Computers in Biology and Medicine 43 (2013) 2001–2006

Contents lists available at ScienceDirect

Computers in Biology and Medicine

journal homepage: www.elsevier.com/locate/cbm

Mitigating the effect of non-stationarity in spectral analysis—An application to neonate heart rate analysis

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ARTICLE INFO

Article history:
Received 10 May 2013
Accepted 21 September 2013

Keywords:
Power spectral analysis
Non-stationarity
Neonatal heart rate
Autonomic nervous system
Birth asphyxia

ABSTRACT

In order to mitigate the effect of non-stationarity in frequency domain analysis of data, we propose a modification to the power spectral estimation, a widely used technique to characterize physiological signals. Spectral analysis requires partitioning data into smaller epochs determined by the desired frequency resolution. The modified approach proposed here involves dividing the data within each epoch by the standard deviation of the data for that epoch. We applied this modified approach to cardiac beat-to-beat interval data recorded from a newborn infant undergoing hypothermia treatment for birth asphyxia. The critically ill infant had episodes of tachyarrhythmia, distributed sporadically throughout the study, which affected the stationarity of the heart rate. Over the period of continuous heart rate recording, the infant's clinical course deteriorated progressively culminating in death. Coinciding with this clinical deterioration, the heart rate signal showed striking changes in both low-frequency and high-frequency power indicating significant impairment of the autonomic nervous system. The standard spectral approach failed to capture these phenomena because of the non-stationarity of the signal. Conversely, the modified approach proposed here captured the deteriorating physiology of the infant clearly.

1. Introduction

Physiological signals exhibit features that have a characteristic time scale. For example, the cardiac beat-to-beat interval (RRi) exhibits: (1) slow changes that are related to both sympathetic and parasympathetic components of the autonomic nervous system (ANS) [1], (e.g. baroreflex activity) and (2) fast changes that are related primarily to the parasympathetic (vagal) component of the ANS, (e.g. respiratory sinus arrhythmia) [1]. Investigation of RRi using appropriate signal processing tools can thus provide clinician opportunity to access the function and integrity of the ANS. Several methods exist to evaluate RRi. Time-domain methods include characterization of (a) low-frequency component (standard deviation of normal to normal [SDNN] intervals), (b) short-term variability or the high-frequency component of the RRi (the root mean square of successive differences [RMSSD]), and (c) the probability that the current normal-to-normal RRi is less than *x*-ms from the previous normal-to-normal RRi [pNN*x*] [2]. Additional methods based on statistical physics such as detrended fluctuation analysis [3] and multifractal analysis [4], have also been used to characterize the low- and high-frequency fluctuations in the RRis. Likewise, novel methods such as phase-rectified signal averaging [5] and phase-plane analysis [6] also have been used to characterize the heart rate in time-domain. In the frequency domain RRis are analyzed using the power spectral approach [2,7–9]. Unlike the time-domain approaches, the spectral approach allows direct assessment of sympathetic and parasympathetic components of the ANS. Power spectral analysis of cardiac inter-beat intervals can be used to characterize the components occurring at different time scales [8–12]. The influence of respiration on the cardiac beat-to-beat interval (respiratory sinus arrhythmia) can also be readily characterized by spectral analysis [13,14]. These features make the power spectral approach superior to the time-domain approach in studies such as heart rate variability analysis. However, an implicit assumption in spectral analysis is that the data must be stationary [2]. Given the non-stationary nature of the physiologic data in clinical practice, this is a potentially significant limitation of spectral analysis in physiologic studies, especially in cases of clinical instability.

The non-stationarity can be caused by extrinsic factors (e.g. such as movement of the subject) or by intrinsic factors (e.g. transient changes within the physiology of the system). While the non-stationarity due to extrinsic factors can be minimized by excluding affected data from the analysis, the non-stationarity caused by the intrinsic factors compromises spectral analysis in a more troublesome manner, and leads to incomplete characterization of the data.

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0010-4825/$ - see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.compbiomed.2013.09.019

In critical care units, a mass of continuous physiological data is acquired by monitors at the bedside. However, there is an enormous redundancy in that a small minority of these data is currently explored for their potential clinically relevant content. There is an urgent need for enhanced anticipation of clinical deterioration since prevention of catastrophic collapse is needed to decrease the acute and long-term complication rates. Real-time integration and processing of the multiple physiological signals monitored may provide valuable early biomarkers of imminent deterioration. However, the methods employed to explore these biomarkers need to perform robustly in the frequent periods of non-stationarity inherent in critical care. This has continued to be a limitation of standard spectral power analyses. In this report we propose a modification to the spectral power analysis (henceforth call the modified approach) that mitigates the effect of non-stationarity in physiologic signals, and compare its performance against standard technique (henceforth call the standard technique).

2. Materials

2.1. Study subject

A newborn female infant with perinatal asphyxia due to nuchal cord and meconium aspiration was treated with a whole body hypothermia protocol proposed by the National Institute of Child Health and Human Development [15]. The infant presented with a cord blood pH of 6.9 and clinical encephalopathy. She was placed on a servo-controlled cooling blanket set to maintain an esophageal temperature of 33.5 °C. The infant underwent continuous physiological monitoring, (i.e. including electrocardiogram [ECG], blood pressure, pulse oximetry, cerebral oximetry) as part of an ongoing prospective observational study. The study was approved by the Children's National Medical Center Institutional Review Board, and informed consent was obtained.

2.2. Data collection

ECG was retrieved from the analog port of the bedside monitor (Philips MP70, Philips, MA, USA) using custom software developed in LabView2010 Professional development system (National Instruments Corporation, TX, USA). The data were sampled at 1 KHz over a continuous period of 23.5 h. All processing was performed using MATLAB (Mathworks, Inc., MA, USA).

3. Methods

3.1. Signal pre-processing

ECG was bandpass filtered between 0.5 and 70 Hz using Butterworth filter with zero-phase distortion. The R-wave was identified using adaptive Hilbert transform approach and beat-to-beat interval (RRi) was computed as successive difference of R-wave occurrence expressed in seconds. The RRi was converted into evenly sampled data using cubic-spline interpolation at a sample rate of 4 Hz. The RRi was divided into 10 min windows with a sliding overlap of 2 min.

3.2. Standard approach

In each 10 min window, the power spectrum was estimated in the standard approach as follows [16]: Step (1) The RRis were partitioned into disjointed (no overlap) 60 s windows (also called fast Fourier transform [FFT] length), and the mean was subtracted from them; this is same as convolving the RRis with a rectangular window of 60 s duration. Step (2) in each 60 s window, the periodogram (i.e. the square of the modulus of the FFT of the RRis) was computed; and Step (3) the periodogram was averaged over all the windows to obtain the estimate of the power spectrum. To express this mathematically

$$P(\omega) = \frac{1}{M}\sum_{k=1}^{M} Per_k(\omega),$$

where $Per_k(\omega)$ is the periodogram in the kth 60 s window and M is the number of 60 s windows, which is 10 in this study. The choice of 60 s was used to capture reliably the low-frequency changes down to 0.05 Hz. However, we would like to mention that the results reported here did not change significantly for the choice of 30 s window. $P(\omega)$ computed as shown above will have a unit of second^2. In the presence of non-stationarity, the periodogram from the non-stationary 60 s region will have significantly different characteristics both in amplitude (usually very high) and frequency. The spurious amplitude from the non-stationary region will dominate the average involved in the calculation of $P(\omega)$ resulting in an incorrect characterization of the data.

3.3. Modified approach

In spectral analysis, the total variance of a signal is decomposed into different frequency components. In other words, the power spectrum is a frequency-domain description of the variance of the RRi. Based on this fact, in a stationary dataset the sum of the powers over all frequency bands is equal to the total variance of the RRis. Thus, for the periodogram from $k$th60 s window, we have the following relation:

$$\int_{-\infty}^{\infty} Per_k(\omega)d\omega = \mathrm{var}(x^{(k)}),$$

where $d\omega$ is the frequency resolution of the spectral estimate, $x^{(k)}$ represents the RRis in the kth 60-s window and $\mathrm{var}(\cdot)$ indicates the variance function. In practice, this integration is performed in the frequency bands from negative half of the sample frequency to positive half of the sample frequency, where the power is calculated.

The proposed modification involves dividing the data after Step 1 (Section 3.2) by its standard deviation. Thus, in the modified approach the periodogram is divided by the variance (recall that the calculation of the spectrum involves squaring of the standard deviation which converts the latter into variance) of the data and the above integral will yield a value of one.

For a stationary dataset the total variance is approximately same as the average of the variance in all the windows (i.e.) $\langle \mathrm{var}(x^{(k)})\rangle_k \approx \mathrm{var}(x)$, where $\langle\cdot\rangle$ denotes the average and x denotes 10-min of RRis. Based on this relation, the integration of the spectral estimate $P(\omega)$ obtained using the modified approach, will also be one. Further, the power spectrum obtained through this modified scheme will be dimensionless because of the normalization by standard deviation. To compare the spectrum obtained using modified approach with standard approach, we rescaled the former by multiplying it with $\langle \mathrm{var}(x^{(k)})\rangle_k$. This rescaling allows to express power in the unit of second^2. Thus, for stationary data, both the standard and modified approaches should yield the same result within the numerical precision of the computation.

However, for non-stationary data, the normalization by standard deviation will ensure that the periodogram corresponding to the non-stationary region (with sudden changes in the signal amplitude) will assume the same or comparable amplitude as rest of the data from stationary regions. Therefore, the periodogram from the non-stationary region will not dominate the average in the calculation of the spectrum. However, the periodogram from the