensitive baroreflex response at stage 1. Moreover, the gain values are low at both stages 2 and 3. It presents a lower sensitivity of baroreflex response at stages 2and 3.

Additionally, we conducted the same analysis to the second and third cases. The analysis results are shown in Fig. 5.



(a)



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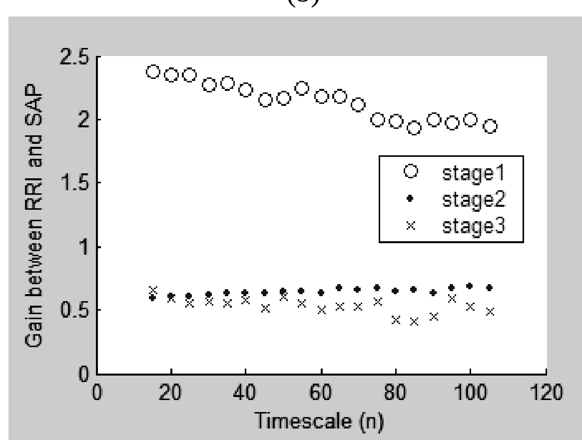
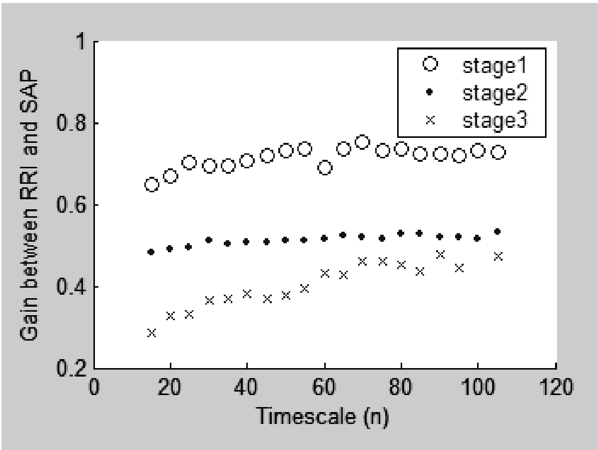


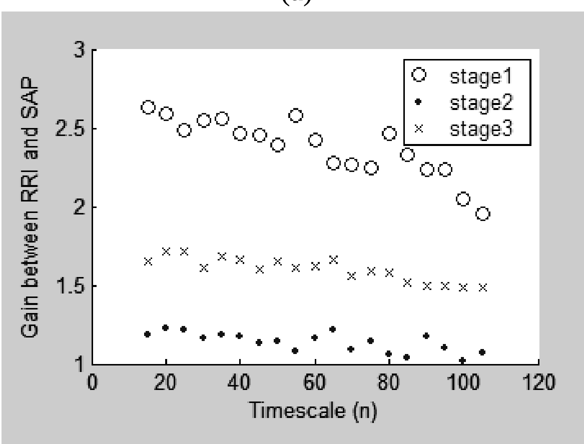
(c)

Fig. 4 A complete analysis result of one patient. (a) The plot of detrended fluctuation of R-R interval. (b) The plot of detrended fluctuation of SAP. (c) The gain values of fluctuation between R-R interval and SAP.

The analysis results of the other two cases are similar to those of the first case. The gain values at the stage 1 are always bigger than those at the other two stages. For different cases, the gain values distribute on various range. It shows the individual property of baroreflex mechanism.



(a)



(b)

Fig.5 Analysis results for the other two patients. (a) Result for the second patient. (b) Result for the third patient.

Furthermore, we made a table to show the final results of three cases. The gain values are shown in average and standard deviation. The values at stage 1 are significantly different from those at the other stages. But, the difference between stages 2 and 3 is not significant.

Table 1 The gain values between fluctuations of SAP and R-R interval at different stages.

	Stage 1	Stage 2	Stage 3
Patient 1	2.15 ± 0.14	0.64 ± 0.03	0.54 ± 0.06
Patient 2	0.71 ± 0.02	0.51 ± 0.01	0.41 ± 0.11
Patient 3	2.38 ± 0.18	1.13 ± 0.06	1.60 ± 0.07

V. Conclusions

In this study, we proposed a different approach of baroreflex response analysis. And, this approach is based on the technique of DFA. Moreover, we applied this new method to find some significant differences among the stages of TKR surgery. We also found the changes of variability of R-R interval and SAP in various stages. But, we have one critical problem unsolved in this investigation. The problem is how to identify the sequences of heart beats which satisfy the definition of baroreflex response.

In the original method of time-domain sequence analysis, only the sequences of beats satisfying a criterion of baroreflex response are included to verify the spontaneous baroreflex sensitivity. The criterion is that sequence of beats in which the SAP and R-R interval changed in same direction on lags of 0 to 2 for 3 or more beats is counted as a sequence of beats for baroreflex response and included in calculation. For the cross-spectral analysis, just the frequencies on which the coherences between SAP and R-R interval are higher than a threshold are included to calculate the gain value. However, we have no criterion to exclude the heart beats which are not satisfied the definition of baroreflex response. We should conduct a further study on this problem in the future investigation.

VI. Future work

As a preliminary study, we proposed a new approach of spontaneous baroreflex response analysis based on DFA. However, there is a problem unsolved in the algorithm. We should take further modification to improve the methodology. On the other hand, we will collect more cases and survey various analysis algorithms to extend our investigation.

References

[1] Fritsch JM, Eckberg DL, Graves LD, Wallin BG. Arterial pressure ramps provoke linear increases of heart period in human, *Am. J. Physiol.* 1986; 251: R1086-R1090.
[2] Bertineri G, Di Reinzo M, Cavallazzi A, Ferrari AU, Pedotti A, Mancia G. Evaluation of baroreceptor reflex by blood pressure monitoring in unanesthetized cats. *Am. J. Physiol.* 1988; 254:H377-H383.
[3] Blaber AP, Tamamoto Y, Hughson RL. Methodology of spontaneous baroreflex relationship assessed by surrogate data analysis. *Am. J Physiol* 1995; 268:H1682-H1687.
[4] Hughson RL, Quintin L, Annat G, Yamamoto Y, Gharib C. Spontaneous baroreflex by sequence and power spectral methods in human. *Clin Physiol* 1993; 13:663-676.
[5] Pagani M, Somers V. Furlan R, Dell Orto S, Conway J, Baselli G. Changes in autonomic regulation induced by physical training in mild hypertension. *Hypertension* 1988; 12:600-610.
[6] Huang NE, Shen Z, Long SR, Wu MC, Shih HH, Zheng Q, Yen NC, Tung CC, Liu HH. The empirical mode decomposition and Hilbert spectrum for nonlinear and

non-stationary time series analysis. *Proc. R. Soc. Lond.* A(1998); 454:903-995.

[7] Costa M, Goldberger AL, Peng CK. Multiscale entropy analysis of complex physiologic time series. *Physical review letters*, 2002; vol. 89; No. 6.

[8] Brockwell PJ, Davis RA. Time series: theory and methods. New York : Springer,1991.

[9] Goldberger AL, Amaral LAN, Hausdorff JM, Ivanov PCH, Peng CK, Stanley HE. Fractal dynamics in physiology: Alterations with disease and aging. *Proc Natural Acad. Sci. USA*, 2002; 99:2466-2472.