

1 **The impact of artifact correction methods of RR series on heart rate**
2 **variability parameters.**

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20 **ABSTRACT**

21 Heart rate variability (HRV) analysis is widely used to investigate the autonomic regulation of the
22 cardiovascular system. HRV is often analyzed using RR time series, which can be affected by different
23 types of artifacts. Although there are several artifact correction methods, there is no study that compares
24 their performances in actual experimental contexts. This work aimed to evaluate the impact of different
25 artifact correction methods on several HRV parameters. Initially, 36 ECG recordings of control rats or rats
26 with heart failure or hypertension were analyzed to characterize artifacts occurrence rates and distributions,
27 in order to be mimicked in simulations. After a rigorous analysis, only sixteen recordings (N=16) with
28 artifact-free segments of at least 10.000 beats were selected. Then, RR interval losses were simulated in
29 the artifact-free (reference) time series according to real observations. Correction methods applied to
30 simulated series were deletion (DEL), linear interpolation (LI), cubic spline interpolation (CI), modified
31 moving average window (mMAW) and nonlinear predictive interpolation (NPI). Linear (time- and
32 frequency-domain) and nonlinear HRV parameters were calculated from corrupted-corrected time series,
33 as well as for reference series to evaluate the accuracy of each correction method. Results show that NPI
34 provides the overall best performance. However, several correction approaches, for example, the simple
35 deletion procedure, can provide good performance in some situations, depending on the HRV parameters
36 under consideration.

37 **Keywords:** Heart rate variability, artifact correction, time domain, frequency domain, nonlinear analysis.

38 **NEW & NOTEWORTHY**

39 This work analyzes the performance of some correction techniques commonly applied to the missing beats
40 problem in RR time series. From artifacts-free RR series, spurious values were inserted based on actual
41 data of experimental settings. Our work has the intention to be a guide to show how artifacts should be
42 corrected to preserve as much as possible the original HRV properties.

43

44 INTRODUCTION

45 Time series of successive RR intervals are widely studied and used as a source to investigate various
46 physiological phenomena related to heart rate variability (HRV). Changes in HRV have been associated
47 with several cardiac and systemic diseases, such as hypertension, heart failure, obesity, epilepsy, diabetes,
48 and sudden death (16, 21, 28). Although RR time series can be easily obtained noninvasively, arrhythmias,
49 HR transients, recording artifacts and beat misdetections influence these time series, leading to
50 misinterpretations in HRV analysis.

51 Spurious values in RR series are mostly consequences of arrhythmias, premature ectopic beats, atrial
52 fibrillation, among others (1, 17). However, in experimental settings, it is very common to find outliers in
53 RR series due, for example, to animal movements, poorly fastened electrodes, power source noise, and so
54 forth.

55 In order to deal with this kind of problems, different correcting methods have been proposed. Some of
56 them are based on simple deletions or interpolation replacements of the problematic segments (1, 4, 14,
57 17). Additionally, methods that are more sophisticated have been proposed claiming to be more efficient.
58 Some of these methods are: comparison and merging (5), predictive autocorrelation (5, 14), nonlinear
59 predictive interpolation (14), exclusion of RR interval segments with divergent duration (17), impulse
60 rejection (18), integral pulse frequency model (18), sliding window average filter (13) and threshold
61 filtering using Wavelet transform (13, 29).

62 Despite the high number of correction methods, it has already not been established a systematic study
63 showing the most suitable methods to deal with artifacts in RR series, and its impact on the different HRV
64 parameters. Therefore, the purpose of this study is to compare some of the most important correction
65 methods, assessing the accuracy of those approaches in preserving the original features of RR series.

66

67 MATERIALS AND METHODS

68 *Database:* Original ECG recordings, obtained from previous studies, were selected (20, 27). These data
69 were collected from 36 recordings of conscious rats with or without pathophysiological conditions such as
70 hypertension or heart failure. The different physiological situations provide a more realistic scenario for
71 evaluating the accuracy of each correction methods on RR interval time series. From the whole dataset, we
72 selected only the animals which ECG recordings have at least 10.000 consecutive beats free of artifacts.
73 All experiments used in the present study were approved by the Committee of Ethics in Animal Research
74 of the Medical School of Ribeirão Preto, University of São Paulo.

75 **Heart Failure:** Heart failure (HF) was induced by myocardial infarction (coronary artery ligation) in male
76 Wistar rats (240-320 g, N=9), according to the procedure described by Pfeffer et al. (23). Additionally,
77 sham-operated rats submitted to a similar surgical procedure without coronary artery ligation (N=18) were
78 used as control animals. Five weeks after coronary artery ligation or sham, rats were implanted with
79 subcutaneous electrodes for ECG recording. Two days after electrodes implantation, conscious animals
80 were connected to an ECG amplifier (8811A, Bioelectric Amplifier, Hewlett-Packard) attached to an
81 analog/digital interface (DI-220, Dataq Instruments), and basal ECG was sampled at 2 kHz for 2 h with the
82 animals freely moving inside their cages (20).

83 **Hypertension:** Male spontaneously hypertensive rats (SHR, N=5) and Wistar-Kyoto (WKY, N=4)
84 normotensive counterparts (210-290 g, N=4), were implanted with telemetry-based biopotential amplifier
85 and transmitter (TR50B, Telemetry Research Auckland, New Zealand) for ECG recording. Three days
86 after the implantation of the telemeter, basal ECG was continuously sampled (2 kHz) with a dedicated
87 receiver (TR180 SmartPad, Telemetry Research) attached to a data acquisition system (PowerLab,
88 ADInstruments, Castle Hill, NSW, Australia). Recordings were carried out during 90 minutes with animals
89 freely moving inside their cages (27).

90 *Study design:* Initially, the entire database was carefully inspected to identify the number of spurious
91 values, due to any reason, in each series. Following, series with at least 10,000 consecutive values
92 completely free of losses or artifacts were selected. Spurious values were then artificially inserted in the

93 artifact-free series based on actual typical rates of loss or misdetections in experimental data. Finally,
94 series with artificial losses were corrected using different approaches, and HRV parameters were
95 calculated for each corrected time series.

96 *Rate of losses:* Table 1 shows the percentage of values and segments of values (lengthening from 1 to 10)
97 found as corrupted (spurious values). We observed an average of 2.5% and a maximum of 5% of the entire
98 HRV series length corrupted.

99 *Simulation of Spurious Values:* From the total amount of 36 time series, 16 fulfilled the criterion of having
100 10,000 consecutive points without any outlier or spurious value, being 6 from sham-operated control rats,
101 3 from rats with HF, 4 from WKY and 3 from SHR. We named these as the reference series for HRV
102 analysis. Missing RR intervals were simulated in the reference series based on the criteria described
103 previously and with the purpose of mimicking the findings from the recorded data. Corrupted series of RR
104 intervals were artificially generated by removing single beats, segments with 3 or 10 consecutive values
105 from the reference series at the proportion of 79%, 11%, and 10%, respectively. We chose these
106 proportions as representative of the distribution shown in Table 1, keeping it consistent with the
107 experimental findings. The overall percentages of removal were selected to be 2.5% or 5% of the total
108 amount of beats. Figure 1 illustrates the loss simulation process in RR interval time series. Then we
109 applied the different correction methods to the corrupted series and calculated all HRV parameters for
110 both, reference (lossless) and corrected series.

111 *Correction techniques:* Different methods are used in the literature to recover information due to signal
112 corruption. In this study, we applied five of the commonly found methods to correct simulated HRV time
113 series that follow the procedures previously described. Simple deletion (DEL) of spurious beats eliminates
114 all inconsistent values on RR series, leading to a reduction in the number of points of corrected series.
115 Linear (LI) or cubic spline interpolation (CI) were used to replace missing beats in RR time series by
116 interpolated ones, maintaining the length of original series (11, 19). Nonlinear predictive interpolation
117 (NPI) is a method that scans all available segments with similar neighbourhood characteristics to the

118 spurious values and uses the most similar segment to replace the affected part of the signal (14). Modified
119 moving average windowing (mMAW), which is a modified version of moving average that replaces each
120 point on a time series by the average formed by the six successive points before and after the missing
121 segment. Usually, these methods have been applied to solve problems of ectopic beats, noise and non-
122 uniform sampling of the RR time series. In a few cases, they were used to correct missing beats (6, 11, 14).

123 *Analysis of ECG and HRV:* The peaks of all R waves were detected from ECG recordings using a
124 computer software (ECG Module from LabChart Software, ADInstruments, Castle Hill, NSW, Australia)
125 and RR time series were created as the intervals between each consecutive R waves.

126 Linear and nonlinear approaches were used to evaluate HRV from original (reference) and corrected RR
127 time series, and estimate the impact of each correction method. Linear techniques involve the
128 quantification of time- and frequency-domain parameters, whereas nonlinear techniques give information
129 about predictability, long-range correlations and patterns of the HRV.

130 In the time domain, we calculated the average, the standard deviation of all RR intervals (AVRR and
131 SDNN) and the root mean squared value of successive differences between RR intervals (RMSSD). The
132 frequency domain parameters correspond to the estimation of the of RR spectra at the standard frequency
133 bands of rats identified as very low (VLF: <0.2 Hz), low (LF: 0.2 to 0.75 Hz) and high-frequency bands
134 (HF: 0.75 to 3.0 Hz) (2, 3). The procedure implies the calculation of the power spectral density (PSD) and
135 the estimation of total power (energy) at each particular frequency band. In this study, the PSD was
136 estimated by the Lomb's periodogram algorithm, introduced by N. Lomb in 1976 (15) as a technique to
137 deal with signals containing unevenly acquired samples. Estimation of PSD based on Fourier transform
138 (FT) requires evenly sampled time series as inputs. Therefore, it requires interpolation of RR series prior to
139 the PSD estimation, as the RR time series are unevenly sampled. We adopted the Lomb algorithm to avoid
140 changing the RR series, as it may introduce some bias to the performance of the correction techniques.
141 Previous studies showed that Lomb's approach results in parameters that are very similar to interpolated
142 FT method (6, 9, 19).

143 Detrended fluctuation analysis (DFA), multiscale entropy (MSE) and symbolic dynamics methods, were
144 selected because they represent three of the most commonly used approaches in the nonlinear analysis
145 (31). DFA allows quantification of long-range correlations on non-stationary time series (22). Scaling
146 properties and fractal structures contained in the signal are evidence of these correlations. Short-term (α_1)
147 and long-term (α_2) scaling exponents, to characterize the RR time series fractal properties, were calculated
148 in this study. The crossover point (n) between α_1 and α_2 was adaptively chosen for each group. From $n=9$
149 to $n=30$, we selected the crossover that gives the lowest cumulative error of the two regression lines
150 regarding α_1 and α_2 range. As a result, it was set $n=10$ for all group of animals (control, HF and for SHR).

151 MSE measures the predictability of time series over multiple time scales (7, 8). MSE analysis is based on
152 the sample entropy (SampEn) calculated for different scales in the signals. SampEn is a refinement of the
153 approximate entropy method introduced by Pincus (24) and widely used in the physiological signal
154 analysis (12, 26). MSE was calculated from scales 1 to 10 and the entropy at scale 1 (MSE1), as well as the
155 sum of the entropy of all scales (MSET), were used as a single number to represent MSE.

156 Symbolic dynamics is a method to characterize the variation patterns of time series in a simple and coarser
157 symbolic notation, capable of retaining the essential dynamic characteristics of the original time series.
158 The conversion of a time series into a set of symbols begins dividing the original signal into six equally
159 distant levels (uniform quantization). Next, patterns of length three are constructed, followed by grouping
160 these patterns into four families, according to the symbol variation: 0V (zero variation), 1V (one variation),
161 2LV (two like variation) and 2UV (two unlike variation). Finally, the rates of occurrence of these families
162 are evaluated (10, 25). Here, only 0V and 2UV variations were used as they have been demonstrated, in
163 previous studies, to be highly correlated with sympathetic and vagal cardiac modulation, respectively (26,
164 30).

165 *Statistical analysis:* Friedman's statistical test was used to verify differences in HRV parameters between
166 the reference and corrected RR time series. Besides, the error for each HRV parameters was calculated as
167 the average of the absolute differences between parameters obtained for each reference and corrected time

168 series. Errors are presented as a median value with their respective 1st and 3rd quartiles (Median [1st;
169 3rd]). On the other hand, ANOVA on ranks method was applied to find statistical differences between
170 error values from different correction techniques to evaluate the performance of each technique for each
171 HRV parameter.

172

173 **RESULTS**

174 Tables 2, 3 and 4 show median and quartile values for HRV parameters calculated from original
175 (reference) and corrupted-corrected series in time and frequency domain, as well as by nonlinear
176 approaches, respectively. The median AVRR interval calculated from series corrected by any of the
177 approaches used in this study was identical to median AVRR derived from reference series. Correction
178 with DEL did not affect time domain parameters of HRV, i.e. SDNN and RMSSD of RR series with 2.5%
179 of losses, while for series with 5% of losses, DEL affected only RMSSD. All other correction methods
180 affected both SDNN and RMSSD.

181 For frequency-domain indices, the RR time series PSD at VLF band in original series was found different
182 from corrected series with DEL (2.5 and 5% of losses) or mMAW (only 5% of losses). Only the series
183 corrected by NPI showed the PSD unmodified at LF band. On the other hand, none of the methods of
184 correction used in the study were able to preserve the RR time series power spectra at HF band. The
185 LF/HF ratio is different from reference series only for those series corrected by interpolation, i.e. either LI
186 or CI.

187 For nonlinear parameters, differences are more exacerbated for corrected series after 5% of losses. While
188 MSE1, i.e. sample entropy itself, presented the lowest number of differences considering all correction
189 methods, the symbolic dynamics 0V showed the greatest number of differences from reference series. NPI
190 gave the lowest number of significant differences from reference series, whereas interpolation-based

191 methods (LI and CI) presented the greatest number of significant differences when considering both 2.5%
192 and 5% of missing points.

193 Figures 2, 3 and 4 show the median error value of HRV parameters calculated between original and
194 corrected series for time-domain, frequency-domain and nonlinear techniques, respectively. For time-
195 domain, one can observe that median error values of corrections with DEL in RMSSD are much lower as
196 compared to the other correction approaches. For AVRR, although the correction with DEL presents the
197 highest median error, the difference between the reference and corrected series are so small that we do not
198 identify any practical relevance in such results. Frequency-domain parameters correction with DEL
199 brought the highest median errors for all parameters, whereas corrections with NPI presented the lowest
200 median error values. For nonlinear parameters, the median error showed a variable behavior. In general,
201 scaling exponents of DFA (α_1 and α_2) present little median error for mMAW and NPI. Indices calculated
202 from MSE (MSE1 and MSET) showed a lower median error for series corrected by DEL or NPI. Symbolic
203 dynamic indices (0V and 2UV) presented lower median error values for series corrected by NPI.

204

205 **DISCUSSION**

206 It is worth noting that the absence of difference between HRV indices calculated from original and a
207 corrected time series does not always imply that the corrected method used is the best approach. The lack
208 of difference means that there is no reliable statistical evidence that the HRV indices calculated from
209 original (reference) and corrected series are different. It may happen, for example, when there is a high
210 variation in the population. Therefore, the calculation of the error provides an additional measure for the
211 evaluation of the correction methods reliability.

212 Results showed that the correction techniques assessed here affect in different ways the HRV indices.
213 While the simple deletion of spurious values (DEL) seems to be one of the best approaches for all time-
214 domain indices, at the same time, it is the worst method for frequency-domain. In the latter case, all other

215 techniques provide similar performances, with emphasis to NPI. For nonlinear methods, the correction
216 techniques are quite variable regarding accuracy.

217 In general, NPI seems to be the best overall approach. One can observe from Tables 2, 3 and 4 that this
218 technique has the least number of statistical differences, and from Figures 2, 3 and 4 it presents the lowest
219 median error value in most situations. However, the simplest method, DEL, can also be used as an
220 excellent correction approach in many cases (see Figure 3).

221 One could expect that the performance of the correction methods be worse when the number of beat
222 losses is higher. Accordingly, the median error values tend to be higher for corrections after 5% of losses
223 in comparison with 2.5%. However, the impact on increasing the number of missing beats was greater for
224 frequency-domain and nonlinear HRV indices than for time-domain.

225

226 **CONCLUSION**

227 Through the simulation of beat losses that mimic real situations in experimental settings, different RR time
228 series correction methods were analyzed. The method with the best overall performance was the NPI.
229 However, for studies on specific HRV indices, other correction techniques can provide quite good
230 performances as well. While for time-domain analysis the deletion technique seems to be an excellent
231 option, it should be avoided for frequency-domain. Moreover, the rate of losses, i.e. 2.5% or 5% of total
232 beats, has less impact on the time-domain indices when compared to the frequency-domain and nonlinear
233 indices.

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- 306

307 **Tables:**

308 Table 1: Mean percentage of spurious values calculated over the entire database. The spurious values
309 were quantified according to their distribution ranging from 1 single beat to 10 consecutive beats.

Number of consecutive spurious values	1	2	3	4	5	6	7	8	9	10
Percentage	1.29	0.41	0.19	0.11	0.11	0.13	0.14	0.13	0.13	0.17

310

311

312 Table 2: Median values with [1st; 3rd] quartiles for time domain indices calculated for the time series
 313 without the presence of spurious values (control group) and after application of each correction method
 314 on both level of correction (2.5 and 5.0%). In these results are indicated if statistical differences were
 315 found using p-value criteria less than 0.05 (* p < 0.05).

Correction Method	AVRR (ms)	SDNN (ms)	RMSSD (ms)
Reference series (Control)	199.2 [188.8; 215.6]	6.9 [2.7; 4.6]	3.6 [2.7; 4.6]
2.5 % of Corrected values:			
Deletion	199.2 [188.8; 215.2]	6.9 [5.5; 10.5]	3.6 [2.7; 4.6]
LI	199.2 [188.7; 215.6]	6.9 [5.5; 10.4]*	3.5 [2.6; 4.5]*
CI	199.2 [188.7; 215.6]	6.9 [5.5; 10.4]	3.5 [2.6; 4.5]
mMAW	199.2 [188.7; 215.6]	6.9 [5.5; 10.4]*	3.6 [2.4; 4.5]*
NPI	199.2 [188.8; 215.6]	6.9 [5.5; 10.4]*	3.6 [2.7; 4.6]*
5% of Corrected Values			
Deletion	199.2 [188.8; 215.6]	6.9 [5.5; 10.4]	3.6 [2.7; 4.6]*
LI	199.2 [188.8; 215.6]	6.9 [5.5; 10.4]*	3.5 [2.6; 4.4]*
CI	199.2 [188.8; 215.6]	6.9 [5.5; 10.4]*	3.5 [2.6; 4.4]
mMAW	199.2 [188.8; 215.6]	6.8 [5.5; 10.4]*	3.5 [2.6; 4.5]
NPI	199.2 [188.8; 215.6]	6.9 [5.5; 10.4]*	3.6 [2.7; 4.5]*

316 LI: linear interpolation, CI: cubic spline interpolation, mMAW: moving average windowing, NPI: non-
 317 linear predictive interpolation.

318

319

320 Table 3: Median values with [1st; 3rd] quartiles for frequency domain indices calculated for the
 321 signals without the presence of spurious values (control group) and after application of each
 322 correction method on both level of correction (2.5 and 5.0%). In these results are indicated if
 323 statistical differences were found using p-value criteria less than 0.05 (* p < 0.05).

Correction Method	VLF (ms ²)	LF (ms ²)	HF (ms ²)	LF/HF
Reference series (Control)	44.6 [22.0; 103.4]	1.3 [0.6; 2.2]	3.8 [2.4; 7.0]	0.4 [0.1; 0.6]
2.5 % of Corrected values:				
Deletion	44.6 [22.5; 104.4]*	1.9 [0.8; 2.9]*	4.5 [3.7; 7.8]*	0.4 [0.9; 0.6]
LI	44.6 [22.5; 103.4]	1.3 [0.6; 2.3]*	3.7 [2.3; 6.7]*	0.4 [0.2; 0.6]*
CI	44.6 [22.5; 103.4]	1.3 [0.6; 2.3]*	3.7 [2.3; 6.7]*	0.4 [0.2; 0.6]*
mMAW	44.6 [22.4; 103.3]	1.3 [0.6; 2.2]*	3.7 [2.3; 6.7]*	0.4 [0.1; 0.6]
NPI	44.6 [22.5; 103.4]	1.3 [0.6; 2.2]	3.8 [2.3; 6.8]*	0.4 [0.1; 0.6]
2.5 % of Corrected values:				
Deletion	44.9 [22.4; 103.1]	2.3 [1.0; 3.6]*	5.6 [4.5; 8.5]*	0.4 [0.2; 0.5]
LI	44.6 [22.5; 103.4]	1.4 [0.7; 2.4]*	3.6 [2.2; 6.4]*	0.4 [0.2; 0.6]*
CI	44.6 [22.5; 103.5]	1.4 [0.7; 2.4]*	3.6 [2.2; 6.4]*	0.4 [0.2; 0.6]*
mMAW	44.5 [22.4; 103.2]*	1.2 [0.6; 2.1]*	3.6 [2.3; 6.5]*	0.4 [0.2; 0.6]
NPI	44.5 [22.4; 103.3]	1.3 [0.6; 2.3]	3.8 [2.4; 6.8]*	0.4 [0.2; 0.6]

324 LI: linear interpolation, CI: cubic spline interpolation, mMAW: moving average windowing, NPI: non-
 325 linear predictive interpolation.

326

327 Table 4: Median values with [1st; 3rd] quartiles for nonlinear indices calculated for the signals without the
 328 presence of spurious values (control group) and after application of each correction method on both level
 329 of correction (2.5 and 5.0%). In these results are indicated if statistical differences were found using p-
 330 value criteria less than 0.05 (* p < 0.05).

Correction Method	α_1 (a.u)	α_2 (a.u)	MSE _I (a.u)	MSE _T (a.u)	0V (%)	2UV (%)
Reference series (Control)	0.7 [0.6; 0.9]	1.1 [1.0; 1.2]	1.4 [1.0; 1.9]	19.9 [16.4; 22.2]	24.3 [11.8; 37.0]	28.7 [23.9; 48.0]
2.5 % of Corrected values:						
Deletion	0.8 [0.6; 0.9]	1.1 [1.0; 1.2]	1.5 [1.0; 1.9]*	20.2 [16.6; 22.5]*	24.8 [12.0; 37.1]	28.9 [24.1; 47.7]
LI	0.8 [0.6; 1.0]*	1.1 [1.0; 1.2]*	1.4 [1.0; 1.8]	20.2 [16.6; 22.6]*	25.7 [12.8; 38.1]*	27.6 [22.6; 46.0]*
CI	0.8 [0.6; 1.0]	1.1 [1.0; 1.2]	1.5 [1.0; 1.8]	20.2 [16.6; 22.7]	26.1 [12.7; 38.3]	27.4 [22.5; 45.9]
mMAW	0.8 [0.6; 1.0]*	1.1 [1.0; 1.2]*	1.5 [1.0; 1.8]	20.2 [16.6; 22.7]	26.1 [12.7; 38.3]*	27.4 [22.5; 45.9]*
NPI	0.8 [0.6; 1.0]	1.1 [1.0; 1.2]	1.4 [1.0; 1.9]	20.1 [16.4; 22.3]*	25.1 [11.8; 37.0]	29.1 [23.0; 47.7]
2.5 % of Corrected values:						
Deletion	0.8 [0.6; 0.9]	1.1 [1.0; 1.2]*	1.5 [1.0; 1.9]*	20.3 [16.9; 22.4]*	27.2 [12.5; 37.6]*	28.7 [22.6; 47.4]*
LI	0.8 [0.6; 1.0]*	1.1 [1.0; 1.2]*	1.5 [1.0; 1.8]	20.4 [17.3; 22.8]*	27.9 [15.0; 39.2]*	26.8 [21.3; 45.1]*
CI	0.8 [0.6; 1.0]*	1.1 [1.0; 1.2]*	1.5 [1.0; 1.8]	20.4 [17.3; 22.9]*	27.5 [15.0; 39.3]*	26.7 [21.7; 44.9]*
mMAW	0.8 [0.6; 0.9]*	1.1 [1.1; 1.2]*	1.4 [1.0; 1.8]*	20.0 [16.3; 22.4]	27.0 [13.5; 39.1]*	27.5 [22.9; 46.9]*
NPI	0.8 [0.6; 0.9]*	1.1 [1.0; 1.2]	1.4 [1.0; 1.9]	20.1 [16.6; 22.4]*	26.6 [12.5; 37.4]*	27.8 [22.8; 48.4]

331 LI: linear interpolation, CI: cubic spline interpolation, mMAW: moving average windowing, NPI: non-
 332 linear predictive interpolation.

333

334 **Figures:**

335

336 Figure 1: Illustrating scheme describing the simulation of losses. Given a reference RR time series (top
337 left corner), the simulation uses a random number generator to produce 1 beat losses with 79%
338 probability, segments of 3 beats with 11% probability and segments of 10 beats with 10% probability. In
339 total, 2.5% or 5% of the reference time series are randomly removed, resulting in the RR series illustrated
340 on the bottom right.

341

342 **Figure 2:** The mean errors for the time-domain HRV measures calculated from corrupted-corrected time
343 series and reference (original) series for different correcting methods over the two levels of correction, i.e.
344 2.5 and 5%. LI: Linear Interpolation; CI: Cubic Interpolation; mMAW: modified Moving Average
345 Window; NPI: Nonlinear Predictive Interpolation; The letters on the top of the bars represent statistical
346 differences, as inferred with ANOVA on ranks, found between correction methods as follows. a: between
347 DEL and LI; b: between DEL and CI; c: between DEL and mMAW; d: between DEL and NPI; e:
348 difference between LI and CI; f: difference between LI and mMAW; g: differs between LI and NPI; h:
349 difference between CI and mMAW; i: difference between CI and NPI; j: difference between mMAW and
350 NPI.

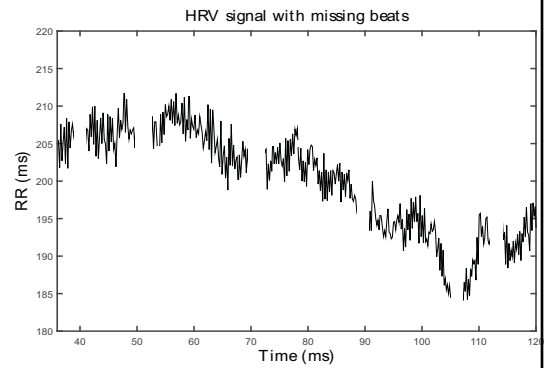
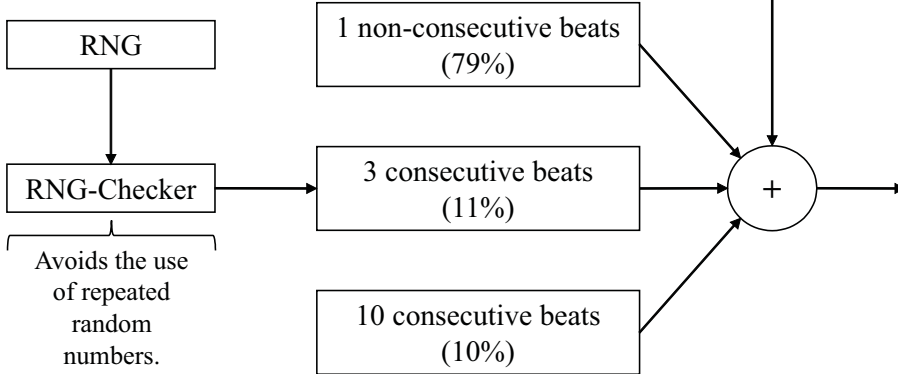
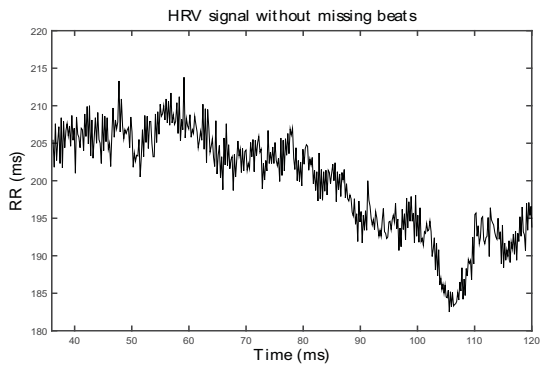
351

352 Figure 3: The mean errors for the frequency-domain HRV measures calculated from corrupted-corrected
353 time series and reference (original) series for different correcting methods over the two levels of
354 correction, i.e. 2.5 and 5%. LI: Linear Interpolation; CI: Cubic Interpolation; mMAW: modified Moving
355 Average Window; NPI: Nonlinear Predictive Interpolation; The letters on the top of the bars represent
356 statistical differences, as inferred with ANOVA on ranks, found between correction methods as follows.
357 a: between DEL and LI; b: between DEL and CI; c: between DEL and mMAW; d: between DEL and

358 NPI; e: difference between LI and CI; f: difference between LI and mMAW; g: differs between LI and
359 NPI; h: difference between CI and mMAW; i: difference between CI and NPI; j: difference between
360 mMAW and NPI.

361

362 Figure 4: The mean errors for the nonlinear HRV measures calculated from corrupted-corrected time
363 series and reference (original) series for different correcting methods over the two levels of correction, i.e.
364 2.5 and 5%. LI: Linear Interpolation; CI: Cubic Interpolation; mMAW: modified Moving Average
365 Window; NPI: Nonlinear Predictive Interpolation; The letters on the top of the bars represent statistical
366 differences, as inferred with ANOVA on ranks, found between correction methods as follows. a: between
367 DEL and LI; b: between DEL and CI; c: between DEL and mMAW; d: between DEL and NPI; e:
368 difference between LI and CI; f: difference between LI and mMAW; g: differs between LI and NPI; h:
369 difference between CI and mMAW; i: difference between CI and NPI; j: difference between mMAW and
370 NPI.



RNG: Random Number Generator.

