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Heart Rate Variability Analysis with the R package RHRV

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ISSN 2197-5736 ISSN 2197-5744 (electronic)
Use R!
ISBN 978-3-319-65354-9 ISBN 978-3-319-65355-6 (eBook)
DOI 10.1007/978-3-319-65355-6

Library of Congress Control Number: 2017948618

Printed on acid-free paper

This Springer imprint is published by Springer Nature
The registered company is Springer International Publishing AG
The registered company address is: Gewerbestrasse 11, 6330 Cham, Switzerland

Foreword

It would be very difficult if not impossible to find a signal processing technique applied to cardiac electrophysiology data that gained more popularity than the methods of heart rate variability. The two decades old HRV standardisation document belongs to the most cited publications in cardiovascular literature and the stream of new technical approaches to HRV analyses and of new clinical HRV studies is not showing any sign of decline.

While this is of course most pleasing to specialists in the HRV field, the widespread popularity also brings problems and challenges. Among others, technical agreement on the details of signal processing and HRV measurement exists practically only with the most simple statistical methods. Only a small number of more advanced techniques are sufficiently standardized. With all others, different nuances in data acquisition, artifact removal, and settings used to implement signal processing methods may influence the numerical values of HRV measurements to that extent that comparisons of results obtained by different research groups are at best problematic and at worst misleading. The more elaborate mathematical apparatus beyond a signal processing method, the more implementation variants exist, hampering both the physiological understanding of the measurements and consequently their clinical and/or epidemiologic potential. Indeed, the recent extension of the HRV standard that aimed at reviewing and organizing the novel nonlinear HRV methods observed growing divergence between technological HRV advances and their clinical utilization. This divergence exists mainly because the clinical researchers find it difficult to be guided by scientific reports from different centers that might agree in principal observations but not in numerical details.

Solution of these problems clearly lies in further standardization. The more research and clinical groups would use the very same technical setting of HRV processing packages, the more mutually comparable measurements would become available for critical scientific review, and consequently the more chances would exist to agree on the correct physiologic and clinical interpretation of the advanced signal processing technologies. Of course, without providing the necessary devices to everybody, this all is easier to declare than to achieve. Obviously, widespread tools are needed. Having this in mind, the authors of this book need to be commended for their contribution to the attempts of standardizing, under a common umbrella, all the different facets of HRV analyses ranging from data preparation and signal inputs to the more mathematically intricate processing tools. Offering the RHRV package for free and unrestricted use by all is an example of welcome assistance to the research community. For this unselfish approach, the developers of the package and the authors of this book deserve our thanks.

February 2016

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Preface

The rhythm of the heart is influenced by both the sympathetic and parasympathetic branches of the autonomic nervous system. There are also some feedback mechanisms modulating the heart rate that try to maintain cardiovascular homeostasis by responding to the perturbations sensed by baroreceptors and chemoreceptors. Another major influence of the heart rate is the respiratory sinus arrhythmia: the heartbeat synchronization with the respiratory rhythm. All these mechanisms are responsible for continuous variations in the heart rate of a healthy individual, even at rest. These variations are referred to as heart rate variability (HRV). Subtle characteristics of these small variations conceal information about all the mechanisms underlying heart rate control, and hence about the health status of the individual.

Since the 1960s, researchers have developed a wide range of algorithms to extract the information hidden in these variations. Using these algorithms, researchers have found markers for many pathologies such as myocardial infarction, diabetic neuropathy, sudden cardiac death, and ischemia. The starting point for all these algorithms is a simple recording of the instantaneous heart rate of the patient, usually extracted from an electrocardiogram. Therefore, a diagnostic based on a HRV marker is inexpensive, simple to perform, and requires no invasive procedure, making it a very attractive test. This is probably the reason behind the increasing amount of research related to HRV (see Fig. 1).

From the point of view of the authors, the main hindrance in the HRV research field is the difficulty in reproducing results from other researchers. When a new analysis technique or a new finding is published in the HRV literature, thinking it will be easy to reproduce the same result on your own data often is a mistake. We have tried it on several occasions. But the exact reproduction of the results was not possible, although we obtained results that qualitatively were similar to the originals. This is due to the lack of standardization in the values of many parameters and other implementation details in the HRV algorithms. Some examples are how exactly ectopic beats are filtered, the algorithm used to interpolate the RR intervals to obtain a time series of constant sampling frequency, how to remove the DC component (from all the RR series, from each window, etc.), the window type

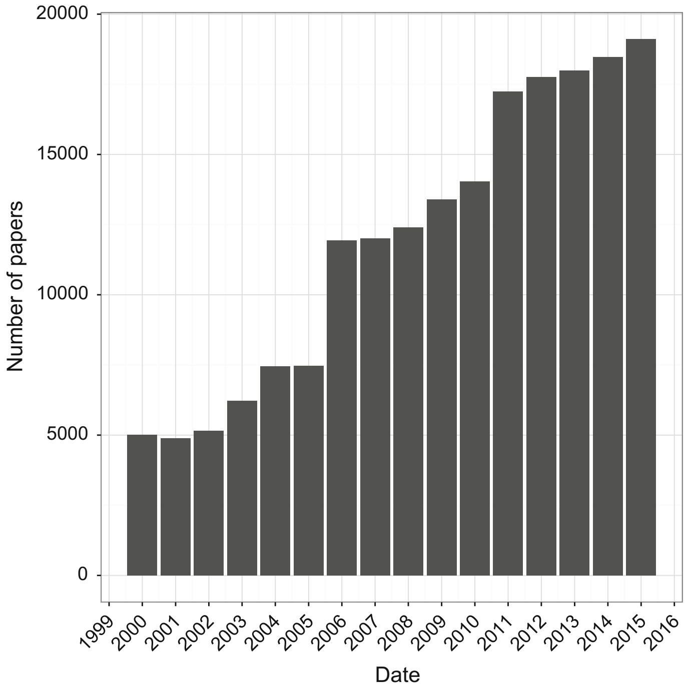

Fig. 1 Papers on HRV published per year according to Google Scholar

(Hamming, Welch, etc.), window size, and window overlap used in the Fast fourier transform, or the mother wavelet used.

Explicitly or implicitly, in any HRV analysis dozens of decisions on either parameters or implementation details are made. Some of these decisions are difficult to document in a scientific paper. But they are essential for the faithful and accurate reproduction of the results. Furthermore, the analyses are often performed with a third party tool, whose source code is probably not available. In this case, many of these decisions have been made by the tool developers, and researchers may be unaware of some (even most) of them.

Another hindrance in the field is that researchers often use analytical techniques that are not the current state of the art, simply because their tool of choice does not support them, and they do not have the time and/or the necessary expertise to implement the techniques themselves. There is often a disconnect in the HRV literature between researchers who develop new and more powerful analysis techniques (often engineers), and those performing applied research in humans or animals (often physicians). The latter still often uses older less powerful techniques and does not benefit from the progress made by the former. For example, in the literature there are many more HRV studies using the Fourier transform than the wavelet transform, despite the theoretically superior properties of the latter for the analysis of nonstationary signals. We believe that the main reason for this is the

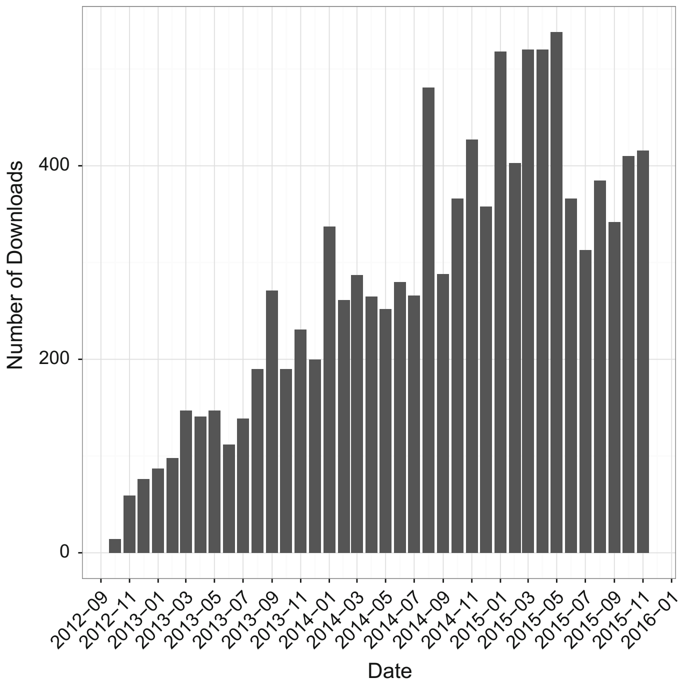

Fig. 2 Monthly RHRV downloads in the RStudio's CRAN mirror

historical lack of HRV analysis tools with support for spectral analysis based on wavelets.

RHRV is our attempt to address these problems. RHRV is a free of charge and open-source package for the R environment that comprises a complete set of tools for heart rate variability analysis. RHRV can import data files containing heartbeat positions in the most broadly used formats and supports time domain, frequency domain, and nonlinear (fractal and chaotic) HRV analysis. The vast majority of the commonly used HRV analysis algorithms used in the literature have already been implemented in the tool. For example, the tool supports frequency analysis using the Fourier transform (with and without Daniell smoothers), short-time Fourier transform, autoregressive models, Lomb-Scargle periodogram, and the wavelet transform. And we will continue adding new functionality to RHRV. Furthermore, as any good open-source project, contributions are welcome.

Beyond being an invaluable help when performing HRV analysis (a typical HRV analysis with RHRV usually has just 10–15 lines of R code), we believe that RHRV can help the whole HRV field. Simply by posting the RHRV analysis script as supplementary material of a paper, the reproduction of the results over the same, or over new data, will be trivial: just run the script. Being RHRV an open and free package, no one should have any impediment to reproduce the results. And given that the state-of-the-art analysis techniques are implemented in RHRV, there is no reason not to use them. For example, in RHRV the difference between carrying out a spectral analysis based on Fourier or wavelets is simply changing a parameter in a function call.

Many researchers have already noticed the advantages of RHRV, and a strong community has already formed around it. During 2015 on average, the package was downloaded 450 times a month just from the RStudio CRAN mirror (see Fig. 2). We hope that the trend shown in Fig. 2 continues, and that RHRV will become the de facto tool for performing HRV analysis. And this book, as the best documentation written so far about RHRV, will contribute to this end.

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December 2015

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Acronyms

ACF	Autocorrelation function
AIC	Akaike information criterion
AMI	Average mutual information
ANS	Autonomic nervous system
AR	Autoregressive
ASCII	American Standard Code for Information Interchange
CI	Confidence intervals
COPD	Chronic obstructive pulmonary disease
DFA	Detrended fluctuation analysis
DFT	Discrete Fourier transform
ECG	Electrocardiogram
EDF	European Data Format
fBm	Fractional Brownian motion
FFT	Fast Fourier transform
fGn	Fractional Gaussian noise
FT	Fourier transform
HF	High frequency
HR	Heart rate
HRV	Heart rate variability
IAPS	International Affective Picture System
ICU	Intensive care unit
IRRR	Interquartile (difference between third and first quartile) Range of the RR intervals series
k-NN	K-Nearest Neighbor
KS	Kolmogorov-Sinai
LF	Low frequency
MADRR	Median of the Absolute Differences between adjacent RR intervals
MODWPT	Maximal overlap discrete wavelet packet transform
OSAH	Obstructive sleep apnea and hypoapnea

pNN50	proportion of successive Normal to Normal differences greater than 50 ms in percent
PSD	Power spectral density
REM	Rapid eye movement
r-MSSD	root Mean Square of Successive heartbeat interval Differences
RP	Recurrence plot
RQA	Recurrence quantification analysis
RSA	Respiratory sinus arrhythmia
SDANN	Standard Deviation of the Averages of Normal to Normal intervals in 5 minutes segments
SDNN	Standard Deviation of Normal to Normal RR intervals
SDNNIDX	mean of the Standard Deviation of Normal to Normal Intervals in 5 minutes segments
SDSD	Standard Deviation of Successive heartbeat interval Differences
STFT	Short-time Fourier transform
SWV	Scaled windowed variance
TINN	baseline width of the Triangular Interpolation of the Normal to Normal intervals histogram
ULF	Ultralow frequency
VARVI	Variability of the heArt Rate in response to Visual stImuli
VLF	Very low frequency
WFDB	WaveForm DataBase
WT	Wavelet transform

Chapter 1
Introduction to Heart Rate Variability

Abstract Searching on Google Scholar the string "heart rate variability" (HRV) provides about half a million references, which gives us an idea of the research activity around this concept. This chapter describes the historical development of this research field, from the pioneering work of the eighteenth and nineteenth centuries to the boom of the final decade of the twentieth century. HRV analysis is important from a clinical point of view because of its direct relationship with the autonomic nervous system (ANS). Therefore, we include a section explaining the physiological basis of HRV and its relationship with the ANS. Finally, we review the most relevant clinical applications of HRV in three distinct lines: patient monitoring, acute care, and chronic disorders. The reader of this chapter must bear in mind that the purpose of this book is to present a software tool, RHRV, which greatly simplifies performing heart rate variability analysis. This chapter does not pretend to be a comprehensive review of the physiology of heart rate variation, but just a brief introduction to the field whose main purpose is building a common language to be able to present concepts more effectively throughout the book.

1.1 Historical Perspective

The heartbeat and pulse were already "known" by Greek physicians like Galen of Pergamon (130–200 AD), who mentioned it on many of his manuscripts relating it to the "vital pneuma" and the "spirited soul." They knew that lack of pulse caused death and, based on its power, frequency, and regularity, they could make diagnoses. Since then, great progress has been made in the analysis of the variations of the heart rate (HR), which can be seen summarized in Fig. 1.1.

In the early eighteenth century, John Floyer (1649–1734) invented the "physician pulse watch" (1707), a precursor of the chronometer, which he began to use to accurately measure the heart rate of patients.

An important proof of the variability of the heart rate was contributed by Stephen Hales (1677–1761) who, in 1733, published a manuscript [12] in which he mentioned that the distance between heartbeats and the blood pressure varied during the respiratory cycle. Later, Carl Ludwig (1816–1895) improved these observations,

C.A. García Martínez et al., *Heart Rate Variability Analysis with the R package RHRV*, Use R!, DOI 10.1007/978-3-319-65355-6_1

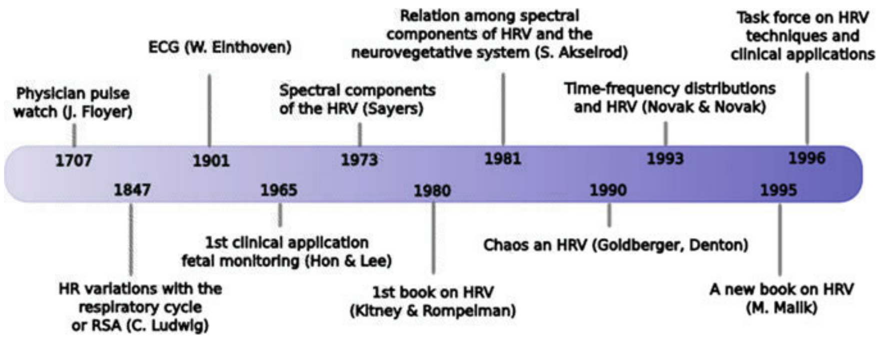

Fig. 1.1 Main heart rate variability analysis historic milestones

clearly stating that the pulse increased during inspiration and decreased during expiration [25], thus laying the foundation of what would be called later respiratory sinus arrhythmia (RSA).

The transition from prehistory to modernity in the field of electrocardiography was given by Willem Einthoven (1860–1927), who recorded the first electrocardiogram (ECG) in 1901 using galvanometers [9]. Figure 1.2 shows one of his early designs, weighting about 270 kg and needing five people to operate it. The current nomenclature of (P, Q, R, S, T) was first used by Einthoven.

The ECG recording techniques improved gradually, and in 1961 Norman Holter (1914–1983) developed a device (that still bears his name, Holter) allowing the registration of long-term ECG records [14].

From the 1970 s on, improvements in measuring equipment and computational techniques caused this research field to take off. In 1970, Caldwell presented the "cardiotachometer" [5], capable of automatically recording beat positions using a small and inexpensive equipment. In 1973, Rompelman [39] presented another device capable of performing a basic statistical analysis of the HR values.

Due to the generalization of these devices and computers, specific studies on HRV started to appear, identifying the basic characteristics of the HR signal, and isolating some well-defined peaks in its spectrum [39, 43]. In 1977, a paper comparing different techniques of HRV analysis was published [37], and in 1982 the first implementation of a system for HRV analysis over a standard PC was developed [38], which made this kind of analysis affordable for any researcher.

It could be considered that the first documented clinical application of HRV was the one published by Hon and Lee in 1963 [15]. They noted that fetal distress was accompanied by changes in HRV, even before there was a detectable change in HR. Another paper that boosted the research in this field was the one by Wolf in 1967 [48], which showed the relationship between HRV and the ANS and its role in sudden cardiac death.

It was certainly in the 1980 s when the field of HRV reached maturity. Methodological issues were fixed, its physiological basis and its relationship with the ANS were demonstrated, and more clinical applications were described. In 1980, the first