Effects of Age, BMI, Anxiety and Stress on the Parameters of a Stochastic Model for Heart Rate Variability Including Respiratory Information

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Abstract: Recent studies have focused on investigating different factors that may affect heart rate variability (HRV), pointing especially to the effects of age, gender and stress level. Other findings raise the importance of considering the respiratory frequency in the analysis of HRV signals. In this study, we evaluate the effect of several covariates on the parameters of a stochastic model for HRV. The data was recorded from 47 test participants, whose breathing was controlled by following a metronome with increasing frequency. This setup allows for a controlled acquisition of respiratory related HRV data covering the frequency range in which adults breathe in different everyday situations. A stochastic model, known as Locally Stationary Chirp Process, accounts for the respiratory signal information and models the HRV data. The model parameters are estimated with a novel inference method based on the separability features possessed by the process covariance function. Least square regression analysis using several available covariates is used to investigate the correlation with the stochastic model parameters. The results show statistically significant correlation of the model parameters with age, BMI, State and Trait Anxiety as well as stress level.

1 INTRODUCTION

Heart rate variability (HRV) is the physiological phenomenon of the variation in the time interval between heartbeats. Especially parameters related to high frequency HRV (HF-HRV) are increasingly used as a proxy of cardiac parasympathetic nervous system regulation (Billman, 2011). However, since many variables influence the measure, the use of HF-HRV power could be difficult and sometimes unreliable.

Recent studies have focused on investigating the different factors that may affect the HRV. In particular, several publications have highlighted the impact of gender and age differences on HRV. Voss et. al. (Voss et al., 2015) have investigated the gender-specific development of HRV indices for different categories of age. A decrease in HF-HRV power was found with increasing age for women as well as for men, but females had an increased HF power for ages 25-54 years in comparison to males. In (Jönsson et al., 2015), HF-HRV power is found to be decreasing with age.

Reduced HF-HRV power is related to attention deficits, depression, various anxiety disorders, long-term work related stress and burnout, (Davari Dolatabadi et al., 2017; Hernando et al., 2016; Lennartsson et al., 2016; Woo and Kim, 2015; Gates et al., 2015). In (Woo and Kim, 2015), the correlation between subjective ratings of stress and HRV in healthy adults is investigated, showing that stress is negatively correlated with HF-HRV power. Reduced HF-HRV power is also found for individuals suffering from clinical burnout (Lennartsson et al., 2016).

Another aspect is the phenomenon of Respiratory Sinus Arrythmia (RSA), i.e. the heart rate variability in synchrony with respiration, by which the heart rate increases during inspiration and decreases during expiration (Billman, 2011). Recent studies claim that the actual respiratory frequency is the main information to be considered in analysis of HRV (Hernando et al., 2016; Choi and Gutierrez-Osuna, 2011; Weippert et al., 2015). These findings have also increased the interest of estimating the respiratory frequency from the HRV signal, e.g., (Khan et al., 2017) and references therein. Joint analysis of respiration and HRV obtains a more reliable characterization of autonomic nervous response to stress, even if classical frequency domain HRV indices scarcely show statistical differ-

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ences during stress (Hernando et al., 2016). Similar results are found in (Choi and Gutierrez-Osuna, 2011) where the HRV is decomposed into a component that is correlated with the respiratory frequency and one residual component. The residual HRV is used to discriminate mental stress conditions from relaxation conditions. In (Weippert et al., 2015), metronome guided breathing during rest is used to investigate effects on HRV indices. The results show that respiration frequency needs to be considered as a contributor when analysing HRV measures.

In this work, we apply a stochastic model suitable for HRV to measurements recorded from 47 subjects. The test participants were told to breathe following a metronome with slowly increasing frequency. This allows for the acquisition of respiratory related HRV-data covering the frequency range in which adults breathe in different everyday situations. Compared to a usual resting measure with spontaneous breathing, this chirp breathing task allows for examination of the dynamics of peripheral nervous system (PNS) mediated cardiac regulation, from slower to faster respiratory related HF-HRV.

The considered stochastic model falls into the practical strand of addressing the non-stationarity of data by assuming stationarity on local scale. This popular approach has led to the several available definitions of locally stationary processes in literature. We will refer to Silverman's definition, (Silverman, 1957). Locally Stationary Processes (LSPs) in Silverman's sense are stochastic processes resulting from a modulation in time of a stationary covariance function. Thanks to the flexibility of the definition, LSPs are suitable for modelling a wide range of time-varying signals and especially physiological signals (Anderson and Sandsten, 2017). We consider an extension of the LSP definition that accounts for the presence of a chirp in the signals, enabling the inclusion of the respiratory frequency information, and we will refer to these kind of processes as Locally Stationary Chirp Processes, as in (Hansson-Sandsten, 2011; Wahlberg and Hansson, 2007).

The final purpose of our work is to investigate the correlation of the model parameters, estimated with a novel inference method, with several available covariates, including Age, Gender, Weight, Body-Mass-Index (BMI), Spielberg State-Trait Anxiety Inventory (STAI) (Spielberger and Gorsuch, 1983) and Shirom-Melamed Burnout Questionnaire (SMBQ) (Shirom, 1989; Melamed et al., 1992; Melamed et al., 2006). State Anxiety refers to a temporary emotional state, as a transient level of physiological arousal and feelings of vigilance, dread and tension, whereas Trait Anxiety reflects a consistent personality attribute, such as the individual disposition to experience anxious feelings, thoughts or behaviours, (Spielberger and Gorsuch, 1983). The SMBQ is a multidimensional measure for burnout consisting of a combination of physical fatigue, emotional exhaustion, and cognitive weariness. According to this conceptualization, burnout represents a separate construct not interchangeable with depression and anxiety (Shirom, 2003), (Lundgren-Nilsson et al., 2012). Therefore, it is of interest to consider both STAI and SMBQ. Previous studies have validated the Swedish version of the STAI (Hansen et al., 2006; Persson and Ørbæk, 2003; Persson et al., 2005) and the SMBQ (Grossi et al., 2003; Lundgren-Nilsson et al., 2012).

The paper is structured as follows. In section 2 test description, data acquisition and preprocessing are presented. Section 3 includes the mathematical background for the general stochastic model, an outline of the novel inference method, the specific stochastic model introduced for this study case and remarks on the regression approach. Results from the fitted regression models are presented and discussed in section 4, followed by the conclusions in section 5.

2 DATA DESCRIPTION

2.1 Test Description

The test participants are 21 women and 26 men with ages in the range 20-65 years old, at different stages of work related burnout. They were told neither to ingest food, caffeine, or tobacco during 2 hours before the experiment, nor alcohol the day before. Patients using medicines or suffering from any disease known to affect the cardiovascular system were not included in the study.

To obtain respiratory related HRV-data covering the frequency range in which adults normally breathe, the recordings were made while the test participants were breathing following a metronome starting at 0.12 Hz and slowly increasing to 0.35 Hz.

Additionally, for each test participant information on general health and stress level has been collected. The available information includes age, gender, height, weight, STAI and SMBQ.

2.2 Data Acquisition and Preprocessing

The heart rate has been recorded through electrocardiography (ECG) using disposable electrodes. Measure of the respiration has been obtained using a strain gauge over the chest. ECG and respiration were recorded at 1 kHz using the ML866 Power Lab data

acquisition system and analysed using its software LabChart8 (ADInstruments Pty Ltd.) and MATLAB (Math-Works, Inc., Natick, MA, USA). The R-waves were detected with LabChart8 and the HRV data are obtained from the HR data, as the time difference between two consecutive heartbeats.

The raw data sequences, consisting of 5 minutes of recording of heart rate and respiratory data, were down-sampled to 4 Hz. After adjusting to zero mean, the middle 960 samples were used, corresponding to 4 minutes of recording. An example of HRV and respiratory data measured from one subject is presented in Figure 1.

3 METHODS

3.1 Locally Stationary Processes

Even though theory of stationary stochastic processes is well developed, the assumption of stationarity is too restrictive for most measured signals, which usually exhibit changes in the behavior over time. Several approaches have been considered, often involving splitting the data into shorter segments for the estimation of time-varying parameters.

An alternative approach revolves around classes of processes with desirable properties extending the stationary case. This is the case for Locally Stationary Processes (LSPs) (Silverman, 1957), assuming stationarity on local scale. This definition of LSPs avoids time-varying parameters and is based on the modulation in time of an ordinary stationary covariance function. More precisely, a zero mean stochastic process $X(t)$, $t \in [T_0, T_f] \subseteq \mathbb{R}$, is a LSP if its covariance $C(s,t) = \mathbb{E}[X(s)X(t)^*]$ can be written as

$$C(s,t) = q\left(\frac{s+t}{2}\right) \cdot r(s-t) \tag{1}$$

with $s,t \in [T_0, T_f] \subseteq \mathbb{R}$, where q is a non-negative function and r is a normalized ($r(0) = 1$) stationary covariance function. When q is a constant, Eq. (1) reduces to a stationary covariance, therefore this definition includes stationary processes as a special case.

The wide range of possibilities for the choice of the functions q and r makes LSPs a flexible tool to model time-varying data. For instance, in (Anderson and Sandsten, 2017), LSPs are used to model electroencephalography data sequences collected within a study on human memory retrieval.

For this application on HRV data, we consider an extension of the model that allows us to include the respiratory frequency information. The covariance matrix of an underlying chirp is included in the model covariance as a multiplicative factor, similarly to the definition of Locally Stationary Chirp Process (LSCP) found in (Hansson-Sandsten, 2011; Wahlberg and Hansson, 2007).

3.2 Inference Method

A novel inference methodology, based on the separability properties of the model covariance, is used to estimate the model parameters for each data sequence. In the following we present an outline of the inference method.

In the sampled data framework, denote with $\mathbf{x}$ a data sequence, consisting of n observations x_k, $k = 1 \ldots n$, sampled at equidistant times $t_k = T_0 + (k-1)\Delta t$, in the time interval $[T_0, T_f] \subseteq \mathbb{R}$, where $\Delta t = t_k - t_{k-1}$ is the constant sampling interval.

To account for the differences among individuals in the interpretation of the task of breathing accordingly to the metronome, the chirp covariance matrix is estimated from the respiratory signal of each subject in the study. Unfortunately, the classical estimator of a non-stationary covariance, the Sample Covariance Matrix (SCM)

$$\hat{C}_{SCM} = \mathbf{x} \cdot \mathbf{x}^T \tag{2}$$

is known to be extremely unreliable if it is based on a single realization (Smith, 2005). Therefore we make use of a surrogate respiratory signal, based on the instantaneous frequency (IF) estimate from the spectrogram of the measured single realization respiratory signal. Using the estimated IF, a number of 1000 surrogate respiratory realizations with different phases are simulated, and the resulting SCMs are averaged. We denote the estimated covariance matrix of the respiratory signal with $\hat{K}$.

Let $Q \in M_{n\times n}$ be the matrix $Q(k,l) \doteq q(\frac{t_k+t_l}{2})$, corresponding to the function q, and $R \in M_{n\times n}$ be the matrix $R(k,l) \doteq r(|t_k - t_l|)$, corresponding to the stationary covariance function r. Clearly, from the definition, it follows that Q is a Hankel matrix, which carries the information about the power schedule, while R is a symmetric Toeplitz matrix.

The function q describes the power schedule of the process $X(t)$, as can be deduced by taking $s = t$ in Eq. (1), $C(t,t) = \mathbb{E}[X(t)^2] = q(t) \cdot r(0) = q(t)$. Consequently, an estimate of the parameters determining q can be obtained through a least squares fitting of the parametric curve to the instantaneous power of a single realization of the HRV data, $P(t_k) = x_k^2$. The parameters define the whole matrix $\hat{Q}$, thanks to its structure.

The final step is the estimation of the stationary covariance R, which can be obtained by least squares fitting of $R \cdot \hat{K}$ to the sample covariance matrix Eq. (2)

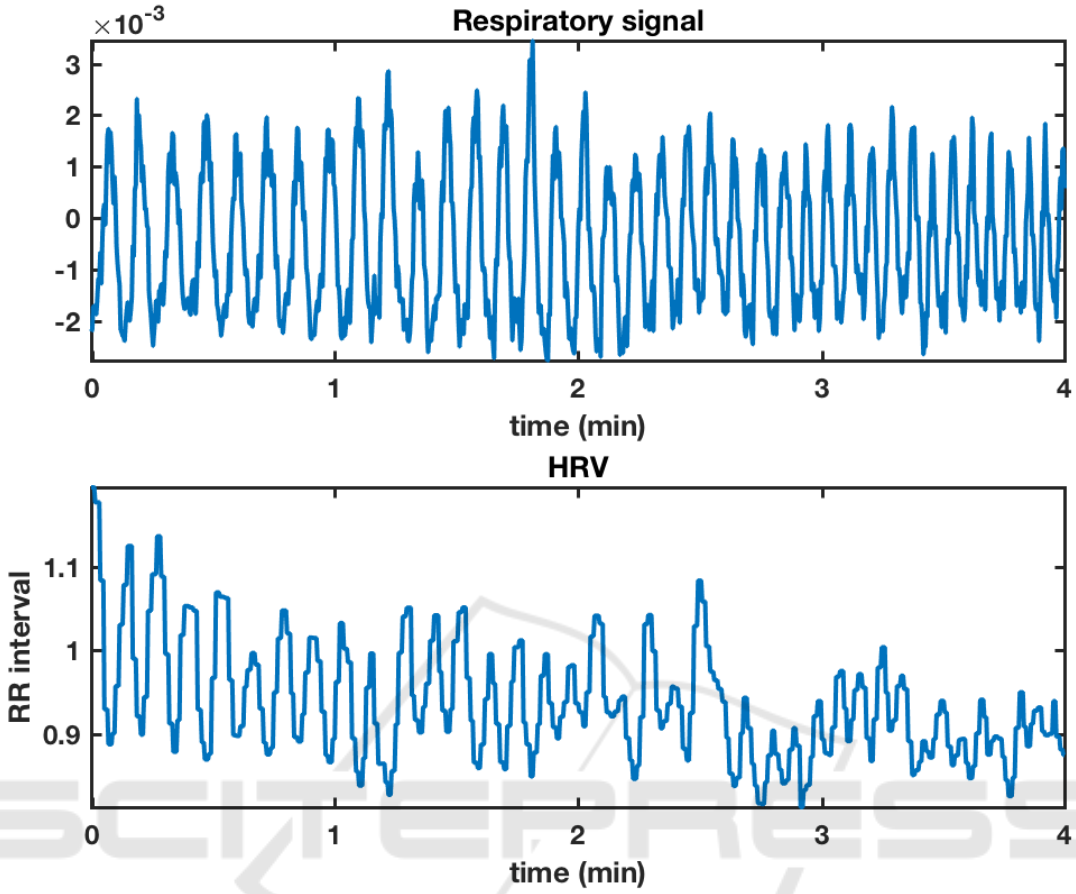

Figure 1: Respiratory signal (upper) and HRV signal (lower) from a subject participating in the study.

of the single realization HRV data divided by the previously estimated $\hat{Q}$. This division does not create stability issues since $\hat{Q}$ is a strictly positive matrix.

3.3 Stochastic Model for HRV Signals

Suitable choices for the families of the functions q and r depend on the data to be modelled. In our application, the family of functions for q should allow the modelling of a typically decreasing instantaneous power, but should also include the exceptions of a stationary or even slightly increasing power. Therefore we choose q to be an exponential function with two parameters $a > 0$ and $b \in [-1, 1]$

$$q_{a,b}(\eta) = a \cdot \exp(b \cdot \eta) \text{ with } \eta = \frac{t+s}{2} \qquad (3)$$

Clearly, the scaling parameter a corresponds to the power at time zero, with a larger value of a corresponding to higher power, whereas the value of b describes the power decrease or increase.

Since the function r should define a stationary covariance function, we choose a Gaussian function for its flexibility and desirable properties

$$r_c(\tau) = \exp\left(-\frac{c}{8} \cdot \tau^2\right) \text{ with } \tau = t - s \qquad (4)$$

with parameter $c > 0$. Intuitively, the parameter c describes the local stationarity of the data, with larger values of c corresponding to a faster decaying auto-correlation. Conversely, a smaller value of c corresponds to a larger standard deviation of the Gaussian bell, meaning longer lasting auto-correlation.

In Figure 2 we exemplify how the different parameters relate to the HRV sequence. In the top panel, we compare a sequence with an estimated large value of a, Figure 2 (a), to a sequence with a smaller estimated a, Figure 2 (b). In the second row, the effect of the parameter b can be observed: typically the estimated value of b is negative and corresponds to the decrease in amplitude of the instantaneous power, Figure 2 (c); however, in a few cases, a value close to 0 or even slightly positive has been observed, Figure 2 (d). The most difficult parameter to interpret is c, related to local stationarity of the underlying stochastic process. In the bottom row, a sequence with an estimated high

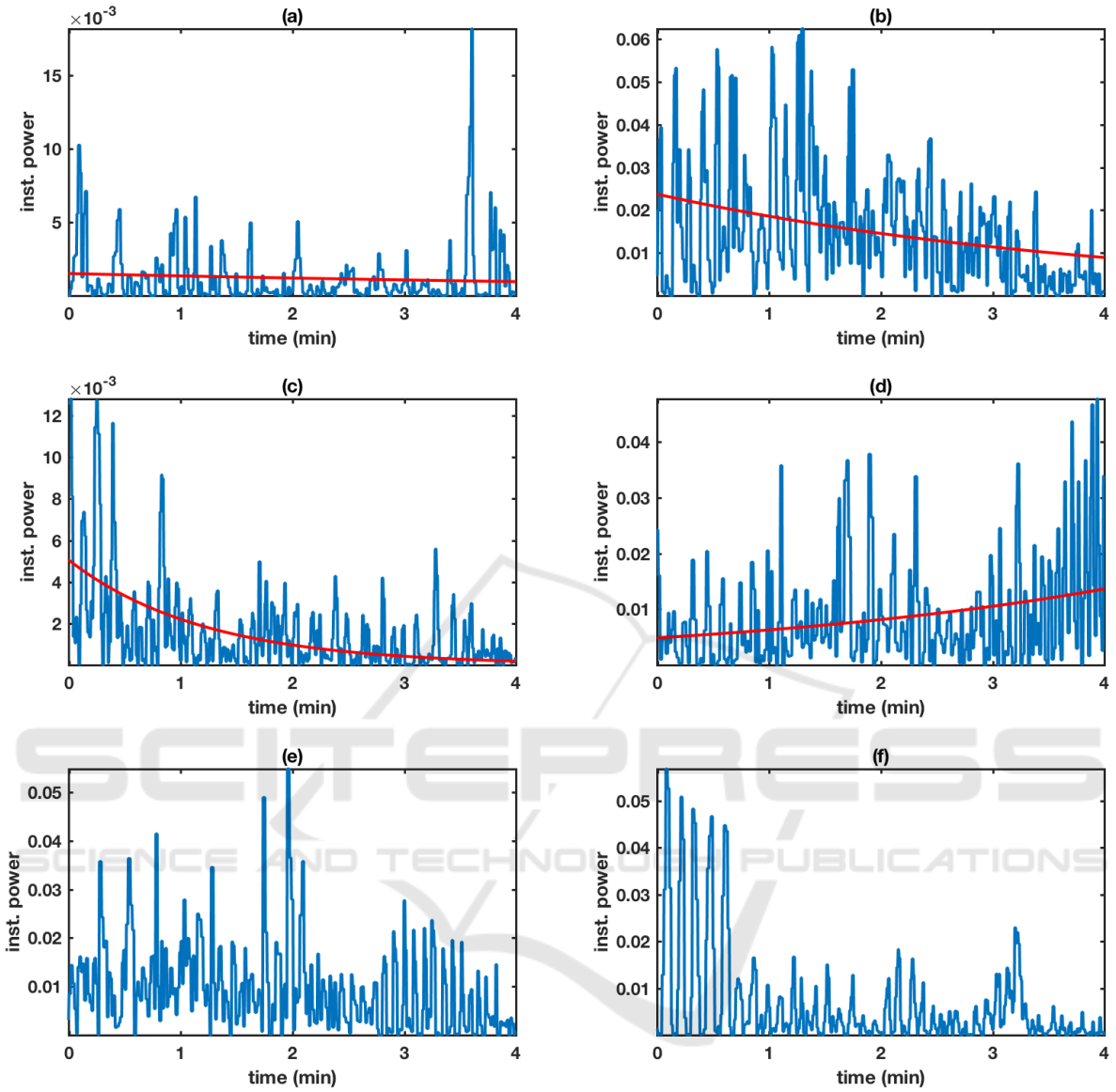

Figure 2: Examples of instantaneous power (blue) and fitted q function (red) for subjects with different estimated parameters:
a) $a = 0.0015$, $b = -0.0019$, $c = 5.7744$;
b) $a = 0.0237$, $b = -0.0041$, $c = 0.0091$;
c) $a = 0.0051$, $b = -0.0138$, $c = 0.0064$;
d) $a = 0.0049$, $b = +0.0043$, $c = 0.0144$;
e) $a = 0.0152$, $b = -0.0040$, $c = 0.0109$;
f) $a = 0.0219$, $b = -0.0152$, $c = 4.3053$.

value of c, Figure 2 (e), is compared to a sequence with a smaller estimated c, Figure 2 (f).

3.4 Linear and Logistic Regression

Least squares regression analysis with each of the LSCP model parameters (a, b, c) as response is performed to explore the correlation of the parameters with several factors of interest (Rawlings et al., 1998). The considered factors are Age, Gender, Weight, BMI, STAI (State Anxiety and Trait Anxiety) and SMBQ. Median, mean and standard deviation for the variables among the participants according to gender are reported in table 1.

To isolate the effect of every factor, regression models with a single explanatory variable (Simple

Table 1: Median, mean and standard deviation (sd) for the variables among the participants according to gender.

	Women (n=21)			**Men** (n=26)		
	Median	Mean	sd	Median	Mean	sd
Age	25	31.14	11.50	30.5	34.69	12.66
Weight	61	63.76	9.67	78.5	78.15	10
BMI	22	22.52	3.32	23.72	24.07	3.06
State Anxiety	35	33.09	6.70	29	30.15	7.70
Trait Anxiety	38	36.95	6.94	33	35.73	10.64
SMBQ	2.86	3.05	1.11	2.64	2.85	1.32

Table 2: Multivariate regression model for parameter a including all observations.

	coeff. est.	S.E.	p-value
Age	-0.0748	0.0114	$5.83 \cdot e^{-08}$ ***
State Anxiety	-0.0635	0.0231	0.0087 **
High Trait Anxiety	0.7261	0.3189	0.0278 *

Table 3: Multivariate regression model for parameter a after removal of influential observations.

	coeff. est.	S.E.	p-value
Age	-0.0873	0.0106	$3.81 \cdot e^{-10}$ ***
State Anxiety	-0.0778	0.0203	0.000433 ***
High Trait Anxiety	0.9471	0.2778	0.001498 **

Regression) has been tested first for each LSCP model parameter and for each covariate.

Afterwards, multivariate models have been evaluated based on statistical significance of the predictors, coefficient of determination R^2 and the Akaike Information Criterion (AIC). Levels of significance considered are 0.001, 0.01, 0.05, 0.1, denoted in the tables with significance codes ***,**,*, . respectively.

Regression diagnostics include residual analysis, F-test for testing inclusion of variables, detection and treatment of outliers and influential observations.

The analysis is performed with open source software RStudio for programming language R (RStudio Team, 2015; R Development Core Team, 2008).

4 RESULTS AND DISCUSSION

4.1 Parameter a

As a is a positive parameter representing the amplitude multiplier that scales the exponential function, it is natural to consider its logarithm transformation to avoid positive skewness of the residuals.

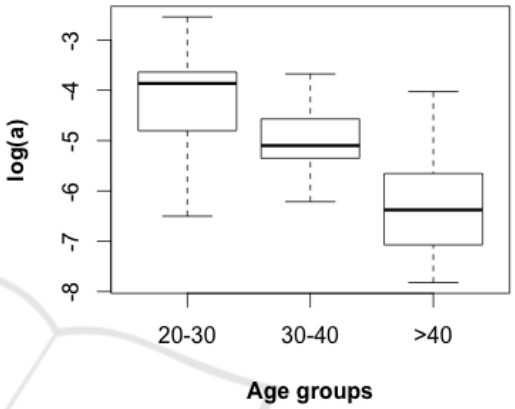

Figure 3: Boxplots of log(a) divided in age groups.

When considering a single explanatory variable, only the covariate Age is a significant predictor, while other covariates become significant only in multivariate models. The simple model with only Age as predictor achieves a coefficient of determination $R^2 = 0.42$. This result is expected, due to the high correlation between HRV amplitude and age, reflected in the scale parameter a, Figure 3.

Step-wise model selection based on AIC starting from a model including all the covariates leads to a multivariate model including Age as well as State and Trait Anxiety. Age and State Anxiety are significant predictors, with $p < 0.001$ and $p < 0.05$ respectively, while Trait Anxiety has a p-value of 0.1013, which is not significant at the usually considered levels.

However, the inclusion of Trait Anxiety in the model improves the predictive power of State Anxiety, which otherwise is not significant. This conflict is solved by considering Trait Anxiety as a categorical variable, distinguishing only between high and low levels of Trait Anxiety, with the median of the population (37) as threshold. Comparison through ANOVA test with respect to the model with only Age and State Anxiety leads to rejection of the null hypothesis at level 0.05, i.e. the categorical variable for Trait Anxiety adds further explanation. Estimated coefficients

Table 4: Multivariate regression model for parameter b.

	coeff. est.	S.E.	p-value
SMBQ	-0.0387	0.0184	0.0413 *
Age	-0.0023	0.0012	0.0641 .
Trait Anxiety	0.0044	0.0024	0.0763 .

Table 5: Simple regression model for the value of b, restricted to 43 subjects with $b > 0$.

	coeff. est.	S.E.	p-value
Intercept	-0.0028	0.0015	0.0662 .
SMBQ	-0.0011	0.0005	0.0217 *

Table 6: Simple regression model for the value of b, restricted to 43 subjects with $b > 0$.

	coeff. est.	S.E.	p-value
Intercept	-0.0047	0.0007	3.11e-07 ***
Stressed Group	-0.0025	0.0010	0.0169 *

Table 7: Logistic regression model for the sign of parameter b.

	coeff. est.	S.E.	p-value
Intercept	-5.4757	1.9033	0.00402 **
Age	0.0806	0.0415	0.05203 .

with standard errors and corresponding p-values are reported in Table 2. The model intercept does not significantly differ from zero, therefore it is omitted. The coefficient of determination is increased to $R^2 = 0.51$.

The fact that both Age and State Anxiety are significant predictors of $\log(a)$ with a similar effect (negative slope and same scale) suggests an analogy between the effect on the HRV instantaneous power of ageing and higher State Anxiety. The effect of an increased anxiety as a temporary emotional state (State Anxiety) is mitigated by the effect of a higher anxiety as a consistent personality attribute (Trait Anxiety).

The removal of potentially influential observations according to Cook's distance (3 out of 47) leads to slightly different model coefficients with smaller p-values and improved coefficient of determination $R^2 = 0.64$, but similar overall conclusions, Table 3.

4.2 Parameter b

As mentioned in section 3, parameter b describes the power decrease or increase. More precisely, a negative b with higher absolute value corresponds to a faster power decrease, while a positive b with higher absolute value corresponds to a faster power increase. Since the increase in respiratory frequency due to the chirp breathing task is usually related to a decrease in power, in most cases the estimated value of b is negative; nevertheless, we have observed a positive b in 4 out of 47 subjects.

To investigate the relation of parameter b with the available covariates, we first consider the estimated value of b for all subjects. Step-wise model selection based on AIC leads to the model presented in Table 4, where the SMBQ is the most significant predictor, $p < 0.05$, followed by Age and Trait Anxiety, $p < 0.1$. The R^2 value for this model is only 0.14. None of the factors are significant if considered as single explanatory variable.

After outliers treatment (removal of 6 out of 47 subjects), the best model according to AIC includes only the SMBQ, which is a significant predictor, $p < 0.05$, with a negative slope, i.e. higher value of the SMBQ corresponds to a faster decrease of the instantaneous power of the HRV, Table 5. However, this model achieves only an R^2 of 0.13, attesting that a large portion of the variability between predictor and response has not been accounted for.

Similar results are obtained when considering the SMBQ as categorical variable, with threshold of 2.75 to distinguish between baseline category (control group) and the stressed group, Table 6. SMBQ above 3.75 is considered as compatible with pre-Exhaustion Disorder (Jönsson et al., 2015); however there is no statistical difference as predictors for the value of the parameter b between the pre-Exhaustion Disorder category (SMBQ above 3.75) and an additional category defined through SMBQ in the range $[2.75, 3.75]$.

Logistic regression to predict the sign of parameter b leads to a single regression model with only Age as covariate, Table 7. Unfortunately this result has limited validity due to the small sample size, since the estimated value of the parameter b is negative only for 4 subjects.

4.3 Parameter c

When considering a single explanatory variable for the parameter c, the covariate Age is highly significant with $p < 0.001$, while BMI and Weight have $p < 0.01$ and $p < 0.05$ respectively. Clearly Weight and BMI are highly correlated covariates, and not surprisingly Weight ceases to be significant once BMI is included in the model. The step-wise selected model according to AIC includes only Age and BMI, Table 8. This model has a coefficient of determination $R^2 = 0.5$. We can observe that both covariates have a positive slope, where an increase of one unit in BMI has roughly the same effect of an increase of two years of age.

If BMI is considered as a categorical variable with levels underweight (BMI$<$ 18), normal weight (18 $\leq$

Table 8: Regression model for parameter c.

	coeff. est.	S.E.	p-value
Intercept	-7.8773	1.9666	0.000235 ***
Age	0.1146	0.0228	$9.04 \cdot e^{-06}$ ***
BMI	0.2416	0.0856	0.007143 **

Table 9: Regression model for parameter c with BMI as categorical variable.

	coeff. est.	S.E.	p-value
Intercept	-2.4395	0.7507	0.002279
Age	0.1115	0.0214	$5.21 \cdot e^{-06}$ ***
Obese	3.7010	0.9318	0.000274 ***

Table 10: Regression model for parameter c with BMI as categorical variable.

	coeff. est.	S.E.	p-value
Intercept	-3.571	0.6885	$6.14 \cdot e^{-06}$ ***
Age	0.1538	0.0210	$5.83 \cdot e^{-09}$ ***
Obese	2.922	0.8821	0.00194 **

BMI < 25), overweight ($25 \leq$ BMI < 30) and obese (BMI ≥ 30), only the category obese is significantly different from the baseline category normal weight, Table 9. This model achieves an R^2 value of 0.57. However, it should be noted that only 4 people in this study have a BMI above 30. Slightly different coefficients and $R^2 = 0.65$ are obtained when 3 outliers and influential observations are removed from the population, Table 10.

5 CONCLUSIONS

In this paper, we have considered a stochastic model based on the definition of Locally Stationary Chirp Processes, which enables the inclusion of the information from the respiratory signal. Suitable families of the functions with parameters defining the model covariance have been selected to fit non-stationary HRV data sequences. The HRV data from 47 subjects is measured during breathing following a metronome with increasing frequency. Respiratory information has been included as a factor in the model covariance matrix.

For each subject, the model parameters are estimated with a novel inference method based on the separability features possessed by the process covariance function. Regression analysis with several available covariates is used to investigate the predictive power with respect to the model parameters. Results show a statistically significant correlation of the model parameters with age, BMI, State and Trait Anxiety and SMBQ.

In particular, both Age and State Anxiety have the effect of decreasing parameter a, which corresponds to a decrease in the scale factor describing the HRV power. This effect is mitigated by the effect of a higher anxiety as a consistent personality attribute (Trait Anxiety). For parameter b, related to the power decrease or increase with the time-varying breathing frequency, the SMBQ is the most significant predictor, followed by Age and Trait Anxiety. After outliers treatment, only SMBQ is significant. Both Age and BMI are statistically highly significant predictors for parameter c ruling the local behavior of the process, with an increase of one unit in BMI, having roughly the same effect of an increase of two years of age.

None of the model parameters has shown significant differences related to gender. It is possible that the demographic composition of the participants, with women younger than men, could have masked possible correlation of the model parameters with gender.

Future research will investigate how the model parameters relate with other commonly used measures for HRV, such as low frequency and high frequency spectral components.

COMPLIANCE WITH ETHICAL REQUIREMENTS

Data collection took place at the Department of Laboratory Medicine, Division of Occupational and Environmental Medicine, Lund University. The study was approved by the central ethical review board at Lund (Dnr 2013/754) and was conducted in correspondence with the Helsinki declaration. All participants signed an informed consent that clearly stated that participation was voluntary and could be discontinued at any time.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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