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A Computer Algorithm to Impute Interrupted Heart Rate Data for the Spectral Analysis of Heart Rate Variability—The ARIC Study[1]

DUANPING LIAO,*[,2] RALPH W. BARNES,† LLOYD E. CHAMBLESS,‡ AND GERARDO HEISS*

For the ARIC investigators

Department of Epidemiology, School of Public Health, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina 27599; †Department of Neurology, Bowman Gray Medical School, Wake Forest University, Winston-Salem, North Carolina 27109; and ‡Department of Biostatistics, School of Public Health, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina 27599

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The shorter term beat-to-beat heart rate data collected from the general population are often interrupted by artifacts, and an arbitrary exclusion of such individuals from analysis may significantly reduce the sample size and/or introduce selection bias. A computer algorithm was developed to label as artifacts any data points outside the upper and lower limits generated by a 5-beat moving average ±25% (or set manually by an operator using a mouse) and to impute beat-to-beat heart rate throughout an artifact period to preserve the timing relationships of the adjacent, uncorrupted heart rate data. The algorithm applies Fast Fourier Transformation to the smoothed data to estimate low-frequency (LF; 0.025–0.15 Hz) and high-frequency (HF; 0.16–0.35 Hz) spectral powers and the HF/LF ratio as conventional indices of sympathetic, vagal, and vagal–sympathetic balance components, respectively. We applied this algorithm to resting, supine, 2-min beat-to-beat heart rate data collected in the population-based Atherosclerosis Risk in Communities study to assess the performance (success rate) of the algorithm ($N = 526$) and the inter- and intra-data-operator repeatability of using this computer algorithm ($N = 108$). Eighty-eight percent (88%) of the records could be smoothed by the computer-generated limits, an additional 4.8% by manually set limits, and 7.4% of the data could not be processed due to a large number of artifacts in the beginning or the end of the records. For the repeatability study, 108 records were selected at random, and two trained data operators applied this algorithm to the same records twice within a 6-month interval of each process (blinded to each other's results and their own prior results). The inter-data-operator

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[2] To whom correspondence and reprint requests should be addressed at Department of Epidemiology, School of Public Health, University of North Carolina at Chapel Hill, 137 E. Franklin Street, NationsBank Plaza, Suite 306, Chapel Hill, NC 27514.

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reliability coefficients were 0.86, 0.92, and 0.90 for the HF, LF, and HF/LF components, respectively. The average intra-data-operator reliability coefficients were 0.99, 0.99, and 0.98 for the HF, LF, and HF/LF components, respectively. These results indicate that this computer algorithm is efficient and highly repeatable in processing short-term beat-to-beat heart rate data collected from the general population, given that the data operators are trained according to standardized protocol. © 1996 Academic Press, Inc.

Introduction

It has long been recognized that the autonomic nervous system plays an important role in cardiac regulation (*1*), that autonomic function changes with increasing age (*2*), and that autonomic dysfunction is associated with various diseases (*3–9*). Further, it has been consistently observed that autonomic function is a predictor of mortality post-myocardial infarction (*10–15*), and it has been found to be associated with sudden cardiac death (*16*) and all-cause mortality (*17*).

As a result of the interaction between sympathetic and parasympathetic activity, beat-to-beat heart rate shows periodicities over time. These periodicities are identified through spectral analysis whereby the observed heart rate is expressed mathematically by a function of time as the sum of a series of sine and cosine functions of varying amplitudes and frequencies. A plot of the square of the amplitudes (called power) of these sine and cosine functions against their cycle frequencies is known as the power spectral density for beat-to-beat heart rate or the heart rate variability (HRV) power spectrum. When the heart rate/time data are reexpressed in this mathematical form, previous work has shown that cycles with a frequency of 0.025–0.15 Hz (called low-frequency power, LF) are under the influence of both sympathetic and parasympathetic nervous system. Cycles with a frequency of 0.16–0.35 Hz (called high-frequency power, HF) are under the influence of the parasympathetic system only and have been regarded as a marker of cardiac vagal function. LF represents the contribution to heart rate variability from the sympathetic and parasympathetic systems, HF represents the contribution to the variability from the parasympathetic, and the ratio HF/LF represents a measure of the balance of parasympathetic and sympathetic functions (*9*, *18–24*).

Beat-to-beat heart rate data often contain artifacts due to occasional body position change, muscular motion, ECG amplifier saturation, or lost contact of ECG leads with the skin. As reported by most of the published studies, it is a common practice to apply spectral analysis to a segment of data which does not contain any artifact and discarding those segments with artifact. However, the beat-to-beat heart rate data collected on samples of the general population are typically short, e.g., 2-min data, and do not permit the option of choosing an uncorrupted segment. Moreover, an arbitrary exclusion of such individuals from analysis may introduce selection bias or significantly reduce the sample size and statistical power.

A computer algorithm was developed to (a) label any data points as artifacts when they were located outside the upper and lower limits generated by a 5-beat moving average ±25% or set manually by an operator using a mouse, (b) impute beat-to-beat heart rate during the period affected by artifact to preserve the timing relationships of the uncorrupted heart rate data, and (c) to apply Fast Fourier Transformation to the smoothed data. The latter was used to estimate LF and HF spectral powers and the HF/LF ratio as conventional indices of sympathetic, vagal, and vagal–sympathetic balance components, respectively. We applied this algorithm to resting, supine 2-min beat-to-beat heart rate data collected in the Atherosclerosis Risk in Communities (ARIC) study.

Data and Methods

Population and Data Collection

Beat-to-beat heart rate records used to test this algorithm were randomly selected from the 15,800 individuals who participated in the baseline examination of the ARIC study. ARIC is a longitudinal study of cardiovascular and pulmonary diseases sponsored by the National Heart, Lung and Blood Institute. It includes a community surveillance and a cohort component. The ARIC cohort was selected as a probability sample of 15,800 men and women between the ages of 45 and 64 years at four ARIC centers in the United States, three of which enumerated and enrolled an ethnically diverse population (selected Minneapolis suburbs, Minnesota; Washington County, Maryland; and Forsyth County, North Carolina). The fourth quarter of the ARIC cohort was sampled from black residents of Jackson, Mississippi, the details of sampling, study design, and cohort examination procedures have been published (*25*). Eligible participants were interviewed at home, invited to a baseline clinical examination, and followed up annually by means of a telephone interview. The baseline examination of the ARIC cohort was conducted in 1987–1989.

A random sample of 526 beat-to-beat heart rate records was selected from the ARIC baseline examinees to test the performance (success rate) of the computer algorithm, and another random sample of 108 records was selected to assess the inter- and intra-data-operator repeatability by using this computer algorithm.

Resting, supine, 2-min beat-to-beat heart rate data were collected after participants remained comfortably in the supine position for at least 20 min during the ARIC B-mode ultrasound and arterial distensibility studies (*26*). Study participants had three ECG electrodes placed on the epigastrium. A dedicated computer and software supporting continuous detection and recording of an ECG *R* wave were used to collect these data. The system then converted the *R* to *R* interval into beat-to-beat heart rate with precision to 2 decimal places, including a record of the real time of each beat (*27*).

Algorithm to Remove Artifacts

We developed a computer algorithm to label as artifacts any data points outside the upper and lower limits generated by a 5-beat moving average ±25% (or set manually by an operator using a mouse) and to impute beat-to-beat heart rate

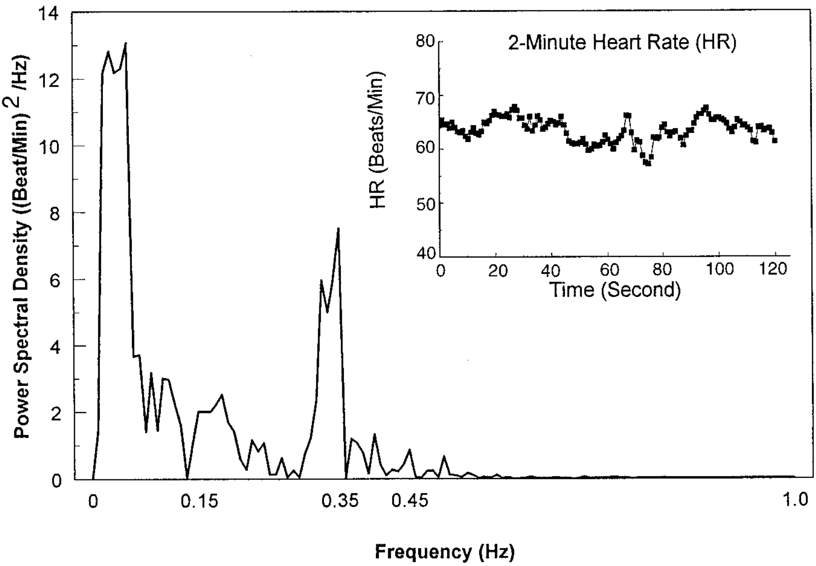

FIG. 1. An example of power spectral density curve from Fast Fourier Transformation with time domain heart rate data in the inset.

throughout an artifact period to preserve the timing relationships of the adjacent, uncorrupted heart rate data. The details of the algorithm are presented in the Appendix.

Spectral Analysis

After the data were smoothed using the algorithm described above, linear interpolation was applied to neighboring heart rate data points, and 256 heart rate data points were resampled with an equal distance of 0.4685 sec. These 256 data points were used to fit a quadratic least-squares model with time and time squared as the predictors, so that the linear and quadratic trends in the data were removed by taking the residuals. From the residuals, Fast Fourier Transformation was performed to estimate Fourier transform of the heart rate residuals, from which the power spectral density (PSD) was computed. A PSD curve for one participant is shown in Fig. 1 as an example. From the PSD curve, two frequency-specific spectral powers (the areas under the PSD curve in given frequency band) were calculated based on a rectangular method: (a) low-frequency spectral power, defined as the power (area) between 0.025 and 0.15 Hz band; (b) high-frequency spectral power, the power (area) between 0.16 and 0.35 Hz band; and (c) the ratio of HF/LF.

Statistical Methods

The performance of the algorithm was assessed by the proportion of records satisfactorily processed. Inter-data-operator and intra-data-operator repeatability in applying this algorithm were assessed using methods briefly described below.

Inter-data-operator reliability. In processing heart rate data with artifacts, the data operators were instructed to apply upper and lower boundaries around the raw data in order to identify the limits between biologically plausible data and artifacts. Although the data operators were trained to apply the boundaries according to specific criteria, differences in judgment and personal style may lead individuals to apply the boundaries differently. As a consequence, variations in the HRV indices might be introduced. To ascertain the degree to which inter-operator differences occurred, we had 79 heart rate data records processed by two data operators blinded to each other's results. We then evaluated the inter-data-operator reliability for each of the HRV indices by fitting a nested random effects model. In this model, total variance comes from two sources for each of the indices of interest,

$$V_{\text{Total}} = V_{\text{BP}} + V_{\text{B-Operator}},$$

where V_{Total} is the total variance, V_{BP} is the between-persons variance, and $V_{\text{B-Operator}}$ is the variance introduced by the data operators. Thus,

$$\text{Reliability Coefficient (RC)} = V_{\text{BP}}/V_{\text{Total}}.$$

The RC was used to assess the inter-data-operator repeatability of applying this algorithm.

Intra-data-operator reliability. This feature was designed to assess the reproducibility of each of two operators in applying the boundary criteria. For this purpose, 78 heart rate records were reprocessed by one data operator (Operator A) after 6 months of first processing, and 27 records were reprocessed by another data operator (Operator B). Operators were blinded to each other's, and their own, previous results. We then evaluated the intra-data-operator reliability for each of the HRV indices by fitting a nested random effects model with the total variance from two sources,

$$V_{\text{Total}} = V_{\text{BP}} + V_{\text{W-Operator}},$$

where V_{Total} is the total variance, V_{BP} is the between-persons variance, and $V_{\text{W-Operator}}$ is the variance within the data operator. Thus,

$$\text{RC} = V_{\text{BP}}/V_{\text{Total}}.$$

Again, the RC was used to assess the intra-data-operator repeatability in applying this algorithm.

TABLE 1

Summary of Inter- and Intra-Data-Operator Repeatability in Applying the Heart Rate Recovery Algorithm, Expressed as Reliability Coefficients for Three Major HRV Indices

Heart rate variability indices	Inter-data-operator reliability coefficient (n = 79)	Intra-data-operator reliability coefficient for Operator A (n = 78)	Intra-data-operator reliability coefficient for Operator B (n = 27)
HF	0.86	0.98	0.998
LF	0.92	0.98	0.999
HF/LF ratio	0.90	0.98	0.962

Note. HF, high-frequency power; LF, low-frequency power; HF/LF, ratio of HF to LF.

To be consistent with the literature, the data were transformed by using natural logarithm.

Results

Performance Results

Of the 526 records processed, 462 (87.8%) of the records could be smoothed by the computer-generated limits, an additional 25 (4.8%) by manually set limits, and 39 (7.4%) could not be processed due to segments with large amounts of artifacts in the beginning or end of the records.

Repeatability Study

The results from the blinded repeatability studies are summarized in Table 1. As shown in this table, the inter-data-operator reliability coefficients were 0.86, 0.92, and 0.90 for the HF, LF, and HF/LF components, respectively, and the averages of intra-data-operator reliability coefficients from two operators were 0.99, 0.99, and 0.98 for the HF, LF, and HF/LF components, respectively.

Discussion

The first step in spectral analysis of beat-to-beat heart rate data is to remove the influence of artifacts. Our computer algorithm was developed to estimate heart rate data in the artifactual period in such a way that the timing relationships among noncorrupted heart rate data were maintained. The test performance on 526 2-min heart rate records collected in the ARIC study indicated that 87.8% of the records can be successfully smoothed by the computer-generated limits, 4.8% by manually set limits, and only 7.4% could not be processed due to large amounts of artifacts in the beginning of the record or the end of the record (lack of consistent heart rate data required for the initialization of the algorithm steps 2 and 3).

The final products of beat-to-beat heart rate data analysis are the indices of the sympathetic and parasympathetic activities and the balance of the vagal–sympathetic function. We tested the inter- and intra-data-operator repeatability in deriving these indices using this algorithm and found a high degree of inter- and intra-data-operator repeatability in the indices of the autonomic cardiac control. The inter-data-operator reliability coefficients were 0.86, 0.92, and 0.90 for the HF, LF, and HF/LF components, respectively. The average intra-data-operator reliability coefficients were 0.99, 0.99, and 0.98 for the HF, LF, and HF/LF components, respectively. These results indicate that this computer algorithm is highly repeatable in processing short records of beat-to-beat heart rate data collected from the general population, provided that the data operators are trained according to standardized protocol.

Evidently, this algorithm has limitations. In our sample of population-based short-term heart rate data, 7.4% could not be processed due to large amounts of artifacts in the very beginning and/or the ending portions of the record. One could have imputed acceptable heart rate data points from such records, had one imputed the data based on a limited number of uncorrupted data points. This practice would not be advisable for short records and would threaten the validity of the estimates.

The visual control exercised by the operator protects against evident error, since the inputed data points are displayed on the screen recognizable as imputed observations in the context of the full record of empirically measured data points. If the fit is not appropriate, the imputation step can easily be repeated under mouse stringent boundaries, in order to satisfy the overall pattern and location of the adjacent, measured data points. In practice, we found it unnecessary to perform such iterations except in extreme cases of corrupted segments of heart rate records.

There is no direct way to assess the validity of the heart rate data imputed by this algorithm. To address the plausibility and consistency of the imputed data, we applied this algorithm to the 2-min beat-to-beat heart rate records collected from the participants in the ARIC cohort to recover the corrupted data and estimate HF, LF, and HF/LF ratio. We found that these HRV indices were significantly associated with age, race, sex, prevalent myocardial infarction, diabetes mellitus, development of hypertension, and coronary heart disease (these results are being published elsewhere). These findings are consistent with the clinical literature and, thus, indirectly support the validity of this algorithm in recovering and estimating HF, LF, and HF/LF ratio from 2-min beat-to-beat heart rate records.

APPENDIX: Algorithm to Remove Artifacts

Assumptions

1. Heart rate raw data are a sequence of terms C(1), C(2), . . . , C(N), where each C(j) is the time difference as determined by the number of clock counts between consecutive R waves of ECG or corrupting artifacts over a period of 2 min.

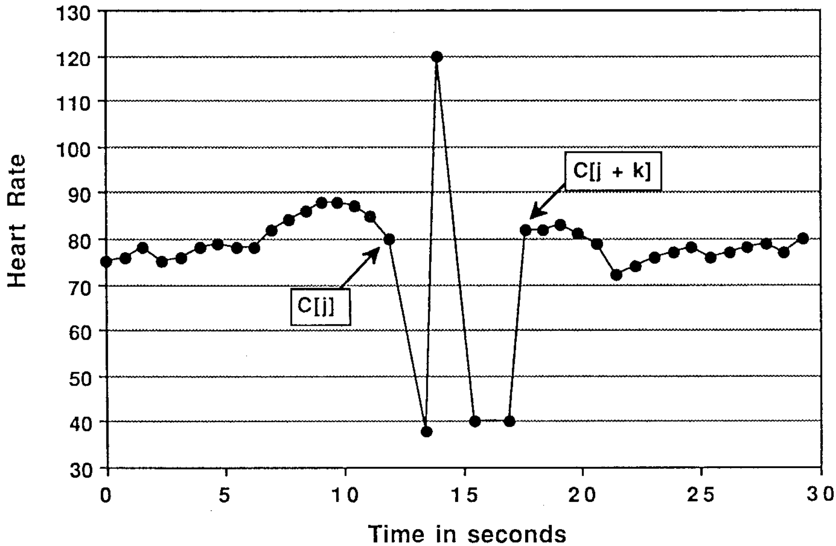

FIG. 2. Heart rate record with artifacts.

2. At least three regions are present in the data as shown in Fig. 2: Stable region before the electronic noise region, the ending term is C(j), electronic noise region between C(j) and C(j + k), stable region after the electronic noise region.

Algorithm

1. Beat-to-beat heart rate (beat/min) is determined by **HR = 60/T,** where **T** is the R to R interval in seconds. In the data, the sequence of terms C(1), C(2), . . . , C(N) represents the number of clock counts between consecutive R waves of ECG. Thus, the **HR(j) = K/C(j)** determines the corresponding heart rate to each C(j), where K is a constant equal to 60 times the clock frequency.

2. C(j) is considered normal if

$$\{(\textbf{LOWER LIMIT})*(\textbf{Aver(j)})\} \leq \textbf{C(j)} \leq \{(\textbf{UPPER LIMIT})*(\textbf{Aver(j)})\},$$

where **Aver** is a 5-beats moving average calculated by

$$\{C(j) + C(j - 1) + \cdot\cdot\cdot + C(j - m)\}/(m + 1),\ m = 5 \text{ in our case.}$$

LOWER LIMIT and **UPPER LIMIT** are determined by average heart rate ±25%.

If the results are acceptable (no artifact), no further processing is performed. The definition of acceptability is that each heart rate data point falls between the lower and upper limits on the moving average generated from the raw data.

If the estimated heart rate data are not within the upper and lower limits generated by the computer as defined above, a limit will be set by manually tracing the biologically plausible lower and upper limits using a mouse. Data from the unacceptable results then can be reprocessed using this manually set limit. If these processed data are not acceptable, no further processing will be performed.

3. Let C(j) be the last acceptable term before an unstable region.

4. Let C($j + k$) be the first acceptable term after the noisy region, such that

$$\{(\mathbf{LOWER\ LIMIT})^*(\mathbf{AVG(j+k)})\} \leq \mathbf{C(j+k)} \leq \{(\mathbf{UPPER\ LIMIT})^*(\mathbf{AVG(j+k)})\},$$

so that the calculated average count is

$$\mathbf{CAV} = (\mathbf{C(j+k)} + \mathbf{C(j)})/\mathbf{2}.$$

5. Calculate the difference in counts,

$$\mathbf{D1} = \mathbf{C(j+k)} - \mathbf{C(j)},$$

which is used to help establish the range of estimated terms between C(j) and C($j + k$).

6. Calculate the sum of the clock counts between C(j) and C($j + k$) in the unstable time series:

$$Sum1 = \sum_{i=1}^{k} C(j+i).$$

7. Estimate the number of terms to be inserted between C(j) and C($j + k$), **Est** = **Trunc (Sum1/CAV)**, where Trunc takes the largest integer less than or equal to (Sum1/CAV).

8. Calculate the estimated average change in the counts per missing heart rate:

$$\Delta 1 = Trunc\ (D1/Est).$$

9. Let the differences in counts between estimated heart rate be

$$d_1 = d_2 = \cdots = d_{Est} = \Delta 1.$$

(a) *If* $\sum_{i=1}^{Est} d_i < D1$, add 1 to d_1, then $d_2, \ldots,$ until

$$\sum_{i=1}^{Est} d_i = D1.$$

(b) *If* $\sum_{i=1}^{Est} d_i > D1$, subtract 1 from d_1, then $d_2, \ldots,$ until

$$\sum_{i=1}^{Est} d_i = D1.$$

10. The first estimated new counts NC(i) between C($j + k$) are

$$\mathbf{NC(1) = C(j) + d_1},$$
$$\mathbf{NC(2) = NC(1) + d_2},$$
$$\vdots$$
$$\mathbf{NC(Est) = NC(Est - 1) + d_{Est}}.$$

11. Calculate the sum of the NC terms,

$$Sum2 = \sum_{i=1}^{Est} NC(i),$$

and then average these terms:

$$Sum2Av = Sum2/Est.$$

The Sum2 term checks to ensure the same number of clock counts in the estimated NC sequence and of clock counts occurring in the original sequence between C(j) and C($j + k$).

12. Calculate the difference $D2$ = Sum1 − Sum2.

13. If $D2 > 0.852^*$ AV then increment Est to Est + 1. Return to step 8 with the new value of Est. This step is an update in case the division (Sum1/Aver) in step 7 is not an integer. The constant 0.825 was determined from reviewing numerous records.

14. If $D2 \neq 0$, then calculate a new difference:

$$\Delta 2 = Trunc\ (D2/Est).$$

15. Let a new difference in counts be

$$d_1 = d_2 = \cdots d_{Est} = \Delta 2.$$

(a) *If* $\sum_{m=1}^{Est} d_m < D2$, add 1 to d_1, then $d_2, \ldots,$ until

$$\sum_{m=1}^{Est} d_m = D2.$$

(b) *If* $\sum_{m=1}^{Est} d_m > D2$, subtract 1 from d_1, then $d_2, \ldots,$ until

$$\sum_{m=1}^{Est} d_m = D2.$$

16. Modify the first NC series by NC(m) = NC(m) + d_m, $m = 1, 2, \ldots,$ Est, where the d_m are obtained from step 15.

17. Checkpoint: if steps 1–16 have been performed correctly, then number of counts in the NC series should be equal to Sum1, the number of counts in the original corrupted time series in region B:

$$Sum1 - \sum_{m=1}^{Est} NC(m) = 0.$$

18. In region B insert the terms NC(1), NC(2), . . . , NC(Est) between C(j) and C($j + k$) as NC(i) = C(j + 1), where i = 1, 2, . . . , Est.

19. Update the running average in region C:

$$\text{New Aver} = (\text{C}(j + \text{Est} + 1) + C(j + \text{Est} + 2) + \cdot \cdot \cdot \text{C}(j + \text{Est} + m))/(m - 1).$$

20. If the entire ECG strip is not finished, go to step 3 with Aver replaced by New Aver.

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