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Biomedical applications
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Modelling and Inference using Locally Stationary Processes
Biomedical applications

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LUND UNIVERSITY

Licentiate Thesis

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Modelling and Inference using Locally Stationary Processes: Biomedical applications

Abstract

This thesis considers statistical methods for non-stationary signals, specifically stochastic modelling, inference on the model parameters and optimal spectral estimation. The models are based on Silverman's definition of Locally Stationary Processes (LSPs). In all the contributions, an example of a biomedical application of the proposed method is provided. In the first two papers, the methods are applied to electroencephalography (EEG) data, while in the third paper the application involves Heart Rate Variability (HRV) data.

In paper A, we propose a method for estimating the parameters of an LSP model. The proposed method is based on the separation of the two factors defining the LSP covariance function, in order to take advantage of their individual structure and divide the inference problem into two simpler sub-problems. We present a simulation study to show the method's performance in terms of speed of convergence, accuracy and robustness. Finally, we provide an illustrative example of parameter estimation from three sets of EEG signals, measured from one person during several trials of a memory encoding task of three different categories of visual memories.

Paper B investigates the estimation of the Wigner-Ville spectrum of time-varying processes, modelled as LSPs. Previous works have provided the theoretical expression of the mean-square error optimal time-frequency kernel, and now, thanks to the introduced inference method, we are able to compute the optimal kernel in real data cases. The derived optimal spectral estimator is compared with the single Hanning spectrogram and the Welch method in a simulation study. As biomedical application, we compute the optimal spectral estimate according to the estimated model parameters for the three EEG data-sets also treated in paper A.

In paper C, we model HRV signals with a model known as Locally Stationary Chirp Processes (LSCP), which is an extension of the LSP model including the presence of a chirp. The inference method proposed in paper A is adapted to take into account the respiratory signal information, in the form of the covariance matrix of the chirp respiratory signal estimated beforehand. We perform least squares regression analysis with each of the LSCP model parameters as the response to explore the correlation of the parameters with several factors of interest. Our results show a statistically significant correlation between the model parameters with age, BMI, State and Trait Anxiety as well as stress level.

Key words

Modelling of Time-Varying Signals, Locally Stationary Processes, Statistical Inference, Time-frequency Estimation, Regression, EEG Signals, HRV Signals

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Modelling and Inference using Locally Stationary Processes
Biomedical applications

Rachele Anderson

Lund University
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Lund, 2017

Rachele Anderson
Abstract

This thesis considers statistical methods for non-stationary signals, specifically stochastic modelling, inference on the model parameters and optimal spectral estimation. The models are based on Silverman’s definition of Locally Stationary Processes (LSPs). In all the contributions, an example of a biomedical application of the proposed method is provided. In the first two papers, the methods are applied to electroencephalography (EEG) data, while in the third paper the application involves Heart Rate Variability (HRV) data.

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interest. Our results show a statistically significant correlation between the model parameters with age, BMI, State and Trait Anxiety as well as stress level.
Popular summary

This thesis considers statistical methods for non-stationary signals. A signal is a physical quantity that varies with some independent variable, e.g. time or space, which conveys information. A signal whose statistical properties are constant in time is called stationary, whereas non-stationary signals, which are more common in real-world cases, are those whose characteristics vary with time. In this thesis a special focus is on biomedical applications: in each paper presented, the statistical methods are applied either to signals measured from the human brain or from the human heart. The brain signals are recorded with electroencephalography (EEG), within a larger study where the final goal is to understand how the human brain decodes different types of visual memories. The heart signals are obtained by measuring the variation in the beat-to-beat time interval and represent a physiological phenomenon called Heart Rate Variability (HRV).

Despite decades of research we still have only a limited knowledge of how the brain works. The strive for this understanding is motivated by a huge panorama of applications, including treatment of brain diseases, development of brain-computer interfaces and the pure interest of understanding our mind and consciousness. EEG is a popular method because of the high time-resolution and because, if the electrodes are placed on the surface of the scalp, it is non-invasive. Recent technologies to collect brain data open new possibilities: for example, EEG wearable caps can provide measurements while doing everyday activities, without having to be in a laboratory. This has a potential that cannot be fully developed without reliable methods to analyse these signals.

Modified HRV has been associated with several clinical conditions. In particular, reduced High-Frequency-HRV power is related to attention deficits, depression, various anxiety disorders, long-term work-related stress and burnout. Investigating the different factors that may affect heart rate variability (HRV) is important since the significance and the meaning of the many different measures of HRV are complex and there is the risk of incorrect conclusions and unfounded extrapolations.

The statistical methods considered are stochastic modelling, estimation of the model parameters and time-frequency analysis. Modelling has the purpose to describe the data through a mathematical representation that mimic a real-
world phenomenon or process. We consider stochastic models, where a source of randomness is included. “All models are wrong” in the sense that they are only approximations of reality; the important fact is whether the model is useful for the purpose. Good models are as detailed as necessary and as simple as possible. Simulations from the model can be used for testing, analysis and prediction of the process behaviour. If we simulate from the stochastic model several times, the results will not be identical. A stochastic model includes parameters which need to be estimated from the data, thus the demand for appropriate inference methods. Time-frequency analysis is one of the most helpful approaches when treating non-stationary signals, where the signal spectrum of frequencies varies with time.
List of papers

This thesis is based on the following papers:

A Rachele Anderson and Maria Sandsten, “Inference for Time-varying Signals using Locally Stationary Processes”, submitted for possible publication in *Journal of Computational and Applied Mathematics*.

B Rachele Anderson and Maria Sandsten, “Optimal Spectral Estimation for Locally Stationary Processes with Application on EEG Signals”, manuscript in progress.


Publications not included in this thesis:


Author Contributions

A Rachele Anderson and Maria Sandsten, “Inference for Time-varying Signals using Locally Stationary Processes”, submitted for possible publication in *Journal of Computational and Applied Mathematics*.

Maria Sandsten (MS) had the idea for the research question. I developed the presented algorithm, made the simulations and had the main responsibility for writing the manuscript. During the whole process MS has provided me with feedback and guidance. The data was collected by Ines Bramao and Mikael Johansson.

B Rachele Anderson and Maria Sandsten, “Optimal Spectral Estimation for Locally Stationary Processes with Application on EEG Signals”, manuscript in progress.

MS had the idea for the research question. I developed the presented algorithm, made the simulations and had the main responsibility for writing the manuscript. During the whole process MS has provided me with feedback and guidance. The data was collected by Ines Bramao and Mikael Johansson.


MS had the idea for the research question. The method was developed by me and MS jointly. I produced the results and had the main responsibility for writing the manuscript. During the whole process MS has provided me with feedback and guidance. The data was collected by Peter Jönsson.
Introduction

All models are wrong, but some are useful.
— George E.P. Box

This licentiate thesis considers statistical methods for non-stationary signals, specifically stochastic modelling, inference on the model parameters and optimal spectral estimation. The following introduction provides a background to the main concepts regarding non-stationary processes and time-frequency analysis, as well as to the biomedical applications treated in the papers.

1 Stationary and non-stationary stochastic processes

Stationary stochastic processes are well studied and it is known that they possess numerous advantageous properties [1, 2]. Several models and inference methods in time series analysis are based on the assumptions that the underlying process is weakly stationary, i.e. the mean function \( m(t) \) is constant in time \( t \) and the covariance function \( r(s, t) \) is finite and depends only on the time difference \( \tau = t - s \). On the other hand, the assumption of stationarity is too restrictive for most measured signals, which usually exhibit changes in their statistical properties over time.

Different approaches have been considered to take into account a time-varying behaviour. Segmentation techniques into stationary frames are common in many fields, e.g. speech processing, where often piece-wise stationary models, such as time-varying AR and ARMA models, are used [3, 4, 5]. An alternative approach revolves around classes of processes with desirable properties extending the stationary case. Cramér [6] studied a class of non-stationary processes including the stationary and harmonizable classes and more recent contributions have considered extensions of this class [7].

In [8], Silverman introduces a definition of Locally Stationary Processes (LSPs) as a generalization of stationary processes, resulting from the modulation in time of an ordinary stationary covariance function. Qualitatively, an LSP has a covariance equal to a stationary covariance multiplied by a sliding power factor,
which renormalizes the average instantaneous power to a representative local level. Besides being a natural generalization of stationary processes, another appealing feature of this definition is that it avoids time-varying parameters.

As the changes in frequency content over time provide insight into the characteristics of the observed time-varying signal, time-frequency analysis is one of the main tools to study non-stationary signals. The time-varying spectral representation of non-stationary processes was initially approached in [9], where the author develops the concept of “evolutionary spectrum”, a time-dependent spectral function. Many recent contributions fall along the lines of Priestley’s work, including [10, 11, 12]. The main limits of the evolutionary spectrum proposed by Priestley are that it is based on the assumption that the process is “slowly time-varying” and that its representation is not unique [13].

2 The short-time Fourier transform and the spectrogram

The fundamental problem of time-frequency analysis is to accurately represent a given signal in both time and frequency domains simultaneously. A common approach to address this problem is based on the use of the short-time Fourier transform (STFT) to determine frequency and phase content of local sections of a signal as it changes over time. The STFT is a natural extension of the Fourier transform for a non-stationary signal $x(t)$ and is defined as

$$X(t, f) = \int_{-\infty}^{\infty} x(s) h^*(s - t) e^{-i2\pi fs} ds$$

(1)

where $h(s)$ is a window function, commonly a Hanning window or Gaussian window centered around zero. From the STFT, the spectrogram of the signal is formulated as

$$S_X(t, f) = |X(t, f)|^2.$$ 

(2)

Intuitively, computing a spectrogram is equivalent to divide the time domain data into shorter sub-sequences, possibly overlapping, and for each sequence, square the magnitude of the Fourier transform and thereby obtaining frequency spectra for all sub-sequences. Consequently, a spectrogram shows how the spectral density of a signal varies with time through a three-dimensional picture, whose dimensions are time, frequency and squared magnitude. Thanks to the Wiener-Khintchine theorem, the power spectrum of a zero-mean non-stationary process $x(t)$ can be defined as the Fourier transform of the time-dependent co-
variance function $r_x(t, \tau) = E[x(t - \tau)x^*(t)]$

$$S_x(t, f) = \int_{-\infty}^{\infty} r_x(t, \tau)e^{-i2\pi f\tau}d\tau.$$  \hspace{1cm} (3)

The advantages of using the spectrogram are possible fast implementation using the FFT, easy interpretation and clear connection with methods for stationary signals, e.g. the periodogram. Nevertheless, this representation is far from being ideal. Indeed, the ideal time-frequency representation is a distribution satisfying a list of conditions:

- It should be positive everywhere, as negative densities imply negative energies (positivity).
- The total energy of the distribution should equal the total energy of the signal (total energy).
- The marginal distribution obtained integrating over time should be equal to the energy spectrum, while the marginal distribution obtained integrating over frequency should be equal to the instantaneous energy (marginals).
- Shifting a signal by a given amount of time should shift its density in time of the same amount, and the same applies to frequency shifts (time- and frequency- shifts invariance).
- If the signal is null out of a given time interval, the distribution should be zero as well, and the same applies to frequency intervals (finite support, weak form).
- The distribution should be zero whenever the signal is null and for any frequency where the signal has not any spectrum component (finite support, strong form).

A distribution respecting the finite support condition in strong form also respects the weak form.

3 The Wigner-Ville distribution

The Wigner distribution was invented in 1932 by E.Wigner [14] in the context of quantum mechanics. It was afterwards introduced in signal analysis by J.Ville [15]. The reason why the Wigner distribution has become one of the main tools
Table 1: Requirements satisfied by the Wigner distribution and the spectrogram respectively.

<table>
<thead>
<tr>
<th>Requirement</th>
<th>Wigner distribution</th>
<th>Spectrogram</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positivity</td>
<td>no</td>
<td>yes</td>
</tr>
<tr>
<td>Total energy</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>Marginals</td>
<td>yes</td>
<td>no</td>
</tr>
<tr>
<td>t,f shift invariance</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>Finite support:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- weak form</td>
<td>yes</td>
<td>no</td>
</tr>
<tr>
<td>- strong form</td>
<td>no</td>
<td>no</td>
</tr>
</tbody>
</table>

for time-frequency analysis is that it satisfies most properties that are expected from an ideal time-frequency representation. In table 1 we present a comparison of the properties satisfied by the Wigner distribution and the spectrogram.

As the Wigner distribution was introduced for deterministic signals, we start from this definition. The Wigner distribution of a deterministic signal \( x(t) \) is defined as

\[
W_x(t, f) = \int_{-\infty}^{\infty} x(t + \frac{\tau}{2}) x^*(t - \frac{\tau}{2}) e^{-i2\pi f\tau} d\tau. \tag{4}
\]

The Wigner distribution can be loosely interpreted as an energy distribution over the time-frequency plane. This interpretation cannot be valid in a point-wise sense, due to the uncertainty principle preventing a point-wise time-frequency localization of any signal, which applies to the spectrogram as well.

A limit of the Wigner distribution is that it can be negative, which is easily solved by transforming the real-valued signal into a complex-valued analytic signal of non-negative frequency content using the Hilbert transform. The Wigner-Ville distribution is the Wigner distribution of the analytic signal, defined as

\[
W_z(t, f) = \int_{-\infty}^{\infty} z(t + \frac{\tau}{2}) z^*(t - \frac{\tau}{2}) e^{-i2\pi f\tau} d\tau \tag{5}
\]

where \( z(t) \) denotes the analytic signal.

Although the only difference between the Wigner distribution and the Wigner-Ville distribution is that the former uses the real signal and the latter uses the analytic signal, the results are very different when frequency components higher than 0.25 are present. When computing the Wigner distribution for a real-valued signal the highest normalized frequency should not be larger than 0.25 in order to avoid aliasing, whereas for the Wigner-Ville distribution the maximum allowed frequency is 0.5.
4 The ambiguity domain

The main drawback of the Wigner-Ville distribution is the presence of cross-terms, located in between the different signal components, which can be twice as large as the auto-terms. To reduce these cross-terms, many different time-frequency kernels have been proposed. The design of these kernels is usually done in the ambiguity domain, also known as the doppler-lag domain, because auto-terms and cross-terms relocalize in a beneficial way. The ambiguity function is formulated similarly to the Wigner-Ville distribution, with the difference that the Fourier transform is made in the $t$-variable instead of the $\tau$ variable

$$A_z(\nu, \tau) = \int_{-\infty}^{\infty} z(t + \frac{\tau}{2}) z^*(t - \frac{\tau}{2}) e^{-i2\pi\nu t} dt$$ \hspace{1cm} (6)

where usually the analytic signal $z(t)$ is used. A filtered ambiguity function is defined as the element-wise multiplication of the ambiguity function and the ambiguity kernel $\phi(\nu, \tau)$

$$A^F_z(\nu, \tau) = A_z(\nu, \tau) \cdot \phi(\nu, \tau). \hspace{1cm} (7)$$

In order to preserve the marginals of the time-frequency distribution, the ambiguity kernel must fulfill $\phi(0, \tau) = \phi(\nu, 0) = 1$.

As the signal auto-term components will always be located at the centre of the ambiguity function and the cross-terms will always be located away from the centre, a natural approach to design a kernel aims to keep the terms located at the centre and reduce the components away from the centre of the ambiguity function. Therefore, by using a properly designed filtered ambiguity function it is possible to preserve the auto-term components while reducing the cross-terms components.

The time-frequency kernel corresponding to (7) is given by

$$W^F(t, f) = \int_{-\infty}^{\infty} \int_{-\infty}^{\infty} \phi(\nu, \tau) e^{-i2\pi(f\tau - \nu t)} d\tau d\nu$$ \hspace{1cm} (8)

and the corresponding smoothed Wigner-Ville distribution is the two dimensional convolution

$$W^F_z(t, f) = W_z(t, f) \ast \ast \Phi(t, f). \hspace{1cm} (9)$$

The original Wigner-Ville distribution has ambiguity kernel $\phi(\nu, \tau) = 1$ for all $\nu$ and $\tau$, and the corresponding time-frequency kernel is $\Phi(t, f) = \delta(t)\delta(f)$. 

5
5 The Cohen’s class

The Wigner-Ville distribution is a prominent member of the Cohen’s class of time-frequency representations, formulated in 1966 by Leon Cohen. All the other representations in Cohen’s class can be derived from the Wigner-Ville distribution with a two-dimensional convolution as in (9) and can thereby always be formulated as the multiplication of the ambiguity function and the ambiguity kernel as in (7).

Using the definition of ambiguity function in (6) we find the most recognized form defining Cohen’s class

\[
W^C_z(t, f) = \int_{-\infty}^{\infty} \int_{-\infty}^{\infty} z\left(u + \frac{\tau}{2}\right) z^*\left(u - \frac{\tau}{2}\right) \phi(\nu, \tau) e^{-i2\pi(\nu t - f\tau - \nu u)} d\nu d\tau. \tag{10}
\]

This class of distributions is time-shift invariant if the kernel is independent of time and frequency-shift invariant if the kernel is independent of frequency. Note that the spectrogram also belongs to Cohen’s class.

6 Stochastic time-frequency analysis

For a non-stationary process \(z(t)\) with instantaneous autocorrelation function (IAF)

\[
r_z(t, \tau) = E\left[z\left(t + \frac{\tau}{2}\right) z^*\left(t - \frac{\tau}{2}\right)\right] \tag{11}
\]

the Wigner-Ville spectrum (WVS) is defined as

\[
W^S_z(t, f) = \int_{-\infty}^{\infty} r_z(t, \tau) e^{-i2\pi f\tau} d\tau \tag{12}
\]

and the ambiguity spectrum as

\[
A^S_z(\nu, \tau) = \int_{-\infty}^{\infty} r_z(t, \tau) e^{-i2\pi \nu t} dt. \tag{13}
\]

Since the expected value computed from one realization is not reliable, one of the main challenges in stochastic time-frequency analysis is the estimation of a reliable time-frequency spectrum from a single realization of the process, [16]. A valuable approach consists in using a proper time-frequency kernel, however many kernels are developed uniquely for deterministic signals. In the last 20 years, the attempts to find optimal estimators for non-stationary processes have increased [17]. In particular, Sayeed and Jones [13] derived the optimal kernel in the mean square error sense for Gaussian harmonizable processes [18], by minimizing the integrated expected squared error.
In this section we discuss some properties of Locally Stationary Processes (LSPs) in Silverman’s sense, which are the base of the modelling approach followed in this thesis. Let \( X(t), \ t \in [T_0, T_f] \subseteq \mathbb{R} \), be a zero mean stochastic process. We say that \( X(t) \) is a locally stationary process (LSP) in the wide sense if its covariance \( C(s, t) = \mathbb{E}[X(s)X(t)^*] \) can be written as

\[
C(s, t) = q \left( \frac{s + t}{2} \right) \cdot r(s - t) = q(\eta) \cdot r(\tau) \tag{14}
\]

with \( s, t \in [T_0, T_f] \subseteq \mathbb{R} \), \( q(\eta) \) a non-negative function and \( r(\tau) \) a normalized \((r(0) = 1)\) stationary covariance function. When \( q(\eta) \) is a constant, (1) reduces to a stationary covariance and this definition therefore includes stationary processes as a special case. The function \( q(\eta) \) describes the instantaneous power of the process as

\[
C(t, t) = \mathbb{E}[(X(t))^2] = q(\eta) \cdot r(0) = q(\eta). \tag{15}
\]

The variety of choices for the functions \( r(\tau) \) and \( q(\eta) \) offers an advantageous flexibility to model time-varying data. Clearly not every choice is suitable, since a function \( C(s, t) \) is a covariance if and only if it is non-negative semi-definite.

One simple example of an LSP is the locally stationary white noise, using the covariance function of stationary white noise and any non-negative function as sliding power factor \([8]\). Another possibility is to use the product of two covariances \([18, 19]\). Silverman has also shown how a pair of functions proposed as components can be made to match each other by suitable smoothing and aperture-limiting operations \([20]\).

In the context of time-varying spectral estimation, the special form assumed by the spectral density of LSPs is of significant advantage. A generalization of the Wiener-Khintchine relations holds for the case of LSPs \([8]\), and as a consequence the generalized spectral density \( \psi(f_1, f_2) \) of an LSP with covariance function defined as in (1), can be written as

\[
\psi(f_1, f_2) = \psi_1 \left( \frac{f_1 + f_2}{2} \right) \cdot \psi_2(f_1 - f_2) \tag{16}
\]

where \( \psi_1(f) = \int_{-\infty}^{+\infty} e^{i2\pi ft} r(\tau)d\tau \) and \( \psi_2(f) = \int_{-\infty}^{+\infty} e^{i2\pi \eta q(\eta)d\eta} \). In \([21]\) the mean square error optimal time-frequency kernel is derived for a class of circularly symmetric LSPs and in \([22]\) the corresponding multitaper spectrograms are evaluated. Therefore, once produced reliable estimates of the model parameters, the optimal time-frequency kernel or multitapers can be applied to compute the
corresponding time-frequency spectral estimates, as in [23]. However, for a practical use of the LSP model, an appropriate non-stationary covariance function must be chosen and the parameters defining the covariance need to be estimated.

8 Biomedical applications

Thanks to their flexibility, LSPs are suitable for modelling a wide range of non-stationary signals. In this thesis a special focus is on biomedical applications: the statistical methods are applied either to signals measured from the human brain or from the human heart. The brain signals are recorded with electroencephalography (EEG), within a larger study where the final goal is to understand how the human brain decodes different types of visual memories. The heart signals are obtained by measuring the variation in the beat-to-beat time interval and represent a physiological phenomenon called Heart Rate Variability (HRV).

8.1 EEG

EEG is a very popular non-invasive method for measuring the electrical activity of the brain, by means of electrodes attached to the scalp. Measurements of EEG are used in many recent studies in the context of cognitive functions, as well as for medical diagnosis. The International 10–20 system is an internationally recognized method to describe the location of scalp electrodes. As illustrative example, in figure 1 we present a multichannel EEG recorded during one trial of a memory encoding task, from 31 electrodes placed on the scalp according to the International 10-20 system.

This method was developed to ensure standardized reproducibility and is based on the relationship between the location of an electrode and the underlying area of cerebral cortex. The ”10” and ”20” refer to the fact that the actual distances between adjacent electrodes are either 10% or 20% of the total front–back or right-left distance of the skull. Each site has a letter to identify the lobe and a number to identify the hemisphere location. The letters F, T, C, P and O stand for frontal, temporal, central, parietal, and occipital lobes, respectively. Even numbers refer to electrode positions on the right hemisphere, whereas odd numbers refer to those on the left hemisphere. A “z” refers to an electrode placed on the midline. The codes A, Pg and Fp identify the earlobes, nasopharyngeal and frontal polar sites respectively. Two anatomical landmarks are used for the essential positioning of the EEG electrodes: the “nasion”, which is the distinctly depressed area between the eyes, and the “inion”, which is the lowest point of
Figure 1: A multichannel EEG recorded during one trial of a memory encoding task, from 31 electrodes placed on the scalp according to the International 10-20 system. Time 0 refers to the instant of the presentation of the visual stimuli.

the skull from the back of the head. A more detailed EEG can be recorded with more electrodes, where extra electrodes are added using the 10% division, filling in intermediate sites between those of the existing 10–20 system. This new electrode system, called Modified Combinatorial Nomenclature (MCN) and
shown in figure 2, has new letter codes that do not necessarily refer to an area of the underlying cerebral cortex [24].

Studies on the neural mechanisms involved in human memory have attracted an increasing attention during the past years, [25, 26, 27]. Recently, time-varying models for EEG signals have been proposed, e.g. in [28], where non-linear autoregressive time-varying systems are applied to EEG, and in [29], where an adaptive and localized time-frequency representation of EEG signals has resulted in improvements in classification accuracy. Similarly, reliable estimation of parameters of an LSP model suitable for EEG signals would allow obtaining optimal time-frequency kernels and extraction of improved features for classification [22, 23].
8. Biomedical applications

8.2 HRV

An electrocardiogram (ECG) describes the electrical activity of the heart recorded by means of electrodes placed on the skin. The electrodes measure the voltage variations caused by the action potentials of the excitable cardiac cells. The resulting heartbeat in the ECG is manifested by a series of waves, named P,Q,R,S,T. The duration of a wave is defined by the two time instants at which the wave either deviates significantly from the baseline. The RR interval represents the length of a ventricular cardiac cycle, measured between two successive R waves, and is an indicator of ventricular rate. In figure 3 an idealized ECG section of a healthy person is presented, with labels on the P, Q, R, S, T waves and R-R interval.

The morphology and timing of these waves convey information which is used for diagnosing conditions related to disturbances of the heart’s activity. The time pattern that characterizes the occurrence of successive heartbeats is also very important. The RR interval is the fundamental rhythm quantity in any type of ECG interpretation and is used to characterize different arrhythmias as well as to study HRV, [30].

Another aspect is the phenomenon of Respiratory Sinus Arrhythmia (RSA), i.e. the HRV in synchrony with respiration, by which the heart rate increases during inspiration and decreases during expiration [31]. Figure 4, reproduced from [30], illustrates HRV in terms of RR intervals for a normal subject who has been instructed to breathe deeply at different respiratory rates. Each of the four respiratory rates was maintained for one minute. As a consequence of the strong relationship between respiration and HRV, the respiratory frequency information must be taken into account when analysing HRV signals. Recent studies actually claim that the respiratory frequency is the main information to
be considered in the analysis of HRV [32, 33, 34].

Modified HRV has been associated with several clinical conditions. In particular, reduced High-Frequency-HRV power is related to attention deficits, depression, various anxiety disorders, long-term work-related stress and burnout. Investigating the different factors that may affect HRV is important since the significance and the meaning of the many different measures of HRV are complex and there is the risk of incorrect conclusions and unfounded extrapolations.
9 Outline of the papers

Paper A: Inference for Time-varying Signals using Locally Stationary Processes

In paper A, we address the lack of suitable methods for estimating the parameters of an LSP model, by proposing a novel inference method. The proposed method is based on the separation of the two factors defining the LSP covariance function, in order to take advantage of their individual structure and divide the inference problem into two simpler sub-problems. First, the estimation of the time-dependent sliding factor is obtained from the global structure of the measured signal, and afterwards the estimated local stationarity property is used to estimate the stationary covariance factor. We present a simulation study to show the performance improvement obtained with the proposed method compared to the least squares estimation of the parameters from the sample covariance matrix. We show that the proposed method achieves considerably faster convergence to the true covariance and the parameter estimates are accurate, independently on the initial values of the optimization. Finally, we provide an illustrative example of parameter estimation from three sets of EEG signals, measured from one person during several trials of a memory encoding task of three different categories of visual memories (i.e. human faces, objects and landmarks). We find that a certain parameter has the same scale for the three categories, due to the common nature of the signals, while the differences in the estimates between the three datasets reflect the expected neural representational differences between various types of encoded memories.

The work in paper A has been submitted for possible publication in *Journal of Computational and Applied Mathematics*.

Paper B: Optimal Spectral Estimation for Locally Stationary Processes with Application on EEG Signals

This paper investigates the estimation of the Wigner-Ville spectrum of time-varying processes, modelled as LSP in Silverman’s sense. Previous works have provided the theoretical expression of the mean-square error optimal time-frequency kernel, but lack of methods for estimating the model parameters was a limit to practical applications. The introduction of a novel inference method for the model parameters (Paper A) permits the computation of the optimal kernel in real data cases. Efficient implementation of the optimal spectral estimator is based on multi-tapers, where the multiple windows are obtained as the
eigenvectors of the rotated time-lag estimation kernel and the spectrograms from the different windows are weighted with the eigenvalues. We present a simulation study to evaluate the performance of the derived optimal spectral estimator, compared with the single Hanning spectrogram and the Welch method, in terms of mean square error. For the same three data-sets used in paper A, we compute the optimal kernels and the multi-tapers for each category, according to the estimated model parameters.

Paper B is a manuscript in progress. It has been published in part as:


The final version of this manuscript will include a classification study for the considered data-sets, in order to verify if the use of the optimal spectral estimator based on the estimated parameters leads to improvements in classification accuracy.

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

In the third paper, we use LSPs to model heart rate variability (HRV) signals. The purpose is to evaluate the effect of several covariates on the parameters of our model for HRV. The data were 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. To include the respiratory frequency information in the model, we consider an extension of the LSP definition that accounts for the presence of a chirp in the signals, known as Locally Stationary Chirp Processes (LSCP). The inference method proposed in paper A is adapted to take into account the respiratory signal information, in the form of the covariance matrix of the chirp respiratory signal estimated beforehand. Recent studies have focused on investigating different factors that may affect HRV, pointing especially to the effects of age, gender and stress level. We perform least squares regression analysis with each of the LSCP model parameters as the response to explore the corre-
lation of the parameters with several factors of interest. The considered factors are Age, Gender, Weight, Body Mass Index, State Anxiety, Trait Anxiety, and Shirom-Melamed Burnout Questionnaire. Our results show a statistically significant correlation between the model parameters with age, BMI, State and Trait Anxiety as well as stress level.

The work in paper C has been accepted for publication in the *Proceedings of the 11th Conference on Bio-inspired Systems and Signal Processing*, Funchal, Madeira, Portugal, January 19-21, 2018.
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Paper A

Inference for Time-varying Signals using Locally Stationary Processes

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Abstract

Locally Stationary Processes (LSPs) in Silverman’s sense, defined by the modulation in time of a stationary covariance function, are valuable in stochastic modelling of time-varying signals. However, for practical applications, methods to conduct reliable parameter inference from measured data are required. In this paper, we address the lack of suitable methods for estimating the parameters of the LSP model, by proposing a novel inference method. The proposed method is based on the separation of the two factors defining the LSP covariance function, in order to take advantage of their individual structure and divide the inference problem into two simpler sub-problems. The method’s performance is tested in a simulation study and compared with traditional sample covariance based estimation. An illustrative example of parameter estimation from EEG data, measured during a memory encoding task, is provided.

Key words: Locally Stationary Process, Time-varying signals, Time-series modelling, Statistical inference, Covariance estimation, EEG signals.
1 Introduction

Theory of stationary stochastic processes is well developed and has been the basis for several models and inference methods in time series analysis [1, 2]. On the other hand, the assumption of stationarity is too restrictive for most measured signals, which usually exhibit changes over time. Different approaches have been considered to take into account a time-varying behaviour. Segmentation techniques into stationary frames are common in many fields, e.g. speech processing, where often piece-wise stationary models, such as time-varying AR and ARMA models, are used [3, 4, 5]. The time-varying spectral representation of non-stationary processes were initially approached in [6], where the author develops the concept of “evolutionary spectrum”, a time dependent spectral function. Many recent contributions fall along the lines of Priestley’s work, including [7, 8, 9].

An alternative approach revolves around classes of processes with desirable properties extending the stationary case. Cramér [10] studied a class of non-stationary processes including the stationary and harmonizable classes and more recent contributions have considered extensions of this class [11]. In [12], Silverman introduces a definition of Locally Stationary Processes (LSPs) as a generalization of stationary processes, resulting from the modulation in time of an ordinary stationary covariance function. Qualitatively, an LSP has a covariance equal to a stationary covariance multiplied by a sliding power factor, which renormalizes the average instantaneous power to a representative local level. Besides being a natural generalization of stationary processes, another appealing feature of this definition is that it avoids time-varying parameters.

One simple example of an LSP is the locally stationary white noise, using the covariance function of stationary white noise and any non-negative function as sliding power factor [12]. Another possibility is to use the product of two covariances [13, 14]. Silverman has also shown how a pair of functions proposed as components can be made to match each other by suitable smoothing and aperture-limiting operations [15]. More recently, in [16] the authors characterize non-stationary processes that can be reduced to local stationarity via a bijective deformation of the time index. Multidimensional models have been considered, as in [17], where parametric covariance models for locally stationary random fields are derived. The theoretical properties have been thoroughly investigated e.g. in [15, 18].

For practical use of the LSP model, an appropriate non-stationary covariance function must be chosen and the parameters defining the covariance need to
be estimated. A maximum likelihood approach for the parameter estimates is not feasible, since a closed form expression of the process distribution is, in the general case, not known. Although the goal is to estimate the model parameters, inference for a LSP is linked to the estimation of a non-stationary covariance from the data, since the LSP is defined by the covariance function. The most natural estimator is the Sample Covariance Matrix (SCM), which is an unbiased and efficient estimator of the covariance matrix. A traditional regression approach would produce the parameter estimates by least squares fitting of the model covariance to the SCM. However, the SCM is not reliable, especially when the sample size is smaller than the number of parameters to be estimated [19] and in presence of outliers, where a singular erroneous observation can damage the estimate [20].

To address these issues, many covariance estimation methods are based on the assumption that the samples follow a particular distribution, frequently the Gaussian distribution or its generalization, the elliptical distribution [21, 22]. Several contributions are based on the Kronecker product structure [23, 24, 25] or on the use of shrinkage estimators based on a convex combination of the sample covariance and a suitable chosen target (e.g. diagonal matrix, constant-correlation model) [26, 27, 28, 29]. The mentioned papers show the benefits of taking into account the covariance structure to produce more accurate estimates. However, these approaches cannot be successfully applied in case of LSP covariances since the model structure is different.

In this paper, we propose a novel inference method based on separation of the two factors of the product defining an LSP covariance function, in order to take advantage of their individual structures. First, the estimation of the time dependent sliding factor is obtained from the global structure of the measured signal, and afterwards the estimated local stationarity property is used to estimate the stationary covariance factor.

The paper is structured as follows. In section 2 the mathematical model of LSPs is presented. In section 3 we introduce the novel inference methodology valid for general LSPs, and in section 4, the performance of the proposed method and reliability of the estimates are evaluated through a simulation study. Section 5 is dedicated to an application to real data, consisting of EEG signals, collected within a study on human memory encoding and retrieval. The paper concludes with some comments and directions for further research in section 6.
2 Locally Stationary Processes

Let $X(t)$, $t \in [T_0, T_f] \subseteq \mathbb{R}$, be a zero mean stochastic process. We say that $X(t)$ is a locally stationary process (LSP) in the wide sense if its covariance $C(s,t) = \mathbb{E}[X(s)X(t)\ast]$ can be written as

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

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

The function $q(\eta)$ describes the instantaneous power of the process as

$$C(t,t) = \mathbb{E} \left[ (X(t))^2 \right] = q(\eta) \cdot r(0) = q(\eta).$$

The variety of choices for the functions $r(\tau)$ and $q(\eta)$ offers an advantageous flexibility to model time-varying data. Clearly not every choice is suitable, since we recall that a function $C(s,t)$ is a covariance if and only if is non-negative definite, i.e. for every finite subset $T_n \subseteq [T_0, T_f]$ and every complex valued function $h(t)$

$$\sum_{s,t \in T_n} C(s,t)h(s)h^\ast(t) \geq 0$$

In figure 1 we present examples of LSP realizations obtained from the model covariance introduced in section 4 with different parametric settings, showing how the realizations vary depending on the parameters. Each set of the displayed realizations has the maximum energy located in the middle of the time interval ($t = 0.25$), but the relation between the functions $q(\eta)$ and $r(\tau)$ reflects a slowly varying behaviour in (a) and a much faster variation in (b) and (c). The only difference between the realizations presented in (b) and (c) is in the parameter $L$, representing the minimum energy level. The increase from $L = 0$ in (b) to $L = 100$ in (c) reflects more additive noise in the realizations, illustrating the use of $L$ to model the additional noise disturbance of the time-varying signal.

In the context of time-varying spectral estimation, the special form assumed by the spectral density of LSPs is of significant advantage. A generalization of the Wiener-Khintchine relations holds for the case of LSPs [12] and as a consequence, the generalized spectral density $\psi(\omega_1, \omega_2)$ of an LSP with covariance function
2. Locally Stationary Processes

Figure 1: Example of simulated realizations with model covariance defined by (12) and the set of parameters \((L, a_q, b_q, c_q, c_r)\) equal to: (a) \((150, 800, 0.25, 250, 3000)\); (b) \((0, 500, 0.25, 1000, 80000)\); (c) \((100, 500, 0.25, 1000, 80000)\).

defined as in (1), can be written as

\[
\psi(\omega_1, \omega_2) = \psi_1(\frac{\omega_1 + \omega_2}{2}) \cdot \psi_2(\omega_1 - \omega_2)
\]  

(4)

where \(\psi_1(\omega) = \frac{1}{2\pi} \int_{-\infty}^{+\infty} \exp(i\tau\omega)r(\tau)d\tau\) and \(\psi_2(\omega) = \frac{1}{2\pi} \int_{-\infty}^{+\infty} \exp(i\eta\omega)q(\eta)d\eta\).

In [30] the mean square error optimal time-frequency kernel is derived for a class of circularly symmetric LSPs and in [31] the corresponding multitaper spectrograms are evaluated. Therefore, once produced reliable estimates of the model parameters, the optimal time-frequency kernel or multitapers can be applied to compute the corresponding time-frequency spectral estimates, as in [32].
3 A novel inference method

We address the problem of fitting a real valued LSP with theoretical covariance $C(s, t) = \mathbb{E}[X(s)X(t)^T]$ to sampled data. Let $x^{(1)}, \ldots, x^{(M)}$ be $M$ independent realizations of a zero-mean non-stationary process $X(t)$. Each realization $x^{(j)}$, $j = 1, \ldots, M$, is observed at $n$ equidistant times $t_k = T_0 + (k - 1) \cdot \Delta t$, in $[T_0, T_f] \subseteq \mathbb{R}$, where $\Delta t = t_k - t_{k-1}$ is the constant sampling interval. Each sampled point of the $j$:th realization is denoted with $x^{(j)}_k$, $k = 1, \ldots, n$. With this notation, the covariance matrix $C \in M_{n\times n}$ of the LSP has elements $C(k, l) = q\left(\frac{t_k + t_l}{2}\right) \cdot r(|t_k - t_l|)$.

We define the matrix $Q \in M_{n\times n}$ as $Q(k, l) \doteq q\left(\frac{t_k + t_l}{2}\right)$ and the matrix $R \in M_{n\times n}$ as $R(k, l) \doteq r(|t_k - t_l|)$. Clearly, $Q$ is a non-negative Hankel matrix, whereas $R$ corresponds to the stationary covariance function $r(\tau)$ and therefore is a symmetric Toeplitz matrix. The proposed inference method is based on the possibility to separate the two factors of the Hadamard product $Q \circ R$ and exploit their individual structures.

Let $\{q_\lambda(\eta)\}$ and $\{r_\rho(\tau)\}$ be the selected parametric family of functions for $q(\eta)$ and $r(\tau)$ respectively. The mean instantaneous power computed from the realizations $P(t_k) = \frac{1}{M} \sum_{j=1}^{M} (x_k^{(j)})^2$ for $k = 1, \ldots, n$ approximates the expected value of the power of the process. Consequently, the estimate of $\lambda$ can be obtained by fitting the parametric curve $q_\lambda$ to $P$, which is equivalent to fitting the function $q_\lambda$ to the diagonal values of the sample covariance matrix, since for all the diagonal elements $r(0) = 1$.

Let $\hat{\lambda}$ be the estimated parameters and $\hat{Q}$ the corresponding estimate of the matrix $Q$. The estimate of the matrix $R$ is found by exploiting the Toeplitz structure. This is possible since the matrix $R$ has already been calculated, therefore the estimate $\hat{R}$ is obtained as

$$
\hat{R}(k, l) = \frac{1}{M - 1} \sum_{j=1}^{M} \left( \frac{1}{N_\tau} \sum_{\tau = |k - l|} \frac{x_k^{(j)} \cdot x_l^{(j)}}{Q(k, l)} \right)
$$

where $N_\tau$ is the cardinality of the set $\{(k, l) : |k - l| = \tau\}$. In other words, even if the total covariance matrix is non-stationary, we are able to use the inherent local stationarity of the model to estimate the matrix $R$, by first estimating and separating the time-varying factor $Q$. The estimates $\hat{\rho}$ are obtained by fitting the parametric function $r_\rho(\tau)$ to the main anti-diagonal of the Toeplitz matrix $\hat{R}$, which contains all the matrix information, since a Toeplitz matrix has constant value on every diagonal.
Since the proposed inference method is based on the possibility to separate the two factors of the Hadamard product \( Q \circ R \) and exploit their individual structures, we will refer to it as HAnkel - Toeplitz Separation (HATS). The estimation procedure is summarized below.

**Algorithm 1 HAnkel - Toeplitz Separation (HATS):** Parametric inference and covariance estimation for LSPs based on separation of the two factors of the Hadamard product \( Q \circ R \).

1. Compute the mean instantaneous power from the data:

\[
P(t_k) = \frac{1}{M} \sum_{j=1}^{M} \left( x_k^{(j)} \right)^2, \text{ for } k = 1, \ldots, n
\]

2. Find \( \hat{\lambda} \) by fitting the function \( q_\lambda \) to \( P \).

3. Compute

\[
\hat{R}(k,l) = \frac{1}{M-1} \sum_{j=1}^{M} \left( \frac{1}{N_T} \sum_{\tau = |k-l|}^{N_T} \left( \frac{x_k^{(j)} \cdot x_l^{(j)}}{\hat{Q}(k,l)} \right) \right)
\]

where \( N_T \) is the cardinality of the set \( \{(k,l) : |k-l| = \tau\} \).

4. Find \( \hat{\rho} \) by fitting the function \( r_\rho \) to the anti-diagonal elements of \( \hat{R} \).

5. Compute covariance matrix estimate \( \hat{C} = \hat{Q} \circ \hat{R} \).
The procedure relates to coordinate descent algorithms, in the sense that the optimization problem is divided in two lower-dimensional sub-problems, each of which can be solved more easily than the full problem [33]. Since the first optimisation is independent of \( r_{\rho}(\tau) \), the procedure terminates with only one iteration of the coordinate descent algorithm.

The choice of the best fitting approach of the curves \( q(\eta) \) and \( r(\tau) \) might depend on the application. Traditional curve fitting choices are least-squares methods (LS) and minimax methods, based on the \( L^2 \) and the \( L^\infty \) approximation respectively. In the following, we will consider the standard regression approach given by LS fitting, i.e.

\[
\hat{\lambda} = \arg\min_{\lambda} \frac{1}{n} \sum_{k=1}^{n} (q_\lambda(t_k) - P(t_k))^2
\]  

(6)

and

\[
\hat{\rho} = \arg\min_{\rho} \sum_{k=1}^{n} \left( r_{\rho}(t_k) - \hat{R}(k, n + 1 - k) \right)^2.
\]  

(7)

4 Evaluation: simulation study

In this section we evaluate the performance of the proposed method using simulated data. For the model covariance (1), we consider functions

\[
q_\lambda(\eta) = L + a_q \cdot \exp \left( -c_q (\eta - b_q)^2 / 2 \right)
\]

\[
r_{\rho}(\tau) = \exp \left( -c_r \tau^2 / 8 \right)
\]  

(8)
where \( \lambda = (L, a_q, b_q, c_q), \rho = (c_r), b_q \in [T_0, T_f], c_r > c_q \). The assumption \( c_r > c_q \) is necessary to assure that the resulting covariance is positive semi-definite. The true parameters used to simulate the data are \( (L, a_q, b_q, c_q, c_r) = (100, 600, 0.20, 1000, 70000) \). This specific choice of parameters is motivated by the real data example, i.e. the parameters for the simulation study are chosen to be in the same scale as those estimated in the real data application presented in section 5. Intuitively, \( L \) can be seen as minimum average energy level (potentially the underlying noise), \( a_q \) is the amplitude of the signal power, \( b_q \) represents the moment when the process power is maximum, while the parameters \( c_q \) and \( c_r \) rule the trade-off between the local stationarity and the time-dependent behaviour.

A realization \( x \) is simulated from the model as \( x = H e \) where \( e = (e_1, ..., e_n) \) is a sequence of i.i.d random variables \( e_i \sim \mathcal{N}(0,1) \) and the process-generating matrix \( H \) is related to the covariance matrix as

\[
C = \mathbb{E}[xx^*] = H \mathbb{E}[ee^*] H^* = HH^*
\]

A few realizations from the parametric setting are presented in figure 3.

For LSPs in Silverman’s sense, no other inference methods have been proposed, making the comparison of HATS with the state-of-the-art difficult. In literature, covariance estimators with a better performance than the SCM have been obtained in special cases, when the data was following a specific distribution or having a certain structure, but not in the case of LSP. Therefore we propose a comparison with the SCM, considering the parameter estimates obtained with a constrained non-linear LS fitting of the model covariance to the SCM (LS SCM).

To evaluate how the number of included realizations affects the inference results, we simulate \( M \in \{1, 5, 10, 20, 30, 40, 50, 60, 70, 80, 90, 100\} \) realizations, each consisting of \( n = 256 \) equidistant points in the time interval \( [T_0, T_f]=[0, 0.5] \).
Figure 4: Normalized Mean-Square Error (NMSE) of the covariance matrix estimates obtained using SCM, LS SCM, and HATS depending on the number of realizations $M$.

seconds. To approximate the expected value we average 100 Monte Carlo simulations for every $M$. For both methods, lower and upper bounds for the parameters are $(0, 1, T_0, 0, 0)$ and $(500, 2000, T_f, 10000, 100000)$ respectively. Initial values for the parameters are randomly initialized in the admissible ranges at every iteration.

The main goal is inference on the model parameters; however, the performance of the proposed method can be evaluated also in term of the covariance matrix estimate. The estimation error is evaluated by the Normalized Mean-Square Error (NMSE)

$$NMSE(\hat{C}) = \frac{\mathbb{E} \left[ \|C - \hat{C}\|_F^2 \right]}{\|C\|_F^2}$$

where $C$ is the true model covariance matrix, $\hat{C}$ is the estimate considered and $\| \cdot \|_F$ denotes the Frobenius norm $\|A\|_F = \sqrt{\sum_{k=1}^{n} \sum_{l=1}^{n} |A(k,l)|^2}$ for a matrix $A \in M_{n \times n}$.

The values of the NMSE in (9) as function of the number of realizations $M$ are shown in figure 4 and reported in table 1 with their standard errors. The results show that HATS performs considerably better than the SCM as well as the LS.
Figure 5: Parameter estimates obtained with LS SCM (a),(c),(e),(g),(i) and with HATS (b),(d),(f),(h),(l) as function of the number of realizations $M$ used. Blue lines indicate the mean estimates, red lines their confidence intervals, dashed black lines are the true values.

SCM. The NMSE is lower than LS SCM already for $M = 1$ and for larger values of $M$ the gain is considerable. The small standard errors of the HATS NMSE
Table 1: NMSE and its standard error depending on the number of realizations using SCM, LS SCM, and HATS.

<table>
<thead>
<tr>
<th>M</th>
<th>SCM</th>
<th>LS SCM</th>
<th>HATS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NMSE</td>
<td>S.E.</td>
<td>NMSE</td>
</tr>
<tr>
<td>1</td>
<td>4.3029</td>
<td>0.1405</td>
<td>0.8445</td>
</tr>
<tr>
<td>5</td>
<td>2.2466</td>
<td>0.0409</td>
<td>0.7331</td>
</tr>
<tr>
<td>10</td>
<td>1.5304</td>
<td>0.0177</td>
<td>0.5944</td>
</tr>
<tr>
<td>20</td>
<td>1.0602</td>
<td>0.0091</td>
<td>0.5610</td>
</tr>
<tr>
<td>30</td>
<td>0.8490</td>
<td>0.0057</td>
<td>0.5113</td>
</tr>
<tr>
<td>40</td>
<td>0.7545</td>
<td>0.0059</td>
<td>0.5528</td>
</tr>
<tr>
<td>50</td>
<td>0.6548</td>
<td>0.0039</td>
<td>0.5108</td>
</tr>
<tr>
<td>60</td>
<td>0.5986</td>
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<td>0.4743</td>
</tr>
<tr>
<td>70</td>
<td>0.5641</td>
<td>0.0034</td>
<td>0.4814</td>
</tr>
<tr>
<td>80</td>
<td>0.5195</td>
<td>0.0032</td>
<td>0.5045</td>
</tr>
<tr>
<td>90</td>
<td>0.4876</td>
<td>0.0023</td>
<td>0.5359</td>
</tr>
<tr>
<td>100</td>
<td>0.4624</td>
<td>0.0022</td>
<td>0.4735</td>
</tr>
</tbody>
</table>

(table 1) show that the estimated covariance matrix is accurate independently on the initial values of the optimization, i.e. the method is robust. It is also clearly seen that the LS SCM is very sensitive to the joint estimation of all parameters.

It should be noted that for a sufficiently large number of used realizations, e.g. in our settings 80 realizations, the LS SCM performs worse than the SCM. This means that, for a sufficiently large number of realizations, the inclusion of the model information does not lead to a more reliable covariance estimate if the model parameters are not estimated with sufficient accuracy. Being a consistent estimator, the SCM converges to the true covariance if an infinite number of realizations is used to produce the estimate; however, the faster convergence obtained with HATS is clearly an advantage in practical applications, where inference should be performed with small amounts of available data.

The parameters estimates obtained with LS SCM and HATS are presented in figure 5, where we restrict to \( M \in \{1, 5, 10, 20, 30, 40, 50\} \) realizations, since for both methods no significant improvement has been observed for larger values of \( M \). For illustrative purpose, the values for \( M = 10 \) and \( M = 30 \) are reported in tables 2 and 3. The joint estimation of all parameters of the LS SCM causes a large variance in the parameter estimates, and very often even the mean value is far away from the truth, e.g. for parameter \( L \) and \( c_q \). The mean values of the HATS estimates quickly approach the true values and the narrow confidence intervals ensure reliable estimates already for \( M = 10 \). With the LS SCM, even when the mean value of the estimated parameter is close to the true value as for the parameter \( b_q \), the coefficient of variation is so high that the estimate based on a single data-set would be unreliable. The only parameter that is well
5. Application to EEG signals from a memory retrieval experiment

Table 2: Using $M = 10$ realizations, mean of the estimated parameters with LS SCM and with HATS, with standard errors (S.E.) for the means, and coefficient of variation $c$ for the parameter estimates.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>LS SCM</th>
<th>HATS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean est.</td>
<td>S.E.</td>
</tr>
<tr>
<td>$L$</td>
<td>165.69</td>
<td>4.53</td>
</tr>
<tr>
<td>$a_q$</td>
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</tr>
<tr>
<td>$b_q$</td>
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<td>0.02</td>
</tr>
<tr>
<td>$c_q$</td>
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</tr>
<tr>
<td>$c_r$</td>
<td>68470</td>
<td>1662</td>
</tr>
</tbody>
</table>

captured with the LS SCM is $c_q$; however, HATS performs better also in this case.

In view of these results, we see the most promising applications when at least 10 realizations of the process are available, although with some care the method can be applied even when only one realization is available.

5. Application to EEG signals from a memory retrieval experiment

Thanks to their flexibility, LSPs are suitable for modelling a wide range of non-stationary signals. In this section we present an application of LSPs and the inference method HATS on measurements of the brain activity recorded through electroencephalography (EEG). EEG is a very popular non-invasive method for measuring activity of the brain, by means of electrodes attached to the scalp. Measurements of EEG is used in many recent studies in context of cognitive functions, as well as for medical diagnosis. In particular, studies on the neural mechanisms involved in human memory have attracted an increasing attention during the past years, [34, 35, 36]. Recently, time-varying models for EEG signals have been proposed, e.g. in [37], where non-linear autoregressive time-varying systems are applied to EEG, and in [38], where an adaptive and localized time-frequency representation of EEG signals has resulted in improvements in classification accuracy. Similarly, reliable estimation of parameters of an LSP model suitable for EEG signals would allow to obtain optimal time-frequency kernels and extraction of improved features for classification [31, 32].

The data was collected as part of a study on human memory encoding and retrieval, conducted at the department of Psychology at Lund University, Sweden. The EEG signals have been measured from one subject participating in the experiment, during 180 trials of a memory encoding task, in which the subject had
Table 3: Using \( M = 30 \) realizations, mean of the estimated parameters with LS SCM and with HATS, standard errors (S.E.) for the means, and coefficient of variation \( c \) for the parameter estimates.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>True value</th>
<th>LS SCM</th>
<th>HATS</th>
</tr>
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<tbody>
<tr>
<td>( L )</td>
<td>100</td>
<td>166.23</td>
<td>100.86</td>
</tr>
<tr>
<td>( a_q )</td>
<td>600</td>
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<td>610.75</td>
</tr>
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<td>( b_q )</td>
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</tr>
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<td>( c_q )</td>
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<td>1085</td>
</tr>
<tr>
<td>( c_r )</td>
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<td>71578</td>
<td>70475</td>
</tr>
</tbody>
</table>

Figure 6: Three random EEG signals, after 70 Hz low-pass filtering, corresponding to three different trials of a memory encoding task, from each category: (a) 'Faces'; (b) 'Objects'; (c) 'Landmarks'.

to associate a presented word with a target picture. Each picture belongs to one of three categories ("Faces", "Objects", "Landmarks") and 60 trials are available for each category. Each time series has 256 equidistant samples during the time interval \([0, 0.5]\) seconds. As primary visual areas can be found below the occipital lobes, we consider signals recorded from channel O1 (International 10-20 system). In figure 6 three realizations from each group are shown as examples.
Assuming that the $M = 60$ realizations in each dataset are realizations of a common LSP, with covariance function (1) as in section 4, we infer the value of the parameters $L, a_q, b_q, c_q, c_r$ with HATS. The choice of the functions $q(\eta)$ and $r(\tau)$ is motivated by a preliminary analysis of the data. To give a measure of the uncertainty of our estimates we use a bootstrap methodology [39]. A bootstrap estimate of the standard error for each parameter is obtained using 100 bootstrap samples, where each bootstrap sample consists of 60 realizations, each sample drawn with replacement from the original data. The estimated parameters for the three categories are reported in table 1 and the fitted functions $q(\eta)$ and $r(\tau)$ are shown in figure 7.

The differences in the parameter estimates for the three data-sets correspond to different underlying LSP for each data-set. The moment when the process energy is maximum is represented by the parameter $b_q$, which is different for the different categories, indicating that the maximum of the signal power is reached at different times for each category. The minimum energy level $L$ is similar.
among the datasets, suggesting a possible interpretation as underlying noise. Similar values of \(a_q\) relate to the comparable amplitude of the power for the signals in each data-set. More difficult the interpretation of the parameters \(c_q\) and \(c_r\), ruling the trade-off between the local stationarity and the time-dependent behaviour, as shown with the simulated realizations for different parameters (figure 1). The estimated covariance matrices for the three classes are presented in figure 8.

The fact that a certain parameter has the same scale for the three categories is due to the common nature of the signals, whereas the differences in the estimates reflect the expected neural representational differences between various types of encoded memories.
Table 4: EEG data application: estimated LSP parameters for the three categories “Faces”, “Objects”, “Landmarks” of the memory encoding task with respective bootstrap standard errors and coefficients of variation.

<table>
<thead>
<tr>
<th></th>
<th>Faces</th>
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<tbody>
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<td>Est.</td>
<td>Std</td>
<td>c</td>
<td>Est.</td>
<td>Std</td>
<td>c</td>
<td>Est.</td>
<td>Std</td>
</tr>
<tr>
<td>$L$</td>
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<td>11.47</td>
<td>0.12</td>
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<tr>
<td>$a_q$</td>
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<td>0.16</td>
<td>447</td>
<td>29.57</td>
<td>0.07</td>
<td>698</td>
<td>47.36</td>
</tr>
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<td>$b_q$</td>
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<td>78676</td>
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</tr>
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</table>

6 Conclusions

In this paper we have proposed a method, named HAnkel - Toeplitz Separation (HATS), to estimate the parameters and the corresponding covariance matrix of a general locally stationary process (LSP) from sampled real data. The method is based on the expression of the non-stationary covariance matrix as the Hadamard product of two matrices: a Hankel matrix, representing the time-varying power, and a Toeplitz matrix, describing the stationary properties. The idea behind HATS is to divide the inference problem in two sub-problems, where the structures of the two matrices are exploited individually.

A simulation study is presented to show the performance improvement obtained with HATS compared to the least squares estimation of the parameters from the sample covariance matrix (LS SCM). The results show that HATS is superior to the LS SCM both in terms of inference on the model parameters and in terms of covariance matrix estimation. Considerably faster convergence to the true covariance is achieved and the parameter estimates are accurate, independently on the initial values of the optimization, attesting robustness. It is shown that HATS can be used to estimate the parameters from a one single realization; however, the most promising applications are those where at least ten realizations from the same process are available.

We have also provided an illustrative example using three data-sets of 60 realizations consisting of EEG signals from a study on memory encoding. Related research is directed to the study of optimal time-frequency kernels for LSPs [30, 31, 32] and their use for extracting improved time-frequency features.
Acknowledgements

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References


Optimal Spectral Estimation for Locally Stationary Processes with Application on EEG Signals

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Mathematical Statistics, Centre for Mathematical Sciences, Lund University, Sweden

Abstract

This paper investigates the estimation of the Wigner-Ville spectrum of time-varying processes, modelled as Locally Stationary Processes in Silverman’s sense. Previous works have provided the theoretical expression of the mean-square error optimal time-frequency kernel, but the lack of methods for estimating the model parameters was a limit to practical applications. The introduction of a novel inference method for the model parameters permits the computation of the optimal kernel in real data cases. Efficient implementation of the optimal spectral estimator is based on multitapers, where the multiple windows are obtained as the eigenvectors of the rotated time-lag estimation kernel and the spectrograms from the different windows are weighted with the eigenvalues. We present a simulation study to evaluate the performance of the derived optimal spectral estimator, compared with the single Hanning spectrogram and the Welch method, in terms of mean square error. The flexibility of the model makes it suitable for a wide range of time-varying signals, e.g. the electrical recordings from the brain, EEG. We provide an illustrative example of application on EEG data measured during a memory encoding task.

Key words: Non-stationary signals, Locally Stationary Processes, Optimal spectral estimation, Time-frequency analysis, EEG signals.
1 Introduction

In this paper, we present a complete procedure to achieve mean square error optimal Wigner-Ville spectrum (WVS) estimators from real-world data. We consider a stochastic parametric model for the signals, based on the definition of Locally Stationary Processes (LSPs), introduced by Silverman in [1]. LSPs are characterized by a covariance function which is the modulation in time of an ordinary stationary covariance function. The optimal kernel for estimation of the WVS for a certain class of LSPs is obtained in [2]. Based on this result, we derive the optimal time-frequency kernel for our model covariance and we use it to compute optimal multitapers and weights, as in [3].

The kernels are parameter dependent and the lack of reliable inference methods has relegated LSPs and their optimal time-frequency representation to a theoretical interest. In [4], we propose a novel inference method based on separation of the two factors of the product defining an LSP covariance function, in order to take advantage of their individual structures. First, the estimation of the time dependent sliding factor is obtained from the global structure of the measured signal, and afterwards the estimated local stationarity property is used to estimate the stationary covariance factor. Thanks to the introduced inference method we obtain a complete procedure to achieve mean square error optimal Wigner-Ville spectrum (WVS) estimators from real-world data.

An example of data that can be modelled through LSPs are measurements of human brain activity recorded through electroencephalography (EEG). EEG is a popular non-invasive method to record electrical activity of the brain, by means of electrodes on the scalp, finding application in recent studies on several cognitive functions, additionally to the traditional uses for medical diagnosis, [5]. In particular, studies on the neural mechanisms involved in human memory have attracted an increased attention during the past years, [6].

The study of a time-frequency image is often the method of choice to address key issues in cognitive electrophysiology. The quality of the time-frequency representation is crucial for the extraction of robust and relevant features, thus leading to the demand for highly performing spectral estimators. In [7] an adaptive and localized time-frequency representation of EEG signals has resulted in improvements in classification accuracy. Similarly, the parameters estimation on a suitable LSP model for EEG signals would allow the extraction of improved features for classification.

The paper is structured as follows. In section 2, we present the mathematical model of LSPs, the inference method valid for general LSP covariance functions
2. Methods

2.1 Locally Stationary Processes

Let \( X(t) \), \( t \in [T_0, T_f] \subseteq \mathbb{R} \), be a zero mean stochastic process. We say that \( X(t) \) is a locally stationary process (LSP) in the wide sense if its covariance \( C(s, t) = \mathbb{E}[X(s)X(t)^*] \) can be written as

\[
C(s, t) = q\left(\frac{s + t}{2}\right) \cdot r(s - t) = q(\eta) \cdot r(\tau)
\]

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

The wide range of possibilities for the choice of the functions offers an advantageous flexibility to model time-varying data. Clearly not every choice is suitable, since we recall that a function \( C(s, t) \) is a covariance if and only if it is positive semi-definite.

2.2 Estimation of the model parameters with HAnkel - Toeplitz Separation (HATS)

We define matrix \( Q \in M_{n \times n} \) as \( Q(k, l) = q\left(\frac{t_k + t_l}{2}\right) \) and matrix \( R \in M_{n \times n} \) as \( R(k, l) = r(|t_k - t_l|) \). Clearly, \( Q \) is a Hankel matrix which carries the information about the power schedule, while \( R \) corresponds to the stationary covariance function \( r(\tau) \) and is a symmetric Toeplitz matrix. Let \( \{q_\lambda\} \) and \( \{r_\rho\} \) be the selected parametric families for the functions composing the process covariance. The function \( q \) describes the power schedule of the process \( X(t) \), as

\[
C(t, t) = \mathbb{E} \left[ (X(t))^2 \right] = q(\eta) \cdot r(0) = q(\eta)
\]
Therefore an estimate of the set of parameters $\lambda$ can be obtained through a least squares fitting of the parametric curve $q_\lambda$ to the mean instantaneous power of the data $P(t_k) = \frac{1}{N} \sum_{j=1}^{N} (x_k^{(j)})^2$, where $x_k^{(j)}$, $k = 1 \ldots n$, in $[T_0, T_f] \subseteq \mathbb{R}$ are independent realizations for $j = 1 \ldots N$.

Let $\hat{\lambda}$ be the estimated parameters and $\hat{Q}$ the corresponding estimate of the matrix $Q$. The estimate of the matrix $R$ is found by exploiting its Toeplitz structure, which is possible since the matrix $\hat{Q}$ has already been calculated. The estimate $\hat{R}$ is obtained as

\[
\hat{R}(k, l) = \frac{1}{M-1} \sum_{j=1}^{M} \left( \frac{1}{N_{\tau}} \sum_{\tau = |k-l|} \left( \frac{x_k^{(j)} \cdot x_l^{(j)}}{Q(k, l)} \right) \right)
\]

where $N_{\tau}$ is the cardinality of the set $\{(k, l) : |k-l| = \tau\}$. In other words, even if the total covariance matrix is non-stationary, we are able to use the inherent local stationarity of the model to estimate the matrix $R$, by first estimating and separating the time-varying factor $Q$. The estimates $\hat{\rho}$ are obtained by fitting the parametric function $r_{\rho}(\tau)$ to the main anti-diagonal of the Toeplitz matrix $\hat{R}$, which contains all the matrix information. The estimation procedure is summarized below.

**Algorithm 2 HAnkel - Toeplitz Separation (HATS):** Parametric inference and covariance estimation for LSPs based on separation of the two factors of the Hadamard product $Q \circ R$.

1. Compute the mean instantaneous power from the data:

\[
P(t_k) = \frac{1}{M} \sum_{j=1}^{M} (x_k^{(j)})^2, \text{ for } k = 1, \ldots, n
\]

2. Find $\hat{\lambda}$ by fitting the function $q_\lambda$ to $P$.

3. Compute

\[
\hat{R}(k, l) = \frac{1}{M-1} \sum_{j=1}^{M} \left( \frac{1}{N_{\tau}} \sum_{\tau = |k-l|} \left( \frac{x_k^{(j)} \cdot x_l^{(j)}}{Q(k, l)} \right) \right)
\]

where $N_{\tau}$ is the cardinality of the set $\{(k, l) : |k-l| = \tau\}$.

4. Find $\hat{\rho}$ by fitting the function $r_{\rho}$ to the anti-diagonal elements of $\hat{R}$.

5. Compute covariance matrix estimate $\hat{C} = \hat{Q} \circ \hat{R}$.
2. Methods

2.3 Mean Square Error optimal kernel

The Wigner-Ville spectrum (WVS) of an LSP is defined as

$$W(t, \omega) = \int_{-\infty}^{\infty} \mathbb{E} \left[ X \left( t + \frac{\tau}{2} \right) X \left( t - \frac{\tau}{2} \right) \right] e^{-i\tau\omega} d\tau$$

where $\mathcal{F}f$ denotes the Fourier transform of the function $f$, [1, 2]. The corresponding ambiguity spectrum is defined as

$$A(\theta, \tau) = \int_{-\infty}^{\infty} \mathbb{E} \left[ X \left( t + \frac{\tau}{2} \right) X \left( t - \frac{\tau}{2} \right) \right] e^{-i\tau\theta} dt$$

and any time-frequency representation member of the Cohen’s class can be expressed as

$$W_C(t, \omega) = \int_{-\infty}^{\infty} \int_{-\infty}^{\infty} A(\theta, \tau) \Phi(\theta, \tau) e^{-i(\tau\omega - \tau\theta)} d\tau d\theta$$

where $\Phi$ is an ambiguity kernel, [8]. The general expression for the optimal ambiguity kernel in the mean square error (MSE) sense was derived in [9] as

$$\Phi_0(\theta, \tau) = \frac{|\mathcal{F}q(\theta)|^2 |r(\tau)|^2}{|\mathcal{F}q(\theta)|^2 |r(\tau)|^2 + (|\mathcal{F}|^2(\theta))(\mathcal{F}^{-1}|\mathcal{F}q|^2(\tau))},$$

and in [2] the authors derived the MSE optimal kernel for LSP where the factors of the covariance are Gaussian functions.

Efficient implementation and estimation are based on multitapers, [2, 3], i.e. a weighted sum of windowed spectrograms, as

$$W_C(t, \omega) = \mathbb{E} \left[ \sum_{k=1}^{K} \alpha_k \left| \int_{-\infty}^{\infty} X(s) h_k^*(t-s)e^{-i\omega s} ds \right|^2 \right],$$

with weights $\alpha_k$, and windows $h_k(t), k = 1 \ldots K$. The weights and windows are derived from the solution of the eigenvalue problem

$$\int_{-\infty}^{\infty} \Psi^{rot}(s, t) h(s) ds = \alpha h(t),$$

where the rotated time-lag kernel is Hermitian and defined as

$$\Psi^{rot}(s, t) = \Psi \left( \frac{s + t}{2}, s - t \right),$$
Figure 1: Example of optimal eigenvectors (a) and eigenvalues (b), corresponding to multitapers and weights of the optimal LSP spectrogram for the model (12) and parameters \((L, a_q, b_q, c_q, c_r) = (150, 800, 0.25, 250, 3000)\).

\[
\Psi(t, \tau) = \int_{-\infty}^{\infty} \Phi(\theta, \tau)e^{it\theta} d\theta. \tag{11}
\]

With a few \(\alpha_k\) that differ significantly from zero, the multitaper spectrogram solution is an efficient solution from implementation aspects.

### 2.4 Stochastic model for the simulation study and the EEG data application

In this study we choose the functions \(q(\eta)\) and \(r(\tau)\) as

\[
\begin{align*}
q(\eta) &= L + a_q \cdot \exp\left(-c_q (\eta - b_q)^2 / 2\right) \text{ with } \eta = \frac{t + s}{2} \\
r(\tau) &= \exp\left(-\frac{c_r}{8} \cdot \tau^2\right) \text{ with } \tau = t - s
\end{align*}
\]

with \(b_q \in [T_0, T_f]\), \(T_0\) and \(T_f\) initial and final times and \(c_r > c_q > 0\). The latter assumption is necessary to assure that the resulting covariance is positive semi-definite. This choice of functions is motivated by the case study presented in section 4.

In figure 2 we present examples of LSP realizations obtained from the model covariance (12) with different parameters settings, showing how the realizations behaviour varies notably depending on the parameters. Each set of realizations presented has power centered in the middle of the time interval \((b_q = 0.25)\), but the relation between the functions \(q\) and \(r\) results in a slowly varying behaviour in (a) and much faster variation in (b) and (c). The only difference between the realizations presented in (b) and (c) lies in the parameter \(L\), representing
the minimum energy level. The passage from $L = 0$ in (b) to $L = 100$ in (c) reflects more realistic realizations, illustrating the possibility of using the level $L$ to model the additional on-going spontaneous EEG activity.

Thanks to (7) we are able to compute the parameter dependent optimal kernel $\Phi_0(\theta, \tau)$ for the introduced model (12), as

$$\Phi_0(\theta, \tau) = \frac{|A(\theta, \tau)|^2}{|A(\theta, \tau)|^2 + B(\theta, \tau)}$$

with

$$|A(\theta, \tau)|^2 = |\mathcal{F}q(\theta)|^2 |r(\tau)|^2$$

$$= \left( L^2 \delta_0(\theta) + \frac{2\pi a_q^2}{c_q} e^{-\frac{\theta^2}{c_q}} + 2a_q L \sqrt{\frac{2\pi}{c_q}} \delta_0(\theta) e^{-\frac{\theta^2}{2c_q}} \right) e^{-\frac{c_q \tau^2}{4}}$$
B(\theta, \tau) = (\mathcal{F}|r|^2(\theta)) (\mathcal{F}^{-1}|\mathcal{F}q|^2(\tau)) \\
= \left(2\sqrt{\frac{\pi}{c_r}}e^{-\frac{\theta^2}{c_r}}\right) \left(\frac{L^2}{2\pi} + a_q^2 \sqrt{\frac{\pi}{c_q}}e^{-\frac{c_q\tau^2}{4}} + a_qL \sqrt{2\pi} \frac{c_r}{c_q}\right)

where \delta_0 denotes the Dirac delta function.

3 Evaluation in simulation study

We present a simulation study to evaluate the method performance in terms of MSE of the derived optimal spectral estimator. We consider 60 realizations of a LSP with covariance function (12), sampled in 256 equidistant points during the time interval \([T_0, T_f]=[0, 0.5]\) seconds. The vector of true parameters used to simulate the data is \((L, a_q, b_q, c_q, c_r) = (100, 600, 0.2, 1000, 10000)\). A few realizations from this parameters setting can be seen in figure 3. The inference method HATS (algorithm 2) is used to estimate the parameters \(\lambda = (L, a_q, b_q, c_q)\) and \(\rho = (c_r)\).

Based on the parameter estimates, the MSE optimal ambiguity kernel and corresponding multitapers are calculated as described in section 2.3 and 2.4. Two other classical estimators are considered for comparison: the single Hanning window spectrogram (HANN) and the Welch method, with 50% overlapping Hanning windows (WOSA). For a fair comparison of the performance of the different estimators, these two methods are optimized to give the smallest possible total MSE. For HANN, the window length \(N_w \in \{16, 32, 64, 128, 256\}\) is optimized, while for WOSA the optimized parameter is the number of windows used \(K \in \{1, 2, ..., 16\}\), where the total length of all included windows is 256.

The expected value of the MSE (mMSE) is computed as the average of 100 independent realizations. In figure 4 we present boxplots of the MSE achieved.
3. Evaluation in simulation study

Figure 4: Boxplots of the MSE on 100 simulation for the spectral estimators considered, all with parameters optimized. Average MSE are 3.8, 2.6 and 1.9, for HANN ($N_w = 32$), WOSA ($K = 10$) and the LSP optimal estimator respectively.

with the different methods in the 100 simulations. The optimal mMSE for HANN and WOSA are 3.8 and 2.6 respectively, obtained respectively with $N_w = 32$ for HANN and $K = 10$ for WOSA. The mMSE value for the LSP optimal estimator with the true parameters or with parameters estimated with HATS is 1.9. Notice that not only the spectral estimate obtained using LSP optimal kernels achieves the best mMSE as expected, but using the true parameters or those estimated with HATS leads to the same result.

To test how the number of realizations used to estimate the model parameters with HATS affects the results in the time-frequency domain, we study the variation of the MSE of the spectral estimator based on parameter estimates obtained using a different number of realizations $N \in \{1, 5, 10, 25, 50\}$. In figure 5 we present the resulting mMSE, computed as average on 100 independent simulations, as function of the number of realizations used, with corresponding 95 % confidence interval.
4 Application to EEG signals

Understanding how cognitive functions are supported by the electrical activity of the brain is the focus of cutting-edge research. In this context, analysis of electroencephalography signals (EEG) is one of the main methodological tools [5]. The study of a time-frequency image is often the method of choice to address key issues in cognitive electrophysiology. Clearly, the quality of the time-frequency representation is crucial for the extraction of robust and relevant features, [5, 7], thus leading to the demand for highly performing spectral estimators.

The data considered has been collected within a study on human memory retrieval, conducted at the department of Psychology of Lund University, Sweden, during the spring of 2015. The EEG signals have been measured from one subject participating in the experiment, during 180 trials of a memory recognition task, in which the subject had to associate a presented word with a target.
4. Application to EEG signals

Figure 6: Three random EEG signals, after 70 Hz low-pass filtering, corresponding to three different trials of a memory task, from each category: (a) ‘Faces’; (b) ‘Objects’; (c) ‘Landmarks’.

picture. Each picture presented belongs to one of three categories: ”Faces”, ”Landmarks”, ”Objects”. For each category, 60 different trials were performed. The measurements were recorded from channel O1 (International 10-20 system), as primary visual areas can be found below the occipital lobes, and downsampled to frequency 512 Hz. Each time series considered has 256 equidistant samples during the time interval [0, 0.5] seconds (figure 6).

Assuming that the 60 realizations in each dataset are realizations of a common LSP, with covariance (12), we infer the value of the parameters $L, a_q, b_q, c_q, c_r$ with HATS. To give a measure of the accuracy of our estimates, a bootstrap estimate of the standard error for each parameter is obtained using 100 bootstrap samples, where each bootstrap sample consists of 60 realizations, each sample drawn with replacement from the original data. The results for the three classes are reported in table 1.

The differences in the parameter estimates for the three data-sets correspond
Table 1: EEG data application: estimated LSP parameters for the three categories “Faces”, “Objects”, “Landmarks” of the memory encoding task with respective bootstrap standard errors and coefficients of variation.

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<td>698</td>
<td>47.36</td>
<td>0.07</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$b_q$</td>
<td>0.20</td>
<td>0.0082</td>
<td>0.04</td>
<td>0.24</td>
<td>0.0050</td>
<td>0.02</td>
<td>0.21</td>
<td>5·$e^{-16}$</td>
<td>2·$e^{-15}$</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$c_q$</td>
<td>1735</td>
<td>629.45</td>
<td>0.41</td>
<td>271</td>
<td>48.78</td>
<td>0.17</td>
<td>1983</td>
<td>247</td>
<td>0.12</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$c_r$</td>
<td>67369</td>
<td>15880</td>
<td>0.23</td>
<td>94939</td>
<td>12194</td>
<td>0.13</td>
<td>78676</td>
<td>17069</td>
<td>0.21</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Figure 7: Spectral estimates using the LSP optimal kernels for the three classes of visual stimuli: (a) Faces; (b) Objects; (c) Landmarks.

to different underlying LSP for each data-set. The moment when the process energy is maximum is represented by the parameter $b_q$, which is different for the different categories, indicating that the maximum of the signal power is reached at different times for each category. The minimum energy level $L$ is similar among the datasets, suggesting a possible interpretation as underlying noise. Similar values of $a_q$ relate to the comparable amplitude of the power for the signals in each data-set. More difficult is the interpretation of the parameters $c_q$ and $c_r$, ruling the trade-off between the local stationarity and the time-dependent behaviour, as shown with the simulated realizations for different parameters (figure 2). The fact that a certain parameter has the same scale for the three categories is due to the common nature of the signals, whereas the differences in the estimates reflect the expected neural representational differences between various types of encoded memories.

Optimal kernel and multitapers for each category are computed according to the estimated model parameters (table 1). For illustrative purpose, the spectral estimates for one randomly selected trial from each category are presented in figure 7.
5 Conclusions

In this paper we have tested the performance of the optimal spectral estimator for Locally Stationary Processes (LSPs) using parameters estimated with a novel inference method, introduced in [4]. The method is based on the possibility of separating the two factors of the Hadamard product composing the covariance matrix to exploit their individual structure. The estimation of the model parameters allows the explicit computation of the corresponding mean square error optimal ambiguity domain kernels and therefore obtain the optimal spectral estimator from real data.

In the simulation study, the optimal time-frequency estimator based on the estimated parameters is compared with other commonly used methods, namely the single Hanning spectrogram and the Welch method, confirming the expected mean square error reduction.

As example of practical application, the LSP model has been applied to EEG signals collected within a research on memory retrieval. Future extensions of this research could consider a multidimensional model to deal with correlated signals and a classification study to verify if the use of the optimal spectral estimator based on the estimated parameters leads to improvements in classification accuracy.

Compliance with ethical requirements

Conflict of Interest

The authors have no conflict of interest to declare.

Statement of human and animal rights

The procedures followed to collect the data were in accordance with the Helsinki Declaration of 1975, as revised in 2000 and 2008.
Acknowledgment

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References


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

Rachele Anderson, Peter Jönsson and Maria Sandsten

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.

Key words: HRV, Chirp Respiratory Frequency, Locally Stationary Chirp Processes, Time-varying signals, Time-series modelling, Linear and Logistic Regression.
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 [1]. 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. [2] 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 [3], 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, [4, 5, 6, 7, 8]. In [7], 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 [6].

Another aspect is the phenomenon of Respiratory Sinus Arrhythmia (RSA), i.e. the heart rate variability in synchrony with respiration, by which the heart rate increases during inspiration and decreases during expiration [1]. Recent studies claim that the actual respiratory frequency is the main information to be considered in analysis of HRV [5, 9, 10]. These findings have also increased the interest of estimating the respiratory frequency from the HRV signal, e.g., [11] 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 differences during stress [5]. Similar results are found in [9] 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 [10], 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, [12]. 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 [13]. 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 [14, 15].

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) [16] and Shirom-Melamed Burnout Questionnaire (SMBQ) [17, 18, 19]. 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, [16]. 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 [20], [21]. Therefore, it is of interest to consider both STAI and SMBQ. Previous studies have validated the Swedish version of the STAI [22, 23, 24] and the SMBQ [25, 21].

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) [12], 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 [13], 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 [14, 15].

### 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 \(x\) 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)
\[
\hat{C}_{SCM} = x \cdot x^T \tag{2}
\]
is known to be extremely unreliable if it is based on a single realization [26]. 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 $Q(k,l) = q(\frac{t_k + t_l}{2})$, corresponding to the function $q$, and $R \in M_{n \times n}$ be the matrix $R(k,l) = r(|t_k - t_l|)$, 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) 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 $b \in [-1, 1]$

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

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

$$r_c(\tau) = \exp\left(-\frac{c}{8} \cdot \tau^2\right) \text{ with } \tau = t - s \quad (4)$$
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 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 [27]. 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.

<table>
<thead>
<tr>
<th></th>
<th><strong>Women</strong> (n=21)</th>
<th><strong>Men</strong> (n=26)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Median</strong></td>
<td><strong>Mean</strong></td>
<td><strong>sd</strong></td>
</tr>
<tr>
<td>Age</td>
<td>25</td>
<td>31.14</td>
</tr>
<tr>
<td>Weight</td>
<td>61</td>
<td>63.76</td>
</tr>
<tr>
<td>BMI</td>
<td>22</td>
<td>22.52</td>
</tr>
<tr>
<td>State Anxiety</td>
<td>35</td>
<td>33.09</td>
</tr>
<tr>
<td>Trait Anxiety</td>
<td>38</td>
<td>36.95</td>
</tr>
<tr>
<td>SMBQ</td>
<td>2.86</td>
<td>3.05</td>
</tr>
</tbody>
</table>

To isolate the effect of every factor, regression models with a single explanatory variable (Simple 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 [28, 29].

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.

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.

![Figure 3: Boxplots of log(a) divided in age groups.](image)

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 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 $R^2 = 0.51$.

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

<table>
<thead>
<tr>
<th></th>
<th>coeff. est.</th>
<th>S.E.</th>
<th>$p$-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>-0.0748</td>
<td>0.0114</td>
<td>$5.83 \times 10^{-8}$ ***</td>
</tr>
<tr>
<td>State Anxiety</td>
<td>-0.0635</td>
<td>0.0231</td>
<td>0.0087 **</td>
</tr>
<tr>
<td>High Trait Anxiety</td>
<td>0.7261</td>
<td>0.3189</td>
<td>0.0278 *</td>
</tr>
</tbody>
</table>

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.

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

<table>
<thead>
<tr>
<th></th>
<th>coeff. est.</th>
<th>S.E.</th>
<th>$p$-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>-0.0873</td>
<td>0.0106</td>
<td>$3.81 \times 10^{-10}$ ***</td>
</tr>
<tr>
<td>State Anxiety</td>
<td>-0.0778</td>
<td>0.0203</td>
<td>0.000433 ***</td>
</tr>
<tr>
<td>High Trait Anxiety</td>
<td>0.9471</td>
<td>0.2778</td>
<td>0.001498 **</td>
</tr>
</tbody>
</table>
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.

<table>
<thead>
<tr>
<th>SMBQ</th>
<th>coeff. est.</th>
<th>S.E.</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>-0.0023</td>
<td>0.0012</td>
<td>0.0641</td>
</tr>
<tr>
<td>Trait Anxiety</td>
<td>0.0044</td>
<td>0.0024</td>
<td>0.0763</td>
</tr>
</tbody>
</table>

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.

<table>
<thead>
<tr>
<th>Intercept</th>
<th>coeff. est.</th>
<th>S.E.</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SMBQ</td>
<td>-0.0011</td>
<td>0.0005</td>
<td>0.0217</td>
</tr>
</tbody>
</table>

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 [3]; 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].

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

<table>
<thead>
<tr>
<th></th>
<th>coeff. est.</th>
<th>S.E.</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>-0.0047</td>
<td>0.0007</td>
<td>3.11e-07 ***</td>
</tr>
<tr>
<td>Stressed Group</td>
<td>-0.0025</td>
<td>0.0010</td>
<td>0.0169 *</td>
</tr>
</tbody>
</table>

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.

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

<table>
<thead>
<tr>
<th></th>
<th>coeff. est.</th>
<th>S.E.</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>-5.4757</td>
<td>1.9033</td>
<td>0.00402 **</td>
</tr>
<tr>
<td>Age</td>
<td>0.0806</td>
<td>0.0415</td>
<td>0.05203</td>
</tr>
</tbody>
</table>

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.

Table 8: Regression model for parameter $c$.

<table>
<thead>
<tr>
<th></th>
<th>coeff. est.</th>
<th>S.E.</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>-7.8773</td>
<td>1.9666</td>
<td>0.000235 ***</td>
</tr>
<tr>
<td>Age</td>
<td>0.1146</td>
<td>0.0228</td>
<td>9.04e^{-06} ***</td>
</tr>
<tr>
<td>BMI</td>
<td>0.2416</td>
<td>0.0856</td>
<td>0.007143 **</td>
</tr>
</tbody>
</table>

If BMI is considered as a categorical variable with levels underweight (BMI < 18), normal weight (18 ≤ BMI < 25), overweight (25 ≤ 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.

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

<table>
<thead>
<tr>
<th></th>
<th>coeff. est.</th>
<th>S.E.</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>-2.4395</td>
<td>0.7507</td>
<td>0.002279</td>
</tr>
<tr>
<td>Age</td>
<td>0.1115</td>
<td>0.0214</td>
<td>5.21·e$^{-06}$ ***</td>
</tr>
<tr>
<td>Obese</td>
<td>3.7010</td>
<td>0.9318</td>
<td>0.000274 ***</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th></th>
<th>coeff. est.</th>
<th>S.E.</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>-3.571</td>
<td>0.6885</td>
<td>6.14·e$^{-06}$ ***</td>
</tr>
<tr>
<td>Age</td>
<td>0.1538</td>
<td>0.0210</td>
<td>5.83·e$^{-09}$ ***</td>
</tr>
<tr>
<td>Obese</td>
<td>2.922</td>
<td>0.8821</td>
<td>0.00194 **</td>
</tr>
</tbody>
</table>

### 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 out-
liers 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.
References


