Heart Rate n-Variability (HRnV): A Novel Representation of Beat-to-Beat Variation in Electrocardiography

Nan Liu*, Dagang Guo, Zhi Xiong Koh, Andrew Fu Wah Ho, Marcus Eng Hock Ong

* Correspondence: liu.nan@duke-nus.edu.sg

Abstract

We propose a novel representation of beat-to-beat variation in electrocardiography, called heart rate n-variability (HRnV), as an alternative to conventional heart rate variability (HRV). The derivation of HRnV parameters are based on multiple RR intervals with or without overlaps. We are able to create many sets of HRnV parameters which are promising at generating extra information from limited data source. We also present three approaches on the use of HRnV, and discuss further on potential applications and future directions. We believe that HRnV is an important addition to HRV, and will contribute to extending the landscape of current studies on HRV.

Index Terms

Heart Rate n-Variability (HRnV); Heart Rate Variability (HRV); Electrocardiography.

1 Introduction

Heart rate variability (HRV), a widely adopted tool in evaluating changes of cardiac autonomic regulation, is believed to strongly associate with autonomic nervous system. Due to its popularity in many clinical applications, the guidelines of HRV measurement, physiological interpretation and clinical use were published in 1996 [1]. Acharya et al. [2] presented a comprehensive review on the analytical methods and applications of HRV. More recently, Billman [3] reviewed HRV from a historical perspective.

The aim of HRV analysis is to explore the beat-to-beat variation in an electrocardiogram (ECG). Over the years, numerous quantitative techniques have been adopted, improved, and implemented to analyze ECG for capturing these variations [4]. For example, geometrical methods are used to extract time domain parameters, the Fourier transform is implemented for deriving frequency domain parameters, and detrended fluctuation analysis is adopted for calculating nonlinear parameters.

HRV has gained reputation in broad clinical applications, particularly in cardiovascular research where reduced HRV is found as a significant predictor of adverse outcomes [5]. However, the autonomic nervous system's impact on HRV remains controversial [3], leaving room for further studies on clinical investigation and the exploration of novel engineered parameters to model the beat-to-beat variation. So far, vast majority of efforts are deriving sophisticated parameters with linear and nonlinear techniques. Furthermore, researchers have been focusing on developing advanced signal processing tools for efficient noise removal and accurate QRS detection, prior to HRV parameter calculation.

N. Liu is with Health Services Research Centre, Singapore Health Services, and Duke-NUS Medical School, National University of Singapore, Singapore.
D. Guo is with TIIM Healthcare Pte Ltd, Singapore.
Z.X. Koh is with Department of Emergency Medicine, Singapore General Hospital, Singapore.
A.F.W. Ho is with SingHealth Emergency Medicine Residency Programme, Singapore Health Services, Singapore.
M.E.H. Ong is with Department of Emergency Medicine, Singapore General Hospital, and Duke-NUS Medical School, National University of Singapore, Singapore.

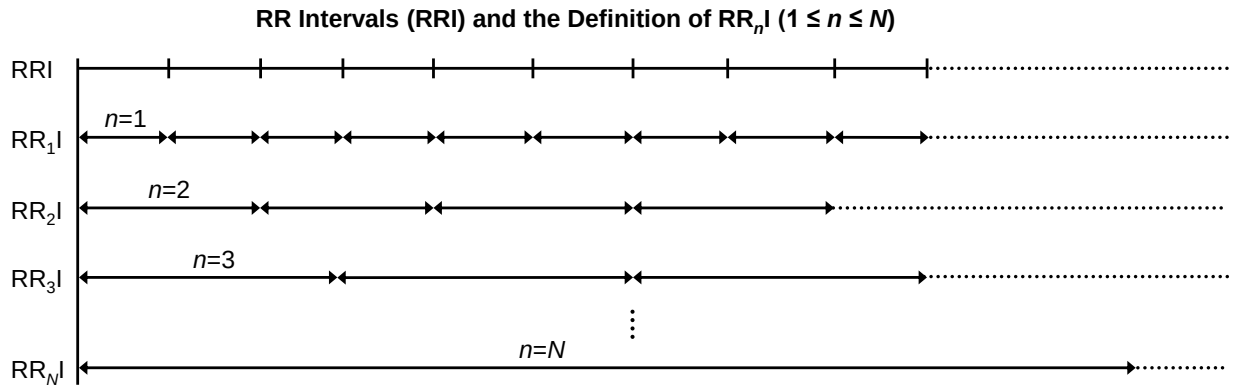

Fig. 1. Illustration of RR intervals and the definition of $\mathrm{RR}_n\mathrm{I}$ where $1 \leq n \leq N$ and $N \ll \hat{N}$. $\hat{N}$ is the total number of RR intervals.

In this paper, we revisit RR intervals, the foundations for computing HRV parameters, and propose heart rate n-variability (HRnV), a novel representation of beat-to-beat variation in ECG. We have developed two specific HRnV measures as alternatives to the conventional HRV and evaluated the feasibility of computing new parameters. We will also discuss the merits, issues, and potential applications of new HRnV measures, and point out the directions for future development.

2 Proposed Heart Rate n-Variability

We elaborate two measures of the novel HRnV representation, namely $\mathrm{HR}_n\mathrm{V}$ and $\mathrm{HR}_n\mathrm{V}_m$. We will introduce the definitions of both measures and illustrate the differences between them and conventional HRV measure.

2.1 $\mathrm{HR}_n\mathrm{V}$: A Novel Measure with Non-Overlapped RR Intervals

Prior to introducing the new $\mathrm{HR}_n\mathrm{V}$ measure, we define a new type of RR intervals (RRI) called $\mathrm{RR}_n\mathrm{I}$ where $1 \leq n \leq N$ and $N \ll \hat{N}$. $\hat{N}$ is the total number of RR intervals. When $n = 1$, $\mathrm{RR}_n\mathrm{I}$ becomes conventional RRI. The definition of $\mathrm{RR}_n\mathrm{I}$ is illustrated in Fig. 1. Note that $\mathrm{RR}_1\mathrm{I}$ is equal to RRI. When $n > 1$, every n adjacent RR intervals are connected to form a new sequence of $\mathrm{RR}_n\mathrm{I}$ intervals. By using this strategy, we are able to create a maximum number of $(N-1)$ new $\mathrm{RR}_n\mathrm{I}$ sequences from the conventional single RRI sequence.

Having these newly generated $\mathrm{RR}_n\mathrm{I}$ sequences, calculation of $\mathrm{HR}_n\mathrm{V}$ parameters is straightforward, by applying existing quantitative methods including time domain analysis, frequency domain analysis, and nonlinear analysis [1],[2]. The computed $\mathrm{HR}_n\mathrm{V}$ parameters include but are not limited to the following: Average of $\mathrm{RR}_n\mathrm{I}$ intervals (aRR_n), standard deviation of $\mathrm{RR}_n\mathrm{I}$ (sdRR_n), square root of the mean squared differences between $\mathrm{RR}_n\mathrm{I}$ (RMSSD_n), the number of times that the absolute difference between 2 successive $\mathrm{RR}_n\mathrm{I}$ intervals exceed 50 ms ($\mathrm{NN50}_n$), $\mathrm{NN50}_n$ divided by the total number of $\mathrm{RR}_n\mathrm{I}$ ($\mathrm{pNN50}_n$), the integral of the $\mathrm{RR}_n\mathrm{I}$ interval histogram divided by the height of the histogram ($\mathrm{HR}_n\mathrm{V}$ triangular index), low frequency (LF_n) power, high frequency (HF_n) power, approximate entropy (ApEn_n), sample entropy (SampEn_n), and detrended fluctuation analysis (DFA_n), among others. We use subscript n to indicate that the parameters are calculated from $\mathrm{RR}_n\mathrm{I}$ sequences.

As noted in the above description, $\mathrm{HR}_n\mathrm{V}$ is a novel measure based on newly generated, non-overlapped $\mathrm{RR}_n\mathrm{I}$ intervals. In the next section, we will introduce another novel measure $\mathrm{HR}_n\mathrm{V}_m$ that is based on overlapped RR intervals.

2.2 $\mathrm{HR}_n\mathrm{V}_m$: A Novel Measure with Overlapped RR Intervals

Similar to $\mathrm{RR}_n\mathrm{I}$ that is used in $\mathrm{HR}_n\mathrm{V}$, in defining the $\mathrm{HR}_n\mathrm{V}_m$ measure, we introduce another type of RR intervals called $\mathrm{RR}_n\mathrm{I}_m$ where $1 \leq n \leq N$, $1 \leq m \leq N-1$, and $N \ll \hat{N}$. In the $\mathrm{RR}_n\mathrm{I}_m$ sequence, m is used

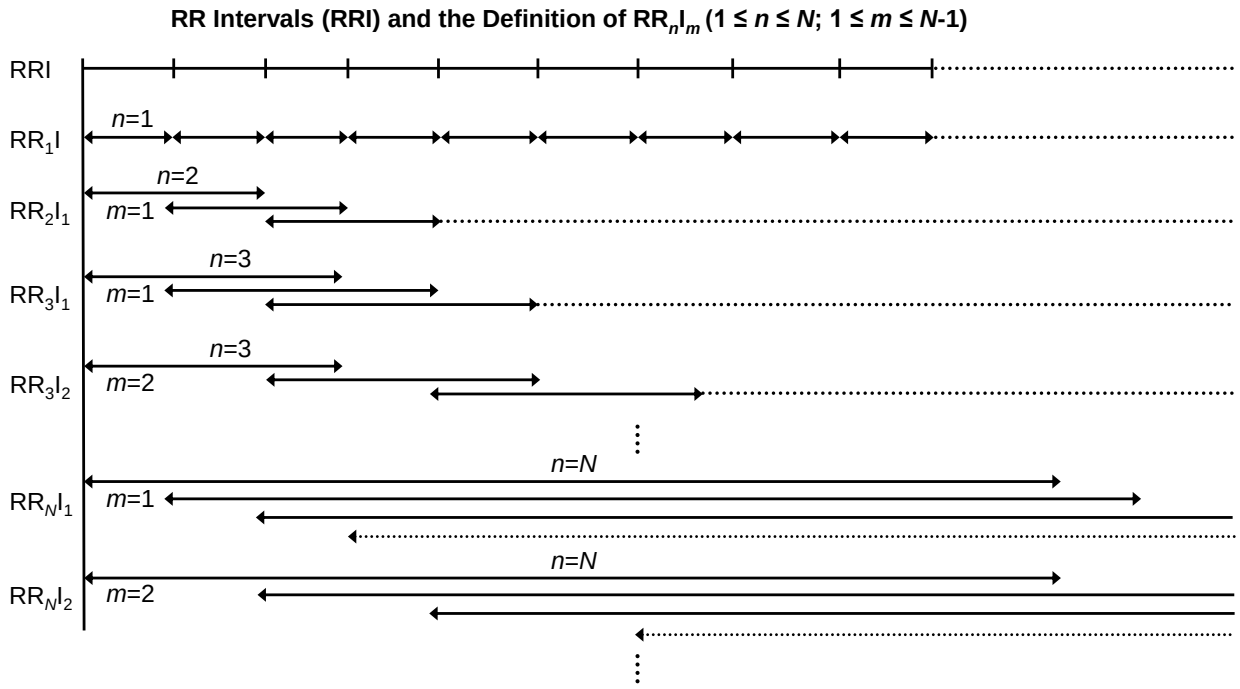

Fig. 2. Illustration of RR intervals and the definition of $\mathrm{RR}_n\mathrm{I}_m$ where $1 \leq n \leq N$, $1 \leq m \leq N-1$, and $N \ll \hat{N}$.

to indicate the level of overlapping between consecutive $\mathrm{RR}_n\mathrm{I}_m$ intervals. As depicted in Fig. 2, $(n-m)$ number of RR intervals form the overlapped portions. Apparently, when $m = n$, $\mathrm{RR}_n\mathrm{I}_m$ becomes $\mathrm{RR}_n\mathrm{I}$. Therefore, the upper limit of m is $N-1$. By controlling the overlaps among newly generated $\mathrm{RR}_n\mathrm{I}_m$ intervals, we are able to create a maximum number of $(N \times (N-1)/2)$ $\mathrm{RR}_n\mathrm{I}_m$ sequences (excluding the $\mathrm{RR}_n\mathrm{I}$ sequence) from the conventional single RRI sequence.

For each of the newly created $\mathrm{RR}_n\mathrm{I}_m$ sequences, we can apply time domain analysis, frequency domain analysis, and nonlinear analysis, to calculate $\mathrm{HR}_n\mathrm{V}_m$ parameters. We add in superscript m to denote that the parameters are computed from $\mathrm{RR}_n\mathrm{I}_m$ sequences. For example, the average of $\mathrm{RR}_n\mathrm{I}_m$ intervals and the sample entropy are written as aRR_n^m and SampEn_n^m, respectively.

Compared with $\mathrm{HR}_n\mathrm{V}$, the $\mathrm{HR}_n\mathrm{V}_m$ measure extracts more information from the raw RR interval sequence, by adopting a strategy of controlling sequence overlapping. $\mathrm{HR}_n\mathrm{V}_m$ measure is particularly useful and suitable when ECG segments are short and thus there are limited number of RR intervals.

3 Experiments

To evaluate the feasibility of calculating HRnV parameters, we conducted a simulation study by using the ECG record of subject #16265 from MIT-BIH Normal Sinus Rhythm Database [6]. We applied the conventional Pan-Tompkins QRS detection algorithm including band-pass filter (5-15 Hz), derivative filter, and moving average to detect QRS peaks. Subsequently, we extracted a 30 minutes segment and derived the $\mathrm{RR}_n\mathrm{I}$ and $\mathrm{RR}_n\mathrm{I}_m$ interval sequences from the original RR intervals, where $n \leq 3$. The conventional RR interval, $\mathrm{RR}_n\mathrm{I}$, and $\mathrm{RR}_n\mathrm{I}_m$ sequences are illustrated in Fig. 3. We observed that there were no obvious changes in the waveforms of conventional and new RR intervals. However, toward the end of sequences, we noted a spike in the original RR interval but more smooth parts in $\mathrm{RR}_n\mathrm{I}$ and $\mathrm{RR}_n\mathrm{I}_m$ sequences, which indicated that sudden significant changes in adjacent R peaks could have been suppressed in the new $\mathrm{RR}_n\mathrm{I}$ and $\mathrm{RR}_n\mathrm{I}_m$ representations where multiple intervals were connected.

Based on the six RR interval sequences shown in Fig. 3, we calculated HRV, $\mathrm{HR}_n\mathrm{V}$, and $\mathrm{HR}_n\mathrm{V}_m$ parameters (Table 1). Among the time domain parameters, we observed that the values were generally incremental with the increase of n. Special attention needs to be given to NN50 and pNN50, where 50 ms is the threshold to assess the difference between pairs of successive RR intervals. Notably, in HRnV

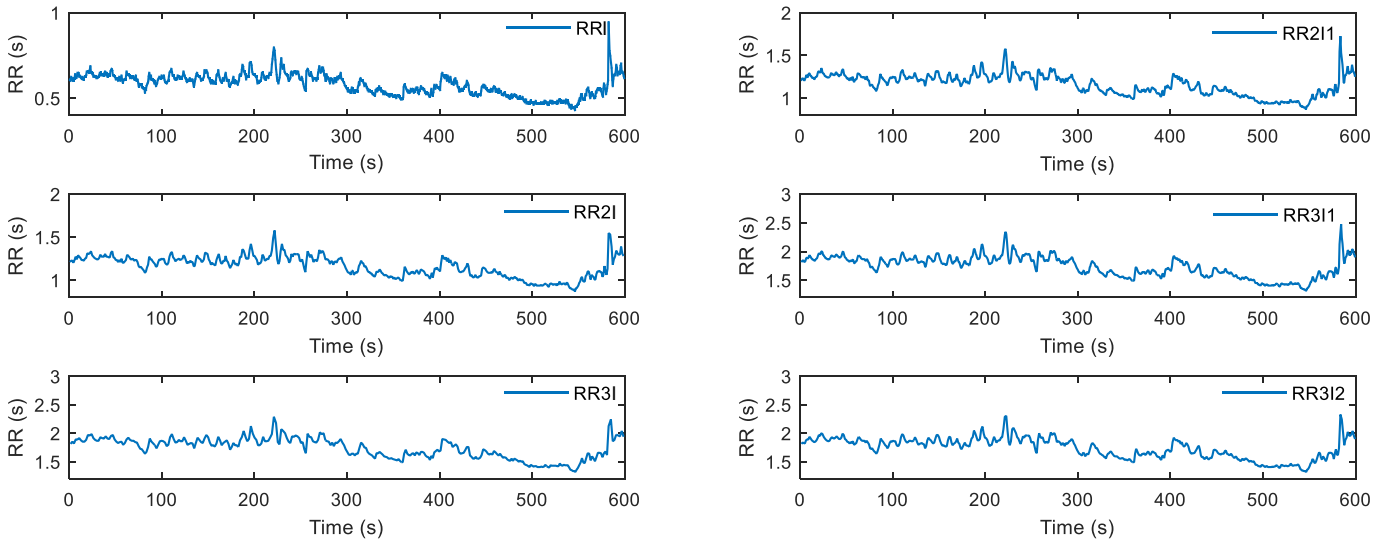

Fig. 3. RR interval and its variations used for calculating HRnV parameters. The six RR interval sequences were RRI, $\mathrm{RR_2I}$, $\mathrm{RR_3I}$, $\mathrm{RR_2I_1}$,$\mathrm{RR_3I_1}$, and $\mathrm{RR_3I_2}$.

measure, the lengths of $\mathrm{RR}_n\mathrm{I}$ and $\mathrm{RR}_n\mathrm{I}_m$ have been extended, thus the threshold needs to be adjusted accordingly. As shown in Table 1, we used 50 ms as the default threshold for all calculations, since we did not aim to study specific parameters in this paper.

Similar to the time domain parameters, we observed the same trend of value change in frequency domain parameters. The exception was HF power norm, where HRnV parameters were smaller than HRV. We also noticed that the change in LF power norm was marginal compared to the value change in HF power norm, which resulted in significant difference in LF/HF values between HRV and HRnV. In nonlinear analysis, the differences between HRV and HRnV on Poincaré plot measures were obvious, while those on entropy and DFA metrics were not. The experimental results reported above were for demonstration purpose, suggesting that they were not meant to provide physiological interpretations. Furthermore, we have to consider many factors such as subject characteristics and length of ECG records in rigorous clinical studies, in order to conduct in-depth investigations on HRnV parameters and their clinical use.

4 Discussion and Future Directions

In this paper, we have introduced heart rate n-variability, a novel representation of beat-to-beat variation in ECG. We proposed two measures, namely $\mathrm{HR}_n\mathrm{V}$ and $\mathrm{HR}_n\mathrm{V}_m$. $\mathrm{HR}_n\mathrm{V}$ is calculated based on non-overlapped $\mathrm{RR}_n\mathrm{I}$ intervals, while $\mathrm{HR}_n\mathrm{V}_m$ is computed from $\mathrm{RR}_n\mathrm{I}_m$ intervals that have overlaps. Heart rate n-variability is not proposed to replace the conventional HRV, instead it is a natural extension. $\mathrm{HR}_n\mathrm{V}$ and $\mathrm{HR}_n\mathrm{V}_m$ measures enable us to create more alternative parameters from raw ECGs, hence empower the extraction of extra information. Therefore, HRnV is complementary to HRV in terms of representing the beat-to-beat variation in ECG.

We have witnessed plentiful clinical investigations using conventional HRV parameters in cardiology [7], diabetes [8], critical care [9], psychiatry [10], cancer [11], and so forth. Similarly, we foresee broad application opportunities for HRnV. With the augmented $\mathrm{RR}_n\mathrm{I}$ and $\mathrm{RR}_n\mathrm{I}_m$ interval sequences, HRnV parameters could possibly capture more dynamic pattern changes from various aspects, comparing to what HRV does.

Given the richness of HRnV parameters, there are many ways of applying them for research and applications. We briefly categorize them into three approaches:

1) Use individual HRnV measures as alternatives to the conventional HRV.
2) Stack various HRnV measures to form a high dimensional feature vector for predictive modeling and disease associations.

TABLE 1
Selected time domain, frequency domain, and nonlinear HRV and HRnV parameters based on 30 minutes ECG segment that was obtained from subject #16265 of the MIT-BIH Normal Sinus Rhythm Database.

Parameters	HRV	HR_2V	HR_3V	HR_2V_1	HR_3V_1	HR_3V_2
Time Domain						
aRR (ms)	651.2	1302.3	1953.4	1302.3	1953.5	1953.4
sdRR (ms)	81.0	160.0	237.8	159.9	237.7	237.7
RMSSD (ms)	25.9	58.9	99.1	34.8	41.3	73.5
NN50	93	347	397	250	372	444
pNN50 (%)	3.4	25.1	43.2	9.1	13.5	32.2
Triangular index	16.8	35.4	35.4	38.4	48.4	49.3
Frequency Domain						
LF power (ms^2)	697.4	2648.5	5549.3	2669.1	5534.0	5581.8
HF power (ms^2)	264.4	702.8	771.9	766.8	1017.5	940.4
LF power norm (nu)	72.5	79	87.8	77.7	84.5	85.6
HF power norm (nu)	27.5	21.0	12.2	22.3	15.5	14.4
LF/HF	2.638	3.769	7.190	3.481	5.439	5.935
Nonlinear						
Poincaré plot SD1 (ms)	18.3	41.7	70.1	24.6	29.2	52.0
Pointcaré plot SD2 (ms)	113.1	222.4	329.0	224.8	334.9	332.2
Approximate entropy	0.926	1.114	1.147	0.763	0.656	1.011
Sample entropy	0.860	1.028	1.049	0.699	0.614	0.930
DFA, $\alpha 1$	1.270	1.167	1.089	1.426	1.594	1.252
DFA, $\alpha 2$	0.988	0.923	1.027	1.003	1.023	0.938

3) Aggregate various HRnV measures to create an ensemble of different models [12] that are built upon individual HRnV measures.

Approaches 2) and 3) are particularly suitable for artificial intelligence and machine learning tools [13] where tons of methods are available for statistical modeling and decision making [14], variable selection [15], and data mining [16].

Although HRnV has promising capabilities in augmenting the conventional HRV parameters, it has many issues to address. Firstly, HRnV lacks physiological interpretations to its numerous parameters. Secondly, choosing of parameter n and m is arbitrary, which has huge impact in various conditions. For example, HRnV may not be feasible for very short ECGs where the number of RR intervals are limited. Thirdly, calculation of certain HRnV parameters needs to be carefully evaluated and rigorously investigated. NN50 in conventional HRV is defined as the number of successive RR intervals pairs that differ more than 50 ms. However, in HR_nV and HR_nV_m, 50 ms seem no longer be a valid indicator. If so, what is a reasonable number, $n \times 50$ ms or another value? Addressing these issues needs collaborative endeavor between clinician scientists and biomedical engineering researchers.

5 Conclusions

We proposed using multiple RR intervals (with or without overlaps) to create novel HRnV measures to represent the beat-to-beat variation. We illustrated the definitions of HR_nV and HR_nV_m and evaluated the feasibility of parameter calculation. HRnV measures enable us to augment the conventional HRV with many more parameters. We have also discussed three approaches with which new HRnV parameters are used and adopted to boost existing research. Although there are issues yet to address, we hope to stimulate a new area of investigations on HRnV, a novel representation of beat-to-beat variation in ECG. We believe that future endeavor in this field will open up the possibility to study in-depth associations between HRnV measures and various human diseases.

AUTHOR CONTRIBUTIONS

N. Liu conceived the idea of heart rate n-variability (HRnV), developed the $\mathrm{HR}_n\mathrm{V}$ and $\mathrm{HR}_n\mathrm{V}_m$ measures, and wrote the first draft of the manuscript. N. Liu, D. Guo, and Z.X. Koh performed the experiments. All authors contributed to evaluation of the HRnV measures and revision of the manuscript.

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