Proceedings of the 2005 IEEE
Engineering in Medicine and Biology 27th Annual Conference
Shanghai, China, September 1-4, 2005

Sensitivity of detrended fluctuation analysis applied to heart rate variability of preterm newborns

Geert Morren[1], Philippe Lemmerling[1], Hans Daniëls[2], Gunnar Naulaers[2], Sabine Van Huffel[1,*]

[1]Department of Electrical Engineering (ESAT/SCD), Katholieke Universiteit Leuven, Leuven, Belgium
[2]Department of Paediatrics, University Hospital Gasthuisberg, Katholieke Universiteit Leuven, Leuven, Belgium
[*] E-mail: sabine.vanhuffel@esat.kuleuven.ac.be

Abstract–**Detrended fluctuation analysis (DFA), a fractal analysis method which is widely used in heart rate variability (HRV) studies, is used to analyze the scaling behaviour of RR interval series of preterm neonates. The average scaling behaviour, calculated using 30000 RR intervals (3 - 4 hours), is characterized by a scaling exponent of 1.4 ± 0.1 at small scales ($n \leq 20$) and a smaller exponent of 1.0 ± 0.1 at larger scales. It is shown that the scaling behaviour is not constant over such long segments and how heart rate patterns, associated with specific physiological mechanisms, contribute to the observed variation of the scaling exponents. The effect of the two most important patterns, spikes (either due to faulty peak detection or true decelerations in heart rate) and periodic fluctuations, on the scaling behaviour is investigated.**

Keywords– **Heart rate variability, RR interval series, tachogram, detrended fluctuation analysis, fractal.**

I INTRODUCTION

Detrended fluctuation analysis (DFA), a method that characterizes power-law scaling in the time-domain, is widely used in HRV analysis since it is considered to be robust and to correctly identify long range correlations in certain types of non-stationary time series [1] (see [2] for a list of references). The scaling exponents α obtained with DFA are reported to have diagnostic and prognostic value for patients with various types of cardiac diseases. A recent study, on a small group of patients, suggests that the DFA scaling exponents allow the discrimination of normal neonates from neonates having experienced an apparent life threatening event (ALTE), which are considered to be at increased risk for sudden infant death syndrome (SIDS) [3]. The DFA scaling exponents are also reported to be dependent on a number of confounding factors such as age, gender, body position [4], physical activity level (rest vs. exercise) [4], sleep stages [5], etc. So far, the observed changes in scaling exponents have usually only been interpreted in terms of changes in correlation properties, without establishing the underlying physiological mechanisms. The main goal of the present paper is to contribute to the understanding of the performance of DFA and its interactions with physiological signals. The time variation of the scaling exponents in continuous heart rate recordings is assessed using a method based on surrogate data. It is shown how specific physiological mechanisms contribute to the observed variation of the scaling exponents. Although the results are based on the analysis of neonatal heart rate data, the methodologies and findings are also useful for the interpretation of the DFA results obtained from other signals.

II MATERIALS AND METHODS

A. Neonatal heart rate data

The heart rate data used in this study were obtained from polysomnographies of 12 preterm infants with post-menstrual age between 31 and 39 weeks (mean: 35 weeks), recorded between 1 and 5 weeks after birth (mean: 3 weeks) at the University Hospitals Gasthuisberg, Leuven, Belgium. During the polysomnographies, the following parameters were measured: ECG, respiratory movements, nasal flow, arterial oxygen saturation, EMG (chin), EOG and EEG. The RR interval series were derived from the ECG signals, which were sampled at 1000 Hz, by a peak detection algorithm using the second order derivatives of the ECG. Consequently, all RR interval series were checked for false and/or missed peaks, and corrected if necessary. The length of each time series was between 30000 and 75000 RR intervals (mean: 55000). Figure 1(a) shows one example of neonatal RR interval series. It can be noted that the mean heart rate of neonates is approximately 150 bpm (2.5 Hz), corresponding to a mean RR interval of 0.4 s, which is higher than in adults.

B. Detrended fluctuation analysis

The DFA algorithm, used to quantify the scaling behaviour of a time series was first described in [1]. The time series (total length N) is first integrated and divided in segments of length n. Each segment is then detrended by subtracting the best linear fit. Finally, the fluctuation function $F(n)$ is calculated as the root mean square of the detrended time series as a function of the segments size n. If the time series is self-similar, the fluctuation function $F(n)$ increases by a power-law: $F(n) \propto n^{\alpha}$. The scaling

0-7803-8740-6/05/$20.00 ©2005 IEEE.

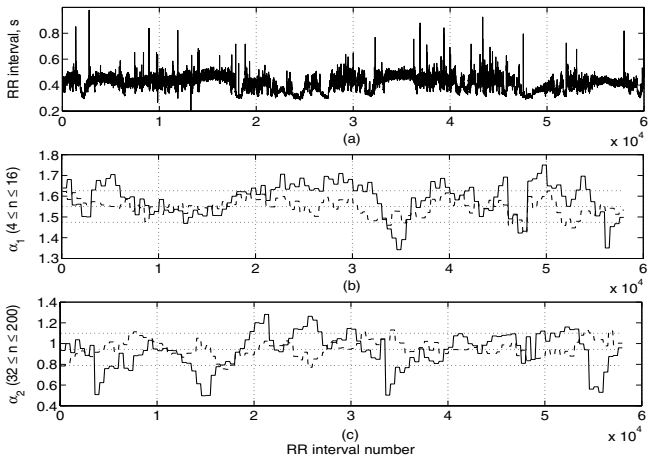


Figure 1. (a) RR interval series and scaling exponents (b) α_1 ($4 \leq n \leq 16$) and (c) α_2 ($32 \leq n \leq 200$) calculated over segments of length $N = 2000$ as a function of time. The horizontal dotted lines in (b) and (c) represent the mean scaling exponent of the surrogate data, and the mean $\pm$ 2 $\times$ standard deviation.

exponent α can be estimated by a linear fit on the log-log plot of $F(n)$ versus n. The scaling exponent α represents the correlation properties of the signal: if $\alpha = 0.5$, the signal is uncorrelated (white noise); if $\alpha < 0.5$, the signal is anticorrelated (negative correlations); if $\alpha > 0.5$, there are positive correlations in the signal.

III TIME VARIATION OF SCALING BEHAVIOUR

The average scaling behaviour, calculated by applying DFA on the whole RR interval series of Fig. 1(a) (N=60000), is characterized by a scaling component $\alpha_1 = 1.57$ up to scales around $n = 20$ and a smaller slope $\alpha_2 = 0.95$ at larger scales, as shown in Fig. 2. The scaling behaviour of the other RR interval series, included in our study, also has a comparable shape, consisting of a steep slope (1.4 ± 0.1) up to scales around $n = 20$ followed by a smaller slope (1.0 ± 0.1) at larger scales. The average scaling exponent at small scales is larger than the short-term scaling exponents reported in the literature for healthy children or adults [6].

In order to distinguish the true time variation of the scaling exponent(s) describing the scaling behaviour, from statistical fluctuation of estimates across time of a constant exponent, an approach based on the technique of (amplitude adjusted) surrogate data is used [7]. In order to assess the time variation of the scaling exponents, the complete RR interval series were divided into shorter segments on which DFA was applied. The segment size was determined as a compromise between the need to track rapid changes (short segments) and the need for accurate estimates (longer segments). One possible source of nonstationarity in the fractal properties which is already described in literature is related to different sleep stages [5]. Therefore, the choice of the segment size was based on the length of the quiet sleep segments, which is on average 2000 RR intervals for our recordings. Hence, segments of length $N = 2000$ were used for DFA, with an overlap of 1500 points between consecutive segments. Visual inspection of the fluctuation functions revealed a downward crossover (a change from a steep slope to a smaller slope) around scale $n = 20$ in most segments (of the different sleep stages). Therefore, two scaling exponents were estimated as a linear fit over a specific scaling range for each segment: α_1 on short scales ($4 \leq n \leq 16$) and α_2 on intermediate scales ($32 \leq n \leq 200$).

Figure 1 shows a neonatal RR interval series consisting of 60000 RR intervals (a), together with the scaling exponents α_1 and α_2 as a function of time, respectively in (b) and (c). In each figure, the scaling exponents calculated on one surrogate data set are also shown (dashed line). The horizontal dotted lines represent the mean scaling exponent of the surrogate data, and the mean $\pm$ 2 $\times$ standard deviation. The range of both α_1 and α_2 calculated on the real data is much wider than that calculated on the surrogate data. For α_1, almost half the estimates on the real data are outside the mean $\pm$ 2 $\times$ standard deviation range. For α_2, the number of points outside this range is somewhat smaller, but there are some remarkable large decreases. Comparing these with the RR interval series, it is clear that these low α_2 values (around 0.5) correspond to the quiet sleep stages. Since similar observations hold for the other RR interval series, it is clear that neither α_1 nor α_2 can be considered stationary over the whole RR interval series. Furthermore, the same approach applied to parts of RR interval series without quiet sleep segments suggests that, in some cases, the scaling exponents can not be considered stationary in between quiet sleep segments either. Therefore, we will first study how spikes and periodic components affect the scaling behaviour estimated with DFA on segments of 2000 points, which will allow us to explain partly the observed variability in scaling exponents.

IV SPIKES

Some (neonatal) RR interval series contain spikes, as shown in Fig. 1(a). Two kinds of spikes are considered: spikes due to faulty peak detection (missed RR peak or false detection) and true decelerations of the heart rate.

The effect of 0.1% missed peak on the scaling behaviour of the RR interval series of Fig. 1(a) is shown in Fig. 2. Hence, in order to get reliable estimates of the scaling exponents of RR interval series, especially on small scales, very good peak detection is necessary. Furthermore, since certain cardiac arrhythmias such as premature beats result in similar spikes, these should be removed before

applying DFA.

The spikes shown in Fig. 1(a) are not due to faults in the peak detection, but are actually short decelerations in heart rate. Their effect on the smallest scales ($n < 16$) is smaller than that of the spikes due to faulty peak detections but they also affect larger scales (up to $n = 150$). To get an idea of the average effect of the decelerations on the scaling exponents, the decelerations were removed from the RR interval series shown in Fig. 1(a). To this end, a simple algorithm that replaced the RR intervals exceeding 120% of the average of the surrounding RR intervals by interpolation was used. For the example of Fig. 1(a), this procedure resulted overall in 0.5% of 'corrected' RR intervals. The scaling exponents estimated on the 'corrected' RR interval series as a function of time were compared to those of estimated on the original time series, as shown in Fig. 1(b-c). It can be noted that, on average, the decelerations decrease the estimates of both scaling exponents α_1 (from 1.64 to 1.59) and α_2 (from 0.99 to 0.93). Other RR interval series with large number of decelerations yield comparable results, which can be explained qualitatively by the fact that, on average, the decelerations cause an increase in the fluctuation function $F(n)$ which is maximal at very small scales and decreases towards larger scales. This effect is also observed in Fig. 2, where the fluctuation functions, calculated on the complete RR interval series of Fig. 1(a)(after removal of the decelerations) are compared. On very large scales ($n > 200$), the effect of the decelerations on the scaling behaviour is negligible.

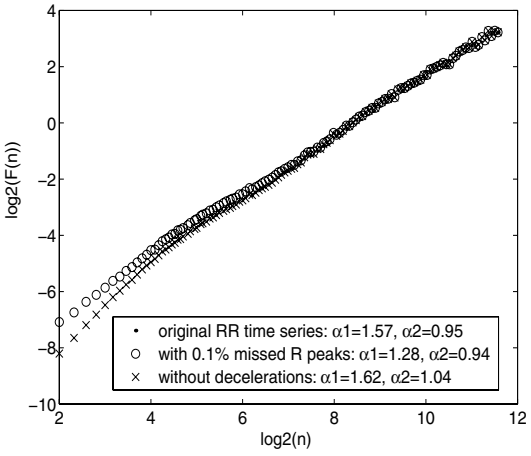


Figure 2. Effect of spikes and decelerations on the scaling behaviour of RR interval series. Comparison of the fluctuation functions calculated on the complete RR interval series of Fig. 1(a), the same time series with 0.1% spikes added and the same RR interval series where the decelerations have been removed.

V PERIODIC FLUCTUATIONS

Sinusoids, and other periodic components, lead to a (positive) deviation from the scaling behaviour of the exact fractal signal in a range of scales around the period of the fluctuation [2]. The deviation can be characterized by two upward -indicating the beginning and the end of the deviation- and one downward crossover at a scale corresponding to the period of the fluctuation, as shown in Fig.3(c). The range of scales over which this deviation extends (i.e. the scales where the upward crossovers occur), increases with increasing amplitude of the periodic fluctuations. In this section, the effect of the two most common periodic fluctuations, i.e. Respiratory Sinus Arrhythmia (RSA) and 10s rhythm, on the scaling behaviour of neonatal RR interval series are discussed.

RSA is the periodic fluctuation of the heart rate

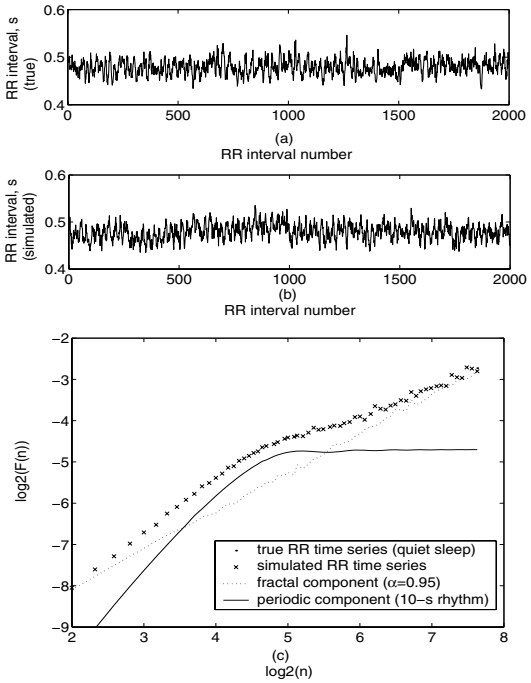


Figure 3. (a) segment of 2000 RR intervals during quiet sleep, (b) simulated RR interval series during quiet sleep, (c) scaling behaviour of the true RR interval series, the simulated RR interval series, and the fractal and periodic components of the simulation.

related with the respiration. The effect of RSA on two segments of different sleep stages was studied (not shown here). As expected, RSA affects the fluctuation function only at small scales ($n < 20$). Using the superposition principle it is easy to see how this effect varies with the strength and the frequency of RSA. Since RSA is not always present, the effect on the global scaling behaviour (calculated over the complete RR interval series) will in general be smaller than that on the segments of 2000 RR intervals.

Figure 3(a) shows a quiet sleep segment of 2000 RR intervals from Fig. 1(a), in which the '10s-rhythm', the cyclical fluctuations with a period around 30 RR intervals, can be observed. Since we cannot simply filter these fluctuations out (this would also remove the fractal content in the corresponding scaling region), the effect of the 10s-rhythm on the scaling behaviour was studied using a simulated RR interval series. An ideal fractal signal, generated with the spectral synthesis method (or Fourier filtering method) [8] with $\alpha = 0.95$, was superimposed onto a sinusoid with a period of 12 s. The amplitude of both components was adjusted so that the scaling behaviour of the resulting signal closely resembled that of the real RR interval series. Figure 3(b) shows that not only the scaling behaviour but also the simulated time series itself is very similar to the real RR interval series. Figure 3(c) shows the fluctuation functions of the real and the simulated RR interval series, and the two components of the simulated time series separately. The periodic component affects the scaling behaviour strongly at all scales. Despite the good linearity of the fluctuation function in the range $32 \leq n \leq 200$, the estimated scaling exponent $\alpha_2 = 0.65$ does not reflect the scaling properties of the underlying fractal signal ($\alpha = 0.95$). It is clear that, due to the 10s-rhythm, it is impossible to determine the scaling exponent of the fractal component by applying DFA on segments of $N = 2000$ RR-intervals, although the power (variance) of both components is approximately equal.

During other sleep stages, the 10s-rhythm is also present, but less marked since the variability on all scales is larger. The larger variability on all scales (in comparison to the 10s-rhythm) results in a smoother crossover in the scaling behaviour (smaller difference between α_1 and α_2). However, although in this case the power of the periodic fluctuations is only 10% of the total power of the signal, the scaling behaviour is still affected by the periodic fluctuations up to large scales ($n = 200$). On very large scales ($n > 200$), the scaling exponent does correspond to the underlying fractal signal.

Non-nutritive sucking (NNS) and periodic breathing (PB) both introduce periodic fluctuations in the RR interval series similar to the 10s-rhythm [2]. They have a similar effect on the scaling behaviour, but NNS and PB are usually only present during a relatively small percentage of the total recording time, respectively up to 10% and 20%.

VI CONCLUSIONS

The scaling behaviour of neonatal RR interval series was analyzed using DFA. Using an approach based on surrogate data, it was shown that the scaling exponents can not be considered as constant over these long segments (30000 RR intervals). Therefore, DFA was applied to segments of 2000 RR intervals in order to calculate the scaling exponents at short (α_1, $4 \leq n \leq 16$) and intermediate (α_2, $32 \leq n \leq 200$) scales as a function of time. Our analysis shows that scaling exponents calculated on predefined scaling ranges, especially in the neighborhood of a crossover in the fluctuation function, might not reflect the correlation properties of the fractal component of the signal. The presence of spikes and/or periodic fluctuations in the RR interval series should be assessed. While spikes are easily detected and can be removed, this is not the case for periodic fluctuations. It is therefore necessary to analyze the complete fluctuation function and take into account the possible effect of periodic fluctuations in order to determine an appropriate scaling range.

ACKNOWLEDGEMENTS

This research is sponsored by the Research Council of the K.U.Leuven (GOA-AMBioRICS), the Flemish Government (FWO: projects G.0360.05, research communities ICCoS & ANMMM), the Belgian Federal Government (DWTC: IUAP V-22 (2002-2006)), and the EU (BIOPATTERN: contract FP6-2002-IST 508803).

REFERENCES

[1] C. Peng, S. Havlin, H. Stanley, and A. Goldberger, "Quantification of scaling exponents and crossover phenomena in nonstationary heartbeat time series," *Chaos*, vol. 5, no. 1, pp. 82–87, 1995.

[2] G. Morren, *Advanced signal processing applied to in-vivo spectroscopy and heart rate variability*. PhD thesis, K.U.Leuven, 2004.

[3] P. Lemmerling, S. Van Huffel, G. Naulaers, H. Daniëls, and H. Devlieger, "Nonlinear analysis of heart rate variability in infants with apparent life-threatening events.," *Adv Exp Med Biol.*, vol. 510, pp. 369–373, 2003.

[4] M. Tulppo, R. Hughson, T. Mäkikallio, K. Airaksinen, T. Seppänen, and H. Huikuri, "Effects of exercise and passive head-up tilt on fractal and complexity properties of heart rate dynamics.," *Am J Physiol Heart Circ Physiol.*, vol. 280, no. 3, pp. H1081–1087, 2001.

[5] T. Penzel, J. Kantelhardt, L. Grote, J. Peter, and A. Bunde, "Comparison of detrended fluctuation analysis and spectral analysis for heart rate variability in sleep and sleep apnea.," *IEEE Trans Biomed Eng.*, vol. 50, no. 10, pp. 1143–1151, 2003.

[6] S. Pikkujämsä, T. Mäkikallio, L. Sourander, I. Räihä, P. Puukka, J. Skyttä, C. Peng, A. Goldberger, and H. Huikuri, "Cardiac interbeat interval dynamics from childhood to senescence : comparison of conventional and new measures based on fractals and chaos theory.,"

[7] B. Pilgram and D. Kaplan, "Nonstationarity and 1/f noise characteristics in heart rate," *Am J Physiol. 276 (Reg, Int, and Comp Physiol.)*, vol. 45, no. 1, pp. R1–R9, 1999.

[8] H.-O. Peitgen and D. Saupe, eds., *The science of fractal images*. Springer-Verlag, 1988.