Editing RR Series and Computation of Long-Term Scaling Parameters

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Abstract

The editing of heart rate variability (HRV) sequences is largely employed in presence of biological (ectopies, arrhythmias) and technical artifacts. Little is know about the effects of these corrections on the estimation of the long-term scaling exponents, especially for long artifacts. We therefore investigated the robustness of three popular scaling exponent estimators (DFA, α-slope and Dispersional Analysis) with an increasing number of missing RR samples. We tested three editing methods: (i) substitution with local mean value, (ii) linear interpolation and (iii) deletion. Starting from long uncorrupted (> 10000 points) NN series, we artificially inserted artifacts. We then evaluated the effect of the editing methods on the estimation of the scaling exponents. As a reference, the same computation was performed simply removing an equivalent number of points at the extreme of the series. The simulations suggest a negligible effect of the corrections, at least as long as the number of points edited is relatively small.

1. Introduction

Long term analysis of Heart Rate Variability (HRV) obtained from 24-hour ambulatory ECG recordings was shown to provide prognostic information, in particular for post-infarction risk stratification [1, 2]. Today, the literature seems to suggest that the usage of metrics describing the long-memory characteristics of the heart rate might be mature. Still a few related issues need to be investigated.

In an acquisition process lasting many hours, movements, sweating or electrodes detachments often corrupt the ECG signal and may introduce gaps in the RR sequences. Furthermore ventricular and supraventricular ectopic beats generate disturbances which need to be removed to study heart rate variability and infer conclusions on the autonomic nervous system activation. When the focus is on short-term variability, the first problem is usually avoided by simply selecting intervals free of missing beats; the second one is routinely treated with linear interpolation as long as the number of ectopies is small. But in dealing with 24-hours recordings, gaps a few minutes long can only be avoided by excluding completely the corrupted ECG from the study unless editing techniques are employed to replace the missing intervals.

While the wealth of studies on time series correction for the subsequent application of linear parameters is large [3–5], when considering long-term scaling parameters, the impact of corrections is still debated. Chen et al. [6] tried to address the issue applying a technique called "detrended fluctuation analysis" (DFA) to fractional Brownian motion (a signal theoretically known to exhibit a long-term scaling behavior) and reported that in most cases randomly removing segments of signal did no significantly changed the value of the estimated scaling parameters. Peltola et al. [7] found that, with respect to DFA's long-term scaling exponents, deletion and local interpolation of premature beats were equivalent for an amount of corrections $< 5\%$ on 8000 points long NN series. Similarly Salo et al. [4] working on RR Holter series found that up to 5% of the data could be deleted without a significant error on long term power-spectral components. Finally, a larger pool of non-linear indexes was consider by Tarkiainen et al. [8] who analyzed the effects of editing ectopic beats on 40 minutes recordings and called for standardized editing practices.

In this paper we tested the consistency of popular estimators, which are typically employed to characterize by mean of a scaling exponent the long memory behavior of HRV, when gaps and artifacts are taken into account. In particular, with respect to previous works [4, 8], which focused on the correction of ectopic beats, our interest is extended also to evaluate the feasibility of long-term scaling estimations in presence of larger gaps of unavailable measurements. The effects of three common RR editing techniques will be investigated.

2. Methods

Dataset. We analyzed 68 high quality Holter recordings. All recordings had at least 15.6h of ECG data and the average duration was 22.5 ± 1.6h. The population age ranged

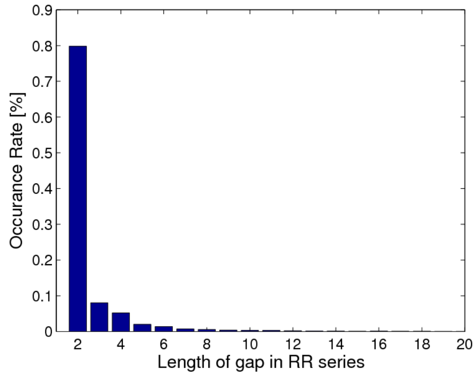

Figure 1. Probability density function of the runs of consecutive intervals which were marked as artifacts or ectopic. The function was estimated from the anomalous beats contained in 68 Holter recordings.

from 20 to 90 years and included normal subjects. A more detailed description of the population can be found in [9].

Data Analysis. The Holter recordings were analyzed using an automatic labeling software. Under the supervision of a trained physician, the labeling procedure produced an annotated RR series for each recording. Among the RR series, we firstly selected the 20 longest segments fulfilling the following two criteria: i) the series were composed of NN intervals only; ii) each NN interval didn't change more than 20% with respect to the preceding NN interval [10]. The length of the selected sequences was 19213 ± 7017 beats, with range $[11286 - 34774]$. These sequences were the longest NN sequences which were also free of gaps and ectopic beats. They will be referred to as *reference series* in the following; they came from 20 different subjects.

The sample histogram of the number of consecutive not normal beats (which were found in 68 Holter recordings) was used to estimate the probability density function (pdf) of the length of the gaps encountered in our dataset. The function is shown in Figure 1. The figure of not normal beats ranged from a minimum of 0.05% to a maximum of 12.7%, being the latter most of an exceptional case than the rule (median: 0.62%, 25 percentile: 0.30%, 75 percentile: 1.92%). As expected, most of the gaps involve two consecutive RR intervals (i.e. ectopic beat and subsequent compensatory longer interbeat interval) but longer runs involving tens of beats may also occurs. Please note that the tail of the distribution is quite "heavy" and about 0.9% of the runs of not normal beats are longer than 20.

In each of the 20 *reference series* several NN intervals were marked as not normal (thus generating "artificial" gaps). The number of such interval ranged from a minimum of 0.5% of the length of the series to a maximum of 5%, covering an extent of practical interest. While the lengths of the gaps were drawn from the pdf in Figure 1, their locations were uniformly distributed over the series,

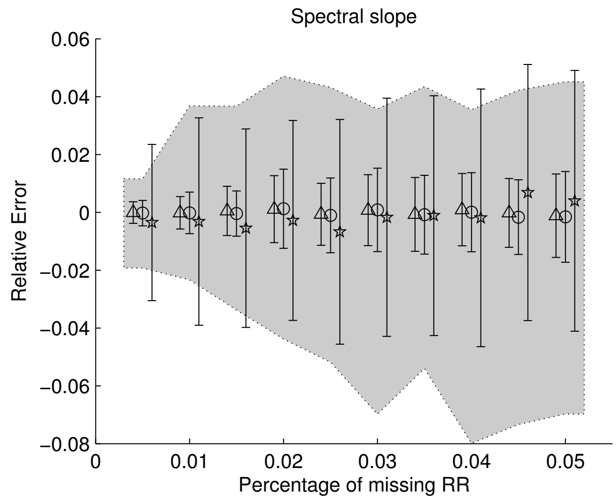

Figure 2. Relative errors on the estimate of the spectral-slope α. The values of α computed on the reference series were compared with the values obtained after marking as anomalous a portion of the interval and a subsequent editing performed with: i) substitution with local mean value (M, triangle); ii) linear interpolation (LI, circle) and iii) deletion (D, star). For each of the 20 reference series and for each percentage of removed intervals, the procedure was repeated 20 times to reach statistical consistency. The values relative to each subject were then averaged and the mean value and the standard deviation collected. Finally, the values reported in the plot are the average of the mean values and standard deviations across the 20 different reference series. The light gray area was instead obtain with the same process but removing intervals from the head and the tail of the series and no subsequent editing. It gives a rough estimation of the standard deviation of the slope of the spectrum.

ensuring that they did not overlap.

The not normal interval in the reference series were then edited as if they were actual anomalous beats. Three editing techniques, routinely employed when computing linear indexes, were considered. We briefly sketch them here.

i) *Linear interpolation* (LI): the number of NN intervals to insert was computed [3] as

$$B = \frac{2\sum_{j=i}^{i+M} \mathrm{RR_j}}{\mathrm{RR_{i-1}} - \mathrm{RR_{i+M+1}}}, \tag{1}$$

where the intervals $\mathrm{RR_j}$ with $j \in [1, M]$ are the ones marked as anomalous. A run of B intervals was then inserted; their lengths were computed with linear interpolation using $\mathrm{RR_{i-1}}$ and $\mathrm{RR_{i+M+1}}$ as endpoints of the line.

ii) *Substitution with local mean value* (M): the number B of intervals to be inserted was computed with equation (1). The interval length was set by computing the local mean

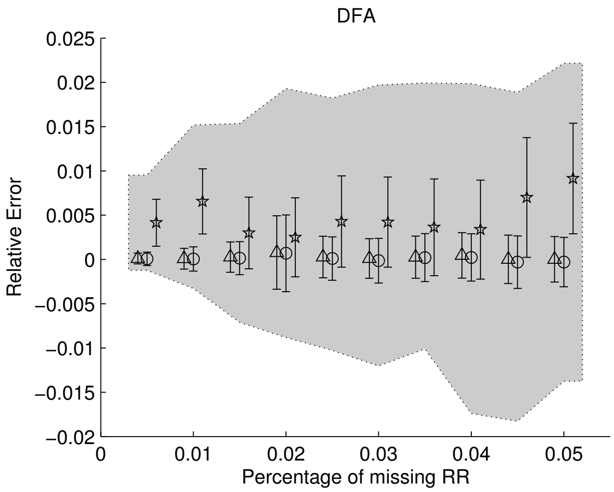

Figure 3. Relative errors on the estimates of the detrended fluctuation analysis (DFA) long-term scaling exponent after editing of anomalous intervals. See figure 2.

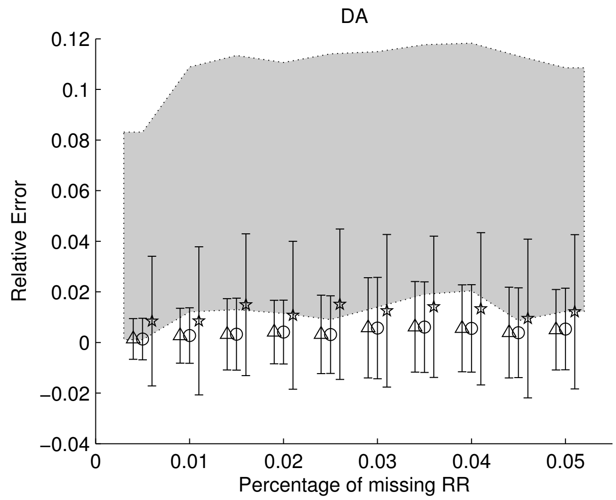

Figure 4. Relative errors on the estimates of the dispesional analysis (DA) long-term scaling exponent after editing of anomalous intervals. See figure 2.

$(\mathrm{RR}_{i-1} + \mathrm{RR}_{i+M+1})/2$.
iii) *Deletion* (D): the anomalous intervals were simply excluded from the series and subsequent beats were shifted down in the sequence to take their place. The final series was thus shorter than the unedited one.

The process of marking as anomalous the intervals of the uncorrupted series with subsequent editing was performed 20 times to reach statistical significance. The scaling exponents computed on the reference series were compared each time with the values obtained after the editing procedure.

Estimator of scaling exponents. Three methods and their correspondent long term scaling parameters were considered: Detrended Fluctuation Analysis (DFA) [11], the slope of the spectrum at low frequencies [12], and Dispersional Analysis (DA) [13]. The indexes were selected as the most representatives among those usually employed in clinical studies. For the reason of brevity, we skip the definition of the parameters here and refer the reader to the bibliography. The scales we considered for DFA and DA were $[127, 2048]$. The fitting of the spectrum was performed in the range $(0, 0.01]$ cycles per beat. The linearity of the fit was checked by visual inspection on a sample and verified with the R^2 statistics.

3. Results

The results we obtained are summarized in figure 2 (spectral slope), figure 3 (DFA) and figure 4 (DA). For each figure, the mean relative error is depicted as a function of the relative number of missing samples. Standard deviation bars are also superimposed. Each correction method is reported with a different symbol.

A few general observations can be derived from the analysis of these graphs. The first one is that the deletion (D) method introduced the larger bias (and standard deviation) in the estimation of the long-term scaling exponents, while substitution with local mean (M) and linear interpolation (LI) yielded similar results with a slightly smaller standard deviation for the former. To verify further this aspect, for each *reference series* and for each percentage of removed intervals, we tested the null hypothesis that the 20 independent estimates obtained were drawn from a normal distribution with mean the value of the scaling exponent as computed on the uncorrupted series. At a correction rate of 5%, the p-values (t-test) were smaller than 0.05% in 13 subjects using D and only in 3 and 2 subjects respectively using LI and M (power slope). Considering DFA the number of subjects became 19, 3 and 3 respectively, while for DA they were 14, 9 and 11. Thus in more than half the reference series a bias (even if small) was present when editing with D.

The results did not favor the editing technique D, which on the contrary was found to have superior performances when dealing with linear parameters [3]. Unfortunately D was inherently different due to the fact that the series was shortened while with the other two editing techniques it remained on average of the same length (e.g. a 5% deletion in a 30000 interval long series is a reduction of 1500 samples). To verify if the shortening itself was to be blamed we also roughly estimated the variability of the estimators at the different lengths by repeating the same computational procedure employed for the scaling exponents but removing samples only on the head or tail of the reference series. In this case too 20 iterations were taken into account to reach statistical significance. The results are reported in figures 2– 4 with a light gray area which corresponds to the mean bias values $\pm$ the average standard deviations. The range of values assumed by the estimators was wide and surely comparable with the values obtained when editing with D. On the shorter series, the null hypothesis was rejected by mean of a t-test in 17 (spectrum slope), 17 (DFA) and 18 (DA) subjects respectively.

4. Discussion and conclusions

The research compared the effects of three different editing techniques prior the computation of three widespread nonlinear indexes on long HRV series. Instead of considering synthetic signals, the problem of locating a set of reference series was bypassed selecting portions of Holter recordings which proved to be free of artifact and ectopic beats. Such portions are not so common so a large collection of recordings had been necessary. The position and length of the runs of anomalous beats were selected resembling as much as possible an actual situation by mean of an estimated pdf of the gaps' lengths.

The results suggest that the absolute values of the bias introduced by editing were $\ll 0.5\%$ for M and LI and $< 1\%$ for deletion. While the first two techniques seemed to perform better than D, once we considered the variability of the estimators due to slightly shortening the series, the three methods appeared pretty much equivalent. In fact, even for series which had only 1% of points less that the reference ones, the variability of the estimates were comparable with the one provided by deletion (when considering the spectrum slope, with 5% of the sample removed, a bias was statistically present in 17 subjects against the 13 observed after D).

In fact, it might be speculated that the shortening itself of the series lead to a larger variability and not to the disruption of the temporal nonlinear dynamics of the series as at first it might have been appeared. This might be rationalized by considering the long scales studied for the computation of the indexes which were typically much larger than the gaps inserted and edited.

As a final remark we stress that the simulations showed that the estimation of the three indexes we considered was quite robust and it was only partially affected by editing. Insertion of a local mean value appears to be slightly superior to the other two techniques so it might become the preferential method in setting up an experimental protocol. Nevertheless, results constructed with other editing methods, as long as the number of edited points is smaller than 5%, are largely comparable.

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