Relating Heart Rate Variability and Age Using Spectral Estimation Methods

Amanda Ledell

Bachelor's thesis
2019:K2

LUND UNIVERSITY

Faculty of Science
Centre for Mathematical Sciences
Mathematical Statistics

CENTRUM SCIENTIARUM MATHEMATICARUM

Abstract

Heart rate variability (HRV) is a measurable property used to describe the naturally occurring time differences between heartbeats and has shown to help with identifying both physiological and psychological disorders. HRV signals of 97 individuals were analyzed using spectral analysis. The data was non-stationary but was analyzed using stationary estimation methods, in which the original data was segmented into shorter, overlapping segments. Different lengths were investigated, all overlapping by 50%. The analysis used different non-parametric spectral estimates in order to find the method which provided the most accurate description of the frequency content. The resulting cross spectrum were related to the age, BMI and sex of the participants using multi-linear regression. For BMI and sex, no significant correlation was found but for age, a negative correlation was determined ($p < 0.001$), consistent with previous research. The model was unable to account for large parts of the inherent variation, indicating that a model with more covariates could be more appropriate. While the spectral estimation techniques showed great promise, more advanced methods such as stationary estimation methods or multi-taper methods might yield better results.

Populärvetenskaplig sammanfattning

Det mänskliga hjärtat slår i genomsnitt mellan 60 och 100 slag per minut, däremot varierar det exakta antalet. Heart Rate Variability, förkortat HRV, är ett kardiologiskt begrepp som mäter den naturliga tidsvariationen mellan hjärtslag. HRV kan användas för att identifiera både fysiska och psykiska åkommor, vilket är möjligt då HRV påverkas av nervsystemet. Det har exempelvis påvisats att man kan identifiera och förhindra hjärtattacker innan de skett med hjälp av HRV-mätningar.

Ett aktivt område inom HRV-forskning är att identifiera relationer mellan HRV och olika variabler. Anledningen till detta är att man vill kunna hitta samband där man, på ett effektivt sätt, kan förhindra samt kontrollera olika åkommor. Det har bland annat identifierats länkar mellan posttraumatiskt stressyndrom och HRV samt diabetes och HRV. Däremot behöver man också fastställa samband mellan enklare parametrar och HRV, så som ålder och kön, för att kunna utesluta och kontrollera för dem i mer komplexa analyser.

I det här arbetet så undersöktes det hur ålder, BMI och kön relaterar till HRV. Det skedde en datainsamling där 97 stycken individer fick andas fortare och fortare, medan deras hjärt- och andningssignaler registrerades. Syftet var att undersöka HRV under en mer påfrestande än avslappnande situation. Spektralanalytiska metoder användes för att analysera HRV och andningssignalerna. Slutligen kunde endast en signifikant länk mellan ålder och HRV bekräftas.

Acknowledgments

There are several people who have helped with this thesis. I would like to begin by thanking my supervisor Rachele Anderson for all of her help and guidance throughout this process as well as Prof. Maria Sandsten for her time and input. Simon Halvdansson, for his tremendous support and help with the programming aspects of this thesis. I would lastly like to thank Dr. Ida Löfman for her help with understanding the cardiological aspects of this thesis and Amanda Ahola Orpana for her constructive criticism.

Amanda Ledell

Contents

1 Introduction

Understanding how variations in heart rate relate to different physiological and psychological factors has been the subject of extensive research during the latest decades [3]. Heart rate has been shown to be an indicator of several health issues and it is also used by individuals in order to optimize their training and recovery [8]. This thesis will analyze the variations in heart rate and investigate possible relationships with the physiological factors, age, BMI and sex.

1.1 Background

The human heart is myogenic which means that the contractions are initiated from the heart itself by the cardiomyocytes, the heart's muscle cells [19, pp. 136-137]. More specifically, it is the sinoatrial node (SA node) which acts as a natural pacemaker and is thereby responsible for the contractions, around 60-100 beats per minute (bpm).

Heart rate variability (HRV) is an important physiological phenomenon which measures the small time changes between consecutive heartbeats. Different methods can be used to measure HRV, both invasive and non-invasive methods. Electrocardiography (ECG) is the most commonly used method since it is non-invasive but also because it registers the electrical impulses that run through the hearts conducting system. ECG may thereby detect heartbeats not initiated by the SA node [12]. This exclusion then ensures that the time, measured in milliseconds, is between two consecutive R's (see Figure 1), known as an RR interval. HRV measures the RR interval to determine the consecutive time changes.

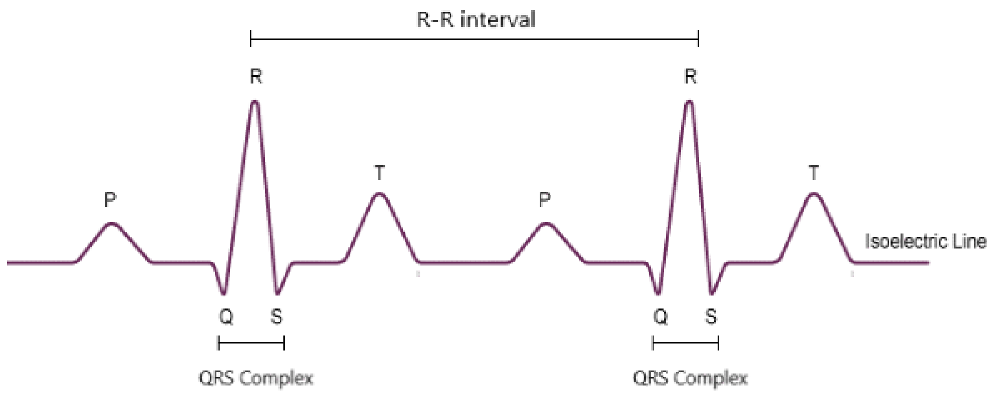


Figure 1: ECG recordings of two consecutive heartbeats and the RR interval between them.

HRV is affected by the autonomic nervous system (ANS), causing HRV to be an important measurement of many different physiological, and psychological reactions [5]. The ANS is responsible for unconscious and involuntary physiological actions, such as heartbeat and breathing. There are two parts to the ANS, the sympathetic nervous system (SNS) and the parasympathetic nervous system (PNS) which both influence bodily functions but in opposite ways. The SNS increases the adrenaline to the SA node, which in turn prepares the body for physical activity by increasing, for example, breathing, heart rate and one's energy level. Additionally, the SNS is also responsible for our stress reaction, known as the "fight or flight" response. PNS, on the other hand, regulates digestion and resting, which relaxes the body and slows down energetic functions [10].

SNS has been associated with the so called low frequency (LF) interval (0.04-0.15 Hz) and PNS with the high frequency (HF) interval (0.15-0.4 Hz) [1]. This creates an opportunity in which frequency domain analysis may give an insight into the balance and strength between the parasympathetic and sympathetic activity [18, p. 590]. A healthy individual's nervous system is efficient in changing between the SNS and the PNS, leading to high variability in heart rate, and thereby a higher HRV value. Lower HRV tends to show that the SNS is in dominance, implying that an individual is in bad health whereas a high HRV means the PNS activity is strong and that the individual is healthy [5]. It has in addition been shown that HRV can be useful in identifying both cardiovascular and non-cardiovascular diseases before their outburst which may help to prevent sudden cardiac death among other disease [1].

There are factors which have a strong impact on HRV such as age, sex and both physiological and psychological conditions and disorders [15]. Age has shown to be strongly correlated with HRV, where infants have the highest HRV values and the values thereafter decrease with age. Women have lower HRV values than men but these inequalities have shown to become less prominent post-menopause [11]. Many disorders have been connected with decreasing HRV, especially somatic diseases. For the past years, there has been an increased focus on psychological disorders, such as depression and post traumatic stress disorders, where tests have shown that such disorders have lower HRV values as well [4].

Respiratory sinus arrhythmia (RSA), which is the natural variability in heart rate during respiration, has been shown to correspond to high-frequency HRV. HRV increases during inspiration and decreases during expiration [14]. RSA is usually present in young and in healthy adults whereas it fades with age and tends to be lacking for individuals with various stages of cardiovascular diseases [9]. It is thereby of great importance to investigate and analyze HRV both by itself and in combination with different factors, in order to obtain valuable information regarding an individuals' health.

1.2 Aim of thesis

The aim of this thesis is to use different spectral estimation methods and time intervals in order to find which combination yields the best estimation of the cross-spectrum between HRV and respiratory signals. The considered methods will be the periodogram, the modified periodogram and the Welch method and the time segments will be either 15 s, 30 s or 60 s. The relation between some covariates (age, BMI and sex) and HRV will be analyzed, with an attempt to find a multi-linear regression model.

2 Mathematical theory

2.1 Spectral Analysis

Spectral analysis is a statistical technique where the spectral properties of a signal are investigated using the Fourier transform. It is sometimes referred to as *frequency domain analysis* since we view signals in the frequency domain, where it is easier to detect periodicities. In applications we use the discrete Fourier transform which we recall to be defined as

$$X(f) = \sum_{t=0}^{n-1} x(t)e^{-i2\pi ft}, \tag{2.1}$$

where x is the input signal and n is the number of data points. Spectral analysis has been shown to be an important tool in several research fields, for example physics and biomedical science, since it can make underlying relations between systems clearer [2]. The following subsections are mainly based on the material in [7].

2.1.1 Power spectral density

The power spectral density (PSD) is a function in the frequency domain which shows where the variation in frequency is strong and where it is weak. The PSD has two interchangeable definitions, either as the Fourier transform of the covariance function (also known as the auto-correlation function), $r(\tau)$, i.e.

$$R_x(f) = \sum_{\tau=-\infty}^{\infty} r(\tau)e^{-i2\pi f\tau} \tag{2.2}$$

or as the average of the squared magnitude of the Fourier transform in the $n \to \infty$ limit

$$R_x(f) = \lim_{n\to\infty} \mathbb{E}\left[\frac{1}{n}\left|X(f)\right|^2\right]. \tag{2.3}$$

As these definitions require an infinite number of samples, methods to estimates the PSD are used in applications. This can be done using parametric or non-parametric methods. The methods presented in this section are solely non-parametric, meaning that they make direct use of the data with no assumptions apart from stationarity.

2.1.2 Periodogram

The periodogram is the simplest and most basic estimate of the PSD and is defined as

$$\widehat{R}_x(f) = \frac{1}{n}\left|X(f)\right|^2. \tag{2.4}$$

This estimate is clearly based on equation (2.3) but can be rewritten to be more similar to equation (2.2) in the following way

$$\begin{aligned}\widehat{R}_x(f) &= \frac{1}{n}X(f)\cdot\overline{X(f)} = \frac{1}{n}\sum_{t=0}^{n-1}\sum_{s=0}^{n-1}x(t)x(s)e^{-i2\pi f(s-t)} \\ &= \frac{1}{n}\sum_{\tau=-n+1}^{n-1}\sum_{t=0}^{n-1-|\tau|}x(t)x(t+|\tau|)e^{-i2\pi f\tau} = \sum_{\tau=-n+1}^{n-1}\widehat{r}_x(\tau)e^{-i2\pi f\tau},\end{aligned} \tag{2.5}$$

where $\tau = s - t$ and $\widehat{r}_x(\tau)$ is the estimate of the covariance function.

A good estimate has an approximate unbiasedness, $\mathbb{E}[\widehat{R}_x(f)] \approx R(f)$, and a low variance, $\text{Var}[\widehat{R}_x(f)] \approx 0$ [2]. From the calculation in [7, pp. 243-244], we know that the variance approaches

$$\text{Var}[\widehat{R}_x(f)] \to \begin{cases} R_x^2(f) & \text{for } 0 < |f| < 0.5, \\ 2R_x^2(f) & \text{for } f = 0 \text{ and } \pm 0.5, \end{cases} \tag{2.6}$$

as $n \to \infty$. We thereby conclude that $\widehat{R}_x$ is an inconsistent estimator which we will combat later by introducing multiple windows. Instead, lets turn to the expectation value which we calculate as follows

$$\begin{aligned}\mathbb{E}[\widehat{R}_x(f)] &= \sum_{\tau=-n+1}^{n-1} = \mathbb{E}[\widehat{r}_x(\tau)]e^{-i2\pi f\tau} \\ &= \sum_{\tau=-n+1}^{n-1}\left(1-\frac{|\tau|}{n}\right)r_x(\tau)e^{-i2\pi f\tau} \xrightarrow[n\to\infty]{} \sum_{\tau=-\infty}^{\infty}r_x(\tau)e^{-i2\pi f\tau} = R_x(f),\end{aligned} \tag{2.7}$$

where we make use of [7, Theorem 2.5] in the second equality. This shows that when n is large, the periodogram is an unbiased estimator of the PSD. However for small n, as is common in applications, we have that

$$\mathbb{E}[\widehat{R}_x(f)] = \sum_{\tau=-\infty}^{\infty}k_n(\tau)r_x(\tau)e^{-i2\pi f\tau}, \tag{2.8}$$

where $k_n(\tau)$ is the *lag window*, defined as $k_n(\tau) = \max(0, 1-\frac{|\tau|}{n})$. We then introduce the *Fejér Kernel*, K_n, as the Fourier transform of the lag window, as

$$K_n(f) = \sum_{\tau=-n+1}^{n-1}k_n(\tau)e^{-i2\pi f\tau} = \frac{\sin^2(n\pi f)}{n\sin^2(\pi f)}. \tag{2.9}$$

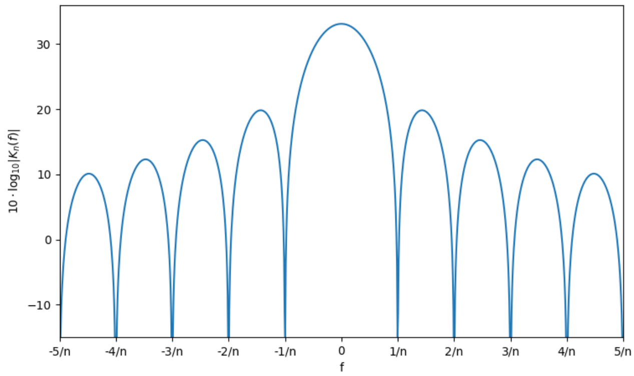


Figure 2: The absolute value of the Fejér kernel $K_n(f)$ in logarithmic scale.

The reason for the bias in the periodogram can be explained by the use of Figure 2. The height of the sidelobes remains high and roughly the same independently of n, causing *leakage* form frequencies with greater powers compared to those with lower powers. Reduced bias can thereby be obtained by changing the "shape" of the the main- and sidelobes which will be discussed next.

2.1.3 Modified periodogram

One method used to reduce the bias is to apply a window by replacing $k_n(\tau)$ with an arbitrary window function $w(\tau)$ yielding what is known as the Modified Periodogram

$$\widehat{R}_x(f) = \frac{1}{n}\left|\sum_{t=0}^{n-1} x(t)w(t)e^{-i2\pi ft}\right|^2. \tag{2.10}$$

The Hanning window is the most commonly used window and is defined as

$$h(t) = \frac{1}{2} - \frac{1}{2}\cos\left(\frac{2\pi t}{n-1}\right), \quad t = 0, 1, \dots, n-1, \tag{2.11}$$

and can be normalized into $w(t)$

$$w(t) = \frac{h(t)}{\sqrt{\frac{1}{n}\sum_{t=0}^{n-1} h^2(t)}}. \tag{2.12}$$

Different windows affect the main- and sidelobes differently, but a rule of thumb is that the wider the mainlobe is, the faster the sidelobes will decrease. It is easiest to compare windows by their corresponding window spectrum, denoted as $K_w(f)$, which is the Fourier transform of $w(t)$.

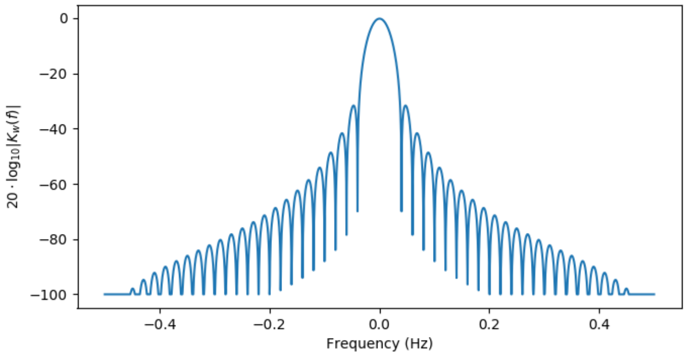


Figure 3: Hanning window spectrum in logarithmic scale.

Comparing Figure 2 and Figure 3 we can see that the Hanning window has a broader mainlobe and lower sidelobes. The width of the mainlobe for the Hanning window is $4/n$ whereas the width of the periodogram mainlobe is $2/n$ which signifies that Hanning is less efficient at resolving close peaks but in return has less leakage than the periodogram, due to a faster decrease for the sidelobes.

2.1.4 The Welch method

There is also the possibility of using multi-window methods such as the Welch method in order to reduce the variance. This method divides the data into shorter segments and uses an overlap technique, resulting in K windows, a specified window-length L and a certain percentile overlap p, which usually is 50%. The Welch method is defined as

$$\widehat{R}_{av}(f) = \frac{1}{K}\sum_{k=1}^{K}\widehat{R}_{x,k}(f). \tag{2.13}$$

This can be viewed as the averaged modified periodogram, given that they use the same window [6]. Given n, p and K, we can determine the length L of each window as

$$L = \frac{n}{pK + 0.5}. \tag{2.14}$$

Reduction of the variance is obtained if the correlation between $\widehat{R}_{x,k}(f)$ and $\widehat{R}_{x,l}(f)$ is small, for $k \neq l$. If that is the case, then

$$\begin{aligned} \mathrm{V}[\widehat{R}_{av}(f)] =& \frac{1}{K^2}\sum_{k=1}^{K}\sum_{l=1}^{K}\mathrm{C}[\widehat{R}_{x,k}(f), \widehat{R}_{x,l}(f)] = \frac{1}{K^2}\sum_{k=l}^{K}\mathrm{V}[\widehat{R}_{x,k}(f)] \\ &\approx \frac{1}{K}R_X^2(f), \end{aligned} \tag{2.15}$$

by the use of the approximation for large n in equation (2.6). The Welch method then reduces the variance by a factor K compared to the normal and modified periodogram.

2.1.5 Cross-spectrum

The cross-spectrum is a tool used in spectral analysis to describe the correlation between two signals. It is a complex-valued function of frequency and is defined as

$$R_{xy}(f) = \sum_{\tau=\infty}^{\infty} r_{xy}(\tau) e^{-i2\pi f\tau}, \tag{2.16}$$

where $r_{xy}(\tau)$ is the cross-covariance function. The cross-spectrum can be written in polar form as $R_{xy}(f) = A_{xy}(f)e^{i\Phi_{xy}(f)}$, where A_{xy} and Φ_{xy} are known as the *amplitude function* and *phase function* respectively. We can estimate the cross-spectrum as

$$\widehat{R}_{xy}(f) = \frac{1}{n} X(f) \cdot \overline{Y(f)} = \sum_{\tau=-n+1}^{n-1} \widehat{r}_{xy}(\tau) e^{-i2\pi f\tau}, \tag{2.17}$$

akin to equation (2.5). Estimating the cross-spectrum can be done using different methods and $X(f)$ and $Y(f)$ can thereby be defined in different ways. Using the periodogram method gives the definitions

$$X(f) = \sum_{t=0}^{n-1} x(t) e^{-i2\pi ft}, \quad Y(f) = \sum_{t=0}^{n-1} y(t) e^{-i2\pi ft}, \tag{2.18}$$

whereas the modified periodogram gives

$$X(f) = \sum_{t=0}^{n-1} x(t) w(t) e^{-i2\pi ft}, \quad Y(f) = \sum_{t=0}^{n-1} y(t) w(t) e^{-i2\pi ft}. \tag{2.19}$$

The Welch method uses equation (2.19) before taking the average.

2.1.6 Coherence spectrum

The magnitude squared coherence spectrum is defined as

$$\kappa^2_{x,y}(f) = \frac{\left|R_{x,y}(f)\right|^2}{R_x(f)R_y(f)} = \frac{A_{xy}(f)^2}{R_x(f)R_y(f)}, \quad \kappa^2_{x,y}(f) \in [0,1] \tag{2.20}$$

and is also known as the normalized cross-spectrum. It is a statistic tool used to determine dependence between the two signals, X and Y, where $\kappa^2_{x,y}(f) = 1$ means that the signals are linearly dependent and $\kappa^2_{x,y}(f) = 0$ means that they are independent. Calculating the coherence spectrum using the periodogram or the modified periodogram gives

$$\widehat{\kappa^2_{x,y}} = \frac{\left|R_{x,y}(f)\right|^2}{R_x(f)R_y(f)} = \frac{\frac{1}{n}X(f)\overline{Y}(f) \cdot \frac{1}{n}\overline{X}(f)Y(f)}{\frac{1}{n}X(f)\overline{Y}(f) \cdot \frac{1}{n}\overline{X}(f)Y(f)} \equiv 1, \tag{2.21}$$

which will not allow us to read off any information about the relationship since it is constant. If we instead use the Welch method, equation (2.13), we have that

$$\begin{aligned} \widehat{\kappa^2_{x,y}} &= \frac{\left|\frac{1}{K}\sum_{j=1}^{K} \widehat{R}_{xy,j}(f)\right|^2}{\frac{1}{K}\sum_{j=1}^{K} \widehat{R}_{x,j}(f) \frac{1}{K}\sum_{j=1}^{K} \widehat{R}_{y,j}(f)} \\ &= \frac{\frac{1}{nK}\sum_{j=1}^{K} X_j(f)\overline{Y_j}(f) \cdot \frac{1}{nK}\sum_{j=1}^{K} \overline{X_j}(f)Y_j(f)}{\frac{1}{nK}\sum_{j=1}^{K} X_j(f)\overline{X_j}(f) \cdot \frac{1}{nK}\sum_{j=1}^{K} \overline{Y_j}(f)Y_j(f)}. \end{aligned} \tag{2.22}$$

Equation (2.22) shows that the use of averaging techniques, such as the Welch method, results in the coherence spectrum being non-constant, as in equation (2.21). Furthermore, a non-constant coherence spectrum is thereby a good measure of dependence between the two signals, $\widehat{R}_x(f)$ and $\widehat{R}_y(f)$, for different frequencies.

2.2 Regression analysis

Regression analysis is a mathematical tool enabling characterization and identification of relationships for a given data set and can be done for multiple factors [16]. There is a dependent variable, Y, and one or more independent variables, X_k, and it is the relation between them which is of interest. There are many methods of regression such as linear, quadratic and logistics, all widely used in fields such as medicine, the social sciences, and business. The theory in this section is mainly based on [13].

2.2.1 Multi-linear regression

In multi-linear regression we have a model with k covariates and n observations. The i:th observation consists of the $k+1$ tuple $(y_i, x_{i,1}, \dots, x_{i,k})$ and we say that Y_i is a dependent variable, whereas $X_{i,j}$ is an independent variable for $j = 1, \dots, k$. They are related as

$$Y_i = \beta_0 + \beta_1 X_{i,1} + \beta_2 X_{i,2} + \ldots + \beta_k X_{i,k} + \epsilon_i, \tag{2.23}$$

where ϵ_i is the random normally distributed error in each observation and $\beta_0, \dots, \beta_k$ are the coefficients which we wish to determine. In order to obtain the estimations we use a method called *the least squares method* in which one minimizes $e_1^2 + \ldots + e_n^2$ in

$$\underbrace{\begin{pmatrix} y_1 \\ y_2 \\ \vdots \\ y_n \end{pmatrix}}_{\boldsymbol{y}} = \underbrace{\begin{pmatrix} 1 & x_{1,1} & x_{1,2} & \dots & x_{1,k} \\ 1 & x_{2,1} & x_{2,2} & \dots & x_{2,k} \\ \vdots & \vdots & \vdots & \ddots & \vdots \\ 1 & x_{n,1} & x_{n,2} & \dots & x_{n,k} \end{pmatrix}}_{\boldsymbol{X}} \underbrace{\begin{pmatrix} b_1 \\ b_2 \\ \vdots \\ b_k \end{pmatrix}}_{\boldsymbol{b}} + \underbrace{\begin{pmatrix} e_1 \\ e_2 \\ \vdots \\ e_n \end{pmatrix}}_{\boldsymbol{e}}, \tag{2.24}$$

where we say that b_j is an estimate of β_j. Minimizing $||\boldsymbol{e}||$ we find that

$$\boldsymbol{b} = (\boldsymbol{X}^T \boldsymbol{X})^{-1} \boldsymbol{X}^T \boldsymbol{y}, \tag{2.25}$$

where we require the existence of the inverse of $\boldsymbol{X}^T \boldsymbol{X}$ in order for a unique solution to exist. After estimating β_j as b_j the discrepancy is accounted for by ϵ_j. From this we can determine the necessary ϵ_j and evaluate the effectiveness of our method. We can finally write our model in matrix form as

$$\boldsymbol{Y} = \boldsymbol{X}\boldsymbol{\beta} + \boldsymbol{\epsilon}. \tag{2.26}$$

Evaluating the effectiveness of the model is done by calculating p-values and the coefficient of determination, also know as R^2. This is a measure of how well a model can account for the inherent variation in the data and is defined as

$$R^2 = 1 - \frac{\sum_i \epsilon_i}{\sum_i (y_i - \bar{y})}, \qquad R^2 \in [0, 1]. \tag{2.27}$$

A high value indicates that the model can account for the variation in the independent variables.

3 Data analysis

3.1 Data descriptions

The data for this thesis was gathered from 47 women and 50 men, aged 20 to 61. Individuals taking medication known to affect the heart rate or who were suffering from any kind of cardiovascular disease were excluded. For every participant, age, BMI, sex, and stress levels were noted, as well as respiratory and heart rate data, each collected during a 5-minute interval with a sampling frequency of 4 Hz. The data was recorded using two devices, a strain gauge attached to the individual's chest for the respiratory signals and electrocardiography (ECG) for the heart rate. The breathing and HRV measurements were made as the participants performed a chirp breathing task, in which the individual was told to breathe following a metronome which began at 0.12 Hz and then slowly increased to 0.35 Hz.

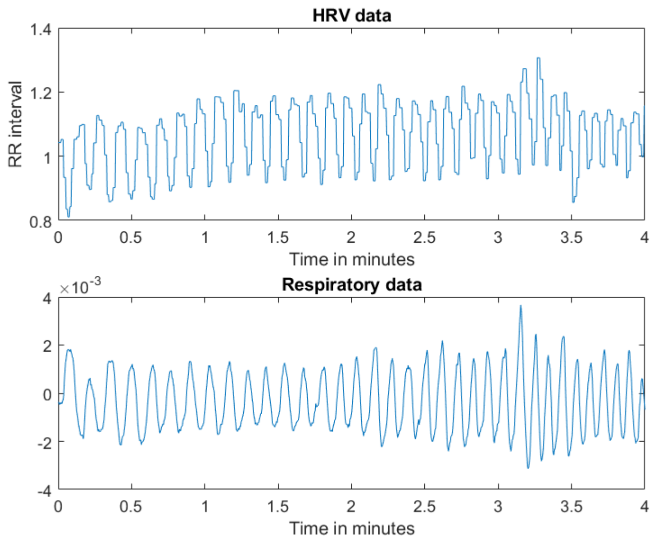


Figure 4: One of the participants' raw HRV and respiratory data.

3.2 Spectral analysis

In order to ensure approximate stationarity, some adjustments were made to the original data. The mean was adjusted to 0 and only the first 4 minutes of measurements were used, corresponding to the first 960 samples. As can be seen in Figure 4, the HRV does not appear to behave like a stationary process and the data was therefore divided into shorter segments, in order to make it more stationary. All segments overlapped by 50% and different segment lengths of 15, 30 and 60 seconds were tested.

All calculations and estimation methods were performed independently for all participants. Zero padding, with $N = 4096$, was used during the FFT calculations in order to make the sample length longer, making it easier to detect peaks. The modified periodogram and the Welch method both used a Hanning window and different numbers of windows were implemented for Welch; 2, 4 and 8. The cross-spectrum was computed between the respiratory and HRV data, and the coherence spectrum was thereafter calculated. For each segment, the cross-spectrum was divided into LF (low frequency, 0.04 - 0.15 Hz) and HF (high frequency, 0.15 - 0.4 Hz) while the rest of the spectrum was discarded. Each participant had their HF and LF powers summed up over all segments, for each estimation method separately. This resulted in a total of three HF values and three LF values per participant.

3.3 Regression analysis

Three covariates were used in the regression analysis; age, BMI, and sex. Previous research indicated that a linear relationship between HRV and the covariates was to be expected which was the motivation for a multi-linear model. To ensure that there were no correlations between the covariates, a correlation coefficient was calculated prior to the analysis which showed no correlation between the covariates. A total of seven regression models were tested and the *p*-values and the coefficient of determination, R^2, were considered in the process of determining whether the models should be rejected or not. The significance levels considered were 0.1, 0.05, 0.01 and 0.001, denoted as ,* **, *** respectively in the tables in the next section.

4 Results and discussion

4.1 Spectral analysis

To determine which time interval Δt yielded the best results, 3 aspects were considered; stationarity, performance for the different estimation methods, and performance of the Welch squared coherence spectrum. In the earlier segments (beginning of the chirp breathing task), a more stationary behavior was observed for $\Delta t = 15, 30$ s than for $\Delta t = 60$ s, while $\Delta t = 15$ s was determined to be the most stationary for the later segments.

Before evaluating the performance of the different estimation methods, the Welch method had to be configured. To decide how many windows, K, should be used, $K = 2, 4, 8$ were tested. For $K = 8$ it was nearly impossible to detect peaks in the cross-spectrum while for $K = 2$ the resulting cross-spectrum was very similar to those obtained using the periodogram and modified periodogram. Therefore, $K = 4$ was chosen together with a 50% overlap, which is customary. This resulted in a window length of 6 seconds, 24 samples. This was then used for all subsequent calculations.

The different time intervals had a similar effect on all of the different estimation methods and their respective cross-spectrum. The peaks got narrower, the longer the segments became and the value of the power decreased as the time intervals got shorter. This can be observed by comparing Figure 5 and 6 below. Note that for all figures, the middle segment of the same participant is shown.

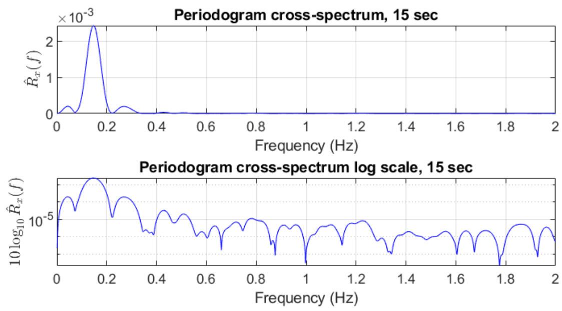


Figure 5: Periodogram cross-spectrum, normal and log scale with $\Delta t = 15$ s.

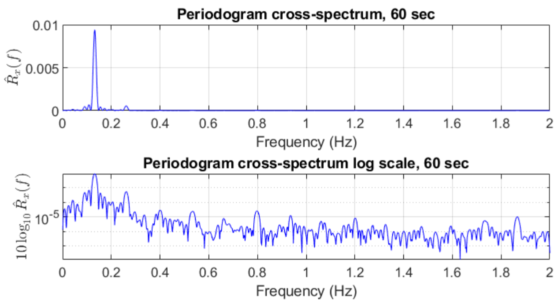


Figure 6: Periodogram cross-spectrum, normal and log scale with $\Delta t = 60$ s.

The Welch coherence spectrum was also greatly affected by the different time intervals. For greater values of Δt, the squared coherence spectrum had an irregular behavior and no clear dependence on frequency, as can be seen in Figure 7.

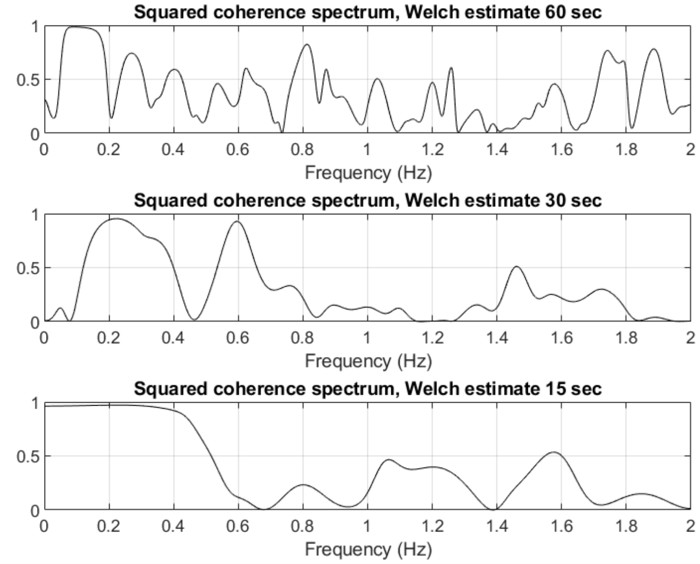
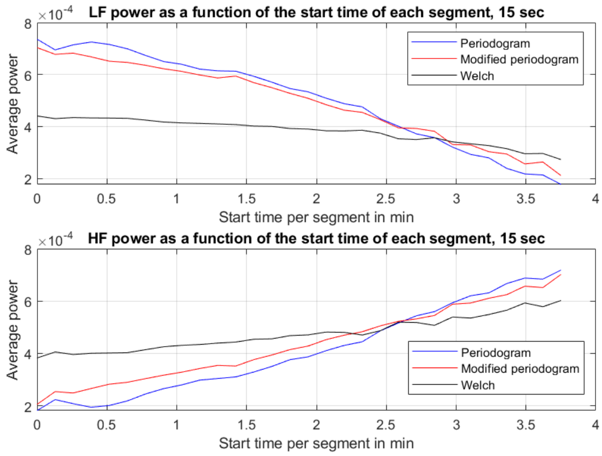


Figure 7: Welch squared coherence spectrum for $\Delta t = 15, 30, 60$ s.

The coherence spectrum for $\Delta t = 15$ s gave some noteworthy result with respect to the LF and HF intervals. For the middle segment, κ_{xy}^2 varied between 0.5 and 1 for the LF interval (0.16 to 0.6 Hz), indicating a strong dependence for most of the interval. For the HF interval (0.6 to 1.6 Hz), however, κ_{xy}^2 varied between 0 and 0.5 indicating some dependence between the respiratory signal and HRV. The same effect, but not as strong, was observed for $\Delta t = 30$ s whereas $\Delta t = 60$ s showed no clear dependence for either interval. The results indicated that $\Delta t = 15$ s was preferable, but it should be noted that the Welch method is less efficient at detecting peaks, which may have caused the coherence spectrum to show greater dependence for lower frequencies than what should be expected. Nonetheless, we still conclude that $\Delta t = 15$ is the most appropriate time interval to choose considering the coherence spectrum.

The chirp breathing task meant that the participants were breathing faster towards the end compared to the beginning. We therefore looked at average power for segments starting at different times. This was done for all time variations, methods, and the LF/HF intervals. This showed no significant difference between the time intervals apart from the graph becoming smoother for $\Delta t = 60$ s in comparison to $\Delta t = 15$ s. All three methods generated similar results, with the exception of the Welch average which was slightly lower than the other two during the LF interval and slightly higher during the HF interval. The graphs also showed that the average Welch powers got closer to the other two estimates as Δt increased. The LF powers decreased as the time increased whereas the HF powers increased, both were consistent with literature as can be seen in the figures below.



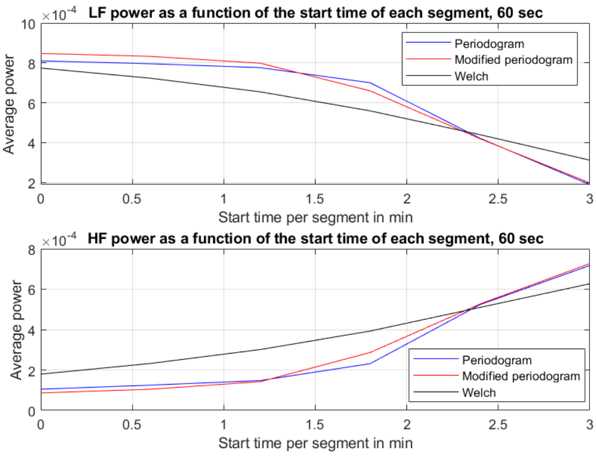


Figure 8: Average LF power as a function of the start time of each segment, for all three methods, $\Delta t = 15$ s.

Figure 9: Average HF power as a function of the start time of each segment, for all three methods, $\Delta t = 60$ s.

Three estimated cross-spectrum, of a random participant, are shown in the Figures 10, 11 and 12. The main noticeable variation was the differences in the widths of the peaks around 0.16 Hz, their ruggedness, and their heights since the Welch peak was lower than the other two. Logarithmic scales are included to highlight behavior in the HF interval.

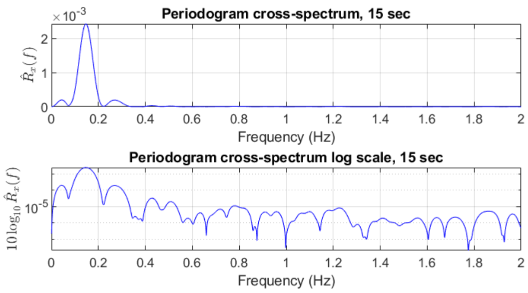


Figure 10: Periodogram cross-spectrum, the middle segment for one of the participants at $\Delta t = 15$ s.

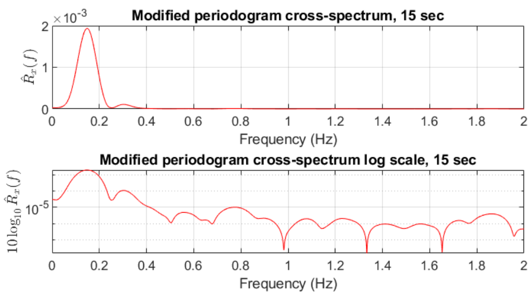


Figure 11: Modifed periodogram cross-spectrum, the middle segment for one of the participants at $\Delta t = 15$ s.

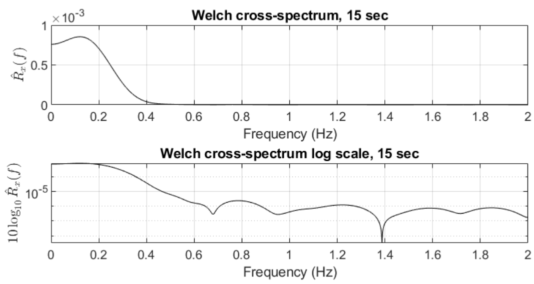


Figure 12: Welch cross-spectrum, the middle segment for one of the participants at $\Delta t = 15$ s.

There was a strong resemblance between the Periodogram and the Modified periodogram as can be seen in Figures 10 and 11, whereas the Welch method behaved differently. This qualitative resemblance is quantized in the table below.

Table 1: Average powers for $\Delta t = 15$ s.

	Periodogram (10^{-3})	**Modified Periodogram (10^{-3})**	**Welch (10^{-3})**
Low Frequency	6.05	6.07	3.96
High Frequency	3.83	4.25	4.44

The HF powers had similar values for all three methods while a significant difference was observed for the LF powers. Powers of the periodogram and the modified periodogram were very close while the Welch method had a much lower value. The difference between these powers was most likely due to the peak of the cross-spectrum being lower in Welch than for the other respective methods, as can be observed in Figures 10, 11 and 12.

4.2 Regression analysis

4.2.1 Covariates

Three covariates were chosen for the regression analysis but they had to be evaluated in order to discard any bias or internal correlation. Evaluating the bias was done by examining the different distributions of the covariates, such as age distribution for the two sexes. This was done in order to determine that, for example, not all females were young and all males old. If that had been the case, then the results may have been influenced negatively and sex would therefore not be a suitable covariate to choose. However, none of the covariates showed any prior bias and example can be seen below between age and sex.

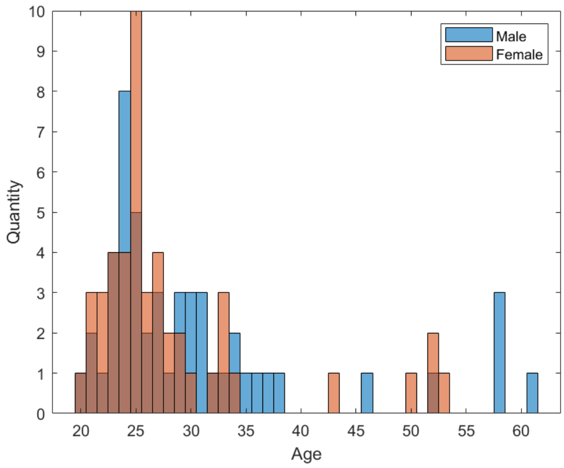


Figure 13: Age distribution for the two sexes.

The average and median age for the respective sexes strengthen the above results due to them being close. The average ages were 30.72 and 28.34, and the median ages were 27 and 25, for males and females respectively. It was shown that females tended to have lower BMIs than males but that should not cause any bias since healthy adult males tend to have a higher BMI's than healthy adult females [17]. The calculation of the correlation coefficients showed no strong correlation, as can be seen in Table 2.

Table 2: Correlation between the covariates.

Age : BMI	**Age : Sex**	**BMI : Sex**
0.154	0.126	0.315

The value between BMI and sex is greater than when they were compared individually with age, which is in agreement with previous statements. The correlation might be of interest for the later regression analysis however, and was therefore noted, but not sufficient enough to be discarded.

4.2.2 Results

All regression models were calculated for all three time intervals $\Delta t = 15, 30, 60$ s. A majority of the models were rejected due to low significant levels in combination with low R^2 values. The only model which was not rejected was the simple regression model for age, at a significance level of less than 0.001. This was true for all values of Δt which only strengthen the dependent relationship between age and HRV, presented in Section 1.1. The age regression results for $\Delta t = 15$ s can be seen in the Table 3.

Table 3: Final age regression model for $\Delta t = 15$ s.

Method	$\boldsymbol{\beta_0}$ $(\mathbf{10^{-3}})$	$\boldsymbol{\beta_1}$ $(\mathbf{10^{-3}})$	$\boldsymbol{p}$**-value** $\boldsymbol{\beta_1}$	$\boldsymbol{R^2}$
Periodogram LF	11.6	−0.19	$3.56 \cdot 10^{-5}$ ***	0.165
Periodogram HF	6.97	−0.11	$21.8 \cdot 10^{-5}$ ***	0.135
Modified periodogram LF	11.6	−0.19	$3.24 \cdot 10^{-5}$ ***	0.167
Modified periodogram HF	7.78	−0.12	$16.3 \cdot 10^{-5}$ ***	0.140
Welch LF	7.6	−0.12	$4.28 \cdot 10^{-5}$ ***	0.162
Welch HF	8.3	−0.13	$8.34 \cdot 10^{-5}$ ***	0.151

The result of the age model for $\Delta t = 30, 60$ s showed very similar result to those in Table 3, implying yet again that age is highly correlated with HRV. Furthermore, all R^2 values were low which in turn meant that the models did not account for most of the inherent variance. This can be seen clearly in Figures 14 and 15.

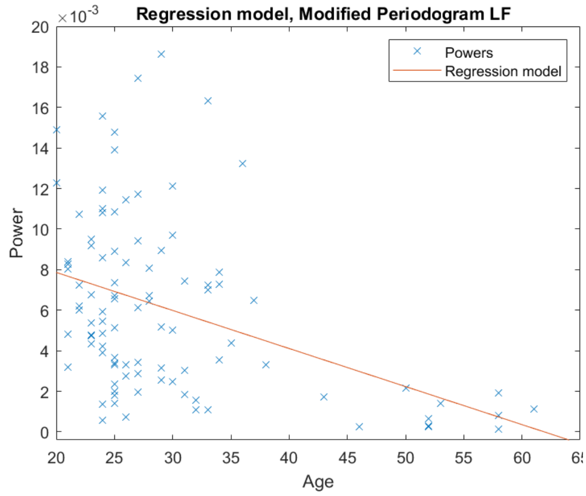


Figure 14: LF power as a function of age, $\Delta t = 15$ s, for the modified periodogram and the associated regression model.

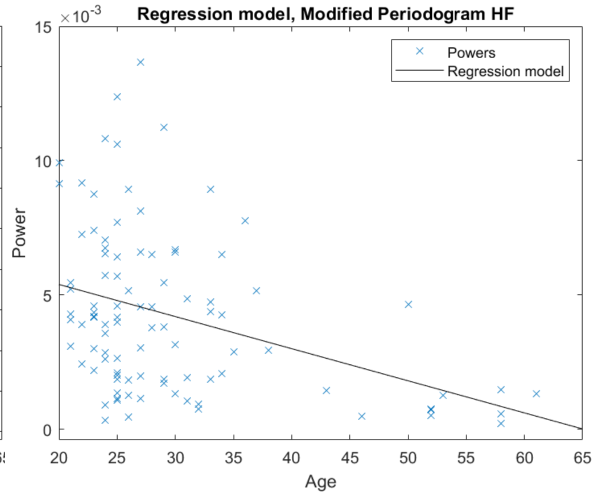


Figure 15: HF power as a function of age, $\Delta t = 15$ s, for the modified periodogram and the associated regression model.

There was a great variation in power for participants between the ages of 20 to 35, which may have been why the model was unable to account for the inherent variations. The obtained powers varied greatly between participants, for all methods, and the average powers may, therefore, have been misleading. In order to highlight this difference, the highest and lowest LF and HF values will be presented. The minimum and maximum values differed by a factor of 1000, as can be seen in Table 4, indicating that there may be something else influencing the results.

Table 4: Differences in the value of power for $\Delta t = 15$ s. All values scaled by 10^{-3}.

	Periodogram			**Modifed periodogram**			**Welch**		
	Min	Max	Difference	Min	Max	Difference	Min	Max	Difference
LF	0.14	18.8	Δ18.7	0.13	18.6	Δ18.5	0.096	12.5	Δ12.4
HF	0.23	13.1	Δ12.9	0.22	13.7	Δ13.4	0.17	14.3	Δ14.2

During the analysis, all models based on either BMI and/or sex were rejected, which was inconsistent with the background information in Section 1.1, this will be discussed later. BMI was chosen as a covariate since it can be used as a measurement to determine if an individual is in a good health and HRV is known to be linked to individual health.

Table 4 showed a great variance between the powers, even within the different LF and HF intervals, which may be one reason why BMI and sex were not suitable covariates. Results which vary as much as these did, tend to imply that there may be other underlying factors present. All participants were interviewed about their individual stress-levels which showed high variations among the participants. Previous studies have shown that psychological disorders influence HRV, indicating that if some participants experienced much stress, that may have masked other "simpler" covariates such as BMI and sex. These ideas are only hypotheses however and needs to be analyzed further in future studies but might have been a reason for the large differences and rejections of the models. Nonetheless, stress was not a covariate of interest in this analysis and the possible influences stress might have had on the results can therefore only speculations. Furthermore, age appeared to have had a stronger correlation with HRV than the other covariates, resulting in the age model not being rejected.

On the other hand, BMI and sex might have been unsuitable covariates because the methods used were not suitable for this data set. All spectral analysis methods assumed stationarity which could have lead to results which complicated the regression analysis. Using non-stationary methods may then give different results, in which BMI and sex are suitable covariates. In addition, combinations of several covariates may sometimes help to bring out relations between covariates which would be hidden otherwise. If such a covariate exists for either BMI or sex, then the lack of that covariate may have lead to inconclusive results. Changing the mathematical methods might, therefore, give different results.

A noticeable difference between the LF and HF intervals were the general results obtained. Evaluating all values of Δt showed that the LF models had lower significance levels throughout, which may have been a result of RSA influence. As RSA is known to be reflected in HF intervals, and only present in youngsters, then that may have led to nonconforming results, since the regression analysis involved both youngsters and older participants. RSA is not reflected in the LF interval and is thereby not a problem for a varying age range. Conclusively, the LF models might have had higher significance levels because there were fewer inconsistencies in comparison to the HF interval as, based on the RSA influence.

Choosing an appropriate value for Δt was difficult because all time intervals yielded more or less the same result. One method to compare them was to look at how the estimated parameters related to the average power. All values of Δt showed that β_1 was $\approx -3\%$ of the average power for the respective method and time interval. This implied that all estimations had roughly the same relation between their powers and the estimated age coefficients. Additionally, it was observed that the LF estimates had a higher percentages than the HF estimates which was in concordance with there being a difference between the two intervals. This is specified further in Table 1.

Table 5: The estimated ratio between the estimated age covariate coefficient and the average power for $\Delta t = 15, 30, 60$ s.

	Average power (10^{-3})			**Estimated β_1 (10^{-3})**			**Percentage**		
	$\Delta t = 15$	$\Delta t = 30$	$\Delta t = 60$	$\Delta t = 15$	$\Delta t = 30$	$\Delta t = 60$	$\Delta t = 15$	$\Delta t = 30$	$\Delta t = 60$
Periodogram LF	6.05	3.26	1.57	-0.19	-0.10 s	-0.050	-3.10%	-3.16%	-3.20%
Modified Periodogram LF	6.07	3.22	1.60	-0.19	-0.10	-0.052	-3.09%	-3.19%	-3.26%
Welch LF	3.96	2.61	1.36	-0.12	-0.083	-0.043	-3.11%	-3.20%	-3.25%
Periodogram HF	3.83	3.26	1.57	-0.11	-0.041	-0.016	-2.77%	-2.63%	-2.38%
Modified Periodogram HF	4.25	3.22	1.60	-0.12	-0.045	-0.013	-2.82%	-2.68%	-2.35%
Welch HF	4.44	2.61	1.36	-0.13	-0.056	-0.019	-2.94%	-2.68%	-2.63%

Regarding the choice of Δt, one thing was particularly distinguishable. Namely the varying significance levels for the estimated age covariate coefficients, as age was linearly combined with none, one or both of the other covariates. All significant levels were lower than 0.001 for $\Delta t = 15$ s whereas the other two Δt had higher significance levels. Conclusively, combining this with the results obtained in the spectral analysis yielded the conclusion that $\Delta t = 15$ s was the most appropriate time interval to choose.

5 Conclusions

This thesis has focused on processing and analyzing a data set obtained from 97 individuals, where their heart rate and respiratory signals were measured. Several factors were also noted and age, BMI, and sex were chosen to be the main focuses of this thesis. Two parts were considered, spectral analysis and regression analysis. Spectral analysis was done with three different methods; the periodogram, the modified periodogram, and the Welch method. Multi-linear regression was used for the regression analysis.

The data was segmented in order to obtain stationarity and three different time intervals were considered; $\Delta t = 15, 30, 60$ s. These time intervals were used for all calculations in both analyses and it was finally concluded that $\Delta t = 15$ s was the most appropriate to choose. Reasons for this included the effects on stationarity, the performance of the estimation methods, the Welch squared coherence spectrum and the significance levels of the regression models.

The three methods did not vary greatly in the estimations they provided. For the LF interval, the periodogram and the modified periodogram showed similar powers for all Δt, whereas the Welch power was significantly lower. During the HF interval, however, all methods generated approximately the same power, where the highest power was obtained by the Welch method. Deciding the best estimation model for this data set was thereby not as straight forward as choosing Δt. All estimations, regardless of method and time difference, indicated an increase in frequency as time increased. During the HF interval, however, the Welch method delivered the lowest p-values and highest R^2 for all Δt and was therefore chosen. For the LF interval, all methods had similar p- and R^2 values, although the modified periodogram had a slight edge and was therefore chosen.

The age regression model was the only model which was not discarded. Some differences were shown for different values of Δt but $\Delta t = 15$ s showed the most preferable result. More specifically, $\Delta t = 15$ s had the lowest significance levels for all methods and for both the LF and HF interval.

Performing analysis based on HRV related data is a noninvasive method to obtain information on different physiological aspects. This can in turn help to identify and prevent both physiological and psychological disorders which is beneficial in many fields. In this analysis, we investigated how age and HRV relate to one another. Despite not being able to draw conclusions about the correlation between HRV and BMI and/or sex, the results indicated that stress might be a covariate of interest in future studies. A possible improvement is, therefore, to do a new analysis with stress as a covariate. Another possible improvement would be to change the mathematical methods and models. The spectral analysis could consist of non-stationary or parametric methods such as ARMA, and the regression analysis could use either more covariates in a multi-linear model or perhaps a different model, i.e. a model with correlated covariates or a quadratic model. Nonetheless, age was significantly correlated with HRV, with $p < 0.001$.

References

[1] Acharya, Rajendra et al. "Heart rate variability: a review". *Medical & Biological Engineering & Computing*, vol. 44 (2006): 1031–51.

[2] Babadi, Behtash and Brown, Emery N. "A Review of Multitaper Spectral Analysis". *IEEE Transactions On Biomedical Engineering*, vol. 61, 5 (2014): 1555-64.

[3] Billman, George E. et al. "An introduction to heart rate variability; methodological considerations and clinical applications". *Frontiers in Psychology*, vol. 6 (2015): 55

[4] Dennis, Paul A. et al. "Posttraumatic stress, heart rate variability, and the mediating role of behavioral health risks". *Psychosomatic medicine*, vol. 76, 8 (2014): 629-37.

[5] Evans, Subhadra et al. "Heart rate variability as a biomarker for autonomic nervous system response differences between children with chronic pain and healthy control children". *Journal of pain research*, vol. 6 (2013): 449-57.

[6] Gupta, Hansa R., Batan, Sushila and Mehra, Rajesh. "Power Spectrum Estimation using Welch Method for various Window Techniques". *International Journal of Scientific Research Engineering & Technology*, vol. 2, 6 (2013): 389-92.

[7] Lindgren, Georg, Rootzén, Holger and Sandsten, Maria. *Stationary stochastic processes for scientists and engineers*. CRC Press, 2013.

[8] Marker, Craig. "Heart Rate Variability: The New Science of Recovery". *Breaking Muscle*. 7 Apr. 2018, `https://breakingmuscle.com/fitness/heart-rate-variability-the-new-science-of-recovery`.

[9] Masi, Christopher M. et al. "Respiratory sinus arrhythmia and diseases of aging: obesity, diabetes mellitus, and hypertension". *Biological psychology*, vol. 74, 2 (2006): 212-23.

[10] McCorry, Laurie Kelly. "Physiology of the autonomic nervous system". *American journal of pharmaceutical education*, vol. 71, 4 (2007): 78.

[11] Moodithaya, Shailaja and Sandhya T. Avadhany. "Gender differences in age-related changes in cardiac autonomic nervous function". *Journal of aging research*, vol. 2012 (2011).

[12] Pieper, Stephen J. and Stanton, Marshall S. "Narrow QRS Complex Tachycardias". *Mayo Clinic Proceddings*, vol. 70, 4 (1995): 371-75.

[13] Rawlings, John O., Pantula, Sastry G. and Dickey, David A. *Applied Regression Analysis, A Research Tool*. Springer Text in Statistics (2nd), 1998.

[14] Ritz, Thomas et al. "Respiratory Sinus Arrhythmia as an Index of Vagal Activity during Stress in Infants: Respiratory Influences and Their Control". *PLOS ONE*, vol. 7 (2012).

[15] Sammito, Stefan and Böckelmann, Irina. "Factors influencing heart rate variability". *International Cardiovascular Forum Journal*, vol. 6, (2016): 18-22.

[16] Schneider, Astrid et al. "Linear regression analysis: part 14 of a series on evaluation of scientific publications". *Deutsches Arzteblatt international*, vol. 107, 44 (2010): 776-82.

[17] Sperrin, Matthew et al. "Body mass index relates weight to height differently in women and older adults: serial cross-sectional surveys in England (1992–2011)". *Journal of Public Health*, vol 38, 3, (2016): 607–613.

[18] Sörnmo, Leif and Laguna, Pablo. *Bioelectrical signal processing in cardiac and neurological applications*. Elsevier Academic Press Inc, 2005.

[19] Walpole, Brenda, Merson-Davies, Ashby and Dann, Leighton. *Biology for the IB Diploma*. Cambridge University Press, 2011.

Bachelor's Theses in Mathematical Sciences 2019:K2
ISSN 1654-6229
LUNFMS-4029-2019

Mathematical Statistics
Centre for Mathematical Sciences
Lund University
Box 118, SE-221 00 Lund, Sweden

http://www.maths.lth.se/