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KARDIA: A Matlab software for the analysis of cardiac interbeat intervals

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ABSTRACT

This article presents KARDIA, a Matlab (MathWorks Inc., MA) software developed for the analysis of cardiac interbeat interval (IBI) data. Available functions are called through a graphical user interface and permit the study of phasic cardiac responses (PCRs) and the estimation of time and frequency domain heart rate variability (HRV) parameters. Scaling exponents of heartbeat fluctuations are calculated with the detrended fluctuation analysis (DFA) algorithm. Grand average and individual subject results can be exported to spreadsheets for further statistical analysis. KARDIA is distributed free of charge under the terms of GNU public license so that other users can modify the code and adjust the program's performance according to their own scientific requirements.

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1. Introduction

Time intervals between successive heartbeats are obtained from electrocardiographical (ECG) recordings and provide a way to measure heart rate patterns, either in resting states (heart rate variability; HRV) or as response to external stimuli (phasic cardiac responses; PCRs). Many commercial data acquisition programs provide algorithms to subtract interbeat intervals (IBIs) from ECG recordings and to calculate some of the most common HRV parameters. The problem of PCR analysis, however, is not addressed by these programs and most researchers depend on custom software to calculate heart rate changes in response to experimental stimuli. In addition, HRV

analysis is a field that has gained considerable interest in recent years and a significant number of new metrics deriving from statistical physics have been proposed as complementary to traditional time and frequency domain measures [1]. At the same time, older algorithms are continuously being refined, and advanced methods are being tested in order to further improve the assessment of autonomic function in health and disease [2].

As an alternative to commercial software, several free HRV analysis programs are also available to cardiovascular researchers. Two of the most sophisticated and user-friendly are Ecglab [3] and POLYAN [4]. Ecglab is a Matlab toolbox that performs not only HRV analysis, but also R-wave peak detection from raw ECG recordings. HRV analysis functions

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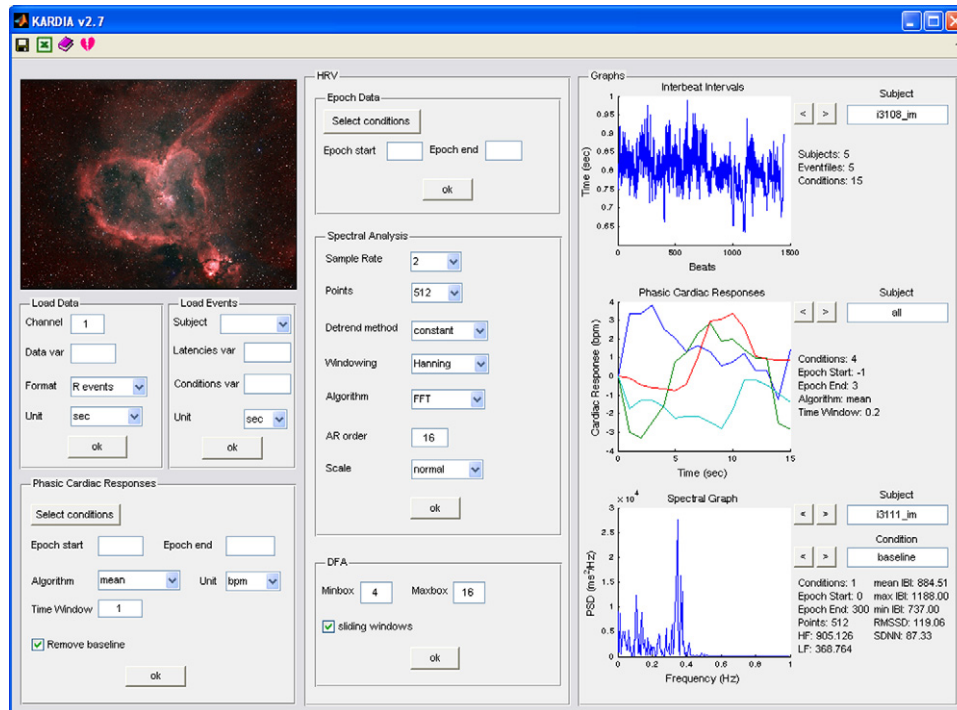


Fig. 1 – The graphical user interface of KARDIA.

calculate most common time domain measures, spectral analysis parameters and also present time–frequency graphs and metrics. Importantly, its open source philosophy allows users to modify the existing algorithms according to their specific needs. POLYAN is another open source Matlab software designed for the simultaneous analysis of several recording signals for the assessment of autonomic regulation. Its HRV analysis algorithms calculate both time and frequency domain metrics and provide elaborate graphs that facilitate the understanding and interpretation of numerical results. Another useful, and freely available HRV analysis program [5], also provides common estimates of time and frequency domain measures.

In this article we present KARDIA (“heart” in Greek), a Matlab software designed for the analysis of PCRs and HRV. Kardia is an open source project hosted by sourceforge, which means that it is subjected to continuous development by an increasing number of researchers [6]. Its main advantage compared to the programs presented above is its capacity for simultaneous analysis of multiple datasets, calculation of grand average statistics across subjects and experimental conditions and generation of analytic spreadsheets that can be directly subjected to further statistical analysis by related software.

Furthermore, KARDIA performs PCR analysis based on event codes corresponding to external stimuli presented under specific experimental conditions. These phasic responses are calculated by coherent averaging which provides a valid estimation of event-related changes as unrelated fluctuations are cancelled out. Results are compared to a baseline period prior to the stimulation where nonspecific fluctuations are expected [7]. The assessment of phasic heart rate responses is a fundamental index of emotional modulation during affective picture processing [8] or an important

measure of orienting and attention [9], just to cite two examples.

2. Program description

KARDIA is intended to be a useful tool for researchers with no specific programming skills and therefore all functionalities are directly available from an intuitive graphical user interface (GUI).

PCRs time-locked to specific events may be calculated using either weighted averages or a range of interpolation methods. Common time and frequency domain HRV statistics are also estimated. The power spectrum is calculated using either fast Fourier transform or parametric methods, and scaling exponents of IBI fluctuations are computed using DFA [10]. Individual subject results and grand average statistics can also be exported to Excel spreadsheets for further statistical analysis.

KARDIA was entirely written in Matlab scripting language. All functions are contained within a single m-file (*kardia.m*), although the complete software package includes the software logo, a matrix with GUI-related information, documentation and sample data stored in different subfolders. The open access policy, guaranteed through the General Public License (GPL), allows more experienced users to adapt the code to address their own specific needs.

2.1. The graphical user interface

KARDIA's GUI is divided into four different panels (Fig. 1): the load data and event information panel (top-left), the PCR analysis panel (bottom-left), the HRV analysis panel (center) and

the results panel (right). The interface allows the user to load several data files simultaneously, manually set the analysis parameters and plot graphs of the results. A toolbar with four icon buttons at the top of the main window offers direct access to specific functionalities, such as save as, export to and help.

2.1.1. Load IBI data and event information panel

IBI data must be provided as a numeric vector saved in a Matlab mat-file. Data from several subjects may be imported simultaneously from different mat-files for analysis. Working with mat-files guarantees compatibility with almost all R-wave detection programs since there are many freely available algorithms that convert from almost any file format to Matlab mat-file. The IBI data vectors can either be in the form of time intervals between adjacent R-waves (IBI series) or R-wave peak times relative to the beginning of the recording (the cumulative sum of IBI series).

Event-related information for each subject needs to be saved in separate mat-files. An event is defined by its onset time in seconds or milliseconds from the beginning of the recording together with an identifying code specific to the type of the event. Onset times are saved as a numeric vector and the codes are stored in a cell structure as string variables. Hence, every event file must include two different variables of the same length: the onset time variable and the event codes variable. According to the experimental design the same event structure can be used for all subjects or different event files can be imported and matched with each subject's dataset. In the latter case, different event structures must be imported individually for each subject.

2.1.2. PCR analysis panel

The first step in performing PCR analysis is to select the events (conditions) that should be averaged. The user then needs to define a baseline period, before the event's onset as well as the event's duration. A drop-down menu offers a choice of algorithms that can be used to calculate the heart rate changes during the event: "mean", "CDR", "constant", "linear" and "spline".

The "mean" algorithm applies the *fractional cycle counts* method described in [11] whereby every IBI $[t_0, t_1], [t_1, t_2]$ is taken as a cardiac cycle. For an analysis window with onset time at T_0 and duration $T_1 - T_0$ the number of cycles within the window $[T_0, T_1]$ is counted. Cycle $[t_{i-1}, t_i]$ is counted as one if $T_0 \leq t_{i-1} < t_i \leq T_1$, as $(t_i - T_0)/(t_i - t_{i-1})$ if $t_{i-1} < T_0 < t_i \leq T_1$, as $(T_1 - t_{i-1})/(t_i - t_{i-1})$ if $T_0 \leq t_{i-1} < T_1 < t_i$ and as $(T_1 - T_0)/(t_i - t_{i-1})$ if $t_{i-1} < T_0 < T_1 < t_i$. Having defined the cycle count within a window, the mean heart rate is given by the ratio of this count to the total window length [11]. Reyes del Paso and Vila [12] showed that this fractional counting procedure is equivalent to the weighted averages method proposed by Graham in 1978 [13] which is the standard procedure used in psychophysiological research.

The algorithm "CDR" can be used to calculate the Cardiac Defense Response, according to the paradigm established by Vila et al. [14]. The heart response elicited by an intense auditory stimulus is calculated during 80s after the onset of the stimulus and is expressed in terms of second-by-second heart rate changes compared to a baseline of 15s prior to the presentation of the stimulus. These second-by-second heart rate

values are subsequently averaged across a group of participants based on 10 points corresponding to the medians of 10 progressively longer intervals: 2 of 3s, 2 of 5s, 3 of 7s and 3 of 13s. This simplified representation facilitates statistical analysis without altering the topographic characteristics of the response [14].

KARDIA also includes algorithms to calculate instantaneous heart rate at a sample rate defined by the user using a choice of three different interpolation methods: "constant", "linear" or "spline" interpolation. The "constant" method assigns the same value to every point between two IBIs. The "linear" method interpolates two adjacent IBIs with a straight line and the "spline" method uses a cubic spline function to interpolate the IBI series.

The user is further required to define the analysis window duration for the "mean" method, or the sample rate for the interpolation algorithms. The option also exists to calculate the heart period instead of heart rate changes and whether or not to subtract the baseline heart rate (or heart period) value when graphically representing the results. When all parameters are set, the program plots a grand average across all subjects for the selected conditions as well as individual graphs for each subject. Clicking on any of KARDIA's embedded graphs opens a new figure with the same plot that can be processed and saved in the same way as ordinary Matlab figures.

2.1.3. HRV analysis panel

HRV analysis is performed on a single epoch over the entire IBI series. The user is asked to select one event code and set the epoch's start and end time relative to the onset of the selected event.

2.1.3.1. Spectral analysis. Spectral analysis of HRV is used for the assessment of the variance of IBI fluctuations in specific frequency bands that correspond to identifiable physiological processes such as the vagally mediated respiratory sinus arrhythmia (RSA) and the baroreflex. As a first step, the IBI series is interpolated by cubic splines at a user-defined sample rate (2 or 4 Hz). The interpolated series is subsequently detrended, either by removing the best straight-line fit, or by subtracting the mean value. Next, the signal is multiplied by a window function (Hanning, Hamming, Blackman or Bartlett) to reduce artifacts on the frequency spectrum due to signal truncation. The discrete Fourier transform (DFT) is calculated by means of fast Fourier transform (FFT) algorithm for a number of points defined by the user (the FFT algorithm requires that the number of data points is a power of 2). The Fourier power spectral density (PSD) is then obtained from the squared absolute value of the DFT which is multiplied by the sampling period and divided by the number of samples in the signal. In addition, a coefficient described in [15] is used to remove the effect of the window function from the total signal power.

Alternatively, Matlab's *arburg* function that uses Burg method to fit an autoregressive (AR) model of variable order to the IBI signal, can be applied [16]. The power spectrum is then calculated from the squared absolute value of the AR system parameters, multiplied by the sample period and the variance of the white noise input to the AR model.

By default, the frequency spectrum is divided into three bands: VLF (0–0.04 Hz), LF (0.04–0.15 Hz) and HF (0.15–0.5 Hz). It is relatively easy, however, to modify these settings in the relevant part of the program code in *kardia.m*. The area under the PSD curve represents the statistical variance and is calculated separately for each frequency band by means of numerical integration. KARDIA graphically represents the PSD for each subject and condition together with key time domain statistics and the HF and LF variance.

2.1.3.2. Detrended fluctuation analysis. DFA is an algorithm introduced by Peng et al. [10] that has proven to be very successful in quantifying the correlation properties of non-stationary time series derived from biological, physical and social systems. DFA has been applied to diverse research fields such as economics [17], climate change [18], DNA [19], neural networks [20] and cardiac dynamics [10]. In its application to HRV, the IBI series (of length N) is first integrated, to calculate the sum of the differences between the i th inter-beat interval $B(i)$ and the mean interbeat interval \bar{B} : $y(k) = \sum_{i=1}^k [B(i) - \bar{B}]$. Next, the integrated series $y(k)$ is divided into boxes of equal length n (measured in number of beats). Each box is subsequently detrended by subtracting a least-squares linear fit, denoted $y_n(k)$. The root-mean-square (RMS) fluctuation of this integrated and detrended time series is calculated by

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

The algorithm is then repeated over a range of box sizes to provide a relationship between the average fluctuation $F(n)$ as a function of box size n . Normally, $F(n)$ will increase as box size n becomes bigger. A linear relationship on a log–log graph indicates the presence of fractal scaling whose exponent is given by the gradient (usually referred to as the α exponent). For uncorrelated time series (white noise), the integrated $y(k)$ is a random walk, which yields an exponent of $\alpha = 0.5$. A scaling exponent larger than 0.5 indicates the presence of positive correlations in the original time series such that a large IBI is more likely to be followed by another large interval, while $0 < \alpha < 0.5$ indicates anti-correlations such that large and small IBI values are more likely to alternate. The special case of $\alpha = 1.5$ is obtained by the integration of highly correlated Brown noise, while $\alpha = 1$ corresponds to $1/f$ noise that reflects a balance between the step by step unpredictability of random signals and highly correlated Brownian noise [21].

KARDIA allows the user to define the minimum and maximum box size for the DFA analysis and whether or not to implement a sliding windows (overlapping) version of the algorithm which increases precision, but is computationally more intensive.

2.1.4. Results panel

KARDIA's results panel is further divided into three sub-panels. The top sub-panel provides information on the number of subjects, event files and conditions imported. After importing data, the IBI series for each subject are plotted

in this sub-panel. Users can use the arrow buttons to scroll through subjects or type the name of a subject to directly see their IBI plot.

The second sub-panel corresponds to the PCR analysis. At any given moment, users can see the conditions selected, the algorithm used as well as the analysis window defined. The graph plots the grand average for each condition, but also allows the user to inspect individual subject's results through the use of the arrows buttons.

The third sub-panel presents the results of the HRV analysis. HRV statistics are instantly updated each time the user runs a new analysis of the data. The graph plots the power spectrum and the DFA graphs for each subject and condition. Once again, users can scroll through subjects by using the arrows or by typing the name of the target subject. The same is also true for differing conditions.

2.1.5. Toolbar buttons

The first toolbar button allows the user to save a mat-file in the current directory containing all the data and event information imported into KARDIA, as well as all the parameter settings relevant to the current analysis. This allows a previously ongoing analysis to be resumed and all the required information, including data and parameter settings, to be saved in a single file thus facilitating data sharing.

The second toolbar button is used to export the numerical results of the last analysis performed (PCR and HRV) to an excel file. The excel spreadsheet generated contains five different tabs: a "General" tab with information about subjects and events, a "PCR" tab with the heart rate (or heart period) estimates for each subject and condition, a "Grand Average PCR" tab with the grand average results for PCR analysis, an "HRV" tab with the measures of all subjects and conditions, and a "Grand Average HRV" tab with the grand average HRV statistics.

The last two toolbar buttons are for launching the "User's Guide" in pdf format and for opening a dialog window displaying the program's copyright agreement, respectively.

2.2. System requirements

KARDIA requires less than 1MB of free hard disk space. The program will run on any operating system supporting Matlab 7.0 (The MathWorks Inc., MA) or later that has the Matlab Signal Processing Toolbox (The MathWorks Inc., MA) installed. The program's current version (v.2.7) has been tested in Matlab R2007b on Mac OS X, version 10.5 (Apple Inc., CA), Ubuntu 8.10 Linux, and Microsoft Windows XP (Microsoft Inc., WA).

2.3. Installation procedure

After downloading and unzipping the KARDIA package, the only step that needs to be followed is to add the package's folder and subfolders to Matlab's path.

2.4. Availability

KARDIA is distributed free of charge under the terms of the GNU General Public License as published by the Free Software

Foundation [22]. Users are free to redistribute and modify it under the terms of the GNU license. KARDIA is freely available for download at <http://sourceforge.net/projects/mykardia/>.

3. Sample runs

KARDIA's PCR module was tested on IBI data obtained from 24 subjects (15 female; 21 years ± 1.7) in a picture viewing paradigm. "Neutral" images (people) and "unpleasant" images (mutilated bodies) drawn from the International Affective Picture System [23] were presented to the subjects on a computer screen while continuous ECG was being recorded. Each picture presentation trial was initiated with a fixation cross lasting from 500 to 900 ms. The picture (neutral or unpleasant) was subsequently presented during 200 ms. A checkerboard mask was then projected during 3 s, until the beginning of the next trial. ECG was recorded from a bipolar chest lead, filtered with a high pass filter (0.5 Hz cutoff frequency) and sampled at 240 Hz. R-wave detection and artifact correction were performed with Ecglab [3].

IBI data for all 24 subjects was imported into KARDIA together with an event file for each subject containing the onsets of the two types of events (neutral and unpleasant picture presentation). In the PCR panel we first chose to analyze both conditions (neutral and unpleasant) and then selected -0.5 s for "epoch start" and 3 s for "epoch end" boxes. The program then uses a 500 ms period before stimulus onset to obtain the baseline heart rate and calculates heart rate changes compared to this baseline value for 3 s post-stimulus. We selected the "mean" option to implement a weighted averages algorithm, "bpm" to obtain the results in heart rate instead of heart period as well as the value 0.2 for the "Time window" to calculate a weighted average heart rate value every 200 ms. We also checked the "Remove baseline" box to plot heart rate changes against the baseline instead of absolute heart rate values in the results graph.

Fig. 2 shows the result of the PCR analysis for the selected parameters as it appears in KARDIA's results panel. The

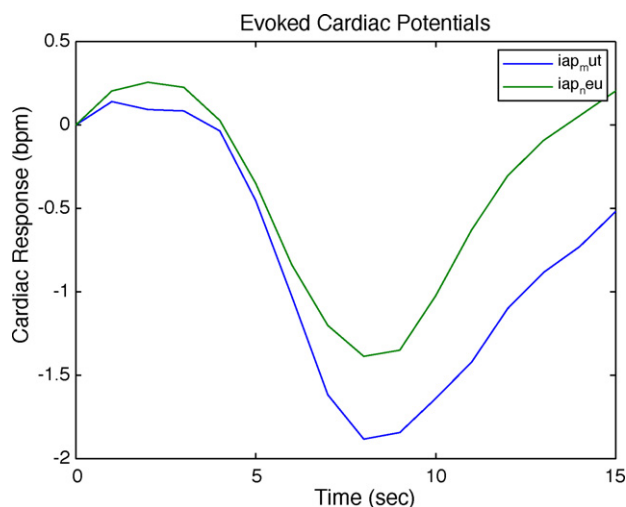


Fig. 2 – The PCR results panel. The grand average over all subjects indicates a potentiated bradycardia in the unpleasant picture condition (blue line) compared to control (green line). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

grand average over all subjects is first plotted, but users can use the arrows to scroll through the results for individual subjects. A potentiated bradycardia is observed in the unpleasant picture condition (blue line) compared to control (green line), as expected according to the literature on the orienting reflex in humans [24]. The embedded graph does not include a legend, but clicking it with the mouse left-button opens the same plot in a new figure window that includes a legend and can be edited and saved in various formats.

The HRV module was tested comparing a 5 min resting period before and after atropine administration. First, in HRV's "Epoch Data" panel, we chose the event code named "before

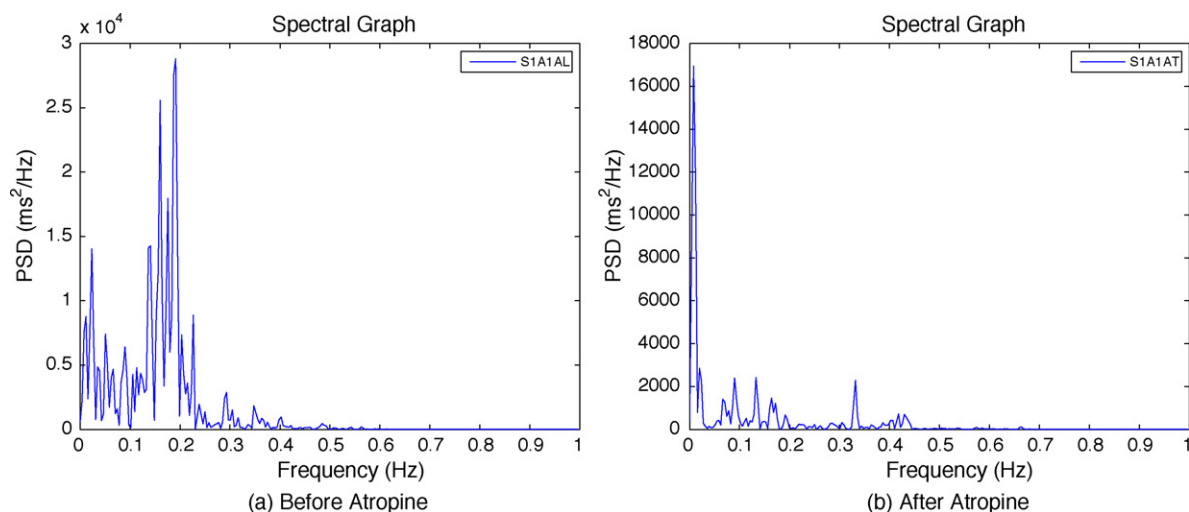


Fig. 3 – The HRV results panel. (a) The spectral graph of a 5 min segment before atropine administration. In (b), which presents a spectral graph for the same subject after atropine administration, we observe the elimination of respiratory-related oscillations due to parasympathetic blockade.

drug” and set “Epoch start” to 0 and “Epoch end” to 300. This defined a specific epoch on the entire IBI record whose onset coincided with the event code named “before drug” (time 0) and lasting 5 min (300 s). Right after epoch selection, the selected IBI epochs for each subject are displayed in the HRV sub-panel of the results panel. The next step was to select the spectral analysis parameters in the corresponding panel. For this example we selected the default values: 2 Hz for the sampling rate, 512 points for the DFT, a “constant” detrending method, Hanning as the window function and FFT for spectral estimation. We repeated the same procedure choosing the label “after drug” as the event code in the “Epoch Data” panel. Fig. 3 presents a comparison between the two conditions. The absence of respiratory-related oscillations due to parasympathetic blockade is obvious in the second condition. Once again users can scroll through subjects to quickly review snapshots of individual spectrograms and statistics.

Finally, the Excel toolbar button can be used to save a specially formatted excel file with the results from all analyses (PCR and HRV) performed. This file provides grand average as well as individual statistics that are then amenable to further processing with statistical packages like R, SPSS, etc.

4. Conclusion

KARDIA is currently in use by research laboratories at Harvard Medical School and Boston University in the USA, at the Universities of Granada and Castellon in Spain, and at the Federal University of Rio de Janeiro in Brasil. It has proven to be very useful in a variety of psychophysiological experiments. Experienced and inexperienced researchers have profited from its graphical user interface, reporting improved analysis time and ease of data manipulation.

One of KARDIA's main advantages over other available software for IBI analysis is its ability to load data from many subjects simultaneously through the GUI and to calculate grand average PCRs and HRV statistics across all subjects. In addition, the program saves all information about imported datasets and numerical results in a single “mat” file that substitutes the numerous IBI and event information files and facilitates data storage and sharing.

KARDIA is being actively maintained and developed. New functionality is expected to be included in future versions, such as algorithms for automatic IBI artifact detection and nonlinear HRV analysis.

Conflict of interest statement

None declared.

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REFERENCES

- [1] P. Mansier, J. Clairambault, N. Charlotte, C. Médigue, C. Vermeiren, G. LePape, F. Carré, A. Gounaropoulou, B. Swynghedauw, Linear and nonlinear analyses of heart rate variability: a minireview, *Cardiovascular Research* 31 (1996) 371.
- [2] A. Camm, M. Malik, J. Bigger Jr., Heart rate variability: standards of measurement, physiological interpretation and clinical use. Task force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, *Circulation* 93 (1996) 1043–1065.
- [3] J. Carvalho, A. da Rocha, F. Nascimento, J. Souza Neto, L. Junqueira Jr., Development of a Matlab software for analysis of heart rate variability, in: B. Yuan, X. Tang (Eds.), 6th International Conference on Signal Processing, vol. 2, Beijing, China, Institute of Electrical and Electronics Engineers, Inc., 2002, pp. 1488–1492.
- [4] R. Maestri, G. Pinna, POLYAN: a computer program for polyparametric analysis of cardio-respiratory variability signals, *Computer Methods and Programs in Biomedicine* 56 (1998) 37–48.
- [5] J. Niskanen, M. Tarvainen, P. Ranta-aho, P. Karjalainen, Software for advanced HRV analysis, *Computer Methods and Programs in Biomedicine* 76 (2004) 73–81.
- [6] P. Perakakis, M. Joffily, M. Taylor, KARDIA project. <http://sourceforge.net/projects/mykardia/> (accessed June 29, 2009).
- [7] J. Jennings, W. Bberg, J. Hutcheson, P. Obrist, S. Porges, G. Turpin, Publication guidelines for heart rate studies in man, *Psychophysiology* 18 (1981) 226–231.
- [8] M. Bradley, M. Codispoti, B. Cuthbert, P. Lang, Emotion and motivation I: defensive and appetitive reactions in picture processing, *Emotion* 1 (2001) 276–298.
- [9] A. Ohman, A. Hamm, K. Hugdahl, Cognition and the autonomic nervous system: orienting, anticipation, and conditioning, *Handbook of Psychophysiology* (2000) 533–575.
- [10] C. Peng, S. Havlin, H. Stanley, A. Goldberger, Quantification of scaling exponents and crossover phenomena in nonstationary heartbeat time series, *Chaos: An Interdisciplinary Journal of Nonlinear Science* 5 (1995) 82.
- [11] T. Dinh, H. Perrault, P. Calabrese, A. Eberhard, G. Benchetrit, New statistical method for detection and quantification of respiratory sinus arrhythmia, *IEEE Transactions on Biomedical Engineering* 46 (1999) 1161–1165.
- [12] G. Reyes del Paso, J. Vila, The continuing problem of incorrect heart rate estimation in psychophysiological studies: an off-line solution for cardiachometer users, *Biological Psychology* 48 (1998) 269–279.
- [13] F. Graham, Constraints on measuring heart rate and period sequentially through real and cardiac time, *Psychophysiology* 15 (1978) 492–495.
- [14] J. Vila, P. Guerra, M. Muñoz, C. Vico, M. Viedma-del Jesús, L. Delgado, P. Perakakis, E. Kley, J. Mata, S. Rodríguez, Cardiac defense: from attention to action, *International Journal of Psychophysiology* 66 (2007) 169–182.
- [15] H. Jokinen, J. Ollila, O. Aumala, On windowing effects in estimating averaged periodograms of noisy signals, *Measurement* 28 (2000) 197–207.

- [16] P. Stoica, R. Moses, *Introduction to Spectral Analysis*, Prentice Hall, Upper Saddle River, NJ, 1997.
- [17] R. Weron, Estimating long-range dependence: finite sample properties and confidence intervals, *Physica A: Statistical Mechanics and its Applications* 312 (2002) 285–299.
- [18] D. Vjushin, R. Govindan, S. Brenner, A. Bunde, S. Havlin, H. Schellnhuber, Lack of scaling in global climate models, *Journal of Physics Condensed Matter* 14 (2002) 2275–2282.
- [19] S. Buldyrev, N. Dokholyan, A. Goldberger, S. Havlin, C. Peng, H. Stanley, G. Viswanathan, Analysis of DNA sequences using methods of statistical physics, *Physica A* 249 (1998) 430–438.
- [20] C. Stam, T. Montez, B. Jones, S. Rombouts, Y. van der Made, Y. Pijnenburg, P. Scheltens, Disturbed fluctuations of resting state EEG synchronization in Alzheimer's disease, *Clinical Neurophysiology* 116 (2005) 708–715.
- [21] C. Peng, S. Buldyrev, A. Goldberger, S. Havlin, F. Sciortino, M. Simons, H. Stanley, Long-range correlations in nucleotide sequences, *Nature* 356 (1992) 168–170.
- [22] Free Software Foundation, GNU General Public License (2007).
- [23] P. Lang, M. Bradley, B. Cuthbert, *International affective picture system (IAPS): technical manual and affective ratings*, The Center for Research in Psychophysiology, University of Florida, Gainesville, FL, 1995.
- [24] P. Lang, R. Simons, M. Balaban, *Attention and Orienting: Sensory and Motivational Processes*, Lawrence Erlbaum Associates, 1997.