Characterizing Artefact in the Normal Human 24-Hour RR Time Series to Aid Identification and Artificial Replication of Circadian Variations in Human Beat to Beat Heart Rate using a Simple Threshold

GD Clifford[1], PE McSharry[1,2], L Tarassenko[1]

[1]Department of Engineering Science, University of Oxford, Oxford OX1 3PJ, UK

[2]Mathematical Institute, University of Oxford, Oxford OX1 3LB, UK

Abstract

The authors present an investigation into the incidences of ectopy and artefact as a function of time of day, heart rate and state changes for 19 normal subjects. State changes are defined to be a statistically significant change in mean or variance over a window of a few minutes. Artefact incidence is shown to be significantly correlated with state change and heart rate in normal humans, whereas ectopy exhibits no significant relationship. Artefact is therefore shown to be a source of information which can aid identification of activity or state changes and facilitate abnormality detection in patient populations.

Timing thresholds are proposed which differentiate between artefact, ectopy and sinus beats. A classification system based upon the frequency of artefact occurrences in relation to state changes is presented which correctly separates 78% of the the real (normal) and artificial RR interval time series in event 2 of the CinC Challenge 2002 (entry number 38).

1. Introduction

Over the last twenty years there has been much interest in methods for characterising the 24-hour RR time series of humans in order to differentiate between patient populations and provide diagnostic information. For example, much work has been done to evaluate 24-hour heart rate variability (HRV) metrics in a clinical setting [1]. However, the utility of results using these metrics is still controversial and clinical communities are reluctant to adopt such metrics as markers of health [2].

Recent studies [1, 2] have shown that variations in physiological activity, at specific times, over the 24-hour period are indicative of health and/or recovery. Although some of the metrics used to assess cardiovascular activity are based upon quantifications of real physiological mechanisms (manifest as spectral peaks around specific frequencies [3]), no explicit allowance is made for circadian changes over the course of a 24-hour period.

Recent work has moved towards a more direct quantification of the behaviour of circadian cardiovascular changes. In particular, Bernaola-Galván *et al.* [4] have attempted to quantify the beat-to-beat variations of human RR intervals over a number of different time scales.

Analyses of such variations often only take into account beat-to-beat changes in normal (sinus) rhythm beats since inclusion of non-sinus (abnormal) beats in the analysis can cause serious errors in estimations of the variability in the RR time series [5]. However, the frequency of abnormal beats has been shown to be an independent predictor of health of patients in high risk groups [1]. Furthermore, for similar recording processes and detection algorithms the frequency of artefact is also related to patient activity [6]. Artefact may therefore provide an independent source of information about the circadian variations over the course of a 24-hour recording.

Methods for describing and quantifying circadian sinus rhythm changes as an aid to detecting normal human cardiovascular activity (and therefore deviations from normality) are presented in an accompanying paper 'A Method for generating synthetic RR time series of normal humans over 24-hours' (entry number 201 in event 1 of the the Physionet/Computers in Cardiology (CinC) Challenge 2002). This paper investigates the incidence of ectopy and artefact in the Physionet Normal Sinus Rhythm database (NSRDB) [7] in relation to means, variances and accelerations in the RR time series. The results are used for generating realistic ectopy and artefact in the above entry for event 1 of the the CinC Challenge 2002.

Simple beat-to-beat RR interval acceleration thresholding is used to label ectopy and artefact. These threshold calculations are used to assess the incidence of ectopy and artefact for all entrants in event 2 of the the CinC Challenge 2002 (entry number 38).
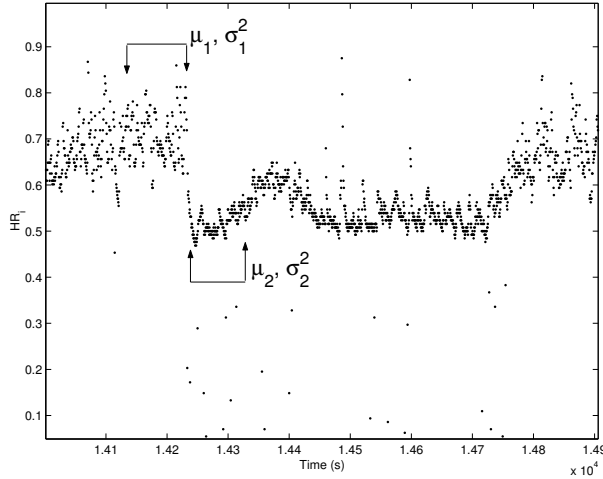
Figure 1. Fifteen minutes of RR interval data for a normal subject (16265) in the Physionet NSRDB. A state change is considered to have occured when adjacent 100 second segments have significantly different means (μ_1,μ_2) or variances (σ_1^2, σ_2^2).

2. Description of data

In the short term, over a period of one to five minutes, a normal healthy human RR time series is characterised by a few dominant frequency components which, together with their variances and the local mean RR interval (averaged over 100 to 300 seconds), tend to change quite slowly. Within such segments, cardiovascular activity is considered to be approximately stationary and frequency domain analysis is often employed [1]. A shift in cardiovascular state is associated with a change in both the local mean RR interval and the relative contributions of the component frequencies as well as a change in variance [4]. Such state switching is often accompanied by changes in physical or mental activity and therefore the frequency of such shifts may be an indication of the overall activity of a subject.

Consider two 100 second segments before and after a given RR interval with means μ_1 and μ_2 and variances σ_1^2 and σ_2^2 respectivley. In this paper, a state state change is considered to have occured if μ_1 is significantly different from μ_2, *or* σ_1^2 is significantly different from σ_2^2. Figure 1 illustrates a *state transition* (at 1.42×10^4 seconds). Note the mean and variance change 100 seconds either side of the transition.

3. Distribution of artefacts and ectopic beats in real data

In this paper, artefacts are defined to be disturbances in the ECG with beat-like morphology (labelled by '|' in the Physionet annotations) such that a conventional R-peak detector would label it as a beat. Ectopic or abnormal beats are defined to be those labelled by L, R, A, a J, S, V, r, F, e, j, n, E, P, f, Q, or ?. These are usually identified by experts because of the associated abnormal morphology and timing with respect to normal sinus beats (labelled 'N'). This paper deals only with aspects of beat to beat timing. Abnormal beats are often defined (in terms of their timing) as occurring either unusually early or late with respect to a sinus beat. It should be noted that the actual time stamp of the abnormal beat or artefact depends both upon the morphology of the beat/artefact *and* the method of detection. The Physionet database has been scored by clinicians who appear to have attempted to locate the top of the R-peak in a lead II configuration. This is effectively the function that many standard beat detectors such as *sqrs* perform [7].

In the absence of morphological information, standard texts define beats to be abnormal if the RR interval changes by more than 20% of the previous normal to normal (N-N) beat [1]. However, abnormal (ectopic) beats can occur within the tolerances of normality. This section presents results quantifying the distribution of timings of sinus to sinus beats (N-N), sinus to ectopic beats (N-E) and sinus to artefact (N-A) in terms of percentage change from the previous N-N interval for the 19 subjects in the Physionet NSRDB. In effect, this quantifies the relative acceleration of the instantaneous heart rate (HR_i). The percentage change in the nth RR interval is calculated using

$$\Delta RR_n = 100 \times \frac{RR_n - RR_{n-1}}{RR_{n-1}}. \qquad (1)$$

If $|\Delta RR_n|$ is greater than some threshold λ, the two beats that constitute the current RR interval are defined to be a non-sinus beat pair (abnormal RR interval) and therefore the following RR interval must be ignored (as it includes the current abnormal beat).

Figure 2 illustrates the distribution of $|\Delta RR|$ for all 3 beats pairs of beat categories (N-N, N-E and N-A). Note that there is only a relatively small overlap between the distributions of each pair, indicating that there might be some optimal thresholds to be chosen for a particular application. Figure 3 illustrates the percentage of N-E and N-A timings that are removed and the percentage of N-N beats that remain for $3 \geq \lambda \leq 24$. The choice of threshold therefore depends on the prevalence of artefact, the application and the associated tolerances.

By inspecting the RR time series from the NSRDB it is possible to observe 'clumping' of artefacts on or near state changes. If this observation is true for all artefacts then short sections of the RR time series (approximately 100 seconds in length) either side of an artefact should exhibit significantly different means (μ_1,μ_2) or variances (σ_1^2, σ_2^2). This is tested by locating all the N-A beat intervals
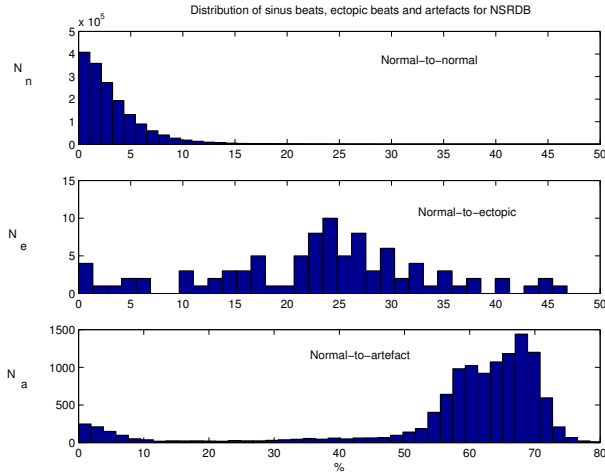
Figure 2. Distribution of absolute percentage change in RR interval ($|\Delta\mathrm{RR}|$) for sinus to sinus beats (upper plot), sinus to ectopic beats (middle plot) and sinus to artefacts (lower plot) for all 19 subjects in the Physionet NSRDB.
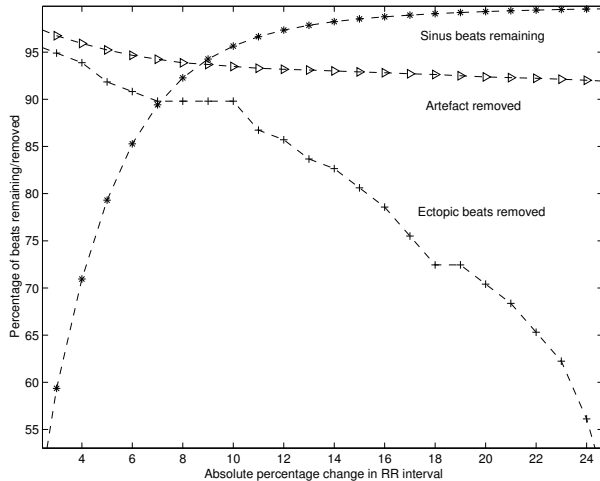

Figure 3. Percentage of N-N beat pairs remaining ($\ast$), N-E ($+$) and N-A ($\triangle$) removed for $3\% < \lambda \leq 25\%$ for all 19 subjects in the NSRDB

and performing Student's t-test on sections of the RR time series either side of the artefactual RR interval. If we cannot reject the null hypothesis that the means are equal, then we test for unequal variances with the F-test [8]. If either the t- or F-test indicates a statistically significant change in mean or variance respectively, a state change is assumed to have occurred at this point. The lower plot in figure 4 illustrates the percentage of N-A beats that have significantly different means or variances 100 seconds either side of the artefact for each of the 19 subjects in the NSRDB. Note that 14 of the 19 subjects have over 80% of their artefacts associated with state changes and the
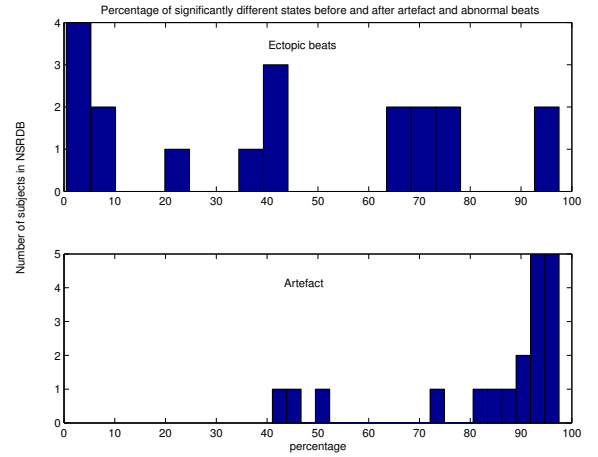

Figure 4. Percentage of significantly different states ($\mu_1 \neq \mu_2$ or $\sigma_1^2 \neq \sigma_2^2$) in 100 second segemts before and after artefact (lower plot) and ectopic beats (upper plot), tested using t- and F-tests for all 19 subjects in the Physionet NSRDB.

remaining 4 subjects have between 40% and 75% of their artefacts associated with state changes. In contrast to this, N-E beat pairs show no particular trend, and are distributed evenly between zero and 100% (figure 4, upper plot).

The frequency of ectopy is therefore independent of time in relation to state changes, and (in subjects with at least some ectopy) the frequency is approximately one abnormal beat per hour. However, the presence of artefact is linked both with state change and mean heart rate. The model (described in the accompanying conference paper, 'Method for generating an artificial RR time series of a typical healthy human over 24-hours'), uses three separate probability distributions are used; P(ectopy), P(artefact in a state), P(artefact at a state change). The latter two distributions are HR dependent.

4. Using $|\Delta\mathrm{RR}_n|$ thresholding to identify ectopy and artefact in unlabelled data for normality classification

The techniques of the previous two sections are applied to unlabelled RR interval data in event 2 of the CinC Challenge 2002. The data consists of 50 RR time series, approximately 50% of which are generated artificially and 50% of which are derived from real ECGs of normal patients similar to those found in the NSRDB. The purpose of this exercise is to ascertain if the activity of the patient is normal or abnormal from an analysis of artefact alone (artificial RR time series are assumed to exhibit abnormal artefact distributions).

However, when analysing unlabelled data, thresholding

using equation 1 alone may lead to problems at state changes. As the HR_i accelerates (as is often the case between states), the ΔRR_n between sinus beats is often greater than 20 %. If the mean HR of a subsequent state is sufficiently different, and the variance, of the next state σ_2^2, sufficiently low, all the following state's N-N beats will be excluded since the last accepted sinus label will be from the previous state (with a much lower or higher associated RR interval value). The solution to this is to check both the current RR interval *and* the next but one, then *AND* the results of each test. i.e. a beat is defined to be abnormal *if* $|\Delta RR_n| > \lambda$ & $|\Delta RR_{n+2}| > \lambda$. Although some N-N timings with large accelerations may be omitted by such a method, recovery is rapid, because the subsequent ΔRR's are likely to be similar to the last accepted RR interval.

Each of the 50 RR time series were tested in two steps. i) The percentage change in each RR interval is measured and if $|\Delta RR_n| \geq 15\%$ the current RR interval and the following RR interval are labelled as 'ectopic' and ignored for the next comparison. If $|\Delta RR_n| \geq 50\%$ then the RR interval and the following RR interval are labelled as artefactual. ii) The t- and F-test are then performed on 100 second segments either side of each artefact label. In order to ensure that outliers (mislabelled artefacts or ectopic beats) do not affect the results, the largest and smallest 10% of the RR intervals in the sections being tested are discarded. A classification is then made for each subject as follows: if more than 70% of the artefacts are significantly associated with a state change, then the RR time series is deemed to come from a normal subject (i.e. it was not artificially generated). This thresholding gave a score of 67 ($\frac{39}{50}$ correctly classified) in event 2 of the CinC Challenge 2002 (entry number 38).

5. Conclusions, limitations and future work

Results indicate that ectopy does not have a significant correlation with time of day or HR, although the total number of ectopic beats is low and analysis of further data sets may give a different result. Artefact incidence is correlated with local mean RR interval such that artefact is lower during low heart rate periods such as sleep, except when local mean HR increases (possibly related to sleep stage changes). Out of sleep, the incidence of artefact is higher, particularly at steep changes in local mean HR, when state changes occur and the mean or variance over a 100 second window changes significantly, again possibly related to changes in levels of activity.

Artefact is therefore associated with changes in activity independent of the information in the RR time series formed from the sinus beats. The increase in artefact incidence at state changes may be linked to the changes in patient activity that precipitate, or are a result of, these state changes.

Due to the overlap of the distribution of RR interval changes, timing techniques will always lead to a small number of errors which may significantly affect results of certain cardiovascular metrics [6, 5]. However, information from the morphology of each beat can significantly improve the beat type classification [9, 10] and could be combined with timing information to improve automatic beat labelling.

Acknowledgements

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Address for correspondence:

Gari D. Clifford
Dept. of Eng. Science / Univ. of Oxford
Parks Road / Oxford Ox1 3PJ / UK
E-mail: gari@robots.ox.ac.uk