Time-Frequency and Point Process Algorithms for Cardiac Arrhythmia Analysis and Cardiorespiratory Control

Sandun V. W. Kodituwakku

B.E. (Hon 1), The University of Adelaide

May 2012

A THESIS SUBMITTED FOR THE DEGREE OF DOCTOR OF PHILOSOPHY
OF THE AUSTRALIAN NATIONAL UNIVERSITY

Research School of Engineering
College of Engineering and Computer Science
The Australian National University
Declaration

The content of this thesis is a result of original research done and has not been submitted for a higher degree in any other university. Most of the work presented in this thesis have already been published in peer-reviewed journals and conference proceedings as listed below:

Journal Publications


Conference Proceedings


The research work presented in this thesis has been performed jointly with A/Prof. Thushara D. Abhayapala (The Australian National University), Prof. Rodney A. Kennedy (The Australian National University), and A/Prof. Ricardo Barbieri (Harvard Medical School/Massachusetts Institute of Technology). The substantial majority of the work is my own.

The following people also contributed to some of the published material: Prof. Emery N. Brown (Harvard Medical School/Massachusetts Institute of Technology), A/Prof. Premananda Indic (University of Massachusetts), A/Prof. Sara W. Lazar (Harvard Medical School), Dr. Zhe Chen (Massachusetts Institute of Technology), A/Prof. Vitaly Napadow (Harvard Medical School), Dr. Jieun Kim (Harvard Medical School), and Dr. Marco L. Loggia (Harvard Medical School).

Sandun V. W. Kodituwakku,
Research School of Engineering,
The Australian National University,
Canberra, ACT 0200, Australia.
Acknowledgements

The work presented in this thesis would not have been possible without the support of a number of individuals and organizations. They are gratefully acknowledged below:

- My supervisors A/Prof. Thushara Abhayapala (The Australian National University), Prof. Rodney Kennedy (The Australian National University), and A/Prof. Riccardo Barbieri (Harvard Medical School/Massachusetts Institute of Technology) for their guidance, insight, support, and encouragement throughout my PhD candidature.

- Prof. Emery Brown (Harvard Medical School/Massachusetts Institute of Technology), A/Prof. Premananda Indic (University of Massachusetts), A/Prof. Sara Lazar (Harvard Medical School), Dr. Zhe Chen (Massachusetts Institute of Technology), A/Prof. Vitaly Napadow (Harvard Medical School), Dr. Jieun Kim (Harvard Medical School), and Dr. Marco Loggia (Harvard Medical School) for their collaboration on some of the work presented in this thesis, and for many fruitful discussions.

- All the academics, students, and administrative staff in the Applied Signal Processing Group, Research School of Engineering, the Australian National University, and in the Neuroscience Statistics Research Laboratory, Massachusetts General Hospital for their effort in providing a friendly and productive research environment.

- The Australian National University for providing me a PhD scholarship and a number of travel grants. Also, Massachusetts General Hospital and Australian Research Council Communications Research Network for providing me travel grants and funding my overseas research visits.
• My friends Tharaka Lamahewa, Sudewa Nawarathna, Sachithra Hemachandra, Terence Tay, and many others for their kind support. Special thanks to Sumila Wanaguru for her continuous support and encouragement during my PhD studies.

• My parents for their tireless efforts in providing me higher education and guidance throughout the life. My sister Anuradha, brother-in-law Manilka, and niece Runi for their kind help and support.
Abstract

Cardiovascular diseases are major causes of disability and premature death globally. In particular, atrial fibrillation is the most common cardiac arrhythmia condition found in clinical practice, and is associated with an increased risk of stroke. Heart rate variability (HRV) and respiratory sinus arrhythmia (RSA) are important indicators of cardiovascular health, and provide useful information on autonomic nervous system inputs to cardiac cycle and cardiorespiratory coupling, respectively. New methods to support the treatment of cardiovascular diseases and identifying efficient ways of measuring cardiovascular health could yield significant benefits. In this thesis, we present a number of advanced algorithms for cardiorespiratory signal processing.

We present algorithms for analyzing atrial fibrillation arrhythmia from electrocardiograms (ECG). We propose an orthonormal basis function based representation for fibrillatory waveforms, and use a regularized least square solution for atrial activity extraction from ECG, suppressing more dominant ventricular components. Time-frequency analysis of atrial activity is used to identify and track fibrillatory frequencies from extracted atrial activity, which provides possible guidance to tailored treatments. In addressing the problem of tracking fibrillatory frequencies, we have developed a framework for generating new classes of time-frequency distributions with many desirable properties. This framework is based on multi-dimensional Fourier transform of a radially symmetric function, and can be used to generate new distributions with unique characteristics. A realization of this framework on a high-dimensional radial delta function results in a new class of time-frequency distributions, which we call radial-δ distributions. The class of radial-δ distributions unifies number of well known distributions, and further provides methods for high resolution time-frequency analysis
of multi-component signals with low interference terms.

We present a maximum likelihood inverse Gaussian point process model for dynamic and instantaneous HRV and RSA estimation from heart beat interval series and respiration recordings. Unlike previous methods, we perform time-frequency analysis of heart beat interval series, respiration, as well as the coherence between the two, and dynamically evaluate RSA transfer function based on instantaneous respiration and maximum coherence frequencies. The point process algorithm and dynamic respiration based RSA estimation methods are applied on two experimental protocols, a meditation experiment and a pain experiment. These applications demonstrate the robustness of the point process model in estimating HRV and RSA under different psychophysiological states. Regardless of the significant variations in respiration during meditation practice, goodness-of-fit tests are still found to be well within the desired confidence bounds, which validate the proposed models. Results indicate a significant increase in RSA during meditation practice, which suggest positive influence of meditation on the cardiovascular health. In the second experiment, reduced RSA during pain indicates the ability of the method to differentiate between different acute pain levels.

Novel time-frequency distributions and orthonormal basis atrial activity representation based analysis provide accurate tracking of fibrillatory frequencies of atrial fibrillation arrhythmia from ECG. The point process model with time-frequency analysis provides accurate estimations of HRV and RSA, and is robust to dynamic changes in respiration and autonomic inputs. These algorithms provide useful tools for monitoring cardiovascular health and particular arrhythmia conditions.
# List of Acronyms

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABS</td>
<td>Average Beat Subtraction</td>
</tr>
<tr>
<td>AF</td>
<td>Atrial Fibrillation</td>
</tr>
<tr>
<td>AIC</td>
<td>Akaike Information Criterion</td>
</tr>
<tr>
<td>AR</td>
<td>Autoregression</td>
</tr>
<tr>
<td>AWGN</td>
<td>Additive White Gaussian Noise</td>
</tr>
<tr>
<td>BSS</td>
<td>Blind Source Separation</td>
</tr>
<tr>
<td>BVP</td>
<td>Blood Volume Pressure</td>
</tr>
<tr>
<td>CWD</td>
<td>Choi-Williams Distribution</td>
</tr>
<tr>
<td>ECG</td>
<td>Electrocardiogram</td>
</tr>
<tr>
<td>HR</td>
<td>Heart Rate</td>
</tr>
<tr>
<td>HRV</td>
<td>Heart Rate Variability</td>
</tr>
<tr>
<td>KS</td>
<td>Kolmogorov-Smirnov</td>
</tr>
<tr>
<td>PI</td>
<td>Pulse Interval</td>
</tr>
<tr>
<td>RID</td>
<td>Reduced Interference Distribution</td>
</tr>
<tr>
<td>RMS</td>
<td>Root Mean Squared</td>
</tr>
<tr>
<td>RP</td>
<td>Respiration Signal</td>
</tr>
<tr>
<td>RR</td>
<td>R-peak to R-peak Interval on Electrocardiogram</td>
</tr>
<tr>
<td>RSA</td>
<td>Respiratory Sinus Arrhythmia</td>
</tr>
<tr>
<td>SNR</td>
<td>Signal to Noise Ratio</td>
</tr>
<tr>
<td>STFT</td>
<td>Short-Time Fourier Transform</td>
</tr>
<tr>
<td>TFD</td>
<td>Time-Frequency Distribution</td>
</tr>
<tr>
<td>WVD</td>
<td>Wigner-Ville Distribution</td>
</tr>
</tbody>
</table>
# Contents

Declaration ................................................. i  
Acknowledgements ......................................... iii  
Abstract .................................................... v  
List of Acronyms ............................................. vii  
List of Figures .............................................. xiii  
List of Tables ............................................... xix  

1 Introduction .............................................. 1  
1.1 Overview ............................................... 1  
1.2 Problem Statement ..................................... 4  
1.3 Contributions .......................................... 6  
1.4 Thesis Outline ......................................... 8  

2 Kernel Design for Quadratic Time-Frequency Distributions ............. 13  
2.1 Introduction ............................................ 13  
2.2 Background ............................................. 16  
2.2.1 Short-Time Fourier Transform .................... 16  
2.2.2 Wigner-Ville Distribution ......................... 17  
2.2.3 Cohen Class ......................................... 17  
2.2.4 Choi-Williams and Reduced Interference Distributions ........ 18  
2.3 Kernel Design Framework ................................ 19  
2.4 Radial-δ Kernel Class ................................... 22
### Contents

#### 2.4 Kernel Methods

- 2.4.1 Derivation of Radial-\(\delta\) Kernel ........................................... 22
- 2.4.2 TFDs of Radial-\(\delta\) Kernel ..................................................... 25
- 2.4.3 Window Interpretation ............................................................. 28
- 2.4.4 Radial-\(\delta\) Kernel Properties .................................................. 29

#### 2.5 Cross-Term Reduction ................................................................. 35

#### 2.6 Discrete Radial-\(\delta\) Distributions ..................................................... 36

#### 2.7 Simulation Results ................................................................. 37

#### 2.8 Kaiser Window based Kernel Design ............................................. 40

#### 2.9 Summary and Contributions ......................................................... 44

#### 3 Time-Frequency Analysis of Atrial Fibrillation Electrocardiograms

- 3.1 Introduction ................................................................. 47
- 3.2 Electrocardiograms .......................................................... 49
- 3.3 Atrial Fibrillation .......................................................... 51
- 3.4 Bessel Distribution based AF Analysis ........................................ 53
  - 3.4.1 Bessel Distribution ................................................... 53
  - 3.4.2 AF Model ............................................................. 55
  - 3.4.3 Results and Comparison with STFT .................................. 56
- 3.5 Orthonormal Basis based Atrial Activity Extraction ....................... 61
  - 3.5.1 Orthonormal Basis Representation .................................. 62
  - 3.5.2 Regularized Coefficient Estimation .................................. 64
  - 3.5.3 Results and Comparison with ABS .................................... 65
- 3.6 Simplified TFD with Missing Data ............................................... 67
  - 3.6.1 Combined AF Reconstruction and TFD Method ....................... 68
  - 3.6.2 Results and Comparison with ABS .................................... 69
- 3.7 Radial-\(\delta\) Kernel based AF Analysis ........................................ 70
- 3.8 Summary and Contributions ......................................................... 72

#### 4 Point Process Algorithms for Cardiorespiratory Dynamics

- 4.1 Introduction ................................................................. 77
- 4.2 Heart Rate Variability .......................................................... 79
- 4.3 Respiratory Sinus Arrhythmia .................................................. 81
### 4.4 Point Process Framework

| 4.4.1 | Point Process Model of Heart Beat Interval Dynamics | 83 |
| 4.4.2 | Point Process Definitions of HR and HRV | 84 |
| 4.4.3 | Heart Beat Spectral Components | 85 |
| 4.4.4 | Bivariate Model for RSA analysis | 86 |
| 4.4.5 | Local Maximum Likelihood Estimation | 88 |
| 4.4.6 | Model Goodness-of-Fit | 89 |

### 4.5 Simulation Results

| 4.5.1 | Constant Respiratory Frequency | 92 |
| 4.5.2 | Varying Respiratory Frequency | 92 |

### 4.6 Application to Pain Administration Protocol

| 4.6.1 | Pain Protocol | 96 |
| 4.6.2 | Pain Experiment Results | 97 |
| 4.6.3 | Discussion of Pain Results | 100 |

### 4.7 Summary and Contributions

| 5 Respiratory Sinus Arrhythmia Analysis during Meditation Practice | 103 |

#### 5.1 Introduction

| 5.2 | Meditation Protocol | 105 |

#### 5.3 Instantaneous PI and HRV Estimation

| 5.4 | Model Goodness-of-Fit | 107 |

#### 5.5 Time-Frequency Analysis of PI and RP

| 5.6 | Instantaneous RSA Estimation | 108 |
| 5.6.1 | Respiration and Coherence based RSA Estimations | 110 |
| 5.6.2 | Dynamic and Static RSA Estimations | 113 |
| 5.6.3 | Flow and Belt Respiration | 113 |

#### 5.7 Standard LF/HF Spectral Analysis

| 5.8 | Statistical Analysis | 114 |
| 5.8.1 | Time Domain Indices | 116 |
| 5.8.2 | Frequency Domain Indices | 118 |
| 5.8.3 | Paced Breathing | 122 |

#### 5.9 Discussion of Meditation Results

| 5.9 | Discussion of Meditation Results | 124 |
5.10 Summary and Contributions ............................................. 125

6 Conclusions and Future Directions ................................. 127
   6.1 Conclusions ................................................................. 127
   6.2 Future Research Directions .......................................... 130

Bibliography ................................................................. 133
List of Figures

1.1 Major questions addressed, and contributions made in Chapters 2 and 3. ............................... 7
1.2 Major questions addressed, and contributions made in Chapters 4 and 5. ............................... 9

2.1 (a) The STFT of a linear chirp with a wide time window, (b) The STFT of the same signal with a narrower time window. .............................. 17
2.2 A fixed scalar-valued univariate function, $\varphi_f(\cdot)$, or equivalently a radially symmetric scalar-valued multivariate function in $n$ variables, $f(r)$, induces an order $n$ radial kernel $\phi^n(\xi, \tau)$. .............................. 21
2.3 Visualization of radial-δ kernels for (a) $n = 1$, (b) $n = 2$, (c) $n = 3$, (d) $n = 4$, (e) $n = 5$, and (f) $n = 6$ in time-lag and frequency-lag domain ($\alpha = 0.5$). .............................. 26
2.4 The effect of the dimension $n$ on the weighting window $W^n(\mu - t)$ for the time correlation (normalized for $\alpha \tau = 1$). .............................. 29
2.5 Time-frequency representation of the two-component signal using (a) Born-Jordan distribution, (b) Bessel distribution, (c)-(e) TFDs based on order 5-7 radial-δ kernels ($\alpha = 0.4$). .............................. 39
2.6 Time-frequency representation of the two-component signal using Choi-Williams distribution with (a) $\sigma = 0.1$, (b) $\sigma = 0.5$, (c) $\sigma = 1$, (d) $\sigma = 5$, and (e) $\sigma = 10$. .............................. 41
2.7 The effect of changing $\beta$ on the time correlated window function. .............................. 43
2.8 Kaiser distribution with $\beta = 12$ for a sum of frequency modulated and linear chirp signals. .............................. 44
2.9 Kaiser distribution with $\beta = 4$ for a sum of frequency modulated and linear chirp signals. ........................................ 45

3.1 A typical ECG waveform of a healthy subject during one cardiac cycle with conventional nomenclature. .......................... 50

3.2 Bessel distribution for sum of two complex exponentials, $\alpha = 0.1$ (left), $\alpha = 0.4$ (right), demonstrates that cross-term energy can be controlled by varying $\alpha$. .................................................... 54

3.3 Bessel distribution for sum of two frequency modulated signals, $\alpha = 0.1$ (left), $\alpha = 0.4$ (right). At a higher value of $\alpha$, cross-term energy reduces but at the slight expense of reduced auto-term resolution. .................................................... 55

3.4 A time window of a 3s interval of simulated AF signal at SNR = 20dB. ................................................................. 56

3.5 Bessel distribution vs. STFT for simulated AF signal with AWGN at SNR = 5dB. ......................................................... 57

3.6 Bessel distribution vs. STFT for simulated AF signal with AWGN at SNR = 0dB. ......................................................... 58

3.7 Bessel distribution vs. STFT for simulated AF signal with AWGN at SNR = −5dB. ......................................................... 58

3.8 RMS error of Bessel distribution and STFT for simulated AF with AWGN at different SNR settings. ......................... 59

3.9 Frequency resolution of Bessel distribution and STFT for simulated AF with AWGN at different SNR settings. ................. 60

3.10 Bessel distribution vs. STFT for the ECG record n02 of PhysioBank AF Termination Challenge Database. .................... 60

3.11 A typical AF ECG waveform segment with the nomenclature used in this thesis. ......................................................... 63

3.12 (a) Synthetic ECG for normal sinus rhythm, (b) P-wave is removed from normal sinus rhythm and AF signal is superimposed, (c) Fiducial points $P_i$ and $Q_i$ are accurately detected. ................. 66
3.13 (a) Simulated AF signal, (b) AF signal reconstructed using orthonormal basis expansion method, (c) AF signal reconstructed using average beat subtraction method. .................................. 67
3.14 Correlation coefficients of reconstructed AF signal using orthonormal basis expansion and average beat subtraction methods, with respect to the simulated AF signal with AWGN. ................. 68
3.15 Time-frequency distributions for (a) simulated AF signal, (b) proposed algorithm based AF reconstruction, (c) average beat subtraction based AF reconstruction. ................................. 70
3.16 Comparison between the proposed algorithm and the average beat subtraction method for AF ECG analysis in terms of RMS error of the estimated AF frequency. .................. ............... 71
3.17 (a) ECG record n09 of PhysioBank AF Termination Challenge Database, (b) TFD generated by the proposed method, (c) TFD generated via average beat subtraction based AF reconstruction. ........................................ 71
3.18 Time-frequency representation of simulated AF signal using (a) Born-Jordan distribution (order 3 kernel), (b) Bessel distribution (order 4 kernel), (c) 5th order kernel based TFD, (d) 6th order kernel based TFD, and (e) 7th order kernel based TFD, ($\alpha = 0.5$). 73
3.19 Time-frequency representation of simulated AF signal using Choi-Williams distribution with (a) $\sigma = 0.1$, (b) $\sigma = 0.5$, (c) $\sigma = 1$, (d) $\sigma = 5$, and (e) $\sigma = 10$. .............................................. 74
4.1 Estimated $f_{RP}$ (top), coherence (middle), and RSA gain (bottom) under constant respiratory rate for the simulated RR and RP signals using the point process algorithm. .............................. 93
4.2 The KS plot (left) and transformed quantiles’ autocorrelation function (right) show the goodness-of-fit of the point process model under constant respiratory frequency. ................................. 93
4.3 Estimated $f_{RP}$ (top), coherence (middle), and RSA gain (bottom) under varying respiratory patterns for the simulated RR and RP signals using the point process algorithm. ................. 94
4.4 The KS plot (left) and transformed quantiles’ autocorrelation function (right) show the goodness-of-fit of the point process model under varying respiratory frequency.

4.5 From top to bottom, original RR-interval series, and point process estimates of HR, HRV, and LF/HF ratio for a 90s segment during a pain run for one representative subject.

4.6 The KS plot (left) and transformed quantiles’ autocorrelation function (right) for the example given in Figure 4.5.

4.7 From top to bottom, original respiration signal, respiratory frequency, coherence between respiration and RR-intervals, and dynamic RSA estimation at the respiratory frequency for the example considered in Figure 4.5.

4.8 Mean RSA gain and LF/HF ratio during the rest epoch and three pain run epochs averaged over all subjects.

4.9 Mean RSA gain and LF/HF ratio at different intensity levels, averaged over three pain epochs and over all subjects.

5.1 From top to bottom, instantaneous mean PI, PI variance, mean HR, and HRV indices estimated by the point process algorithm for an expert meditator subject.

5.2 From top to bottom, instantaneous mean PI, PI variance, mean HR, and HRV indices estimated by the point process algorithm for a control subject.

5.3 KS plots (left) and transformed quantiles’ autocorrelation functions (right) for an experienced meditator (top) and a control subject (bottom).

5.4 Time-frequency distributions of PI power (top), RP power (middle), and coherence between PI and RP (bottom) for the expert meditator (left) and the control subject (right).
5.5 Dynamic frequencies where maximum RP power is observed ($f_{RP}$) and coherence between PIs and RP is maximum ($f_{coh}$) (top), coherence at $f_{RP}$ and maximum coherence (middle), RSA gain estimated at $f_{RP}$ and $f_{coh}$ by the point process model (bottom) for the expert meditation subject. 112

5.6 Dynamic frequencies where maximum RP power is observed ($f_{RP}$) and coherence between PIs and RP is maximum ($f_{coh}$) (top), coherence at $f_{RP}$ and maximum coherence (middle), RSA gain estimated at $f_{RP}$ and $f_{coh}$ by the point process model (bottom) for the control subject. 112

5.7 Comparison of RSA estimations based on dynamic frequencies with maximum coherence, and a fixed mean respiratory frequency for the expert meditator subject. 114

5.8 Comparison of RSA estimations obtained using flow RP and belt RP signals for the expert meditator subject. 115

5.9 From top to bottom, PI power in the LF band, PI power in the HF band, LF/HF ratio, and percentage RP power in the LF band for the expert meditator subject. 115

5.10 Mean values and standard errors of dynamic RSA estimates for meditator and control groups during rest, practice, and number generation phases. 122

5.11 Paced breathing: middle epoch reproduces slow breathing pattern as in meditation, but no significant changes in RSA were found compared to the baseline epoch. 123
List of Tables

2.1 Radial-δ kernels for lower \( n \) dimensions \hspace{1cm} 25
2.2 Desirable distribution properties (P#) and kernel constraints (C#) of the Cohen class TFDs \hspace{1cm} 30
4.1 Parameters used in two dynamic RSA simulation studies with constant and time-varying respiratory rates \hspace{1cm} 91
5.1 Statistical comparison of point process heart beat indices between meditation and control groups, along with the standard time domain indices \hspace{1cm} 117
5.2 Statistical comparison of RP, coherence, and estimated RSA indices between meditation and control groups along with the standard frequency domain HRV measures \hspace{1cm} 120
Chapter 1

Introduction

1.1 Overview

Biomedical signal processing plays an increasingly important role in patient care in clinical practice including monitoring, diagnosing and treatment. Biomedical signals carry vital information on the living systems, and clever processing of these signals provides important physiological and clinical information. Digital signal processing techniques have been widely used in biomedical signal processing. They may vary from traditional first and second order statistical analysis of linear stationary systems to more sophisticated methods of nonstationary and nonlinear systems analysis [29]. Efficient and reliable signal processing is a key to the development of many pieces of medical equipment used in the clinical practice today. From simple linear time-invariant noise filtering to more advanced methods such as non-linear adaptive or time-variant filtering, time-frequency or wavelet decomposition, source separation, or complexity analysis contribute to the development of advanced biomedical signal processing for better patient care. In addition to the desire for continuous improvements in the health care, the aging population in most developed countries demands fast, cheap, and individualistic health care solutions in which advanced signal processing algorithms could make a significant contribution.

In this thesis, we focus on some specific problems in cardiac and cardiorespiratory signal processing. Cardiovascular diseases are major causes of disability and premature death globally, and contribute substantially to the escalating costs of
Cardiac arrhythmia is an irregular rhythm of the heart, and some arrhythmia conditions could be life threatening. Among number of arrhythmias, atrial fibrillation is the most common arrhythmia condition in clinical practice. It affects 0.4% to 1% of the general population, but increases up to 8% for the population over age of 80 [127]. Atrial fibrillation is associated with an increased risk of stroke [52, 127]. A significant part of this thesis is devoted to the better characterization of the atrial fibrillation arrhythmia condition from the electrocardiogram (ECG) signal. We address the problem of extracting low amplitude atrial fibrillation signal from ECGs avoiding residues from dominant ventricular activity. Further, we address how to identify and then track fibrillatory frequencies accurately from the extracted atrial fibrillation signal in order to facilitate efficient and tailored treatments for this arrhythmia condition.

Heart rate variability is an important indicator of the cardiovascular health of a subject. It is regulated by the autonomic nervous system activity, thus accurate quantification of heart rate variability provides vital information on subject’s autonomic modulation, and cardiovascular health. Further, respiratory sinus arrhythmia is characterized as the heart rate oscillations which occur simultaneously with the respiratory cycle. Though named as an arrhythmia, respiratory sinus arrhythmia is a normal physiological process which characterizes the variations in the heart rate during inspiratory and expiratory phases of the respiratory cycle [47, 124]. It serves an important role in providing synchrony between the respiratory and cardiovascular systems. Accurate quantification of respiratory sinus arrhythmia provides critical insights into the mechanisms involved in short-term and long-term cardiopulmonary coupling [47, 124]. Number of algorithms have been presented in the literature for characterizing heart rate variability and respiratory sinus arrhythmia in time and frequency domains, but
with number of shortcomings. Problems remain as to how to quantify heart rate variability and respiratory sinus arrhythmia instantaneously, how to account for the fast dynamic changes in respiration and autonomic inputs in the model, and how to model the discrete heart beat generation process accurately without interpolation. The novel algorithms presented in this thesis are capable of estimating heart rate variability and respiratory sinus arrhythmia instantaneously, and robust to fast changes in the underlying physiological processes.

It is important to test and validate these novel algorithms on experimental data. In this regard, we apply the algorithms for quantifying heart rate variability and respiratory sinus arrhythmia on two experimental protocols. It serves dual purpose. First, it helps to test and validate the robustness of the algorithms. Second, it helps to analyze a particular psychophysiological state using estimated cardiorespiratory indices. The first experiment is consisted of a group of experienced meditators engaging in meditation practice. We investigate how systematic changes occur in respiratory sinus arrhythmia during meditation sessions, and thus potential benefits of meditation on cardiovascular health. The second experiment is consisted of a group of subjects experiencing acute pain administered at different intensities. We investigate possible relationships between pain at different intensities and respiratory sinus arrhythmia, and subsequently the possibility of using respiratory sinus arrhythmia estimation as an indicator of the pain level.

Though our focus is on the cardiorespiratory signal processing, some of the signal processing algorithms we develop in this thesis may have wide range of applications, and contribute to the general signal processing theory. For example, we develop new algorithms and a framework for efficient joint time and frequency representation of nonstationary signals. These algorithms could be readily applicable to time-frequency analysis of any nonstationary signal. Similarly, the methodology we introduce for efficient time-frequency analysis of incomplete data, could be applicable to any type of signals with incomplete or missing data segments.

In the next Sections of this Chapter, we define the scope and the problems investigated in this thesis more precisely, briefly describing the solutions and contributions made in specifically addressing those problems, and then outlining
the following Chapters.

1.2 Problem Statement

In analyzing atrial fibrillation cardiac arrhythmia, atrial component should be extracted from the ECG. The ECG signal consists of electrical signals generated by the different parts of the heart, namely atria and ventricles. Waveforms due to ventricular sources are dominantly present in the ECG compared to the waveforms due to atria. Additionally, spectral components of the atrial and ventricular waveforms overlap with each other, thus linear filtering techniques fail to isolate atrial activity. This raises the importance of a reliable method to extract atrial activity from atrial fibrillation ECG signals. During an atrial fibrillation episode atrial waveform is narrowband, and there exist a dominant fibrillatory frequency. Different types of atrial fibrillation conditions exhibit different fibrillatory frequencies. Additionally, atrial fibrillation waveforms are nonstationary in nature. Thus, a problem rises as to how to identify and then track the main fibrillatory frequency of atrial fibrillation, which would help the diagnosis and treatment of atrial fibrillation arrhythmia condition in clinical practice.

Time-frequency distributions have been used extensively in analyzing nonstationary signals in joint time-frequency domain, thus could be used for tracking the dominant fibrillatory frequency in time. There are a large number of time-frequency distributions with different characteristics, thus a systematic way of generating a smaller set of distributions, and finding a simplifying relationship between those members becomes relevant. We address this problem in order to generate novel time-frequency distributions with desirable distribution properties. Further, as the ECG signal is dominated by the ventricular activity, the extracted atrial waveform usually consists of corrupted data segments. Thus, it is not straightforward to perform time-frequency analysis directly on a signal with missing or corrupted data segments.

In the second part of the thesis, we focus on a different aspect of cardiorespiratory signal processing. Heart rate variability and respiratory sinus arrhythmia are physiological processes which are triggered by the autonomic nervous system activity and the cardiorespiratory coupling. A dynamic and robust methodology
for quantifying heart rate variability and respiratory sinus arrhythmia reveals important information on the underlying autonomic activity, which are indicators of the cardiovascular health. A point process framework for heart beat dynamics [8, 9] has been proposed to assess heart rate variability indices dynamically and instantaneously. In light of these previous developments, here we propose a new algorithm to assess respiratory sinus arrhythmia in the presence of dynamic respiratory patterns. Validation of the algorithms is critical, and two experimental protocols have been used to test the methodology. In doing so, first we address how respiratory sinus arrhythmia changes during meditation practice in experienced meditators, accounting for altering respiratory activity. Second, we address how respiratory sinus arrhythmia changes when subjected to different pain intensities.

In summary, the main questions addressed in the thesis are,

1. How to extract the atrial activity from atrial fibrillation ECG without ventricular residues?
2. How to identify and track dominant fibrillatory frequencies of atrial fibrillation episodes?
3. How to define kernel functions in a systematic way to generate well-defined time-frequency distributions with desirable characteristics?
4. How to perform time-frequency analysis of a signal in the presence of missing or corrupted data segments?
5. How to improve the point process heart beat model to estimate respiratory sinus arrhythmia instantaneously in the presence of dynamic autonomic inputs?
6. How to estimate respiratory sinus arrhythmia accurately during meditation practice where dynamic respiratory activity is observed?
7. How does respiratory sinus arrhythmia change in response to different intensities of acute pain?
1.3 Contributions

In addressing the above questions, we develop important and novel signal processing algorithms in this thesis work. In order to extract atrial activity from atrial fibrillation ECG, we propose a representation of atrial activity by mode limited short-time expansion of an orthonormal basis. This representation is used to estimate the atrial activity during the ventricular dominant period by interpolating known atrial fibrillation data segments to give a minimum least square solution. The method preserves the morphology and frequency content of the underlying atrial fibrillation signal, and the resulting signal is free from any ventricular residues. In order to improve the stability of the algorithm, we have introduced Tikhonov regularization into the model.

We investigate suitable time-frequency distributions for tracking the dominant fibrillatory frequency of atrial fibrillation waveforms. As results obtained from existing time-frequency distributions were not totally satisfactory, we develop novel time-frequency distributions with desirable characteristics. We introduce a generic framework based on multi-dimensional Fourier transform of a radially symmetric function for deriving kernels for quadratic time-frequency distributions. This framework is used to derive a new class of distributions called radial-$\delta$ distributions with highly structured kernels with distinctive characteristics. It subsumes number of existing and well known distributions, thus introduces a unifying kernel formula. We demonstrate that this radial-$\delta$ distributions reduce interference terms for multi-component signals in the time-frequency plane, while achieving good time and frequency resolutions.

Additionally, we derive simplified analytical expressions for time-frequency analysis of signals with missing or corrupted data segments. This algorithm is applied to atrial fibrillation waveforms where significant amount of ventricular residues are present. Figure 1.1 shows a summary of problems addressed, contributions made, and future research directions of the work presented in Chapters 2 and 3 of this thesis.

In second instance, we introduce a maximum likelihood point process model for instantaneous heart rate variability and respiratory sinus arrhythmia estimation. Different to previous methods, time-frequency analysis of heart beat
Figure 1.1: Major questions addressed, and contributions made in Chapters 2 and 3. Shaded ovals represent new algorithms and contributions made in the thesis. Rectangles represent the significant problems addressed using these new algorithms and techniques. Unshaded ovals represent future research directions based on current contributions and findings.

intervals, respiration, and coherence between heart beat intervals and respiration signal is used for the dynamic evaluation of respiratory sinus arrhythmia. The model has been developed closely resembling the underlying physiology of the cardiorespiratory control, thus estimated indices accurately represent the autonomic control and cardiorespiratory coupling. These new algorithms are comprehensively tested on experimental data, and validated using model goodness-
of-fit tests. Traditionally, rigid frequency bands were used to estimate the heart rate variability parameters, and have inherited problems when autonomic inputs or respiration changes dynamically. But our new model overcomes such shortcomings as it estimates the relevant indices dynamically based on instantaneous respiratory frequency. Therefore, it provides a better characterization of cardiorespiratory control compared to the standard time or frequency domain methods.

This maximum likelihood point process algorithm is applied to a pain administered protocol where subjects experience series of pressure stimuli at different intensities. The analysis verifies the applicability of the proposed model in experimental settings. Our results indicate reduced vagal tone during the pain experience, and demonstrate the ability of the method to differentiate between different pain levels. Further, the proposed point process algorithm is applied to physiological data obtained from subjects practicing meditation who are experienced meditators, and a control group who were asked to relax under equal conditions. First, it demonstrates the robustness of the proposed algorithm under significant variations in respiration which occur during meditation, as goodness-of-fit tests are still found to be within the desired confidence bounds. Second, the analysis provides an opportunity to investigate the effects of meditation techniques on cardiovascular control, and the potential benefits of meditation on cardiovascular health. Our results show a significant increase in respiratory sinus arrhythmia during meditation practice, which is not evident in the control group, suggesting meditation practice may have a positive influence on the cardiovascular health. Figure 1.2 shows a summary of problems addressed, contributions made, and future research directions of the work presented in Chapters 4 and 5 of this thesis.

1.4 Thesis Outline

In this Section we provide an outline of the following Chapters of the thesis:

Chapter 2 contains a kernel design framework for quadratic time-frequency distributions, and develops novel radial-δ distributions for reduced interference and high resolution time-frequency representation. First, we provide a back-
1.4 Thesis Outline

**Dynamic and instantaneous HRV and RSA estimation**

- **Maximum likelihood point process model**
- **Time-frequency analysis of heart beat intervals, respiration and their coherence**

- **Applied to a meditation protocol, found increase in RSA during meditation practice**
- **Applied to a pain protocol, found reduced vagal tone during pain experience**

- **Potential benefits of meditation on cardiovascular health**
- **RSA measure as an indicator of the pain level**

- **Better characterization of RSA and sympathovagal balance compared to standard indices**
- **Readily applicable to any experiment requiring dynamic measures of cardiorespiratory control**

Figure 1.2: Major questions addressed, and contributions made in Chapters 4 and 5. Shaded ovals represent new algorithms and contributions made in the thesis. Rectangles represent the significant problems addressed using these new algorithms and techniques. Unshaded ovals represent future research directions based on current contributions and findings.
ground on existing time-frequency representation techniques such as short-time Fourier transform, Wigner-Ville distribution, Choi-Williams distribution, and reduced interference distributions. We show quadratic time-frequency distributions achieve better time and frequency resolutions in the expense of interference terms, and the Cohen class provides a generic formula for most quadratic time-frequency distributions. Then, we introduce a novel framework for obtaining appropriate kernel functions for the Cohen class of time-frequency distributions based on multi-dimensional Fourier transform of radially symmetric functions. We use this framework on a radial delta function for deriving a new class of kernels, which we call radial-$\delta$ kernels. We derive time-frequency distributions corresponding to these radial-$\delta$ kernels, and prove that radial-$\delta$ kernels satisfy all known desirable properties including time and frequency support. We show how radial-$\delta$ distributions reduce cross-terms for multi-component signals, and also derive discrete-time versions of the new distributions. We demonstrate the superiority of radial-$\delta$ distributions over the Choi-Williams distribution by performing time-frequency analysis of a two-component signal consisting of frequency modulated and linear chirp components. Additionally, we derive a sinhc kernel formula which generates a Kaiser window based time-frequency distribution.

Chapter 3 analyzes atrial fibrillation arrhythmia condition from surface ECG using time-frequency distributions. First, we give a brief overview on how ECG signals are generated by the electrical activity of the heart, and provide a brief overview of existing signal processing algorithms for ECG analysis. We also provide a background to the signal processing challenges in atrial fibrillation analysis, and clinical importance of the problems addressed. Then, we perform a preliminary study of atrial fibrillation analysis using the Bessel distribution, and its results are compared to the short-time Fourier transform in order to demonstrate better time and frequency resolutions of quadratic distributions. A sum of frequency modulated sinusoidal model is used to represent the atrial fibrillation waveform throughout the Chapter, in addition to the results obtained using real signals. Next, we introduce a method for reconstructing the atrial activity from ECG by mode limited short-time expansion of an orthonormal basis. Regularization is incorporated into the model in order to achieve a stable solution. The performance of the new algorithm is compared to the traditional average
beat subtraction method. Further, we integrate atrial activity extraction and
time-frequency analysis of atrial fibrillation into a single algorithm, thus more
efficient real-time analysis of atrial fibrillation from ECG is viable. Finally, we
analyze atrial fibrillation arrhythmia with radial-δ kernel based time-frequency
distributions. The performance of the novel time-frequency distributions are
compared to the existing time-frequency distributions such as the Choi-Williams
distribution.

Chapter 4 develops a point process algorithm for dynamic estimations of
heart rate variability and respiratory sinus arrhythmia. First, we give a brief
overview on physiology behind heart rate variability and respiratory sinus ar-
rhythmia, and existing time-domain, frequency-domain, and nonlinear methods
for analyzing them. Then, we present a maximum likelihood point process model
for heart beat interval dynamics, and analytical expressions for heart rate and
heart rate variability are derived. We further develop the algorithm to include a
bivariate model incorporating heart beat intervals and respiration signal for res-
piratory sinus arrhythmia analysis. Respiratory sinus arrhythmia is dynamically
estimated based on time-frequency analysis of respiration and coherence between
heart beat intervals and respiration. Goodness-of-fit of the proposed model is
evaluated using a Kolmogorov-Smirnov (KS) test, as well as using transformed
quantiles’ autocorrelation function. Algorithms are first tested on simulated data
under constant and dynamic respiration, and dynamic autonomic inputs. Then,
we apply the proposed algorithms to a pain administered protocol where series of
pressure stimuli were delivered at different intensities. The experimental analysis
is used to verify the robustness of the algorithms, as well as to find reduced vagal
tone during the pain experience, demonstrating the ability of the algorithm to
differentiate between different pain levels.

Chapter 5 presents a detailed analysis of a meditation experimental proto-
col using the point process algorithms developed in Chapter 4. The data were
acquired from experienced practitioners of insight meditation, a form of ‘mind-
fulness’ meditation. The optimal model parameters for the point process model
are obtained by minimizing the Akaike information criterion for the maximum
likelihood estimation, as well as the KS distance on the KS plot. Time-frequency
analysis of the pulse intervals and respiration is performed in order to identify the
dynamic changes in respiratory frequency and autonomic inputs. Time-varying coherence between pulse intervals and respiration is also computed to characterize respiratory sinus arrhythmia more accurately. Comparisons are made between static evaluation of respiratory sinus arrhythmia and new dynamic measures. Comparisons are also made between estimates based on respiratory signals obtained through different measurements. We show that point process model based estimates overcome shortcomings of standard hear rate variability indices which are based on subdivision of fixed frequency bands. A comprehensive statistical analysis is also done in order to illustrate the significance of the results. As a compliment to the main experiment, a paced breathing protocol is analyzed to isolate the physiological effects of the meditation from similar breathing patterns. The results supporting the hypothesis that the increased respiratory sinus arrhythmia during meditation practice may reflect possible benefits of meditation on cardiovascular health.

**Chapter 6** presents conclusions of the thesis and future research directions.
Chapter 2

Kernel Design for Quadratic Time-Frequency Distributions

2.1 Introduction

Fourier transform and its derivatives have been used extensively in signal processing applications in analyzing signals in the frequency domain. They allow decomposition of a time domain signal into its frequency components, and quantify the relative intensity of each frequency component. Though it has been used in diverse applications, the major drawback in Fourier transform is that it fails to represent at which time instances each frequency component has occurred. It does not account for the time evolution of the signal, thus assumes that the signal is stationary. As a result, Fourier transform does not have any time resolution, and therefore fails to represent the signals whose frequency content change in time accurately. In order to avoid such shortcomings, time-frequency distributions (TFDs) have been proposed, where signal is represented simultaneously in time and frequency domains. The TFDs are well suited for analyzing nonstationary signals.

TFDs have been used in wide range of applications, including acoustics, radar, and physiological signal processing. In fact, nonstationary nature of the human speech led to the creation of first type of TFDs, known as speech spectrogram [77]. Since then it has been used widely in analyzing nonstationary signals. In recent times, TFDs have been employed in number of medical applications analyzing
various physiological signals. Time-frequency analysis of electroencephalograms (EEG) has been used in epilepsy detection and characterization \[5, 142\]. TFDs and time-frequency based filtering techniques have been employed in characterizing heart related disorders such as ventricular fibrillation and atrial fibrillation conditions using electrocardiograms (ECG) \[80, 82, 132\]. Analysis and decomposition of electromyogram (EMG) signals can be done using TFDs for detecting and characterizing muscle fatigues \[43, 141\]. Also, TFDs have been applied in detecting dysrhythmia in electrogastrograms (EGG) \[31, 87\]. In addition to the applications in electrophysiological signals such as EEG, ECG, EMG, and EGG, TFDs have also been used in bio-acoustic signal processing applications such as understanding temporomandibular disorders from temporomandibular joint sounds \[146\], study of heart sounds \[41\], and ultrasound signals of blood flow measurements \[63\].

TFDs are capable of representing a signal in time and frequency domains simultaneously. The simplest way of generating a TFD is to apply a window to the signal centered around a particular time instance, and slide that window along time to generate Fourier transforms at each instance. This is known as the short-time Fourier transform (STFT). The previously mentioned spectrogram is defined as the squared of STFT. Though STFT satisfies the basic requirement of a TFD, the choice of the window length leads to a trade-off between time and frequency resolutions. A wide time window fails to capture the localized events, whereas a narrow time window reduces the frequency resolution.

In order to overcome time and frequency resolution trade-offs in linear TFDs such as STFT, quadratic TFDs have been introduced. Most famously, the Wigner-Ville distribution (WVD) has been proposed which is capable of achieving excellent resolutions in time and frequency at the same time. The Wigner distribution was originally introduced in the context of quantum mechanics \[143\], and was later reintroduced in the context of signal analysis \[140\]. Though it achieves good time and frequency resolutions simultaneously, cross-terms appear in the time-frequency plane when applied to a multi-component signal due to the quadratic nature of the distribution. As most physical and physiological signals are multi-component in nature, these cross-terms or the interference terms limit the ability to interpret the resulting distribution of such signals. In order to
2.1 Introduction

overcome these cross-terms, smoothing functions have been applied to the WVD to smear out interference terms, while preserving good time and frequency resolutions. These smoothing functions are known as the kernel of the distribution.

Number of kernel functions have been introduced in the literature, which give rise to different TFDs with unique properties. Among them, the Choi-Williams distribution (CWD) [35] is well known for its effective cross-term suppression by using a Gaussian shaped kernel function. TFDs based on different kernels have their inherit advantages and disadvantages, and it is important to note that not a single distribution will work well for all kinds of signals and applications. Thus depending on the context, a kernel function should be carefully chosen to produce a TFD with desirable properties.

As a large number of kernels exist which give rise to TFDs with different characteristics, a systematic way of generating a smaller set of kernels, and finding a simplifying relationship between those members becomes relevant. This may lead to finding the best kernel suitable for representing given signals in the time-frequency domain. Jeong and Williams proposed a systematic procedure for generating kernels by introducing reduced interference distributions (RIDs) [69], which preserves desirable distribution properties while suppressing interference terms. However, this class can be regarded as too broad and insufficiently well-structured.

In this Chapter, we introduce a novel framework for generating well-structured kernel functions based on multi-dimensional Fourier transform of a specified radially symmetric function. We show that by varying a single integer parameter, newer, related, highly structured kernels can be revealed. When the specified function takes the simplest form, a delta function, we are lead to a general set of kernels where the kernel function takes the form of Bessel functions of different orders. Interestingly, we find that kernels corresponding to existing Margenau-Hill [95], Born-Jordan [38], and Bessel distribution [62] can be obtained by our formula for dimensions 1, 3, and 4, respectively. We also show applications of higher order radial kernels (dimension greater than 4), and their superiority over existing lower order kernels by analyzing atrial fibrillation ECG signals in Chapter 3. TFDs corresponding to the proposed set of kernels can be easily generated by varying only the dimension, and the best suited TFD within the
set for a given application can be found by inspecting auto-term resolution and cross-term interference.

2.2 Background

2.2.1 Short-Time Fourier Transform

The Fourier spectrum of a continuous-time function $s(t)$, $t \in \mathbb{R}$ and $s(t) \in \mathbb{C}$, is given by

$$F_s(\omega) = \frac{1}{\sqrt{2\pi}} \int_{-\infty}^{\infty} e^{-j\omega t}s(t)dt.$$  \hspace{1cm} (2.1)

Though highly useful, the Fourier spectrum $F_s(\omega)$ fails to identify the temporal evolution of the spectrum. In order to overcome such drawbacks associated with the Fourier spectrum, the short-time Fourier transform (STFT) [3, 77] has been proposed as

$$STFT_s(t, \omega) = \frac{1}{\sqrt{2\pi}} \int_{-\infty}^{\infty} e^{-j\omega \tau}s(\tau)w(t-\tau)d\tau.$$  \hspace{1cm} (2.2)

In the STFT, the time resolution is achieved by using a time localized sliding window, $w(\cdot)$. Thus, by using an appropriate window function, time localization can be achieved for nonstationary signals. However, signals exist whose frequency content is changing rapidly that assigning a short time interval is not practical, since there may not be any interval which the signal is stationary. Additionally, reducing the time window to highlight the local events reduces the frequency resolution. Therefore, the STFT has an inherit trade-off between time and frequency resolutions.

This time and frequency trade-off of the STFT has been demonstrated in Figure 2.1 for a simulated linear chirp signal. Figure 2.1(a) uses a wide Hamming window, thus achieves a good frequency resolution, but at the expense of poor time resolution. On the other hand, Figure 2.1(b) uses a narrower Hamming window in the time domain, thus is capable of achieving a better time localization, but displays an unsatisfactory frequency resolution. Therefore, quadratic TFDs such as the WVD have been proposed to overcome time and frequency resolution trade-offs in the STFT.
2.2 Background

Figure 2.1: (a) The STFT of a linear chirp with a wide time window, (b) The STFT of the same signal with a narrower time window.

2.2.2 Wigner-Ville Distribution

The Wigner-Ville distribution (WVD) [140,143] of signal $s(t)$ is given by

$$WVD_s(t, \omega) = \frac{1}{2\pi} \int_{-\infty}^{\infty} e^{-j\omega \tau} s\left(t + \frac{\tau}{2}\right) s^*\left(t - \frac{\tau}{2}\right) d\tau.$$  \hspace{1cm} (2.3)

The WVD is capable of achieving better time and frequency resolutions compared to the STFT, but at the expense of some artifacts. The quadratic nature of the WVD generates cross-terms for multi-component signals, and also could produce negative values which can not be physically interpreted. But regardless of these disadvantages, the WVD has been well known for its excellent time and frequency resolutions, and has been widely used in many different applications.

2.2.3 Cohen Class

Since the introduction of the WVD, a number of other quadratic TFDs have been proposed in the literature. Among them, some of the historically significant distributions are Margenau-Hill [95], Rihaczek [115], Page [39], and Born-Jordan [38]. Cohen [38], in his pioneer work, generalized most of these quadratic TFDs into a single class, with a kernel function being the only distinction be-
between each distribution. This class of TFDs is often referred as the Cohen class of TFDs. The generic form of a TFD which belongs to the Cohen class is given by

$$C_s(t, \omega; \phi) = \frac{1}{4\pi^2} \int\int e^{j(\xi \mu - \tau \omega - \xi t)} \phi(\xi, \tau) s(\mu + \tau/2) s^*(\mu - \tau/2) d\xi d\mu d\tau, \quad (2.4)$$

where \(s(\cdot)\) is the time signal to be analyzed, \(s^*(\cdot)\) is its complex conjugate, \(t\) and \(\omega\) are time and frequency, respectively, \(\tau\) and \(\xi\) are time-lag and frequency-lag, respectively, and \(\phi(\xi, \tau)\) is the kernel defining a particular distribution [38, 39]. The limits of each integral are from \(-\infty\) to \(\infty\).

Within the Cohen class, different TFDs are identified by their corresponding kernel functions: Wigner-Ville with \(\phi(\xi, \tau) = 1\); Margenau-Hill [95] with cosine kernel, \(\phi(\xi, \tau) = \cos(\eta \xi \tau/2)\); Rihaczek [115] and Page [39] with complex exponential kernels, \(\phi(\xi, \tau) = \exp(j\eta \xi \tau/2)\) and \(\phi(\xi, \tau) = \exp(j\eta \xi \tau/2)\), respectively; and Born-Jordan [38] with sinc kernel, \(\phi(\xi, \tau) = \sin(\alpha \xi \tau)/(\alpha \xi \tau)\). Since then, substantial work has been done in order to find the optimal kernel functions for the Cohen class of TFDs. Familiar among these are: Choi-Williams [35] with Gaussian kernel, \(\phi(\xi, \tau) = \exp(-\xi^2 \tau^2/\sigma)\); reduced interference distributions [69]; and Bessel distribution [62], \(\phi(\xi, \tau) = J_1(2\pi \alpha \xi \tau)/(\pi \alpha \xi \tau)\). The scope of this Chapter is limited to the product kernels where \(\phi(\xi, \tau) = \phi(\xi \tau)\), as they satisfy many desirable mathematical properties of TFDs.

### 2.2.4 Choi-Williams and Reduced Interference Distributions

Choi and Williams [35] introduced an exponential distribution with the kernel \(\phi(\xi, \tau) = \exp(-\xi^2 \tau^2/\sigma)\), which is later known as the Choi-Williams distribution (CWD). The CWD is given by

$$CWD_s(t, \omega) = \frac{1}{2\pi} \int e^{-j\omega \tau} \left[ \int \frac{1}{\sqrt{\tau^2/\sigma}} \exp \left( -\frac{(\mu - t)^2}{4\tau^2/\sigma} \right) s(\mu + \tau/2) s^*(\mu - \tau/2) d\mu \right] d\tau. \quad (2.5)$$

The CWD is well known for its successful suppression of cross-term interference, as opposed to the WVD. But the CWD does not satisfy some of the
desirable TFD properties such as time-support and frequency-support which will be discussed later. The kernel design framework presented in this Chapter, and the subsequently derived kernel functions overcome such shortcomings.

Further, reduced interference distributions (RIDs) [69] have been proposed to reduce cross-terms while preserving the desirable TFD properties. Though it describes a set of guidelines for efficient kernel design, it does not introduce a systematic way of selecting an appropriate TFD for a given signal. Also RID class can be regarded as too broad, and insufficiently structured. Our proposed framework for kernel design, which is based on the multi-dimensional Fourier transform of a radially symmetric function addresses above issues, and introduces highly structured kernel functions for the Cohen class of quadratic TFDs.

2.3 Kernel Design Framework

In this Section, we introduce a novel generic framework for obtaining appropriate kernel functions for the Cohen class of TFDs. Later, we show a realization of the framework based on a radial-δ function and its desirable properties. As kernels are derived based on multi-dimensional radial functions, we name these new kernels radial kernels. The multi-dimensional Fourier transform has been used in deriving these kernel sets.

Let \( r \in \mathbb{R}^n \) be a vector in \( n \)-dimensional space, and \( \|r\| \) be its Euclidean norm.

\[
\begin{align*}
  r &= \begin{pmatrix} a_1 \\ a_2 \\ \vdots \\ a_n \end{pmatrix} \\
  \|r\| &= \sqrt{\sum_{k=1}^{n} |a_k|^2}
\end{align*}
\]

Then we choose a scalar-valued multivariate function \( f: \mathbb{R}^n \rightarrow \mathbb{R} \) in \( n \) variables, such that \( f \) satisfies following three conditions:

R1: \( f(r) \) is radially symmetric, i.e., \( f(r) = \varphi_f(\|r\|) \) for some scalar-valued univariate function \( \varphi_f: \mathbb{R} \rightarrow \mathbb{R} \).
R2: \( f(r) \) has a unit volume, i.e., \( \int \int f(r) \, dv(r) = 1 \), where \( dv(r) \) is the volume element at \( r \) in \( n \)-dimensional space.

R3: \( f(r) \) has finite support of \( \|r\| \leq 1/2 \), i.e., \( f(r) = 0 \) for \( \|r\| > 1/2 \).

The condition R1 introduces symmetry to the final kernel expressions, and is an essential defining property in our definition of radial kernels. The conditions R2 and R3 induce key properties such as marginals, and time and frequency support which are shared by most of the well defined kernels. In Section 2.4.4, we further discuss how these desirable properties are satisfied by the proposed kernel functions.

The \( n \)-dimensional Fourier transform of \( f(r) \) is given by

\[
F(k) = \int \int f(r) \exp(2\pi j r \cdot k) \, dv(r), \quad k \in \mathbb{R}^n,
\]

where \( k \) is a vector in \( n \)-dimensional space, and \( r \cdot k \) is the scalar product. Due to the radially symmetric nature of \( f(r) \), \( F(k) \) will also be radially symmetric. Thus, we could map \( F(k) \) to some univariate scalar function \( \varphi_F : \mathbb{R} \rightarrow \mathbb{R} \),

\[
F(k) = \varphi_F(\|k\|).
\]

The Hankel transform [15] of order \( n - 1 \) given below can be used to obtain the scalar function \( \varphi_F(\cdot) \) from the scalar function \( \varphi_f(\cdot) \),

\[
\varphi_F(k) = \int_0^\infty r J_{n-1}(rk) \varphi_f(r) \, dr.
\]

We identify the scalar \( \|k\| \) with the product of time-lag \( \tau \) and frequency-lag \( \xi \), \( \|k\| = \xi \tau \), to define our order \( n \) radial kernel, to be used as the kernel in the Cohen class of TFDs, in terms of the \( n \)-dimensional Fourier transform \( F(\cdot) \). In the notation, the superscript \( n \) serves to distinguish this kernel from the more general \( \phi(\xi, \tau) \) in (2.4),

\[
\phi^n(\xi, \tau) \triangleq \varphi_F(\xi \tau).
\]

This procedure to generate our order \( n \) radial kernels is illustrated in Figure 2.2. Multivariate scalar functions \( f(\cdot) \) and \( F(\cdot) \) are multi-dimensional Fourier transforms of each other, and they can be mapped to univariate functions \( \varphi_f(\cdot) \)
The above kernel generation procedure has been described in an abstract way without mentioning a particular function in order to stress the generality of the framework and its independency from a specific function. Any function could be chosen for \( f(\cdot) \) given it satisfies the conditions R1-R3, although a careful choice will lead to a kernel set which result in TFDs with good time and frequency resolutions and better cross-term suppression.

The proposed framework can be viewed as a generalization of RIDs [69] as all the RIDs can be obtained by setting the dimension \( n = 1 \), and varying the scalar function \( \varphi_F(\cdot) \). RIDs use an extra condition which state that the function should taper smoothly towards both ends so that its frequency response has little high frequency content. This last condition in RIDs is ambiguous as it is a qualitative statement as opposed to a strict mathematical relationship. The proposed method here overcomes such shortcomings. In the given method, smoothness is achieved through increasing the dimensionality (\( n \)) of the base function \( f(\cdot) \), thus additional conditions are not required on \( \varphi_f(\cdot) \).

Additionally, with RIDs one chosen function gives rise to one kernel function, therefore in order to chose an appropriate TFD for a given signal, a number of base functions need to be tried. On the other hand, the proposed method uses a single base function which gives rise to a family of kernels, thus within the family appropriate kernel for a given signal can be chosen much easily. Also, it
results in more convenient practical implementation as the comparison within
the set can be easily done by varying the dimensionality $n$ as an integer variable,
as opposed to trying out unrelated and different types of TFDs. Therefore, a
simpler picture emerges when a fixed scalar-valued univariate function $\varphi_f(\cdot)$ is
chosen, and vary only the dimension $n$. In fact, of all possible valid choices of
the scalar function $\varphi_f(\cdot)$, we show that the choice of the delta function accounts
for some existing kernels simply by varying $n$. This is illustrated in the following
Section.

2.4 Radial-$\delta$ Kernel Class

2.4.1 Derivation of Radial-$\delta$ Kernel

The above framework for kernel generation can be realized by using an appro-
priate function for $f(r)$. A natural choice for $f(r)$, equivalently $\varphi_f(\|r\|)$, is the
delta function which is given by

$$f_\delta(r) = C\delta(\|r\|^2 - \alpha^2), \quad r \in \mathbb{R}^n,$$
(2.12)

where $C$ is a constant and $f_\delta(r)$ is non-zero only on the surface of the hyper-
sphere of radius $\alpha$. The function $f_\delta(r)$ is radially symmetric, thus satisfies the
condition R1. The constant $C$ needs to be chosen so that the condition R2,
which states that $f(\cdot)$ has a unit volume, is satisfied. Thus, we need to find $C$
such that

$$\int \ldots \int C\delta(\|r\|^2 - \alpha^2) \, dv(r) = 1.$$
(2.13)

The volume element in $n$-dimensional space $dv(r)$ can be written in terms of
hyper-spherical polar coordinates $(r, \theta, \phi_1, \ldots, \phi_{n-2})$, where $r$ represents radial
axis, $(\theta, \phi_1, \ldots, \phi_{n-3})$ angles have the range $(0, \pi)$, and $\phi_{n-2}$ has full-turn range
$(0, 2\pi)$, as

$$dv = r^{n-1} \sin^{n-2}(\theta) \sin^{n-3}(\phi_1) \ldots \sin(\phi_{n-3}) dr d\theta d\phi_1 d\phi_{n-2}.$$
(2.14)
Since $\delta(\|r\|^2 - \alpha^2)$ is a radial function and is independent of the angles,

\[
C \int_0^\infty r^{n-1} \delta(\|r\|^2 - \alpha^2) dr \int_0^\pi \sin^{n-2}(\theta) d\theta \int_0^\pi \sin^{n-3}(\phi_1) d\phi_1 \ldots \int_0^{2\pi} d\phi_{n-2} = 1.
\] (2.15)

But

\[
\int_0^\pi \sin^{n-3}(\phi_1) d\phi_1 \ldots \int_0^{2\pi} d\phi_{n-2} = \frac{2\pi^{n/2-1/2}}{\Gamma(n/2 - 1/2)},
\] (2.16)

and

\[
\int_0^\pi \sin^{n-2}(\theta) d\theta = \frac{\sqrt{\pi} \Gamma(n/2 - 1/2)}{\Gamma(n/2)},
\] (2.17)

where $\Gamma(\cdot)$ is the Gamma function given by

\[
\Gamma(n) = \int_0^\infty t^{n-1} e^{-t} dt.
\] (2.18)

Thus, we get the normalization constant

\[
C = \frac{\Gamma(n/2)}{\pi^{n/2}\alpha^{n-2}}.
\] (2.19)

The finite support condition R3 will be satisfied provided $\alpha \leq 1/2$, as function takes a non-zero value only on the surface of the hyper-sphere of radius $\alpha$. Thus, $f_\delta(r)$ can be rewritten as

\[
f_\delta(r) = \frac{\Gamma(n/2)}{\pi^{n/2}\alpha^{n-2}} \delta(\|r\|^2 - \alpha^2), \quad r \in \mathbb{R}^n, \quad \alpha \leq 1/2.
\] (2.20)

Then we estimate the $n$-dimensional Fourier transform [139] of $f_\delta(r)$. The $n$-dimensional Fourier transform $F(k)$ of a function $f(r)$ is given by

\[
F(k) = \int \ldots \int f(r) \exp(2\pi j r \cdot k) dv
\] (2.21)

where $k$ is a $n$-dimensional vector in the Fourier space. The $n$-dimensional Fourier transform of $f_\delta(r)$ is given by

\[
F_\delta(k) = \frac{\Gamma(n/2)}{\pi^{n/2}\alpha^{n-2}} \int \ldots \int \delta(r^2 - \alpha^2) \exp(2\pi j kr \cos(\theta)) dv.
\] (2.22)
Integrating over the angles \((\phi_1, \ldots, \phi_{n-2})\) and \(r\), we get

\[
F_\delta(k) = \frac{\Gamma(n/2)}{\sqrt{\pi} \Gamma(n/2 - 1/2)} \int_0^\pi \exp(2\pi jk\alpha \cos(\theta)) \sin^{n-2}(\theta) d\theta,
\]

(2.23)

which reduces to

\[
F_\delta(k) = \frac{2\Gamma(n/2)}{\sqrt{\pi} \Gamma(n/2 - 1/2)} \int_0^{\pi/2} \cos(2\pi k\alpha \cos(\theta)) \sin^{n-2}(\theta) d\theta.
\]

(2.24)

Now, the Bessel function of first kind of order \(\nu\) can be expressed by a definite integral \([14]\) as

\[
J_\nu(z) = \frac{2(z/2)^\nu}{\sqrt{\pi} \Gamma(\nu + 1/2)} \int_0^{\pi/2} \cos(z \cos u) \sin^{2\nu}(u) du.
\]

(2.25)

Thus, \(F_\delta(k)\) can be rewritten in terms of \(J_\nu(z)\) as

\[
F_\delta(k) = 2^{n/2-1}\Gamma(n/2) \frac{J_{n/2-1}(\alpha \|k\|)}{(\alpha \|k\|)^{n/2-1}}.
\]

(2.26)

Finally, we set \(\|k\| = \xi \tau\), the product of time and frequency lags to obtain the order \(n\) radial-\(\delta\) kernel function

\[
\phi^n_\delta(\xi, \tau) \triangleq 2^{n/2-1}\Gamma(n/2) \frac{J_{n/2-1}(\alpha \xi \tau)}{(\alpha \xi \tau)^{n/2-1}}, \quad \alpha \leq 1/2, \ n \geq 1.
\]

(2.27)

In the notation the addition of the subscript \(\delta\) in \(\phi^n_\delta(\xi, \tau)\), serves to distinguish this radial-\(\delta\) kernel from the more general radial kernel, \(\phi^n(\xi, \tau)\) defined in (2.11). As \(n\) varies (2.27) gives rise to set of kernels with distinctive properties, as we shall see later in the examples. Thus, starting from a simple radial-\(\delta\) function, we derived a class of functions to be used as kernels for the Cohen class.

Radial-\(\delta\) kernels for lower dimensions are shown in Table 2.1, and equivalent mathematical forms are given. Note that, \(j_\nu(\cdot)\) denotes spherical Bessel function of first kind of order \(\nu\) which can be given in terms of \(J_\nu(\cdot)\) as

\[
j_\nu(z) = \sqrt{\frac{\pi}{2z}} J_{\nu+1/2}(z).
\]

(2.28)

The formula given in (2.27) defines a family of kernels indexed by \(n\) for the
Table 2.1: Radial-δ kernels for lower \( n \) dimensions

<table>
<thead>
<tr>
<th>( n )</th>
<th>Radial-δ kernel ( \phi_\delta^n(\xi, \tau) )</th>
<th>TFD</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>( \cos(\xi \tau/2) )</td>
<td>Margenau-Hill [95]</td>
</tr>
<tr>
<td>2</td>
<td>( J_0(\alpha \xi \tau) )</td>
<td>this thesis</td>
</tr>
<tr>
<td>3</td>
<td>( \sin(\alpha \xi \tau)/\alpha \xi \tau )</td>
<td>Born-Jordan [38]</td>
</tr>
<tr>
<td>4</td>
<td>( 2J_1(\alpha \xi \tau)/\alpha \xi \tau )</td>
<td>Bessel [62]</td>
</tr>
<tr>
<td>5</td>
<td>( 3j_1(\alpha \xi \tau)/\alpha \xi \tau )</td>
<td>this thesis</td>
</tr>
<tr>
<td>6</td>
<td>( 8J_2(\alpha \xi \tau)/(\alpha \xi \tau)^2 )</td>
<td>this thesis</td>
</tr>
</tbody>
</table>

Cohen class of TFDs. When \( n = 1, 3, \) and 4, (2.27) simplifies to \( \cos(\alpha \xi \tau) \), \( \sin(\alpha \xi \tau)/\alpha \xi \tau \), and \( 2J_1(\alpha \xi \tau)/\alpha \xi \tau \), the kernels of Margenau-Hill, Born-Jordan and Bessel distributions, respectively. Thus, (2.27) is a unified formula for three existing and well known kernels, and for higher dimensions it generates novel kernels whose applicability is shown in the Section 2.7.

Radial-δ kernels for dimensions 1 to 6 are visualized in Figure 2.3 in the time-lag and frequency-lag domain. In this domain, radial-δ kernels show characteristics of two dimensional low-pass filters. Dimensionality of the base function controls the bandwidth of this low-pass filter, and higher dimensions result in broader bandwidth. Recalling that under the Cohen class shape of the kernel function of the WVD is a plane, it can be seen that as the dimensionality of the radial function increases, the radial-δ kernel asymptotically moves towards the kernel of the WVD.

### 2.4.2 TFDs of Radial-δ Kernel

The TFDs corresponding to radial-δ kernel \( \phi_\delta^n \) can be obtained by substituting the kernel formula into generic Cohen equation (2.4), and integrating with respect to frequency-lag \( \xi \). This order \( n \) radial-δ kernel based TFD of the time signal \( s(\cdot) \) is given by

\[
C_s^n(t, \omega) = \frac{1}{\pi} 2^{n/2-2} \Gamma(n/2) \int_{\tau} e^{-j\omega \tau} \int_{\mu} \left[ \int_{\xi} e^{-j\xi(t-\mu)} \frac{J_{n/2-1}(\alpha \xi \tau)}{(\alpha \xi \tau)^{n/2-1}} d\xi \right] d\mu / d\tau, \quad (2.29)
\]
Figure 2.3: Visualization of radial-$\delta$ kernels for (a) $n = 1$, (b) $n = 2$, (c) $n = 3$, (d) $n = 4$, (e) $n = 5$, and (f) $n = 6$ in time-lag and frequency-lag domain ($\alpha = 0.5$).
which further simplifies to

\[
C_s^1(t, \omega) = \frac{1}{4\pi} \int e^{-j\omega\tau} \left( s(t - \alpha\tau + \tau/2) s^*(t - \alpha\tau - \tau/2) + s(t + \alpha\tau + \tau/2) s^*(t + \alpha\tau - \tau/2) \right) d\tau, \quad n = 1
\]  

(2.30)

and

\[
C_s^n(t, \omega) = \frac{\Gamma(n/2)}{2\alpha\pi^{3/2}\Gamma(n/2 - 1/2)} \int \frac{1}{\tau} e^{-j\omega\tau} \int \left[ 1 - \left( \frac{\mu - t}{\alpha\tau} \right)^2 \right]^{(n-3)/2} \times \Pi\left( \frac{\mu - t}{2\alpha\tau} \right) s(\mu + \tau/2) s^*(\mu - \tau/2) d\mu d\tau, \quad n > 1
\]

(2.31)

where \( \Pi(\cdot) \) is the rectangle function given by

\[
\Pi\left( \frac{\mu - t}{2\alpha\tau} \right) = \begin{cases} 
1 & |\mu - t| \leq \alpha|\tau| \\
0 & \text{elsewhere.}
\end{cases}
\]

(2.32)

The expression \( C_s^n(t, \omega) \) represents the order \( n \) radial-\( \delta \) kernel based TFD of the time signal \( s(\cdot) \).

Now we reveal some special cases of the derived TFD. For \( n = 1 \) and \( \alpha = 1/2 \), (2.30) simplifies to

\[
C_s^1(\alpha=0.5)(t, \omega) = \text{Re} \frac{1}{\sqrt{2\pi}} s(t) e^{-j\omega t} S^*(\omega),
\]

(2.33)

which is the Margenau-Hill distribution [38, 95]. The Margenau-Hill distribution is an historically important TFD which was first derived by Ville and Moyal [97, 140]. It is simpler to use than the WVD for certain problems [39].

For the special case where \( n = 1 \) and \( \alpha = 0 \), (2.30) simplifies to

\[
C_s^1(\alpha=0)(t, \omega) = \frac{1}{2\pi} \int e^{-j\omega\tau} s(t + \tau/2) s^*(t - \tau/2) d\tau,
\]

(2.34)

which is the expression for the WVD. Thus, the WVD too could be considered as a special case of the class of radial-\( \delta \) kernel based TFDs.
For $n = 3$, (2.31) simplifies to

$$C_3^s(t, \omega) = \frac{1}{4\pi\alpha} \int \frac{1}{\tau} e^{-j\omega\tau} \int \Pi \left( \frac{\mu - t}{2\alpha\tau} \right) s(\mu + \tau/2)s^*(\mu - \tau/2) \, d\mu \, d\tau, \quad (2.35)$$

which is the Born-Jordan distribution [38, 39] with the sinc kernel.

Also, for $n = 4$, (2.31) simplifies to

$$C_4^s(t, \omega) = \frac{1}{\alpha\pi^2} \int \frac{1}{\tau} e^{-j\omega\tau} \int \left[ 1 - \left( \frac{\mu - t}{\alpha\tau} \right)^2 \right]^{1/2} \Pi \left( \frac{\mu - t}{2\alpha\tau} \right) \times s \left( \mu + \tau/2 \right) s^* \left( \mu - \tau/2 \right) \, d\mu \, d\tau, \quad (2.36)$$

which is known as the Bessel distribution [62]. It should be noted that Guo et al. [62] named this particular TFD “Bessel distribution” as its kernel contained a Bessel function of order one, and there were no other TFD kernels existed at that time which incorporate Bessel functions in their kernels. Our proposed radial-\(\delta\) kernels contain Bessel functions of different orders, thus calling the TFD proposed by Guo “Bessel distribution” is rather misleading. Nevertheless, going with the conventional nomenclature, we call the TFD based on Bessel function of first kind of order one “Bessel distribution”. The Bessel distribution has been successfully applied in the analysis of Doppler ultrasound signals of the femoral artery [63].

We have shown that radial-\(\delta\) kernel formula derived from our proposed framework contains at least four existing TFDs, thus is a generalization of some of the existing TFD kernel functions. We have also shown the relationship between them by demonstrating that each of these kernels corresponds to a particular dimension of the original radial-\(\delta\) function. Thus, our framework unifies number of existing TFDs, and also introduces novel high-order TFDs (for dimension > 4), which has unique characteristics and applications.

### 2.4.3 Window Interpretation

A careful examination of the radial-\(\delta\) TFDs given in (2.30) and (2.31) suggest that they both contain weighting windows for the time correlation of the signal.
2.4 Radial-δ Kernel Class

Figure 2.4: The effect of the dimension $n$ on the weighting window, $W^n(\mu - t)$ (2.37), for the time correlation (normalized for $\alpha \tau = 1$).

This window can be explicitly written as

$$W^n(\mu - t) \triangleq \begin{cases} 
\frac{1}{4\pi} (\delta(\mu - t - \alpha \tau) + \delta(\mu - t + \alpha \tau)), & n = 1 \\
\Gamma(n/2) \left[ 1 - \left( \frac{\mu - t}{2\alpha \tau} \right)^2 \right]^{(n-3)/2} \Pi \left( \frac{\mu - t}{2\alpha \tau} \right), & n > 1.
\end{cases}$$

(2.37)

The Figure 2.4 shows the effect of the dimensionality on the resulting window for $\alpha \tau = 1$. It is clear that the shape of the weighting window is based on the dimensionality of the radial-δ function, and as the dimensionality $n$ increases windows become more concentrated at the center, and less weighted at the ends. Thus, by varying the dimensionality of the kernel interference terms can be controlled more effectively, as we shall see in Section 2.5.

2.4.4 Radial-δ Kernel Properties

In this Section, we show that the novel radial-δ kernels derived in this Chapter satisfy all the desirable properties of the Cohen class of quadratic TFDs. A list of desirable properties of the distribution (P#) and the constraints on the kernel
(C#) are listed in Table 2.2. Properties P1–P7 were added by Cohen [38], and P8–P9 were later introduced by Claasen and Mecklenbrauker [36]. A distribution property P# will hold given that the kernel is constrained to C#.

Table 2.2: Desirable distribution properties (P#) and kernel constraints (C#) of the Cohen class TFDs. C# ⇒ P#.

<table>
<thead>
<tr>
<th>P#</th>
<th>Property</th>
</tr>
</thead>
<tbody>
<tr>
<td>P1</td>
<td>Real valued: ( C_s(t, \omega; \phi^n_{\delta}) = C^*<em>s(t, \omega; \phi^n</em>{\delta}) )</td>
</tr>
<tr>
<td>C1</td>
<td>( \phi^n_{\delta}(\xi, \tau) = \phi^n_{\delta}^*(-\xi, -\tau) )</td>
</tr>
<tr>
<td>P2</td>
<td>Time shifting: if ( g(t) = s(t - t_0) ), then ( C_g(t, \omega; \phi^n_{\delta}) = C_s(t - t_0, \omega; \phi^n_{\delta}) )</td>
</tr>
<tr>
<td>C2</td>
<td>( \phi^n_{\delta}(\xi, \tau) ) is independent of ( t )</td>
</tr>
<tr>
<td>P3</td>
<td>Frequency shifting: if ( g(t) = s(t)e^{j\omega_0 t} ), then ( C_g(t, \omega; \phi^n_{\delta}) = C_s(t, \omega - \omega_0; \phi^n_{\delta}) )</td>
</tr>
<tr>
<td>C3</td>
<td>( \phi^n_{\delta}(\xi, \tau) ) is independent of ( \omega )</td>
</tr>
<tr>
<td>P4</td>
<td>Time marginal: ( \int C_s(t, \omega; \phi^n_{\delta})d\omega =</td>
</tr>
<tr>
<td>C4</td>
<td>( \phi^n_{\delta}(0, \tau) = 1 ) ∀( \tau )</td>
</tr>
<tr>
<td>P5</td>
<td>Frequency marginal: ( \int C_s(t, \omega; \phi^n_{\delta})dt =</td>
</tr>
<tr>
<td>C5</td>
<td>( \phi^n_{\delta}(0, \tau) = 1 ) ∀( \tau ), and ( \frac{\partial}{\partial \tau} \phi^n_{\delta}(\xi, \tau)</td>
</tr>
<tr>
<td>P6</td>
<td>Instantaneous frequency: ( \frac{\int \omega C_s(t, \omega; \phi^n_{\delta})d\omega}{\int C_s(t, \omega; \phi^n_{\delta})d\omega} = \omega_s(t) )</td>
</tr>
<tr>
<td>C6</td>
<td>( \phi^n_{\delta}(0, \tau) = 1 ) ∀( \tau ), and ( \frac{\partial}{\partial \tau} \phi^n_{\delta}(\xi, \tau)</td>
</tr>
<tr>
<td>P7</td>
<td>Group delay: ( \frac{\int t C_s(t, \omega; \phi^n_{\delta})dt}{\int C_s(t, \omega; \phi^n_{\delta})dt} = t_s(\omega) )</td>
</tr>
<tr>
<td>C7</td>
<td>( \phi^n_{\delta}(0, \tau) = 1 ) ∀( \tau ), and ( \frac{\partial}{\partial \xi} \phi^n_{\delta}(\xi, \tau)</td>
</tr>
<tr>
<td>P8</td>
<td>Time-support: if ( s(t) = 0 ) for (</td>
</tr>
<tr>
<td>C8</td>
<td>( \int e^{-j\xi \tau} \phi^n_{\delta}(\xi, \tau)d\xi = 0 ) for (</td>
</tr>
<tr>
<td>P9</td>
<td>Frequency-support: if ( S(\omega) = 0 ) for (</td>
</tr>
<tr>
<td>C9</td>
<td>( \int e^{-j\omega \tau} \phi^n_{\delta}(\xi, \tau)d\tau = 0 ) for (</td>
</tr>
</tbody>
</table>

**Reality**

It is desirable to have positive real values for the TFD of a given signal. Though Cohen class does not necessarily guarantee a positive distribution, reality of the distribution could be guaranteed by having a kernel such that \( \phi^n(\xi, \tau) = \)
2.4 Radial-δ Kernel Class

$\phi^{n*}(\xi,\tau)$. For the proposed radial-δ kernels, it is clear that $\phi^n_\delta(\xi,\tau) = \phi^{n*}_\delta(\xi,\tau)$. Thus, resulting TFD will always be real-valued.

**Time and Frequency Shifting**

If the original signal is shifted by an amount $t_0$, i.e., $s(t) \rightarrow s(t + t_0)$, we expect the TFD to be shifted by the same amount, i.e., $C_s(t, \omega) \rightarrow C_s(t + t_0, \omega)$. Given that kernel is independent of $t$, this time shifting property will hold [36]. The proposed radial-δ kernels are product kernels of time-lag and frequency-lag, thus are independent of the time $t$. Therefore, time shifting property will be upheld for the resulting TFDs.

Similarly, in the frequency domain, if the spectrum is shifted by a fixed frequency, i.e., $s(t) \rightarrow s(t)e^{-j\omega_0 t}$, the resulting TFD should also be shifted by the same amount, i.e., $C_s(t, \omega) \rightarrow C_s(t, \omega + \omega_0)$. Again, the kernel’s independence of $\omega$ will guarantee this property, thus the proposed radial-δ kernel based TFDs satisfy the frequency shifting property.

**Time and Frequency Marginals**

The time and frequency marginal properties (P4 and P5) are important as they ensure that the time-frequency representation can be interpreted as an energy distribution of the signal over time and frequency. When the frequency variable is integrated out from the TFD, we expect to have the instantaneous power $|s(t)|^2$.

By integrating the Cohen TFD with respect to $\omega$, we get

$$\int C_s(t, \omega)d\omega = \frac{1}{2\pi} \iint \delta(\tau)e^{j\xi(\mu-t)}\phi(\xi,\tau)s(\mu + \tau/2) s^*(\mu - \tau/2) d\xi d\mu d\tau$$

$$= \frac{1}{2\pi} \int \delta(\tau)e^{j\xi(\mu-t)}\phi(\xi,0)s(\mu)|^2 d\xi d\mu. \quad (2.38)$$

In order this to be equal to $|s(t)|^2$, we require

$$\frac{1}{2\pi} \int e^{j\xi(\mu-t)}\phi(\xi,0)d\xi = \delta(t - \mu), \quad (2.39)$$
which implies

$$\phi(\xi, 0) = 1. \quad (2.40)$$

In order to show that the above kernel constraint is valid for the radial-\(\delta\) kernel class, we use the Taylor series expansion of the proposed kernel formula (2.27), which can be written as

$$\phi_n^\delta(\xi, \tau) = \Gamma(n/2) \sum_{m=0}^{\infty} \frac{(-1)^m}{m! \Gamma(m + n/2)} \left( \frac{\alpha \xi \tau}{2} \right)^{2m}$$

$$= 1 + \Gamma(n/2) \sum_{m=1}^{\infty} \frac{(-1)^m}{m! \Gamma(m + n/2)} \left( \frac{\alpha \xi \tau}{2} \right)^{2m}. \quad (2.41)$$

By setting \(\tau = 0\) we get \(\phi_n^\delta(\xi, 0) = 1\), thus time marginal property is held by the proposed kernels.

Similarly, we require \(\phi_n^\delta(0, \tau) = 1\) to fulfill the frequency marginal property,

$$\int C_s(t, \omega) dt = |S(\omega)|^2. \quad (2.42)$$

Now, by setting \(\xi = 0\) in the Taylor series expansion (2.41) we get \(\phi_n^\delta(0, \tau) = 1\), therefore proposed radial-\(\delta\) kernels satisfy the frequency marginal property as well.

**Instantaneous Frequency and Group Delay**

The average frequency \(\omega_s(t)\) of the distribution at a certain time is given by

$$\omega_s(t) = \frac{\int_{-\infty}^{\infty} \omega C_s(t, \omega; \phi) d\omega}{\int_{-\infty}^{\infty} C_s(t, \omega; \phi) d\omega}, \quad (2.43)$$

and this is called the instantaneous frequency of the signal. The above expression of instantaneous frequency holds for a complex-valued signals, and for a real-valued signal its corresponding analytic signal should be used [36].

Given that the signal is expressed in terms of its amplitude \(A(t)\) and phase \(\phi(t)\),

$$s(t) = A(t)e^{j\phi(t)}, \quad (2.44)$$
we require the instantaneous frequency to be equal to the derivative of the signal phase,

$$\omega_s(t) = \frac{d\varphi(t)}{dt}.$$  \hspace{1cm} (2.45)

This requirement for the instantaneous frequency will hold given that the kernel function satisfies \(\phi(\xi, 0) = 1\), and \(\frac{\partial}{\partial \tau} \phi(\xi, \tau)|_{\tau=0} = 0\) for \(\forall \xi\). We have already shown in the previous Section that the first condition holds for the radial-\(\delta\) kernel class. In order to show that the second condition is also satisfied, we take the partial derivative of the Taylor series expansion given in (2.41) with respect to \(\tau\) to get

$$\frac{\partial}{\partial \tau} \phi_\delta^n(\xi, \tau) \bigg|_{\tau=0} = \alpha \xi \Gamma(n/2) \sum_{m=1}^{\infty} \frac{(-1)^m}{(m-1)!} \Gamma(m + n/2) \left(\frac{\alpha \xi \tau}{2}\right)^{2m-1} \bigg|_{\tau=0} = 0.$$  \hspace{1cm} (2.46)

Thus, the proposed radial-\(\delta\) kernels satisfy the required instantaneous frequency property.

The average time \(t_s(\omega)\) of the distribution at a certain frequency is given by

$$t_s(\omega) = \frac{\int_{-\infty}^{\infty} t C_s(t, \omega; \phi) dt}{\int_{-\infty}^{\infty} C_s(t, \omega; \phi) dt},$$  \hspace{1cm} (2.47)

and this is called the group delay of the signal. Similarly, the novel TFDs will hold the group delay property given that the kernel function satisfies \(\phi(0, \tau) = 1\), and \(\frac{\partial}{\partial \xi} \phi(\xi, \tau)|_{\xi=0} = 0\) for \(\forall \tau\). The first condition is already shown in the previous Section, and the second condition is shown below.

$$\frac{\partial}{\partial \xi} \phi_\delta^n(\xi, \tau) \bigg|_{\xi=0} = \alpha \tau \Gamma(n/2) \sum_{m=1}^{\infty} \frac{(-1)^m}{(m-1)!} \Gamma(m + n/2) \left(\frac{\alpha \xi \tau}{2}\right)^{2m-1} \bigg|_{\xi=0} = 0.$$  \hspace{1cm} (2.48)

Thus, the proposed radial-\(\delta\) kernels satisfy the group delay property.
Time and Frequency Support

If the signal is zero in a certain time range, it is desirable to have the corresponding TFD zero in the same range as well [36], i.e., if \( s(t) = 0 \) for \( |t| > T \), then \( C_s(t, \omega; \phi) = 0 \) for \( |t| > T \). TFD will satisfy this time-support property given that the kernel function satisfies

\[
\int_{-\infty}^{\infty} e^{-j\xi t} d\xi = 0 \quad \text{for} \quad |\tau| < 2|t|. 
\]

(2.49)

For the radial-\( \delta \) kernels we get

\[
\int_{-\infty}^{\infty} e^{-j\xi t} \phi_{\delta}^n(\xi, \tau) d\xi = \frac{2\sqrt{\pi} \Gamma(n/2)}{\alpha \tau \Gamma(n/2 - 1/2)} \left[ 1 - \frac{t^2}{\alpha^2 \tau^2} \right]^{(n-3)/2} \Pi \left( \frac{t}{2\alpha \tau} \right) = 0 \quad \text{for} \quad |\tau| \leq |t|/\alpha.
\]

(2.50)

Thus, provided that the scalar constant \( \alpha \leq 1/2 \), the proposed class of kernels satisfies the time-support property.

Similarly, if the signal is band-limited, it is desirable to have a resulting TFD limited to the same band, i.e., if \( S(\omega) = 0 \) for \( |\omega| > \Omega \), then \( C_s(t, \omega; \phi) = 0 \) for \( |\omega| > \Omega \). This frequency-support property holds given the kernel follows

\[
\int_{-\infty}^{\infty} e^{-j\omega \tau} d\tau = 0 \quad \text{for} \quad |\xi| < 2|\omega|.
\]

(2.51)

Fourier transform of the radial-\( \delta \) kernel gives

\[
\int_{-\infty}^{\infty} e^{-j\omega \tau} \phi_{\delta}^n(\xi, \tau) d\tau = \frac{2\sqrt{\pi} \Gamma(n/2)}{\alpha \xi \Gamma(n/2 - 1/2)} \left[ 1 - \frac{\omega^2}{\alpha^2 \xi^2} \right]^{(n-3)/2} \Pi \left( \frac{\omega}{2\alpha \xi} \right) = 0 \quad \text{for} \quad |\xi| \leq |\omega|/\alpha.
\]

(2.52)

Thus, provided that \( \alpha \leq 1/2 \) frequency-support property holds.

We have shown that proposed radial-\( \delta \) kernels satisfy all the desirable properties shared by the known kernels, thus resulting TFDs are easily interpretable for information extraction, and directly comparable with the existing distributions.
2.5 Cross-Term Reduction

Due to the quadratic nature of the Cohen class of TFDs, cross-terms appear in the distribution for the multi-component signals. These cross-terms or interference terms are hard to interpret, and do not represent the true spectral content of the original signal, thus are considered to be artifacts. In this Section, we derive analytical expressions for the auto-terms and cross-terms for a simple multi-component signal, and in the next Section we show, using simulated signals, that the proposed radial-δ kernels are capable of reducing these cross-terms effectively, while achieving good time and frequency resolutions.

We illustrate auto-term and cross-term generation by using a two-component signal. For simplicity, we use a sum of two sinusoids with constant amplitudes, where the analytic form is given by

\[ s(t) = A_1 e^{j \omega_1 t} + A_2 e^{j \omega_2 t}. \]

Then we have

\[ s(\mu + \tau/2) s^*(\mu - \tau/2) = A_1^2 e^{j \omega_1 \tau} + A_2^2 e^{j \omega_2 \tau} + 2A_1A_2 e^{j(\omega_1 + \omega_2)\tau/2} \cos(\omega_1 - \omega_2)\mu. \] (2.53)

Thus, \( n \)th order radial-δ kernel based TFD can be written as

\[ C_n^s(t, \omega) = C_{n AT1}^m(t, \omega) + C_{n AT2}^m(t, \omega) + C_{n CT}^m(t, \omega), \] (2.54)

where \( C_{n AT1}^m(t, \omega) \) is the first auto-term resulting from \( A_1^2 e^{j \omega_1 \tau} \), \( C_{n AT2}^m(t, \omega) \) is the second auto-term resulting from \( A_2^2 e^{j \omega_2 \tau} \), and finally \( C_{n CT}^m(t, \omega) \) is the cross-term resulting from the last term of (2.53).

The first auto-term \( C_{n AT1}^m(t, \omega) \) simplifies to

\[
C_{n AT1}^m(t, \omega) = \frac{A_1^2 \Gamma\left(\frac{n}{2} + 1\right)}{\alpha \sqrt{\pi} \Gamma\left(\frac{n}{2} + rac{1}{2}\right)} \int \frac{1}{\tau} e^{-j(\omega_1 - \omega_2)\tau} \int \left[1 - \frac{(t - \mu)^2}{\alpha^2 \tau^2}\right]^{\frac{\alpha^2 - \frac{1}{2}}{2}} \Pi\left(\frac{t - \mu}{2\alpha \tau}\right) d\mu d\tau
= 2\pi A_1^2 \delta(\omega - \omega_1), \] (2.55)

where \( \delta(\cdot) \) is the Dirac delta function, and similarly for \( C_{n AT2}^m(t, \omega) \). Thus, auto-terms represent the true energy of the signal at each frequencies.

The cross-term \( C_{n CT}^m(t, \omega) \) is given by
\[ C_{CT}^n(t, \omega) = \frac{2A_1A_2\Gamma\left(\frac{n}{2} + 1\right)}{\alpha \sqrt{\pi} \Gamma\left(\frac{n}{2} + \frac{1}{2}\right)} \int \frac{1}{\tau} e^{-j(\omega - \frac{\omega_1 + \omega_2}{2})\tau} \times \int \left[ 1 - \frac{(t - \mu)^2}{\alpha^2 \tau^2} \right]^{\frac{n}{2} - \frac{1}{2}} \Pi\left(\frac{t - \mu}{2\alpha \tau}\right) \cos (\omega_1 - \omega_2)\mu \, d\mu \, d\tau \]

\[ = \frac{8A_1A_2}{\alpha \omega_d} \cos \omega_d t \sqrt{1 - \left(\frac{\omega - \omega_m}{\omega_d}\right)^2} \Pi\left(\frac{\omega - \omega_m}{2\omega_d}\right), \quad (2.56) \]

where \( \omega_m \) is the average of the two frequencies, i.e., \( \omega_m = (\omega_1 + \omega_2)/2 \), and \( \omega_d \) is the difference between the two frequencies, i.e., \( \omega_d = |\omega_1 - \omega_2| \). The cross-term is centered at \( \omega_m \), thus appears in between the auto-terms in the time-frequency plane. Also, it should be noted that cross-term amplitude is inversely proportional to \( \omega_d \), thus closer the auto-term frequencies, higher cross-term energy appears in the TFD. The cross-terms do not correspond to the original signal, and therefore we require the TFD to suppress these cross-terms. In Section 2.7, we show how radial-\( \delta \) kernel based TFDs effectively suppress the cross-terms while maintaining a good auto-term resolution.

### 2.6 Discrete Radial-\( \delta \) Distributions

In this Section, we derive discrete-time versions of the proposed radial-\( \delta \) distributions for a complex valued discrete-time signal \( s(m) \). Discrete versions are useful for the numerical implementation of the TFDs. The discrete radial-\( \delta \) TFD can be written as

\[ C_{s}^n(m, \omega) = \frac{\Gamma(n/2)}{2\alpha \pi^{n/2}} \sum_{\tau = -\infty}^{\infty} \frac{1}{\tau} e^{-2j\omega\tau} \sum_{\mu = -\infty}^{\infty} \left(1 - \left(\frac{\mu - m}{2\alpha \tau}\right)^2\right)^{(n-3)/2} \times \Pi\left(\frac{\mu - m}{4\alpha \tau}\right) s(\mu + \tau) s^*(\mu - \tau), \quad (2.57) \]

where \( m \) and \( \tau \) are discrete variables of time and time-lag, respectively, and \( \omega \) is a continuous variable. The rectangle function limits the inner summation to the interval \([m - 2\alpha|\tau|, m + 2\alpha|\tau|]\). Also by changing the variables \((\mu - m) \rightarrow \mu\), we
have
\[
C_n^s(m, \omega) = \frac{\Gamma(n/2)}{2\alpha \pi^{3/2} \Gamma(n/2 - 1/2)} \sum_{\tau=-\infty}^{\infty} \frac{1}{\tau} e^{-2j\omega\tau} \sum_{\mu=-2\alpha|\tau|}^{2\alpha|\tau|} \left(1 - \left(\frac{\mu}{2\alpha\tau}\right)^2\right)^{(n-3)/2} \\
\times s(m + \mu + \tau) s^*(m + \mu - \tau),
\]
(2.58)

Similar to other Cohen class of quadratic TFDs, radial-δ distributions are periodic with respect to the frequency variable \(\omega\), with a period of \(\pi\). Thus, by letting \(\omega = \pi k/M\), fast Fourier transform (FFT) can be used to compute the radial-δ TFDs efficiently. Also, for practical computation outer summation limits should be finite. Therefore, we use a rectangle window of \(M + 1\) samples to slide along the time axis at each instance \(m\). By setting \(\omega = \pi k/M\) and limiting \(\tau\) to \(M + 1\) rectangle window, we get
\[
C_n^s(m, k) = \frac{\Gamma(n/2)}{2\alpha \pi^{3/2} \Gamma(n/2 - 1/2)} \sum_{\tau=-M/2}^{M/2} e^{-2j\pi k\tau/M} \sum_{\mu=-2\alpha|\tau|}^{2\alpha|\tau|} \frac{1}{|\tau|} \left(1 - \left(\frac{\mu}{2\alpha\tau}\right)^2\right)^{(n-3)/2} \\
\times s(m + \mu + \tau) s^*(m + \mu - \tau),
\]
with
\[
\frac{\Gamma(n/2)}{2\alpha \pi^{3/2} \Gamma(n/2 - 1/2)} \sum_{\mu=-2\alpha|\tau|}^{2\alpha|\tau|} \frac{1}{|\tau|} \left(1 - \left(\frac{\mu}{2\alpha\tau}\right)^2\right)^{(n-3)/2} s(m + \mu + \tau) s^*(m + \mu - \tau)\bigg|_{\tau=0} = s(m) s^*(m),
\]
(2.59)

where \(m\) and \(k\) correspond to discrete time and frequency variables, respectively.

2.7 Simulation Results

In this Section, we apply proposed radial-δ kernel based TFDs in analyzing a simulated multi-component signal with added Gaussian noise. The simulation results show the superiority of novel higher order kernels introduced in this Chapter compared to those previously derived. Further, we perform a comparison of the proposed kernel class with the CWD.
We use a two-component signal consisting of a frequency modulated (FM) component, and a linear chirp component given by

$$s(t) = \cos\left(2\pi f_1 t + \frac{\Delta f}{f_m} \sin(2\pi f_m t)\right) + \cos\left(2\pi (f_2 + \frac{\ell}{2}) t\right) + n(t),$$  \hspace{1cm} (2.60)

where the FM component has a center frequency of $f_1$, a maximum frequency deviation of $\Delta f$, and a modulation frequency of $f_m$. The chirp component has a starting frequency of $f_2$ and a chirp rate of $\ell$. Additive white Gaussian noise (AWGN) component is represented by $n(t)$.

Radial-$\delta$ kernel based TFDs are used to perform the time-frequency analysis of the simulated two-component signal with the parameters set to $f_1 = 14$Hz, $\Delta f = 5$Hz, $f_m = 0.04$Hz, $f_2 = 2$Hz, $\ell = 0.16$Hz/s, and SNR = 15dB. Signal parameters were chosen to simulate both close and remote interactions of the two components, i.e., both large and small $\omega_d$ will occur at different points in time.

Simulation results are shown in Figure 2.5. The scalar constant $\alpha$ is set to 0.4, thus all the desirable TFD properties including time and frequency support are satisfied. Figure 2.5 (a) and (b) show Born-Jordan and Bessel distributions respectively for the simulated two-component signal. Both Born-Jordan and Bessel distributions have considerable amounts of cross-terms in the time-frequency plane. Thus, existing kernels, i.e., kernels up to and including order $n = 4$ suffer from large interference terms, as well as show poor auto-term resolution. On the other hand, TFDs based on radial-$\delta$ kernels of order 5 and above show a sharp auto-term resolution as shown in Figure 2.5 (c)-(e), and their cross-terms are significantly low compared to the lower order kernels. It should be emphasized that order 5 and above radial-$\delta$ kernels are newly derived using the $n$-dimensional Fourier transform based framework introduced in this Chapter. Among higher order kernel based TFDs the order 5 radial-$\delta$ kernel based TFD shows the least interference terms, thus we conclude that $\phi_5^\delta(\xi, \tau) = 3j_1(\alpha \xi \tau)/\alpha \xi \tau$, a novel kernel introduced in this Chapter, gives the best representation within the radial-$\delta$ kernel class for the simulated two-component signal.

The CWD [35] is well known for its successful suppression of cross-terms. Here, we compare the proposed radial-$\delta$ kernel based TFDs with the CWD. The
Figure 2.5: Time-frequency representation of the two-component signal (2.60) using (a) Born-Jordan distribution, (b) Bessel distribution, (c)-(e) TFDs based on order 5-7 radial-$\delta$ kernels ($\alpha = 0.4$).
CWD uses a parameter $\sigma$ to control the cross-terms, and it is suggested that a good choice of $\sigma$ is in the range from 0.1 to 10 [35]. We present the CWD for the same two-component signal described above for a range of $\sigma$ values. The Figure 2.6 shows the simulation results for $\sigma = 0.1, 0.5, 1, 5,$ and 10. Distributions with $\sigma < 0.5$ or $\sigma > 5$ suffer from large interference terms, and simulations show that the best Choi-Williams time-frequency representation is achieved at $\sigma = 1$ (Figure 2.6(c)). Both the 5th order radial-$\delta$ kernel based TFD in the proposed class and the CWD with $\sigma = 1$ do not contain significant cross-terms, but the auto-term resolution of the 5th order radial-$\delta$ kernel based TFD is better compared to the CWD.

Thus, simulation results indicate the superiority of the novel radial-$\delta$ kernels in terms of cross-term reduction and auto-term resolution compared to the existing distributions such as Born-Jordan, Bessel, and Choi-Williams.

### 2.8 Kaiser Window based Kernel Design

The Kaiser window has been used extensively in designing finite impulse response digital filters, and various other digital signal processing applications [66,73]. It provides an asymptotic approximation to the prolate spheroidal wave functions, which have been shown to provide the greatest concentration of energy simultaneously in time and frequency [73]. As prolate functions are difficult to compute, Bessel function based Kaiser window provides a good alternative to achieve concentration of energy in time and frequency. The Kaiser window is given by

$$w_K(t) = \begin{cases} I_0 \left( \beta \sqrt{1 - \left( t/\tau \right)^2} / I_0(\beta) \right) & |t| \leq \tau \\ 0 & |t| > \tau, \end{cases}$$

(2.61)

where $I_0(\cdot)$ is the zeroth order modified Bessel function of the first kind.

As described in the Section 2.4.3, the shape of the window function in the TFD effectively controls the auto-term resolution and cross-term reduction. Thus in order to utilize the desirable energy concentration properties of the Kaiser window, we define a kernel function based on the Fourier transform of the Kaiser
Figure 2.6: Time-frequency representation of the two-component signal (2.60) using Choi-Williams distribution with (a) $\sigma = 0.1$, (b) $\sigma = 0.5$, (c) $\sigma = 1$, (d) $\sigma = 5$, and (e) $\sigma = 10$. 
window as
\[
\phi_K(\xi, \tau) = \frac{\sinh \left( \beta \sqrt{1 - \frac{\alpha^2 \xi^2 + \tau^2}{\beta^2}} \right)}{\sinh(\beta) \sqrt{1 - \frac{\alpha^2 \xi^2 + \tau^2}{\beta^2}}},
\]
(2.62)
where \( \alpha \) and \( \beta \) are real parameters. In the special case where \( \beta = 0 \), the kernel is reduced to the sinc kernel [38], given by \( \phi(\xi, \tau) = \sin(\alpha \xi \tau) / (\alpha \xi \tau) \). It will result in the Born-Jordan distribution which has been previously discussed.

We call this novel kernel, the sinhc kernel. The sinhc kernel satisfies all the desirable criteria of the Cohen class of distributions given in Table 2.2. As it is a real-valued product kernel, the reality property is satisfied. Also the kernel is independent of time and frequency variables, thus time shifting and frequency shifting properties are satisfied. We have \( \phi_K(\xi, 0) = 1 \forall \xi \), and \( \phi_K(0, \tau) = 1 \forall \tau \), thus time marginal and frequency marginal properties are satisfied, respectively. Additionally, we get
\[
\frac{\partial}{\partial \tau} \left[ \frac{\sinh \left( \beta \sqrt{1 - \frac{\alpha^2 \xi^2 + \tau^2}{\beta^2}} \right)}{\sqrt{1 - \frac{\alpha^2 \xi^2 + \tau^2}{\beta^2}}} \right] \bigg|_{\tau=0} = 0,
\]
(2.63)
thus instantaneous frequency property is satisfied, and similarly for the group delay property. Finally, we have
\[
\int_{-\infty}^{\infty} e^{-j\xi t} \frac{\sinh \left( \beta \sqrt{1 - \frac{\alpha^2 \xi^2}{\beta^2}} \right)}{\sinh(\beta) \sqrt{1 - \frac{\alpha^2 \xi^2}{\beta^2}}} d\xi = \begin{cases} 
\frac{\beta}{2\alpha \tau \sinh(\beta)} I_0 \left( \beta \sqrt{1 - \left( \frac{t}{\alpha \tau} \right)^2} \right) & |\tau| > |t| / \alpha \\
0 & |\tau| \leq |t| / \alpha,
\end{cases}
\]
(2.64)
thus provided that the scalar constant \( \alpha \leq 1/2 \), the time-support property is satisfied, and the frequency-support follows similarly.

The resulting TFD of the sinhc kernel can be derived by using the generic formula for Cohen class TFDs (2.4). By substituting (2.62) into (2.4) and integrating with respect to \( \xi \) we get
\[
K_s(t, \omega) = \frac{1}{4\alpha \pi \sinh(\beta)} \int \frac{1}{\tau} e^{-j\omega \tau} \int I_0 \left[ \beta \sqrt{1 - \left( \frac{\mu - t}{\alpha \tau} \right)^2} \right] \\
\times \Pi \left( \frac{\mu - t}{2\alpha \tau} \right) s(\mu + \tau/2) s^*(\mu - \tau/2) d\mu d\tau.
\]
(2.65)
We name $K_s(t, \omega)$, the Kaiser distribution, due to the appearance of a Kaiser window in the TFD. The Kaiser distribution is a member of Cohen class, and it satisfies all the desirable distribution properties as already proven in terms of its kernel function.

The shape of the Kaiser window can be used to control the trade-off between auto-term resolution and cross-term energy in the TFD. This is analogous to use of parameter $\beta$ in the Kaiser window to trade-off main-lobe width and relative side-lobe amplitude in the digital filter design applications. The parameter $\beta$ controls the shape of the time correlated window function in the Kaiser distribution, and Figure 2.7 shows two instances of the window for different $\beta$ values. When $\beta = 12$ a narrow and sharp window is observed, and this is suited for mono-component signals or multi-component signals where components have a wide separation in the time-frequency plane to achieve high time and frequency resolutions. On the other hand, $\beta = 4$ yields to a slightly wider window, and is suited for multi-component signals with components located in close proximity in the time-frequency plane to effectively reduce the possible interference terms.

Figure 2.7: The effect of changing $\beta$ on the time correlated window function.

The Kaiser distribution is used to perform the time-frequency analysis of two-component signal described in Section 2.7. The parameters of the FM signal are
set to $f_1 = 12\text{Hz}$, $\Delta f = 4\text{Hz}$, $f_m = 0.04\text{Hz}$, and those of the linear chirp signal set to $f_2 = 2\text{Hz}$, and $l = 0.2\text{Hz/s}$. AWGN level is set to SNR = 15dB. Figures 2.8 and 2.9 show the simulation results for $\beta = 12$ and $\beta = 4$, respectively. Simulations confirm that low values of $\beta$ can smooth out the interference terms effectively in the time-frequency plane, but at the expense of slightly reduced auto-term resolution.

Figure 2.8: Kaiser distribution with $\beta = 12$ for a sum of frequency modulated and linear chirp signals.

2.9 Summary and Contributions

1. A general framework based on multi-dimensional Fourier transform of a radially symmetric function is proposed for deriving kernels for the Cohen class of quadratic TFDs. The framework guarantees that resulting distributions satisfy all the desirable distribution properties including time and frequency support. The proposed method generalizes and extends the currently existing reduced interference distributions framework.

2. Under the proposed framework, a kernel formula, the order $n$ radial-$\delta$ kernel, is derived from a radial delta function. This radial-$\delta$ kernel formula
subsumes existing and known kernels of Margenau-Hill, Born-Jordan, and Bessel distributions. Radial-δ kernel class not only unifies number of known kernels, but also introduces highly structured new kernels with distinctive characteristics by only varying the dimension of the base radial function.

3. Higher order radial-δ kernels are shown to be more effective in the time-frequency analysis of multi-component signals. Compared to the existing low order kernels, they are capable of reducing interference terms in the time-frequency plane for multi-component signals, while achieving good time and frequency resolutions.

4. A novel sinhc kernel, which generates a Kaiser window based TFD is introduced. The Kaiser distribution belongs to the Cohen class of TFDs, and satisfies desirable distribution properties. By controlling the shape of the Kaiser window, auto-term resolution and cross-term magnitudes can be successfully traded.
Chapter 3

Time-Frequency Analysis of Atrial Fibrillation Electrocardiograms

3.1 Introduction

The electrocardiogram (ECG) is used as the gold standard for detecting cardiovascular disorders, and is the most widely used method for measuring and diagnosing abnormal rhythms of the heart [23]. The ECG records body surface potentials of a subject, which is generated due to the electrical activity of the heart. In the early days of ECG, making electrodes sensitive enough to measure small potential differences in the order of milli-Volts was a challenge. The Dutch scientist Willem Einthoven won the Nobel prize in medicine in 1924 for his invention of the string galvanometer, in which he introduced the first practical ECG measuring mechanism. Since then ECG has been widely used in clinical practice, and also for research purposes in assessing cardiovascular health. Due to non-invasive nature of the ECG, it has very low risk, and convenient to undertake in clinical as well as in non-clinical conditions. Among number of other usages, ECG has been used for diagnosing and analyzing number of cardiac arrhythmia conditions. In this Chapter, we focus on atrial fibrillation (AF), one of the most common cardiac arrhythmia condition which could be detected from the ECG.

AF is the most common sustained cardiac arrhythmia condition in clinical
practice increasing in prevalence with age [52]. AF accounts for approximately one-third of the hospitalizations due to cardiac rhythm disturbances. During an AF episode, one regular wave (P-wave) of the ECG is replaced by rapid oscillations called fibrillatory waves. Thus, ECG signal is a convenient source of detecting AF episodes. Though AF detection from the ECG is relatively straightforward, further analysis of AF poses several problems. First, atrial activity is significantly weak compared to the ventricular activity, thus a typical ECG is dominated by the electrical signals due to the depolarization and repolarization of the ventricles. Thus, extracting atrial activity requires canceling out more dominant ventricular components. In order to solve this problem, we introduce an orthonormal basis based interpolation technique for atrial activity extraction. Second, fibrillatory wave frequency, which contains the information on the severity and possible duration of the AF episodes, changes in time. Thus, by monitoring changes in fibrillatory wave frequencies, treatment methods can be tailored. The novel time-frequency distributions (TFDs) discussed in Chapter 2 are well suited for analyzing such time-varying AF frequencies.

A number of TFD based techniques have been proposed in the literature for tracking dominant AF frequency. Stridh et al. [131, 133] employed Wigner-Ville and Choi-Williams TFDs for analyzing time variation of spectral content of AF, but the accuracy and noise robustness of the algorithms are inconclusive. As AF activity has a substantially lower amplitude in the ECG compared to the ventricular activity and almost undistinguishable from noise and other ECG artifacts, it is important that a given method has a significant robustness to noise. Sandberg et al. [120] employed hidden Markov model based technique for frequency tracking of AF, but the performance at low SNR values has not been studied. Thus, accurate estimation of time-varying AF frequencies still poses a challenge. In this Chapter, we introduce a method for extracting the AF content from ventricular-dominant single lead ECG, and further apply novel TFD techniques for accurate estimation and tracking of AF frequencies.

This Chapter is organized as follows: In Sections 3.2 and 3.3, we provide a background on ECG and AF respectively, linking the physiological basis and current signal processing techniques used in ECG and AF analysis. Then in Section 3.4, we conduct a preliminary study of AF characterization based on
Bessel distribution, an existing member of the proposed radial-$\delta$ class described in the previous Chapter. In Section 3.5, we address the problem of extracting the low amplitude atrial activity from the surface ECG suppressing the dominant ventricular components by introducing an orthonormal basis based interpolation technique. In the following Section, we combine the atrial activity extraction and time-frequency analysis into a single algorithm generating a fast, one-step method for time-frequency analysis of AF ECGs. Finally, we show the superiority of the novel higher order radial-$\delta$ kernel based TFDs in time-frequency analysis of AF ECGs compared to the existing TFDs.

### 3.2 Electrocardiograms

The electrical activity of the human heart during a cardiac cycle induces a potential difference on the body surface in the order of milli-Volts. This potential difference can be measured by placing two surface electrodes, one on the subject’s upper torso, while using a second electrode as a reference. This signal is known as the ECG signal, and is used as the gold standard for diagnosing cardiac disorders. A typical ECG signal of a healthy subject for one cardiac cycle is shown in Figure 3.1. Conventionally, one ECG cycle is divided into four parts, P-wave, QRS complex, T-wave, and U-wave. The U-wave is hardly noticeable in an ECG obtained in a typical experiment, and therefore of less practical importance. The P-wave of the ECG is created by the depolarization of the atria (two upper chambers of the heart), while the QRS complex and the T-wave are generated by depolarization and repolarization of the ventricles (two lower chambers of the heart), respectively [37]. The QRS complex is refereed to as the heart beat, and the time interval between two R-peaks is known as the inter beat interval or the RR-interval. The analysis of RR-intervals gives important information on control of the autonomic nervous system, and we shall discuss new point process algorithms for inter beat interval analysis in the following Chapters. In this Chapter, however, we analyze the ECG waveform for AF arrhythmia analysis.

In general, beat detection and classification are prerequisites for most ECG signal processing techniques. Beat detection involves detecting QRS complexes and R-peaks from the ECG signal. This is crucial in basic heart rate monitoring
Time-Frequency Analysis of Atrial Fibrillation Electrocardiograms

50

Figure 3.1: A typical ECG waveform of a healthy subject during one cardiac cycle with conventional nomenclature.

systems, and also as a preprocessing stage for other ECG applications. A number of techniques have been used in beat detection including neural networks [105], matched filtering and wavelet transforms [46], hidden Markov and state space models [33], and Hermite expansion based models [78].

Once the beats are identified, they need to be classified based on their morphological features. This is of special interest in the Holter monitoring systems. The Holter monitor is an ambulatory ECG monitoring system which is usually worn for extended period of time during normal daily activities. As the patient is not closely monitored by a qualified health professional during the ambulatory monitoring, an intelligent Holter monitor should be able to identify and classify between the sinus beats (normal healthy beats), ectopic beats, and escape beats. Ectopic beats occur when depolarization originates outside the sinoatrial node of the heart. This unusual depolarization results in premature atrial and ventricular waveforms. Escape beats are similar to ectopic beats, in that they are an initiation of a depolarization wavefront outside the sinoatrial node. However, escape beats are normal, compensatory response, and a fail-safe functionality of the heart [37]. Linear discriminant analysis, support vector machines [104], hidden Markov models [33], artificial neural networks and hybrid fuzzy networks [105] are often used in the beat classification applications. It has been shown that beat classification based on artificial intelligence based supervised and unsupervised
3.3 Atrial Fibrillation

learning algorithms could give insight into individual subject classification [19].

ECG data compression, and noise and artifacts cancelation is necessary in any practical ECG data collection system. Data compression could be loss or lossless, and discrete cosine transform [4], Karhunen-Loève transform [101], wavelet transform [30, 45], and recently Burrows-Wheeler transform [6] have proven to be good compression techniques for ECG data. Noise and artifacts of a typical ECG mainly consist of power-line interference, thermal noise, and motion artifacts. The power-line interference can be canceled out by applying a notch filter (a band-stop filter with a narrow stop-band) at 50 or 60Hz [51]. Thermal noise can be suppressed by using linear filtering, Wiener filtering [81], Bayesian filtering [119], or wavelet denoising techniques [1]. The artifacts due to motion and muscle activity is the hardest to discriminate, and techniques such as Kalman filtering [118], principal component analysis, independent component analysis [12], and neural networks [145] have proven to yield good results.

Fiducial points extraction and segmentation of ECG is also useful in analyzing a particular ECG wave segment. It helps separating atrial and ventricular segments in the ECG, and also provides quantitative measures for ST and QT segments for ischemia analysis. Fuzzy logic, hidden Markov models, and wavelet transforms based techniques have been employed in extracting fiducial points in the ECG [37]. After these preprocessing stages, ECG signal can be used in number of different applications such as arrhythmia analysis or ischemia detection. In the next Section, we introduce atrial fibrillation, a common arrhythmia condition detectable from the ECG.

3.3 Atrial Fibrillation

Atrial fibrillation (AF) is the most commonly found cardiac arrhythmia condition, and results in significant morbidity, mortality, and health care cost [52]. AF is characterized by the replacement of consistent P-waves on the ECG by rapid oscillations (fibrillatory waves) that vary in amplitude, frequency, and shape. Additionally, an irregular ventricular response is usually associated with an AF episode. The changes in the P-wave are due to the uncoordinated atrial activation with deterioration of the atrial mechanical function. The prevalence of AF is
0.4% to 1% in the general population, but increases up to 8% for the population over age of 80 [127]. AF is also associated with an increased risk of stroke [52,127]. AF may occur in association with other arrhythmia conditions like atrial flutter or atrial tachycardia, thus a given detection and analysis method should be sensitive enough to differentiate these different atrial arrhythmia conditions.

Depending on the time taken for an AF episode to terminate spontaneously, it has been divided into two categories, called paroxysmal and persistent. Persistent AF is defined as sustained beyond seven days without terminating spontaneously, regardless of the possibility of treatment based early termination. Otherwise, it is called paroxysmal AF. Though paroxysmal AF is characterized as AF episodes up to seven days, even episodes smaller than 30 seconds may be of importance in certain clinical conditions, especially when assessing the effectiveness of a therapeutic intervention [52,83]. Therapeutic intervention for AF involves either pharmacological therapy or direct current cardioversion. AF episodes with low fibrillatory frequency are more probable to terminate spontaneously, and respond better to antiarrhythmic drugs or cardioversion. On the other hand, AF episodes with high fibrillatory frequency are more often persistent [21].

The P-wave of the ECG reflects the atrial activity, whereas the QRS complex and T-wave reflect ventricular activity. One of the major challenges is to extract the atrial activity from the ECG, as it has substantially low amplitude compared to the ventricular activity. Extracting atrial activity is highly useful in analyzing number of atria related disorders like AF or atrial flutter. Several approaches have been taken for this purpose, including average beat subtraction (ABS), template matching [22, 125], and spatiotemporal cancelation of ventricular activity [28]. Later, principal component analysis and independent component analysis techniques have been used to estimate the atrial activity [113,114], but they have not been able to show total satisfactory solutions.

Previous studies have shown that spectrum of the atrial activity of the ECG under AF has a dominant peak (AF frequency), and there is a significant correlation between spontaneous or drug induced termination of AF and the time variation of AF frequency [22], indicating the importance of accurately tracking the AF frequency in time. This dominant fibrillation frequency decreases as atrial activation progressed in patients with paroxysmal AF [83]. Thus, esti-
ation of AF frequency not only gives insight into type of AF, but also helps identifying a particular treatment method, if required. Stridh et al. [131, 133] employed Wigner-Ville distribution and Choi-Williams distribution for analyzing time variation of the spectral content of AF, but the accuracy and noise robustness of the algorithms are inconclusive. As AF activity has a substantially low amplitude in the ECG, and almost undistinguishable from noise and other ECG artifacts, it is important that a given method has a significant robustness to noise. Sandberg et al. [120] employed hidden Markov model based method for frequency tracking of AF, but the performance at SNR less than 0dB has not been studied. In this Chapter, we propose the Bessel distribution and novel higher order radial-δ kernel based TFDs for tracking AF frequency in ECG with a good frequency resolution and a low RMS error.

3.4 Bessel Distribution based AF Analysis

3.4.1 Bessel Distribution

Bessel distribution [62] is a member of the Cohen class of TFDs [39]. In Chapter 2, we showed that Bessel distribution also belongs to the radial-δ class of TFDs, which is a new sub-class which we developed in the previous Chapter. The kernel of the Bessel distribution is given by

\[ \phi(\xi, \tau) = \frac{2 J_1(\alpha \xi \tau)}{\alpha \xi \tau}, \]

where \( J_1(\cdot) \) is the Bessel function of first kind of order one, and \( \alpha > 0 \) is a scaling factor. The time and frequency support properties of the distribution are preserved under the condition \( \alpha \leq 0.5 \). The explicit form of the Bessel distribution is given by

\[
BD_s(t, \omega) = \frac{1}{\alpha \pi^2} \int \frac{1}{\tau} e^{-j\omega \tau} \int \left[ 1 - \left( \frac{\mu - t}{\alpha \tau} \right)^2 \right]^{1/2} \Pi \left( \frac{\mu - t}{2\alpha \tau} \right)
\times s(\mu + \tau/2) s^*(\mu - \tau/2) d\mu d\tau.
\]

Due to the nonlinear nature of the Bessel distribution, cross-terms appear
in the time-frequency plane for a multi-component signal. In Chapter 2, we showed that for a sum of two complex exponentials with constant amplitudes, i.e., \( s(t) = A_1e^{j\omega_1t} + A_2e^{j\omega_2t} \), the cross-term energy distribution is given by

\[
BD_{s,CT}(t, \omega) = \frac{8A_1A_2}{\alpha \omega_d} \cos \omega_d t \sqrt{1 - \frac{(\omega - \omega_m)^2}{\alpha^2 \omega_d^2}} \Phi \left( \frac{\omega - \omega_m}{2\alpha \omega_d} \right), \tag{3.3}
\]

where \( \omega_m = (\omega_1 + \omega_2)/2 \), and \( \omega_d = |\omega_1 - \omega_2| \). At a given time \( t = t_0 \), (3.3) is a half an ellipse centered at \((\omega_m, 0)\) and has semi axes \( (8A_1A_2 \omega_d t_0)/(\alpha \omega_d) \) and \( \alpha \omega_d \). Thus, the energy distribution of the cross-term can be controlled by varying \( \alpha \), as shown in Figure 3.2. Large \( \alpha \) reduces cross-term energy but at the expense of slightly reduced auto-term resolution. Also, there is an upper limit on \( \alpha \), i.e., \( \alpha \leq 0.5 \) in order to satisfy time and frequency support.

Cross-term energy distribution given in (3.3) is a good approximation for a sum of frequency modulated signals as shown in Figure 3.3, provided that \( \| \max(\Delta \omega_1, \Delta \omega_2) \| \ll \| \omega_1 - \omega_2 \| \), and given

\[
s(t) = A_1 \cos [\omega_1 t + \frac{\Delta \omega_1}{\omega_{f_1}} \sin (\omega_{f_1} t)] + A_2 \cos [\omega_2 t + \frac{\Delta \omega_2}{\omega_{f_2}} \sin (\omega_{f_2} t)]. \tag{3.4}
\]

\( s(t) \) comprises of two sinusoidally frequency modulated components, where \( A_k \) (\( k = 1, 2 \)) is the amplitude, \( \omega_k \) is the center frequency, \( \omega_{f_k} \) is the frequency of the frequency modulation, and \( \Delta \omega_k \) is the maximum deviation from the center fre-
quency. Inequality holds if two components are relatively distant compared to the maximum frequency deviations of each component.

Figure 3.3: Bessel distribution for sum of two frequency modulated signals, $\alpha = 0.1$ (left), $\alpha = 0.4$ (right). At a higher value of $\alpha$, cross-term energy reduces but at the slight expense of reduced auto-term resolution.

AF signal has been often modeled as a sum of frequency modulated signals [130]. Therefore, we assert that the Bessel kernel and similarly other higher order radial-$\delta$ kernels based TFDs are suited for analyzing time variation of AF frequency in the presence of noise.

### 3.4.2 AF Model

Fibrillatory waves generated during AF episodes are time-varying sinusoidal in nature, and also include harmonic components of the fundamental fibrillatory waves. Thus, AF signal has been mathematically modeled by a sum of frequency modulated sinusoidal with time varying amplitude and its harmonics [130], and is given by

$$s(t) = \sum_{k=1}^{M+1} a_k(t) \cos \left( k\omega_0 t + \frac{\Delta \omega}{\omega_m} \sin(\omega_m t) \right) + n(t),$$

where $a_k(t) = e^{-\gamma (k-1)} \left( a + \Delta a \sin(\omega_a t) \right)$, $\omega_0$ is the fundamental AF frequency, $\omega_m$ is the frequency of frequency modulation, $\Delta \omega$ is the maximum frequency deviation, $M$ is the number of harmonics excluding the fundamental, $\gamma$ is the decaying factor of harmonics, $a$ is the average amplitude of the fundamental, $\omega_a$
Figure 3.4: A time window of a 3s interval of simulated AF signal (3.5) at
SNR = 20dB ($\omega_0 = 14\pi$rad/s, $\omega_m = 0.08\pi$rad/s, $\Delta \omega = 2\pi$rad/s, $M = 3$,
$\gamma = 1$, $a = 100\mu V$, $\omega_a = 0.16\pi$rad/s, $\Delta a = 20\mu V$).

is the frequency of amplitude modulation, and $\Delta a$ is the maximum amplitude
deviation. $n(t)$ represents Gaussian noise, artifacts from insufficient ventricular
activity cancelation, and other ECG artifacts. According to the model, AF
frequency is given by

$$\omega_{AF}(t) = \omega_0 + \Delta \omega \cos(\omega_m t).$$

The objective is to accurately estimate $\omega_{AF}(t)$, especially when $n(t)$ is sig-
nificant compared to the amplitude of the fundamental $a_1(t)$ as AF activity has
a low amplitude within the ECG. A time window of the simulated AF signal is
shown in Figure 3.4.

3.4.3 Results and Comparison with STFT

Simulations were performed using (3.5) to generate AF signals where AWGN was
used for $n(t)$ at different SNR settings. A numerical implementation of the Bessel
distribution can be obtained from the discrete radial-$\delta$ distributions described in
Chapter 2. $\alpha$ was set to 0.5 in order to minimize the cross-term effects, and at the
same time preserving time and frequency support properties of the distribution.
In order to analyze the performance of the Bessel distribution, it was compared to
the short-time Fourier transform (STFT). Results for SNR = 5dB, 0dB, and -5dB
are shown in Figures 3.5, 3.6, and 3.7, respectively. The results were analyzed using two performance measuring criteria, RMS error and frequency resolution.

Figure 3.5: Bessel distribution vs. STFT for simulated AF signal with AWGN at SNR = 5dB.

RMS error was used as the first performance measuring criteria of the algorithm. It measures the noise robustness and accuracy of a particular method in estimating the AF frequency under a noisy environment, and is given by

$$E_{RMS} = \sqrt{\langle [\omega_N(t) - \omega_{AF}(t)]^2 \rangle},$$  \hspace{1cm} (3.7)

where $\omega_N(t)$ is the estimated AF frequency using TFD under AWGN, $\omega_{AF}(t)$ is the actual AF frequency, and $\langle \cdot \rangle$ is the average over time. Simulation results for RMS error is given in Figure 3.8 for a range of SNR settings.

For all the SNR settings considered, i.e., SNR$\in [-5, 5]$, low RMS error was observed in Bessel distribution based AF frequency estimation compared to the STFT based estimation. Specially at low SNR levels Bessel distribution outperforms the STFT, and at an SNR of -5dB the RMS error was reduced by approximately 1Hz, from 1.8Hz to 0.8Hz. Given that atrial activity is less present in practical ECGs due to more dominant ventricular components, we observe high noise levels in the extracted AF waveforms. Thus, the improved performance of Bessel distribution at low SNR settings is highly desirable.
Figure 3.6: Bessel distribution vs. STFT for simulated AF signal with AWGN at SNR = 0dB.

Figure 3.7: Bessel distribution vs. STFT for simulated AF signal with AWGN at SNR = −5dB.
3.4 Bessel Distribution based AF Analysis

Figure 3.8: RMS error of Bessel distribution and STFT for simulated AF with AWGN at different SNR settings.

Frequency resolution was used as the second performance measuring criteria, and is estimated by the time average of 3dB bandwidth of the distribution. It is another measure of noise robustness in terms of the energy concentration in a noisy environment and is given by

\[
\hat{\omega}_{\text{max}}(t) + \frac{1}{2} \omega_r(t) \leq \int_{-\infty}^{\omega_r(t)} P_s(t, \omega) d\omega = 0.5 \int_{-\infty}^{\omega_{\text{max}}(t)} P_s(t, \omega) d\omega, \quad (3.8)
\]

where \( \omega_r(t) \) is defined as the frequency resolution, \( \omega_{\text{max}}(t) \) is the frequency where maximum power is observed, and \( P_s(t, \omega) \) is a particular TFD of a given AF signal. Frequency resolution indicates the level of unambiguity in estimating the AF frequency from the TFD. Frequency resolution at a particular SNR setting will be given by \( \langle \omega_r(t) \rangle \). Simulation results for the frequency resolution is given in Figure 3.9 for the same SNR range as above.

Bessel distribution achieves a better frequency resolution compared to the STFT for all SNR settings. For SNR values of 0dB and above, it is capable of concentrating more than half of AF signal power within a 0.5Hz frequency band. For the same range, the STFT only achieves a resolution of 1.5Hz on average, thus we observe an improvement of approximately 1Hz. For low SNR settings, the advantage of Bessel distribution over the STFT is even more apparent with
Figure 3.9: Frequency resolution of Bessel distribution and STFT for simulated AF with AWGN at different SNR settings.

Figure 3.10: Bessel distribution vs. STFT for the ECG record n02 of PhysioBank AF Termination Challenge Database [56].

A gain of around 4.5Hz at a SNR of -5dB. Thus, better AF frequency estimation with a high resolution can be obtained by Bessel kernel based TFD compared to the STFT. Later, we show that results could be further improved by applying higher order radial-δ kernel based TFDs on AF signals.

PhysioBank [56] is an annotated archive of recordings of physiological signals
widely used by the biomedical research community. One of the ECG databases in PhysioBank is the AF Termination Challenge Database, which includes one minute long ECG recordings exhibiting either self-terminating or sustained AF. We have applied Bessel distribution and STFT in analyzing AF frequency in AF Termination Challenge Database recordings, and Figure 3.10 shows an example. The results indicate that Bessel distribution achieves a high resolution without cross-terms, while STFT fails to indicate a continuous trace of the dynamic AF frequency.

3.5 Orthonormal Basis based Atrial Activity Extraction

Atrial activity extraction from the ECG is a prerequisite in analyzing the AF waveform. As spectral contents of atrial and ventricular components overlap with each other, linear filtering techniques fail to extract an uncorrupted atrial signal. Also, higher dominance of ventricular activity in the ECG makes the extraction of atrial activity non-trivial [21,113]. Two types of methods have been found in the literature for extracting atrial activity from the ECG, broadly named average beat subtraction (ABS) based methods, and blind source separation (BSS) based techniques.

First type of methods refereed to as ABS methods generate a template for the combined QRS complex and T-wave (QRS-T), which are dominant by the ventricular sources, and that template is subtracted by the ECG beat by beat in order to estimate the atrial signal. ABS methods assume the stationarity of the ECG signal, as reasonable number of beats are required to generate such a template based on the mean statistics. They also assume the time invariance of wave morphology, as the same template is subtracted from multiple beats. But both these assumptions do not hold in the presence of ectopic beats, movement of electrodes, random nature of the physiological processes, and the thermal noise. Thus, the resulting atrial signal of ABS methods often contain significant amount of residual QRS-T [130]. These residuals could be quite significant due to the order of magnitude difference in atrial and ventricular signals. The performance
could be further limited for signals with short durations, as constructing a good QRS-T template become difficult [86].

Second type of methods known as BSS based techniques, explore the spatial diversity of multi-lead ECG. The methods such as independent component analysis, and principal component analysis are employed for separating atrial and ventricular sources [28,113]. BSS methods rely on the assumption of linear mixing of uncoupled atrial and ventricular activities in generating surface ECG. They use non-Gaussianity criteria such as kurtosis for separating atrial and ventricular sources, and are capable of estimating a global atrial activity for multi-lead ECG. The inherit downside of BSS methods is that they assume multiple ECG leads are recorded during monitoring. Thus, the performance of the source separation techniques reduces significantly for fewer number of leads. Especially for Holter recordings where only few electrodes are available, the performance of the source separation techniques are not satisfactory [2].

In order to address above shortcomings in atrial activity estimation, in this Chapter we introduce a method for reconstructing the AF activity from AF ECG by mode limited short-time expansion of an orthonormal basis. Atrial activity during the QRS-T duration is estimated by interpolating immediately preceding and following segments of AF signal. The method preserves the morphology and frequency content of the underlying AF signal, and is free from any QRS-T residues. Tikhonov regularization is used to obtain a stable solution for the coefficients of the basis functions, leading to a bounded AF signal uncorrupted from ventricular residues. Compared to previously described ABS and BSS methods, our proposed method conserves the localized spectral content of the underlying AF signal which improves the accuracy of the dynamic AF frequency estimation. In the next Sections we present our proposed method for atrial activity estimation.

3.5.1 Orthonormal Basis Representation

In constructing the AF signal, the observed ECG is first considered as the AF signal which has been corrupted by the ventricular activity and other artifacts. Let \( s(t) \) be the observed signal with corrupted data segments. By replacing the
corrupted segments by zeros, the known segments of the AF signal $\tilde{s}(t)$ can be written as

$$\tilde{s}(t) = \sum_{i=1}^{N} \mathcal{X}_{[P_i, Q_i]}(t)s(t),$$

(3.9)

where $\mathcal{X}_{[,]}$ is the indicator function, i.e.,

$$\mathcal{X}_{[P,Q]}(t) = \begin{cases} 
1 & t \in [P, Q] \\
0 & t \notin [P, Q]. 
\end{cases}$$

(3.10)

Timings of starting point of the QRS complex, and end point of the T-wave of the $i^{th}$ beat are named $Q_i$ and $P_{i+1}$, respectively as shown in Figure 3.11. Here, without loss of generality, we assume that signal is correctly known in the intervals $t \in \{[P_i, Q_i]_{i=1}^{N}\}$, and corrupted in between intervals. Now consider the interval $[P_i, Q_{i+1}]$. We use the information available in the intervals $[P_i, Q_i]$ and $[P_{i+1}, Q_{i+1}]$ to reconstruct the corrupted segment $(Q_i, P_{i+1})$. This construction based on localized information results in a good localization in the time-frequency plane as we shall see in the later analysis.

Let $f_i(t)$ be the underlying AF signal in the interval $[P_i, Q_{i+1}]$. In general,
most signals have a frequency band of interest, and in the case of AF signal, fibrillatory frequencies are practically limited to 15Hz with possible harmonics. Thus, a mode limited orthonormal basis can be used to represent $f_i(t)$. Let $\{\phi^i_n(t)\}$ be an orthonormal basis with the fundamental period $T_i = Q_{i+1} - P_i$. Assuming that $f_i(t)$ is mode limited to $N$ with respect to $\{\phi^i_n(t)\}$,

$$f_i(t) = \sum_{n=-N}^{N} c^i_n \phi^i_n(t) \quad P_i \leq t \leq Q_{i+1},$$

(3.11)

where $\{c^i_n\}$ is the localized coefficients of the basis functions for the beat $i$. The best number of modes is a trade-off between capturing the detailed underlying signal and improving the noise robustness, and can be optimized empirically.

The limited number of modes which capture the underlying AF signal preserves the spectral content of the signal, and improves the noise robustness.

Due to the frequency modulated harmonic nature of the AF signal, the natural choice for the basis is considered to be the complex exponential functions,

$$\phi^i_n(t) = e^{j2\pi nt/T_i}.$$ 

(3.12)

Coefficients $c^i_n$ can be estimated via regularized least square solution given below. Using the known information in the intervals $[P_i, Q_i]$ and $[P_{i+1}, Q_{i+1}]$, we get

$$\begin{bmatrix}
\tilde{s}(P_i) \\
\vdots \\
\tilde{s}(Q_i) \\
\tilde{s}(P_{i+1}) \\
\vdots \\
\tilde{s}(Q_{i+1})
\end{bmatrix} =
\begin{bmatrix}
\phi^-_i(P_i) & \cdots & \phi^-_i(P_i) \\
\vdots & \ddots & \vdots \\
\phi^-_i(Q_i) & \cdots & \phi^-_i(Q_i) \\
\phi^-_i(P_{i+1}) & \cdots & \phi^-_i(P_{i+1}) \\
\vdots & \ddots & \vdots \\
\phi^-_i(Q_{i+1}) & \cdots & \phi^-_i(Q_{i+1})
\end{bmatrix}
\begin{bmatrix}
c^-_i \\
\vdots \\
c^-_i \\
c^+_i \\
\vdots \\
c^+_i
\end{bmatrix},$$

(3.13)

or $\tilde{s} = \Phi c$ in short.

### 3.5.2 Regularized Coefficient Estimation

The above system will be over-determined given $(Q_i - P_i) + (Q_{i+1} - P_{i+1}) > 2N + 1$, and that will be the usual case provided observed signal is sufficiently sampled.
Otherwise the given system will be under-determined. Regardless of the undeterministic nature, regularization can be applied to overcome the associated problems. It also avoids modeling of noise, and guarantees a bounded solution, thus any remaining QRS-T residues will be suppressed. We use Tikhonov regularization [112] in solving the above system, and the solution can be written in the form

\[ c = (\Phi^\top \Phi + \lambda^2 I)^{-1} \Phi^\top \tilde{s}, \]  

(3.14)

where \( I \) is the identity matrix, \( \lambda \) is the regularization parameter, and \( ^\top \) stands for the transpose of the matrix.

### 3.5.3 Results and Comparison with ABS

The above atrial activity reconstruction algorithm is first applied to simulated AF ECG. ECG signals are generated from a dynamical model of motion [96]. This model generates realistic synthetic ECG signals with much of the beat-to-beat variation in morphology and timing of the human ECG, including QT dispersion and R-peak amplitude modulation [96]. It is then modified by removing the P-waves, and adding simulated AF signal described in Section 3.4.2. For the simulations, following parameters are used in the AF model: \( \omega_0 = 10\pi \text{rad/s} \), \( \omega_m = 0.1\pi \text{rad/s} \), \( \Delta \omega = 6\pi \text{rad/s} \), \( M = 3 \), \( \gamma = 0.9 \), \( a = 0.05 \text{mV} \), \( \omega_a = 0.2\pi \text{rad/s} \), and \( \Delta a = 0.01 \text{mV} \). Figure 3.12(a) shows the simulated ECG for normal sinus rhythm, and Figure 3.12(b) shows the AF ECG.

Once the AF ECG is generated, baseline wander is removed by passing through a high-pass filter with a 0.5Hz cut-off frequency. Then, R-peaks are detected using Hilbert transform based peak detection technique [16]. Following R-peak detection, fiducial points \( P_i \) and \( Q_i \) are identified by \( P_i = R_{i-1} + 0.5\overline{RR} \), and \( Q_i = R_i - 0.1\overline{RR} \), where \( \overline{RR} \) is the mean RR-interval. Accurate identification of fiducial points \( P_i \) and \( Q_i \) is shown in Figure 3.12(c). Correct fiducial points detection helps constructing the intervals \([P_i, Q_i]\) accurately.

Following the identification of fiducial points, the proposed orthonormal basis expansion based algorithm is applied to reconstruct the AF signal from the ECG. Number of modes \( N = 16 \), and regularization parameter \( \lambda = 1.8 \) are found to be optimal by maximizing the correlation with the original AF signal.
Figure 3.12: (a) Synthetic ECG for normal sinus rhythm [96], (b) P-wave is removed from normal sinus rhythm and AF signal (3.5) is superimposed, (c) Fiducial points $P_i$ and $Q_i$ are accurately detected.

ABS method is also applied to the same ECG data in order to compare the performance of the proposed method. The ABS method involves constructing a mean QRS-T template, and subtracting this QRS-T template from each beat after temporal alignment and scaling with the corresponding R-peak. Figure 3.13 shows the simulated AF generated by the model in (3.5), and reconstructed AF signals using proposed orthonormal basis expansion method, and the ABS method. QRS-T residues are apparent in the ABS method at times $t = 6, 7, 8$s, whereas orthonormal basis expansion method has successfully suppressed all the ventricular activity.

Correlation coefficient is used to evaluate the performance of the proposed method, and is given by

$$\text{Cor. Coef.} = \frac{\int_{-\infty}^{\infty} f(\tau)g^*(\tau - t)d\tau}{\sqrt{\int_{-\infty}^{\infty} f(\tau)f^*(\tau - t)d\tau \int_{-\infty}^{\infty} g(\tau)g^*(\tau - t)d\tau}}$$

where $g(t)$ is the simulated AF signal, and $f(t)$ is the reconstructed AF signal.
3.6 Simplified TFD with Missing Data

In this Section, we further improve the proposed AF analysis technique by integrating atrial activity extraction and time-frequency analysis into a single algorithm, thus more efficient real-time analysis of AF from ECG is viable. In the previous Section, atrial activity during the QRS-T duration was estimated by a mode limited short-time expansion of an orthonormal basis. Here, an analytical expression for the TFD is derived solely based on these empirically found coefficients of the basis, thus time-frequency plots can be constructed with less

Figure 3.13: (a) Simulated AF signal (3.5), (b) AF signal reconstructed using orthonormal basis expansion method, (c) AF signal reconstructed using average beat subtraction method.

from a particular method. Figure 3.14 shows the correlation coefficients for orthonormal basis expansion method and the ABS method at $t = 0$, with AWGN, for a range of SNR settings. It is clear that the proposed method outperforms the ABS for all the noise settings, and at 0dB SNR correlation is improved by 16%.

3.6 Simplified TFD with Missing Data

In this Section, we further improve the proposed AF analysis technique by integrating atrial activity extraction and time-frequency analysis into a single algorithm, thus more efficient real-time analysis of AF from ECG is viable. In the previous Section, atrial activity during the QRS-T duration was estimated by a mode limited short-time expansion of an orthonormal basis. Here, an analytical expression for the TFD is derived solely based on these empirically found coefficients of the basis, thus time-frequency plots can be constructed with less
computations to observe the time variation of the dominant AF frequency. Additionally, the proposed algorithm can be generally applicable to time-frequency analysis of any nonstationary signal with missing or corrupted data segments.

3.6.1 Combined AF Reconstruction and TFD Method

We use estimated coefficients \( \{c_i^m\} \) to derive an analytical expression for the TFD. The Wigner-Ville distribution is used here to demonstrate how to derive such an analytical expression using the orthonormal basis coefficients. Nevertheless, it should be emphasized that any TFD can be applied here, for example members of Cohen class, but simplified analytical expressions may not be always found depending on the corresponding kernel function. As previously discussed, the Wigner-Ville distribution is given by

\[
WVD(t, \omega) = \frac{1}{2\pi} \int e^{-j\omega \tau} s(t + \tau/2) s^*(t - \tau/2) d\tau. \tag{3.16}
\]

Replacing \( s(\cdot) \) by the reconstructed AF signal in (3.11), and with the coeffi-
The integral in (3.17) can be further simplified as \( \{\phi^n_i(t)\} \) is only dependent on the beat \( i \). Given that the complex exponentials are used as the basis, i.e.,

\[
\phi^n_i(t) = \exp(j2\pi nt/T_i),
\]

(3.17) further simplifies to

\[
WVD_i(t, \omega) = \frac{1}{2\pi} \sum_{n=-N}^{N} \sum_{m=-N}^{N} c^n_i c^m_i^* \int e^{-j\omega \tau} \phi^n_i(t+\tau/2) \phi^m_i(t-\tau/2) d\tau.
\]

(3.18)

The expression in (3.18) provides a computationally efficient way of constructing the TFD using the estimated coefficient vectors without explicitly reconstructing the AF signal.

### 3.6.2 Results and Comparison with ABS

Figure 3.15 shows TFDs for the original and reconstructed AF signals using the proposed combined AF reconstruction and TFD method and the ABS method. It is evident that the proposed scheme closely resembles the original AF time-frequency plot compared to the ABS based reconstruction. Deviations in the ABS reconstructed time-frequency plot are mainly due to the insufficient QRS-T cancelation. Also, it should be emphasized that the ABS method required reconstructing the signal and performing the time-frequency analysis as a two step process, whereas the proposed method has constructed the time-frequency plot straight from the coefficients vector of the basis functions, thus less processing time is required.

We compute the RMS errors in dominant AF frequency estimation for a range of SNR values to quantify the performance of the proposed method, and similar analysis is done for the ABS method for comparison. Results are shown in Figure 3.16. Dominant AF frequency is estimated as the frequency where maximum energy is observed in the time-frequency plane. For all considered SNR values proposed method performs better than the ABS method, and at low SNR
values, which is of high interest, it outperforms the ABS method considerably. The proposed scheme reduces the error to be within 0.5Hz for all SNR settings greater than 0dB, whereas to achieve the same error limits the ABS method requires SNR to be greater than 8dB.

We show the applicability of the proposed method in analyzing real ECG with AF episodes by applying the algorithm on ECG records in PhysioBank AF Termination Challenge Database [56]. The example shown in Figure 3.17 shows that the proposed scheme estimates the dominant AF frequency to a higher degree of resolution compared to the standard ABS method.

### 3.7 Radial-δ Kernel based AF Analysis

In this Section, we analyze AF arrhythmia condition with novel radial-δ kernel based TFDs. Same AF model described in Section 3.4.2 is used to evaluate the performance of the novel TFDs compared to the existing TFDs such as the Choi-Williams distribution (CWD).
Figure 3.16: Comparison between the proposed algorithm and the average beat subtraction method for AF ECG analysis in terms of RMS error of the estimated AF frequency.

Figure 3.17: (a) ECG record n09 of PhysioBank AF Termination Challenge Database [56], (b) TFD generated by the proposed method, (c) TFD generated via average beat subtraction based AF reconstruction.
Figure 3.18 shows simulation results for the AF signals with $\alpha = 0.5$. Radial-$\delta$ kernels up to order 3 (including Margenau-Hill, and Born-Jordan distributions) show poor results with considerable cross-terms. Orders 4-6 (including Bessel distribution) show less interference terms compared to the lower order kernels. Orders 7 and above achieve a good resolution for the auto-terms, but suffer greatly from cross-term interference. Among orders 4-6 (Figure 3.18(b)-(d)), a careful visual inspection suggests order 6 radial-$\delta$ kernel based TFD has the least interference terms, while no significant differences are found in the auto-term resolution. Thus, we conclude that $\phi^\rho_{6}(\xi, \tau) = 8 J_2(\alpha\xi\tau)/(\alpha\xi\tau)^2$ gives the best representation within the radial-$\delta$ kernel set for the AF signals. Note that $\phi^\rho_{6}(\xi, \tau)$ is a novel kernel derived in this thesis.

Then we compare the proposed radial-$\delta$ kernel distributions with the CWD. The CWD has a control parameter $\sigma$, which could be used to minimize the cross-terms effectively. Figure 3.19 shows the CWD of AF signals for a range of $\sigma$ values. For the AF signal, the radial kernel of order 6 (Figure 3.18(d)), and the CWD with $\sigma = 0.5$ (Figure 3.19(b)) give best results within each category, and there is no significant difference between these two distributions in terms of auto-term resolution or cross-term interference. But radial-$\delta$ kernel of order 6 ($\alpha = 0.5$) preserves time-support and frequency-support properties, which the CWD does not satisfy.

### 3.8 Summary and Contributions

1. An orthonormal basis based interpolation method is proposed for atrial activity extraction from AF ECG. The method uses short-time expansion of an orthonormal basis, and regularized least squares solution is used to compute stable coefficients for the basis. The algorithm successfully extracts the fibrillatory waveform from ECG, canceling out dominant ventricular components. Its advantages over the conventional ABS method have been demonstrated.

2. Dynamic changes in fibrillatory frequencies have been accurately tracked using Bessel distribution and novel radial-$\delta$ kernel based TFDs. We show
Figure 3.18: Time-frequency representation of simulated AF signal (3.5) using (a) Born-Jordan distribution (order 3 kernel), (b) Bessel distribution (order 4 kernel), (c) 5th order kernel based TFD, (d) 6th order kernel based TFD, and (e) 7th order kernel based TFD, ($\alpha = 0.5$).
Figure 3.19: Time-frequency representation of simulated AF signal (3.5) using Choi-Williams distribution with (a) $\sigma = 0.1$, (b) $\sigma = 0.5$, (c) $\sigma = 1$, (d) $\sigma = 5$, and (e) $\sigma = 10$. 
that higher order radial-$\delta$ kernel based TFDs achieve better time and frequency resolutions with less cross-terms in the AF analysis.

3. Atrial activity extraction from ECG during AF episodes, and tracking of dominant AF frequency have been combined into a single algorithm for efficient computation. A simplified analytical expression is derived for time-frequency analysis of AF ECG, which is based only on the coefficient vector of the basis. The method can also be applied to time-frequency analysis of any nonstationary signal with missing or corrupted data segments.

4. The proposed algorithms have been successfully applied to simulated as well as real ECGs with AF episodes. Their advantages over current AF extraction and time-frequency analysis methods have been demonstrated.
Chapter 4

Point Process Algorithms for Cardiorespiratory Dynamics

4.1 Introduction

Heart rate and heart rate variability (HRV) are important indicators of cardiovascular health of a subject. It has long been understood that HRV is regulated by the autonomic nervous system [93]. The sympathetic and parasympathetic branches of the autonomic nervous system regulate the heart rate and HRV, thus analyzing HRV gives insights into subject’s autonomic nervous system and the cardiovascular system [18]. Heart beats can be detected from the ECG recordings as R-wave events, or as peaks (pulses) on the blood volume pressure (BVP) recordings. Traditionally, heart rate is defined as the average of the reciprocal of intervals between consecutive R-wave events (RR-intervals), or between consecutive pulses (pulse intervals, PIs) in a given time window. HRV can be quantified in the time domain using simple statistical measures such as standard deviation of the heart beat intervals. In the frequency domain, HRV is decomposed mainly into three distinct spectral bands in order to reflect the sympathetic and parasympathetic outflow variations. Further, nonlinear methods such as chaos analysis, Lyapunov exponents, detrended fluctuation analysis, and approximate entropy have been employed in characterizing HRV [93]. All these techniques provide a range of indices associated with HRV, although significant inaccuracies may rise from some of the assumptions made, as we shall discuss later.
Respiratory sinus arrhythmia (RSA) is a cardiorespiratory phenomenon characterized by heart rate fluctuations which occur simultaneously with the respiratory cycle [61]. This phenomenon is a direct result of the interaction between the cardiovascular and respiratory systems. In normal conditions, heart beat intervals shorten during the inspiration, and prolongs during expiration. Accurate quantification of RSA provides vital information on cardiorespiratory coupling, and also gives an index to the vagal tone. Further, evidence suggests that reduced RSA is often associated with physiological and psychological morbidity [75], and therefore RSA could be used as a marker of risk. Similar to HRV, time and frequency domain methods have been employed in characterizing RSA from heart beat intervals and respiratory recordings. These methods may vary from simple time domain peak-valley methods to more comprehensive transfer function approaches [122].

Several shortcomings exist in the current HRV and RSA quantification methods. Heart beats are resulted from the electrical impulses of the heart due to ventricular contractions. These impulses are discrete set of events in time as opposed to a continuous time signal. But most existing algorithms interpolate inter beat intervals in order to obtain a continuous signal for their analysis. Therefore, these algorithms fail to represent the intrinsic point process nature of the heart beat generating process [8]. Second, most algorithms assume the stationarity of the inter beat interval series for a certain time period, thus failing to capture nonstationarities and fast dynamics in HRV. Additionally, RSA is also influenced by the dynamic respiration patterns, thus the stationarity assumption usually does not hold under most circumstances. Third, most approaches do not estimate HRV and RSA measures in between heart beats, thus failing to provide true instantaneous estimates of HRV and RSA. Also, most existing algorithms do not statistically validate the inter beat interval series models using goodness-of-fit tests [9].

In this Chapter, we introduce a maximum likelihood point process framework for instantaneous estimation of HRV and RSA. This estimation method has been selected for its robust dynamic identification properties, and because it is less sensitive to parameter initialization and numerically more stable than other adaptive recursive point process filters. The proposed method allows time
increments for parameter update at arbitrary small time intervals, thus achieving
instantaneous estimations of HRV and RSA measures. As a consequence, rapid
RSA changes at time intervals smaller than pulse or respiratory cycles can be
monitored and accounted for, without waiting till the next respiratory cycle or the
next pulse as required by the existing methods. Importantly, as measures based
on the traditional subdivision in oscillatory frequency components might not be
reliable in the presence of nonstationary respiratory patterns, we further propose
a new method for dynamically estimating the RSA gain within a transfer function
spectrum, based on time-frequency characterization of the respiratory cycle and
time-varying coherence between respiration and inter beat intervals. Such a
combined method is capable of computing reliable, instantaneous estimates of
RSA by accounting for rapid dynamic changes in both respiration patterns and
autonomic inputs.

The structure of this Chapter is as follows: In Sections 4.2 and 4.3, we present
some background and existing methodologies for estimating HRV and RSA, re-
spectively. In Section 4.4, we present the maximum likelihood point process
framework, the methods for evaluating model goodness-of-fit, and the methods
for estimating instantaneous RSA gain within the framework. Sections 4.5 and
4.6 report on results obtained from applying the proposed algorithms on simu-
lated signals with varying respiration and autonomic inputs, and on results of a
pain protocol with nonstationary respiration patterns, respectively. Finally, in
Sections 4.6.3 and 4.7, we present discussions and final conclusions.

4.2 Heart Rate Variability

The variation in the time period between consecutive heart beats is known as
the heart rate variability (HRV). Inter beat intervals can be measured from the
ECG signal as the time period between two consecutive R-peaks, or as pulse
intervals from the BVP signal. The sympathetic and parasympathetic branches
of the autonomic nervous system regulate the sinoatrial node, which acts as a
pacemaker of the heart, thus analyzing HRV gives an insight to subject’s auto-
nomic nervous system functions [93]. The typical rate of the sinoatrial pacemaker
is between 60 to 100 beats per minute, which is the fastest compared to other
potential pacemaker areas of the heart, thus under normal conditions sinoatrial node determines the heart rate. An ECG waveform with a normal heart rate is called the sinus rhythm. A heart rate above the normal is referred as sinus tachycardia, and below the normal as sinus bradycardia. The heart rate is controlled by a number of sensors throughout the body, including blood pressure in arteries, acid-base conditions in blood, pressure within the wall of the heart, and signals from the respiratory cycle [37].

Conventionally, the analysis of HRV is based on separate time domain and frequency domain analysis of the inter beat interval series. Standard time domain measures usually fall into two categories, those derived directly from inter beat intervals, and those derived from the differences between inter beat intervals [93]. The standard deviation of the inter beat intervals (SDNN), and the standard deviation of the average inter beat intervals calculated over short periods (usually 5 minutes intervals) fall under the first category. Interval difference based measures include the square root of the mean squared differences of successive inter beat intervals (RMSSD), and the percentage of number of interval differences of successive inter beat intervals greater than 50ms (pNN50). The measurements of short-term variation estimate high frequency variations in heart rate, and are highly correlated [93].

Frequency domain measures are derived from power spectral density of the inter beat interval series, and can be computed by either non-parametric or parametric methods [93]. Non-parametric methods use fast Fourier transform (FFT) or similar algorithms, are simple to implement, and have a higher processing speed. On the other hand, parametric methods are based on autoregression or similar methods, have higher complexity, but have the advantage of smoother spectral components which can be distinguished independently for pre-selected frequency bands. The spectrum of the inter beat interval series can be computed either from the inter beat interval tachogram or from the discrete event series of inter beat intervals. The inter beat interval tachogram is obtained from plotting inter beat interval durations against number of progressive beats, whereas the discrete event series is obtained from plotting inter beat durations against the time of corresponding beat occurrence.

Three main spectral components can be identified in short-term recordings,
4.3 Respiratory Sinus Arrhythmia

A large number of autonomic and hemodynamic parameters are influenced by respiratory activity. Among them, respiratory sinus arrhythmia (RSA) is defined as the variations in heart rate during inspiratory and expiratory phases of the respiratory cycle [47, 124]. At typical resting respiratory frequencies, heart rate increases during inspiration, decreases during expiration, and respiratory frequency also influences the phase relationship between respiration and heart rate oscillations [47, 123]. RSA serves an important role in providing synchrony between the respiratory and cardiovascular systems, together responsible for maintaining the metabolic equilibrium over a wide range of physical and psychological conditions. RSA magnitude is dependent on both respiratory frequency and tidal volume, even when the autonomic tone remains stable [67]. A key problem in cardiorespiratory physiology modeling is to efficiently and accurately quantify and monitor RSA under different physiological and behavioral conditions, where
frequent variations in respiration and autonomic inputs are present. A solution to this issue could yield critical insights into the mechanisms involved in short-term and long-term cardiorespiratory coupling [47,124].

Accurate quantification of RSA serves several purposes. First, it is an indirect measure of parasympathetic cardiac control, and it has been shown that pharmacologically induced changes in cardiac vagal tone (e.g., atropine administration) can be accurately tracked by RSA measures [49,59]. Thus, RSA mainly reflects cardiac vagal efferent effects on the sinoatrial node [48, 58], though at lower respiratory frequencies sympathetic cardiac control can contribute to RSA as well [124]. RSA could be used as a stable measure of parasympathetic cardiac control not only in controlled environments but also during ambulatory recordings [55]. Second, evidence has been given for using RSA as a predictive marker of risk of physiological morbidity [75], as well as psychological deficiencies [68]. Generally, it has been found that lower RSA is associated with high risk of morbidity. Third, RSA has become a central point in evolution theory of central and vagal control of cardiorespiratory interactions [61].

In early work, RSA was defined using simple time domain measures of beat interval series [60,74]. One proposed algorithm measures RSA as the difference between the shortest RR-interval during inspiration and the longest RR-interval during expiration within one respiratory cycle, and has been referred as the peak-valley method. When using peak-valley based RSA estimations respiratory parameters need to be controlled carefully, which may not be possible under some behavioral conditions [58]. Several other methods have been devised in the last decades, both in the time and frequency domains, successfully relating measures of HRV to RSA and cardiopulmonary coupling [18, 20, 42, 50, 54, 70, 98, 99, 102, 126, 135]. In particular, filtering and transfer function approaches were used in quantifying RSA [123, 144], and a bivariate autoregressive model was further proposed to estimate the time-varying RSA gain [7,11]. As most of these methods are not able to completely overcome nonstationarity issues and not capable of estimating the fast changes in RSA at arbitrarily small time scales, a point process framework for heart beat dynamics [8,9] has been proposed to assess RSA within an adaptive point process filtering algorithm [32]. However, the above approaches do not account for irregular respiration dynamics when
assessing RSA.

The maximum likelihood point process framework introduced in the next Section estimates RSA instantaneously accounting for dynamic respiratory patterns and fast changes in the autonomic inputs. It also overcomes problems associated with traditional subdivision of frequency bands by computing the estimations based on instantaneous respiratory frequency and coherence. The proposed algorithm is validated on simulated data, as well as on data obtained during a pain administration protocol.

4.4 Point Process Framework

4.4.1 Point Process Model of Heart Beat Interval Dynamics

Heart beats are initiated by the polarization of pacemaker cells of the heart starting from the sinoatrial node, and propagating through to the other parts of the heart. After each depolarization, membrane potential of these cells falls to a resting state, and begins to rise gradually preparing for the next beat [64]. The next heart beat occurs when the membrane potential crosses a threshold. The waiting time between two threshold crossings marks the inter beat interval or the RR-interval. Thus, integrate and fire models are regularly used to simulate the heart beats [128].

The rise of membrane potential to a threshold has been modeled as a Gaussian random walk [128]. Such models postulate that the resulting times between two firing events have statistical properties of an inverse Gaussian process [9, 128]. Further, sympathetic and parasympathetic inputs to the sinoatrial node could occur in milliseconds, but their effects may last for several seconds. Thus, resulting heart beats are not an independent random process, but dependent on the recent history of autonomic inputs. Additionally, autonomic inputs to the sinoatrial node are part of the cardiovascular control circuitry, thus the RR-interval variations are dynamic, or time-varying [9]. For this reason, we here model the R-wave events as a history dependent, inverse Gaussian point process model with time-varying model parameters.
Assume in a given observation interval \((0, T]\), \(K\) successive R-wave events are recorded: \(0 < u_1 < u_2 < \ldots < u_K \leq T\). Given any R-wave event \(u_k\), the waiting time until the next R-wave event (i.e., next RR-interval), obeys a history dependent inverse Gaussian probability density \(f(t)\) given by

\[
f(t|u_k) = \left[ \frac{\theta(t)}{2\pi(t-u_k)^3} \right]^\frac{1}{2} \exp \left\{ -\frac{1}{2} \frac{\theta(t)[t-u_k-\mu_{RR}(t)]^2}{\mu_{RR}^2(t)(t-u_k)} \right\},
\]

where \(t\) is any time satisfying \(t > u_k\), and \(\mu_{RR}(t) > 0\) is the mean of the distribution, which is an estimation of the instantaneous mean RR-interval. \(\theta(t) > 0\) is the shape parameter of the inverse Gaussian distribution. The standard deviation of the above RR probability model [34] is given by

\[
\sigma_{RR}(t) = \left[ \frac{\mu_{RR}^3(t)}{\theta(t)} \right]^\frac{1}{2}.
\]

Because of the lasting effects of autonomic inputs to the sinoatrial node, \(\mu_{RR}(t)\) in the point process probability model should be modeled as dependent on the recent history of the previous RR-intervals,

\[
\mu_{RR}(t) = a_0(t) + \sum_{k=1}^{p} a_k(t) RR_{t-k}.
\]

Thus, the mean value of the distribution is modeled as a univariate \(p\)-order autoregressive (AR) process. According to the model, the mean RR-interval is influenced by the past \(p\) RR-intervals, thus dependent on the AR coefficients \(\{a_k(t)\}_{k=0}^{p}\), whereas the RR-interval variance is determined by \(\{a_k(t)\}_{k=0}^{p}\) and \(\theta(t)\). All the model parameters are time-varying, taking into account the nonstationary behavior of heart beat dynamics, and allowing for definition of instantaneous estimates of HRV. Later we shall see an extension of above AR model in Section 4.4.4, which accounts for the nonstationarities in respiration.

### 4.4.2 Point Process Definitions of HR and HRV

The probability density given in (4.1), which characterizes the stochastic nature of the RR-intervals, can be used to formulate definitions of heart rate and HRV. Heart rate is often defined as the reciprocal of the RR-intervals [11,93,122,137].
For RR-intervals measured in seconds, \( r = c/(t - u_k) \), where \( c = 60\text{s/min} \), gives the estimation of heart rate in beats per minute (bpm). By using a standard change of variables formula [117], we get heart rate probability density \( f(r) = f(c/(t - u_k)) \) as

\[
f(r) = \left| \frac{dt}{dr} \right| f(t) = \left[ \frac{\theta(t)}{2\pi cr} \right]^\frac{1}{2} \exp \left\{ -\frac{1}{2} \frac{\theta(t)[c - \mu_{RR}(t)r]^2}{\mu_{RR}^2(t)cr} \right\}.
\] (4.4)

Mean and standard deviation of the heart rate probability density are given by [9]

\[
\mu_{HR}(t) = c \left( \frac{1}{\mu_{RR}(t)} + \frac{1}{\theta(t)} \right), \quad (4.5)
\]

\[
\sigma_{HR}^2(t) = c \left[ \frac{2\mu_{RR}(t) + \theta(t)}{\mu_{RR}(t)\theta^2(t)} \right]^\frac{1}{2} \quad (4.6)
\]

Instantaneous estimates of heart rate and HRV are characterized by \( \mu_{HR}(t) \), and \( \sigma_{HR}^2(t) \), respectively. Though our point process framework and HRV estimates are defined using RR-interval series, it is equally applicable to any data series of inter beat intervals.

### 4.4.3 Heart Beat Spectral Components

Spectral analysis of HRV has been deemed useful in measuring the sympathovagal balance of a subject. The frequency response of the RR-interval series in the proposed method is given by

\[
H_1(\omega, t) = \frac{1}{1 - \sum_{k=1}^{p} a_k(t)z^{-k}|z=e^{2\pi f_s}|}, \quad (4.7)
\]

where \( f_s \) is the beat rate. We can then evaluate the dynamic power spectrum, or the parametric auto-spectrum [13] by

\[
P_{RR}(\omega, t) = \sigma_{RR}(t)|H_1(\omega, t)|. \quad (4.8)
\]

The main spectral components can be identified from the above auto-spectrum by subdividing it into the three frequency bands as given by the current HRV
standards [93], and described in Section 4.2. The low frequency component (LF, 0.04 – 0.15Hz) indicates the slow autonomic effects (a combination of sympathetic and parasympathetic) on the sinoatrial node, whereas the high frequency component (HF, 0.15 – 0.4Hz) indicates only the parasympathetic modulation. As a consequence, an instantaneous estimation of LF/HF power ratio would provide important information about the sympathovagal balance of a subject. Our formula in (4.8) is capable of estimating the LF/HF dynamically, accounting for fast changes in the autonomic inputs. Furthermore, later we shall redefine the HF band, dynamically centered around the respiratory frequency [102], which would overcome possible biases of using fixed frequency bands.

### 4.4.4 Bivariate Model for RSA analysis

We further develop the univariate AR model for $\mu_{RR}(t)$ by incorporating respiration measures into the model in addition to the past RR-intervals. The influence of past autonomic inputs and respiration activity on the RR-intervals are modeled by defining a bivariate regression on the mean of the point process probability density,

$$
\mu_{RR}(t) = a_0(t) + \sum_{k=1}^{p} a_k(t)RR_{t-k} + \sum_{k=1}^{q} b_k(t)RP_{t-k}.
$$

(4.9)

The dependency of $\mu_{RR}(t)$ on past $p$ RR-intervals and past $q$ respiration values accounts for past autonomic input driven and respiration driven RR-interval modulation, respectively. The original respiration signal (RP) is resampled at the R-wave events, so that both respiration and RR-intervals are synchronized. Resampling of RP can be performed quite accurately, as current respiration measuring techniques offer high sampling rates.

RSA can then be defined as the transfer function from RP to RR,

$$
H_{12}(\omega, t) = \frac{\sum_{k=1}^{q} b_k(t)z^{-k}|_{z=e^{2\pi f_s}}}{1 - \sum_{k=1}^{p} a_k(t)z^{-k}|_{z=e^{2\pi f_s}}}.
$$

(4.10)

We propose two methods of estimating the RSA gain from above transfer function. First, the time-varying respiration spectrum $P_{RP}(\omega, t)$ is used to esti-
mate the frequency $\omega_{RP}(t)$, where maximum respiration power is concentrated at each time instance, i.e.,

$$P_{RP}(\omega_{RP}, t) = \max_{\omega} [P_{RP}(\omega, t)]. \quad (4.11)$$

Then, time-varying RSA gain can be estimated by evaluating (4.10) at $\omega_{RP},$

$$RSA^a_{gain}(t) = |H_{12}(\omega_{RP}, t)|. \quad (4.12)$$

Alternatively, we evaluate the RSA gain at the frequency where maximum interactions between RR-intervals and respiration occur. In this regard, we use the time-varying coherence spectrum

$$Coh(\omega, t) = \frac{|P_{RR-RP}(\omega, t)|}{\sqrt{P_{RR}(\omega, t)P_{RP}(\omega, t)}}, \quad (4.13)$$

where $P_{RR-RP}(\omega, t)$ is the cross-spectral density between respiration and the RR-intervals, while $P_{RR}(\omega, t)$ and $P_{RP}(\omega, t)$ are the auto-spectral densities of RR-intervals and respiration, respectively [144]. This time-varying coherence spectrum is then used to estimate the frequency $\omega_{coh}(t)$ where coherence is maximum at each time instance, i.e.,

$$Coh(\omega_{coh}, t) = \max_{\omega} [Coh(\omega, t)], \quad (4.14)$$

and RSA gain is dynamically evaluated at $\omega_{coh},$

$$RSA^b_{gain}(t) = |H_{12}(\omega_{coh}, t)|. \quad (4.15)$$

Although computed differently, both above RSA indices are expected to yield similar results, as RR-intervals are highly correlated with the breathing cycle, and coincident with the main respiratory frequency in spectral terms. In Chapter 5, we test the validity of this assumption, pointing at both $RSA^a_{gain}(t)$ and $RSA^b_{gain}(t)$ as reliable estimates of instantaneous RSA.
### 4.4.5 Local Maximum Likelihood Estimation

A local maximum likelihood method [89, 136] is implemented to estimate the unknown time-varying parameter set $\xi = \{\{a_k\}_{k=0}^p, \{b_k\}_{k=1}^q, \theta\}$ in the point process model. In estimating $\xi$ at time $t$, we take a local likelihood interval $(t - l, t]$, where $l$ is the length of the local likelihood observation window. Within $(t - l, t]$, we may observe $n$ pulses, $t - l < u_1 < u_2 < \ldots < u_n \leq t$. Then, we consider the local joint probability density of $u_{t-l,t}$, where $u_{t-l,t} = \{u_1, \ldots, u_n\}$. The log-likelihood associated with this joint probability density is given by

$$
\log f(u_{t-l,t}) = \sum_{j=2}^{n} w(t - u_j) \log f(u_j - u_{j-1}) \\
+ w(t - u_n) \log \int_{t-u_n}^{\infty} f(\nu) d\nu,
$$

(4.16)

where $w(t - u_j) = \alpha^{t-u_j}$, $0 < \alpha < 1$, is a weighting function for the local likelihood estimation [9, 89]. The weighting time constant $\alpha$ governs the degree of influence of a previous event observation $u_j$ on the local likelihood at time $t$. The second term of (4.16) represents the likelihood of the partially observed interval since the last observed pulse $u_n$ (right censoring). To maximize the local log likelihood given in (4.16) we use the Newton-Raphson method, and obtain the local maximum likelihood estimate of $\xi$. Of note, the time increment $\Delta$ for computing the next $\xi$ from $t$ to $t + \Delta$ can be chosen as arbitrarily small, thus yielding instantaneous estimates of heart rate and HRV.

In computing the maximum likelihood estimations, orders of the bivariate regression ($p$ and $q$), local observation window ($l$), and the weighting constant $\alpha$ can be simultaneously chosen by minimizing the Akaike Information Criterion (AIC) for the local maximum likelihood analysis. These model orders and the parameters used in the estimation method need to be empirically chosen before obtaining the point process HRV and RSA estimations. The model goodness-of-fit tests described in the next Section could also be utilized in choosing appropriate model orders.
4.4.6 Model Goodness-of-Fit

In order to evaluate how well the proposed point process model describes a series of inter beat intervals, it is necessary to compute goodness-of-fit statistics for the model. The goodness-of-fit of the proposed model is evaluated using Kolmogorov-Smirnov (KS) test based on the time-rescaling theorem \cite{10,25,100}. The KS test uses the conditional intensity function given by

$$\lambda(t) = \frac{f(t)}{1 - \int_{u_n}^t f(\nu)d\nu},$$ \hspace{1cm} (4.17)

which is the history dependent rate function for the point process. Then, time-scaled or transformed RR-intervals can be defined as

$$\tau_k = \int_{u_{k-1}}^{u_k} \lambda(t)dt,$$ \hspace{1cm} (4.18)

where \(\tau_k\) values are independent, exponential random variables with a unit rate. Further transformation, \(z_k = 1 - \exp(-\tau_k)\) results in \(z_k\) values, which are independent, uniform random variables on the interval \([0,1]\). The construction of the KS plot \cite{25,100} allows to test the agreement between the transformed observations \((z_k)\) and the ideal uniform probability density function. If the model is correct, the KS plots should align with the 45 degrees diagonal. Additionally, KS distance can be computed as the largest distance between the cumulative distribution function (cdf) of \(z_k\) and the cdf of ideal uniform distribution on \([0,1]\).

In addition to the KS plot, the transformed quantiles’ autocorrelation function is computed to check the independence of the transformed intervals \(\tau_k\) \cite{9}. According to the time-rescaling theorem \cite{25}, \(\tau_k\) values should be independent regardless of the dependencies in the original RR-intervals. We plot the serial correlation function of the \(\tau_k\) values at different lags, in order to assess the correlation structure. Small values of the serial correlation function at all lags would suggest that the \(\tau_k\) values are uncorrelated, hence consistent with independence criteria \cite{9}, indicating that the point process model is appropriate for the RR-interval data series.
4.5 Simulation Results

Algorithms are tested with simulated signals for both constant and dynamic respiratory conditions in order to evaluate the robustness of the proposed methods under altered respiratory patterns. A simple sinusoidal model is used for both RR-intervals and RP signals as given by

\[
RR(t) = \mu_{RR} + \alpha(t) \sin(2\pi f_1(t)t) + \beta(t) \sin(2\pi f_2(t)t) + n_1(t), \quad (4.19)
\]

\[
RP(t) = \gamma(t) \sin(2\pi f_2(t)t) + n_2(t). \quad (4.20)
\]

The LF and HF components of the simulated RR-intervals are modeled by \( f_1(t) \) and \( f_2(t) \) with amplitude factors \( \alpha(t) \) and \( \beta(t) \), respectively. With the basic assumption that the HF component of RR-intervals is coherent with the respiration, the respiratory frequency is also given by \( f_2(t) \). The amplitude of the RP waveform is modeled by \( \gamma(t) \). \( n_1(t) \) and \( n_2(t) \) are noise in the RR-interval and respiration measurements, and are modeled by AWGN.

Such formulation is capable of simulating dynamic autonomic inputs via setting the \( \alpha(t) \) and \( \beta(t) \) parameters, thus varying the LF and HF powers. The LF/HF ratio, which is given by \( (\alpha(t)/\beta(t))^2 \), can consequently also be varied. The model is also capable of altering the RSA gain by changing the ratio \( \beta(t)/\gamma(t) \). Respiratory frequency can also be varied by setting \( f_2(t) \) appropriately. The proposed point process algorithm is used to perform two sets of simulations, which estimate the dynamic RSA gain at both constant and dynamic respiration conditions by varying only \( \beta(t) \), and then varying both \( \beta(t) \) and \( f_2(t) \), respectively. Two sets of simulations are reported here with parameters given in Table 4.1.
Table 4.1: Parameters used in two dynamic RSA simulation studies with constant and time-varying respiratory rates (rpu=respiratory units)

<table>
<thead>
<tr>
<th></th>
<th>$\mu_{RR}$</th>
<th>$f_1(t)$</th>
<th>$f_2(t)$</th>
<th>$\alpha(t)$</th>
<th>$\beta(t)$</th>
<th>$\gamma(t)$</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Constant RP</td>
<td>1s</td>
<td>0.1Hz</td>
<td>0.3Hz</td>
<td>0.1s</td>
<td>0.2s, 0 &lt; t &lt; 500s</td>
<td>0.1rpu, 0.2s, 0 &lt; t &lt; 500s</td>
</tr>
<tr>
<td>B. Time-varying RP</td>
<td>1s</td>
<td>0.1Hz</td>
<td>0.35Hz, 500 &lt; t &lt; 1000s</td>
<td>0.1s</td>
<td>0.25Hz, 500 &lt; t &lt; 1000s</td>
<td>0.2s, 0 &lt; t &lt; 500s</td>
</tr>
</tbody>
</table>


4.5.1 Constant Respiratory Frequency

The first set of simulations is devised to show that the proposed algorithm is capable of accurately estimating the RSA gain while respiratory frequency remains relatively constant, and the results are shown in Figure 4.1. $\beta(t)$ is set to have a step change from 0.2s to 0.1s at 500s, and then a linear increment from 0.1s to 0.2s between 1000s and 1500s in order to demonstrate the ability of the algorithm to track step changes as well as gradual changes in RSA gain while respiratory frequency remains constant. AWGN is used for $n_1(t)$ and $n_2(t)$ with SNR set at 20dB. A bivariate AR model is used to estimate the time-varying respiratory frequency, and the coherence between RR-intervals and respiration at the beats. The regression is defined at the beats, thus neither interpolation nor resampling was necessary.

Results demonstrate the ability of the proposed point process algorithm to track step changes as well as gradual changes in RSA gain while respiratory frequency remains relatively unchanged. Respiratory frequency is accurately estimated to be 0.3Hz, and a very high coherence (close to 1) is observed between RR-intervals and RP at that frequency. The step change at 500s is tracked accurately, and the point process algorithm is capable of reaching 95% of the lower RSA level within 41s. Additionally, gradual changes in RSA from 1000s to 1500s are also followed accurately. The KS plot and the transformed quantiles’ autocorrelation function for 60 lags are shown in Figure 4.2. The KS plot stays well within the 95% confidence bounds, and the autocorrelation function also lies within the 95% confidence intervals for most lags.

4.5.2 Varying Respiratory Frequency

The second set of simulations is done to show that the proposed algorithm is robust under sudden and gradual changes in the respiratory frequency, and still capable of accurately estimating the RSA gain. The simulation results for the dynamic respiration is shown in Figure 4.3. In this case, respiratory frequency $f_2(t)$ is linearly increased from 0.25Hz to 0.35Hz between 0s and 500s, suddenly dropping back to 0.25Hz at 1000s. All the other parameters are set at same values as in Section 4.5.1.
Figure 4.1: Estimated $f_{RP}$ (top), coherence (middle), and RSA gain (bottom) under constant respiratory rate for the simulated RR and RP signals using the point process algorithm (dotted curve shows the theoretically expected RSA gain).

Figure 4.2: The KS plot (left) and transformed quantiles’ autocorrelation function (right) show the goodness-of-fit of the point process model under constant respiratory frequency (dashed lines indicate the 95% confidence bounds).
According to Figure 4.3, a drop in coherence is observed at 1000s down to approximately 0.7 due to the step change in the respiratory frequency. More precisely, the coherence drop occurs at 1026s, 26s after the actual frequency drop due to the transient effect. The estimated RSA gain during the gradual increase in respiratory frequency (from 0s to 500s) fluctuates just below 2, which demonstrates the robustness of the point process algorithm under altered respiratory conditions. Note that the step change in the respiratory frequency at 1000s does not have an impact on accurate estimation of RSA gain during that period. Figure 4.4 shows the KS plot and the transformed quantiles’ autocorrelation function, which validate the goodness-of-fit of the model.

The simulation results indicate that the proposed point process method is capable of estimating the RSA gain accurately under dynamic respiration patterns and autonomic inputs. The algorithm appropriately tracks fast changes in RSA, thus providing precise instantaneous RSA estimates.
4.6 Application to Pain Administration Protocol

In this Section, we apply the proposed point process algorithms for HRV and RSA estimations in a pain administered experimental protocol. The autonomic nervous system is modulated to provide an adaptive response to the pain experience. The pain experience has been found to increase the heart rate [90,134,138] and decreases HRV [26, 88, 129]. Cain et al. reported lower HF power and higher LF/HF ratio in women with irritable bowel syndrome who have severe gut pain [26]. Storella et al. found increase in HRV with the relief of chronic pain which was attributed to the restoration of cardiovascular health [129]. A study on new-born infants suggests a clear stress response provoked when the heel was squeezed for blood sampling, indicated by an increased heart rate and a decreased spectral power in the HF band [88]. Campbell et al. reported long-term relationships between pain sensitivity and the autonomic tone [27], and found that average pain sensitivity is associated with the HF component and the LF/HF ratio of HRV, suggesting increased sympathetic and reduced parasympathetic tone among individuals less sensitive to pain. In addition to these frequency domain methods, time domain methods of HRV analysis have also been used in pain/analgesia evaluation [91]. To date, there has not been an attempt to link
continuous estimates of RSA with evoked pain administration.

In order to characterize the cardiorespiratory dynamics during an acute pain experience, we apply the maximum likelihood point process algorithm in a short-term pain administration protocol. During the experiment, subjects received, and then rated, pain stimuli on the left calf at different individually calibrated intensities. The experiment was conducted at Massachusetts General Hospital in Boston, MA, USA. We present a summary of the experimental protocol, and then the results obtained by proposed point process algorithms.

4.6.1 Pain Protocol

The experimental protocol consisted of a series of pressure stimuli (each 14s long, 2s ramp up, 10s at target pressure, 2s ramp down), which were delivered on the left calf muscle using a velcro-adjusted pressure cuff connected to a rapid cuff inflator. The cuff inflator was adapted to ramp up more gradually to target pressure over 2 seconds, to minimize abrupt subject motion. Ten seconds after the end of each stimulus, subjects used a button box to complete two pain rating scales, both on 0 – 100 numerical scales: pain intensity (0 = ‘no pain’, 100 = ‘the most intense pain tolerable’), and pain unpleasantness (0 = ‘neutral’, 100 = ‘extremely unpleasant’). Subjects received each of the p0−p70 (p0 = ‘no pressure’, p70= ‘highest target pressure’) stimuli three times, for a total of 24 stimuli. Of note, stimulus pressure had a highly significant linear effect on both ratings of pain intensity and unpleasantness. The stimuli were delivered in a pseudorandom order in three separate runs, 8 stimuli per run. All physiological signals, including ECG and respiration, were collected at a sampling frequency of 400Hz. Written informed consent was obtained from all participants, and the protocol was approved by the Human Research Committee of Massachusetts General Hospital.

Before the actual experiment, a training session was conducted to familiarize subjects with the stimuli and rating procedures, and to determine appropriate stimulus intensities to be used subsequently. The highest pressure value which was consistently rated as non-painful was selected as p0, and thereafter stimulus intensities were individually calibrated.
4.6 Application to Pain Administration Protocol

Figure 4.5: From top to bottom, original RR-interval series, and point process estimates of HR, HRV, and LF/HF ratio for a 90s segment during a pain run for one representative subject (shaded areas indicate periods where pain is administered).

4.6.2 Pain Experiment Results

The proposed maximum likelihood point process algorithm is applied to each subject during three pain runs, and during the preceding resting epoch. Optimal model parameters were found to be $p = 4$, $q = 6$, $l = 90s$, and $\alpha = 0.98$ by initial empirical testing. Minimization of both AIC for the maximum likelihood estimation, and the KS distance on the KS plot are used as the optimization criteria. Figure 4.5 shows the original RR-interval series together with the estimated mean heart rate, HRV, and LF/HF ratio. Shaded areas show periods where pain is administered, i.e., two periods correspond to target pain intensities of p20 and p70, respectively. While HRV slightly decreases during the pain administration, which agrees with previous findings, we observe an increase in LF/HF ratio during pain compared to the immediately preceding period, suggesting reduced vagal inputs during pain. The KS plot and transformed quantiles’ autocorrelation function shown in Figure 4.6 confirm the goodness-of-fit of the model for the subject considered in Figure 4.5. Both the KS distance and autocorrelation values at different lags mostly stay within the 95% confidence intervals.
Figure 4.7 shows the original respiration signal together with the estimated respiratory frequency, coherence between respiration and RR-intervals at the respiratory frequency, and the dynamic RSA gain estimated for the same pain run and same subject considered above. Respiration is fairly constant, and respiratory frequency stays between $0.3 - 0.34$Hz. We observe a high coherence ($> 0.8$), which indicates that respiration and RR-intervals are highly correlated at the respiratory frequency. Importantly, we observe a decrease in RSA gain during the pain administration. During the second pain epoch (target intensity of p70), RSA gain drops even lower compared to the first epoch (target intensity of p20), suggesting that higher pain level is associated with lower RSA.

Mean RSA gain and LF/HF ratio during the rest epoch and three pain run epochs averaged over all subjects are shown in Figure 4.8. Results show that, in comparison to the resting period, all three pain runs elicited a significant decrease in RSA by over 21%. Wilcoxon signed-rank test is performed to test the hypothesis that RSA estimates significantly decrease during pain runs compared to the baseline resting period. The test results ($p = 0.05, 0.02, 0.05$) point at an overall reduction in parasympathetic tone during pain. Then, we compare our RSA estimates with the LF/HF ratio estimates. We found that LF/HF ratio expectedly increased during pain runs compared to the rest epoch, but the increments are not statistically significant ($p = 0.73, 0.10, 0.49$).

Figure 4.9 shows the correlation between estimated RSA gain and LF/HF
4.6 Application to Pain Administration Protocol

Figure 4.7: From top to bottom, original respiration signal, respiratory frequency, coherence between respiration and RR-intervals, and dynamic RSA estimation at the respiratory frequency for the example considered in Figure 4.5.

Figure 4.8: Mean RSA gain and LF/HF ratio during the rest epoch and three pain run epochs averaged over all subjects.
Figure 4.9: Mean RSA gain and LF/HF ratio at different intensity levels, averaged over three pain epochs and over all subjects.

The inverse Gaussian point process model of heart beat interval dynamics is applied to derive continuous estimates of RSA during a short-term pain administration experiment. Overall, a significant decrease in RSA is found when pain is administered as compared to the resting stage, in line with previous findings suggesting reduced vagal tone during pain experience. The results also show a negative correlation between RSA estimates and the target pain intensities. In comparing our RSA quantification with the standard sympathovagal balance indices, we found that the novel RSA assessment provides higher significance and sensitivity than any other time-varying instantaneous autonomic measure as computed within the proposed point process framework (including LF/HF). These encouraging results indicate that the proposed method may be able to differentiate pain stages, and fast transitions in protocols where pain is administered in short windows of time.
Future analysis will include assessing the correlations between the RSA estimation and subjects’ perspective of intensity and unpleasantness ratings of the pain. Also, future improvements to the model may consider frequency-dependent filters consistent with autonomic modulation physiology in order to obtain more direct estimates of vagal tone. Additionally, devising a multivariate model including arterial blood pressure as further covariate and accounting for directionality and causality will enable to disentangle the closed-loop blood pressure control dynamics from the respiratory-driven effects. Further, consideration of nonlinear models to comprise the nonlinear interactions observed in cardiovascular control and cardiorespiratory coupling may also lead to more accurate instantaneous HRV and RSA estimates. A precise dynamic RSA assessment could provide a useful complement to current standard HRV measures with the prospect of including RSA quantification into standard clinical or ambulatory monitoring systems to achieve better patient care.

4.7 Summary and Contributions

1. A maximum likelihood point process model is introduced for instantaneous HRV and RSA estimation. Differently than previously employed methods, time-varying spectral analysis of respiration, and coherence between inter beat intervals and respiratory signal is used for the dynamic RSA evaluation. Thus, the novel framework allows for robust tracking of RSA changes at any time resolution.

2. The problems associated with traditional subdivision in frequency bands were overcome by introducing the RSA estimations centered around the instantaneous respiratory frequency where, in general, maximum coherence between inter beat intervals and respiration is observed. Thus, the proposed method is robust to distinctive respiratory dynamics, where standard rigid subdivision of frequency band based methods may fail. The dynamic RSA estimation provides a better characterization of cardiorespiratory control compared to the standard time or frequency domain methods.

3. The proposed point process algorithm is applied to a pain protocol where
subjects experience series of pressure stimuli at different intensities. We found a reduced vagal tone during the pain experience, and also demonstrated the ability of the proposed method to differentiate between increasing pain stages.

4. The dynamic statistical measures computed from our point process framework provide the basis for potential real-time indicators for ambulatory monitoring, and instantaneous assessment of the autonomic control.
Chapter 5

Respiratory Sinus Arrhythmia Analysis during Meditation Practice

5.1 Introduction

In this Chapter, we study cardiorespiratory dynamics during meditation practice by applying the maximum likelihood point process algorithms and the dynamic respiratory sinus arrhythmia (RSA) estimation methods introduced in Chapter 4. Numerous reports have documented phase-locked decreases in respiratory rate during meditation periods [85, 106], thus a meditation protocol is an ideal setting for evaluating the robustness of the novel estimation methods under time-varying respiration activity concurrent with dynamic autonomic inputs. During the experiment, a group of experienced meditators practice ‘insight’ meditation, where distinctive respiratory dynamics are observed as a result of the meditation technique. The analysis also helps exploring the psychophysiological effects of meditation, and possible benefits of meditation on long-term cardiovascular health.

Meditation is a form of mental exercise that is becoming increasingly popular in the Western world. There are different types of meditation techniques available, but most of them are focused on training the mind to achieve a specific state of consciousness. Regular meditation practice produces psychophysiological
effects which are beyond the period of actual meditation [92]. Considerable attention has been given to analyze potential health benefits of meditation techniques, and its possible effects on neuroautonomic functions [107]. Findings suggest the existence of steady autonomic and cardiovascular adaptations that meditation practitioners experience along years of practice in order to gain deeper meditative states [109].

Meditation shows a high degree of cardiorespiratory synchronization compared to spontaneous breathing. Low respiratory frequencies during meditation result in decrease in high frequency (HF, 0.15 – 0.4Hz) power, and increase in low frequency (LF, 0.04 – 0.15Hz) power in heart rate variability (HRV), as well as pronounced and in-phase RSA [17, 40]. Jovanov [71] found significant increase in RSA and LF/HF ratio, and decrease in respiratory frequency following very slow yogic breathing exercises. Furthermore, Peng et al. [106, 107] challenged the notion of meditation as an autonomically quiescent state, and found active patterns of autonomic response during meditation, with prominent LF heart rate oscillations accompanied by an increase in mean resting heart rate. It has also been found that heart rate oscillations are highly correlated with respiration at the respiratory frequency during meditation practice [106, 107]. However, the HRV and RSA estimation methods used in these studies are static, and do not account for dynamic changes in autonomic inputs and respiration. The application of the proposed point process algorithms on meditation data provides dynamic and instantaneous HRV and RSA estimates, also accounting for underlying slow respiratory frequency patterns.

This Chapter is organized as follows: First, we introduce the meditation protocol, statistical description of the participating subjects, and experimental methods. Then, we estimate instantaneous heart rate and HRV parameters using the maximum likelihood point process model, and validate the model by goodness-of-fit tests. We perform time-frequency analysis of inter beat intervals, respiration, and estimate coherence between inter beat intervals and respiration, in order to compute the instantaneous frequencies which maximum respiration power and maximum coherence are observed. Then, we apply the bivariate AR model to estimate dynamic RSA, and compare the results of different RSA estimation methods. We also perform standard LF/HF spectral analysis in order
to demonstrate the superiority of the novel RSA estimation methods. Finally, we perform a comprehensive statistical analysis to highlight the significance of the findings, and to draw conclusions of our findings.

5.2 Meditation Protocol

The data were acquired from 13 experienced practitioners of Buddhist insight (a.k.a. Vipassana) meditation. The main focus of the insight meditation is the cultivation of attention and mindfulness. Mindfulness is defined as non-judgmental awareness of the present moment without cognitive elaboration [57, 72, 110]. The study participants were instructed to perform a breath awareness meditation technique, which consists of focusing attention on breathing sensations (flow of air through the nose, or rise and fall of the abdomen), and passively ignoring everyday thoughts. In total 4 females and 9 males, (25 to 49 years old, average 38.4), were included. They had been practicing insight meditation for between 1 and 20 years (average 8.7), and were required to have been practicing 40 minutes per day at least 5 days per week for at least 1 year, and to have attended at least one week long meditation retreat. The meditation retreat entailed approximately 10 hours of meditation per day. These subjects are compared to a demographically matched control group of 10 subjects, 4 females and 6 males, (24 to 49 years old, average 35.7), with no previous yoga or meditation experience. The meditation and control participants were matched for age, race, and years of education. All participants were physically and psychologically healthy, and none reported taking any medication or having any cardiovascular disease.

The experiment, which was conducted inside a magnetic resonance imaging (MRI) scanner as part of a larger study [84], started with a 6 minutes of baseline period, followed by 1 minute of fixation, then 24 minutes of meditation, followed by 1 minute of fixation, and finally 6 minutes of silent random number generation. The control group did not meditate, but rather simply rested throughout the corresponding 24-minute period. For analytical purposes, the meditation session was divided into three epochs (early, middle, late) of 8 minutes each, referring to the temporal stage of the meditation. Thus, in our results the experiment is divided into 5 epochs, baseline, early, middle, and late meditation, and
number generation phase. During the experiment, the blood volume pressure (BVP) signal was recorded, and it was used to identify the pulse intervals (PIs). Additionally, two respiration signals, a flow signal proportional to the airflow changes of the breath, and a belt signal proportional to lung volume changes, were recorded. All the raw signals obtained were initially sampled at 1kHz. Respiration signals were resampled at the pulse timings to obtain the respiration values at the beats, after low-pass filtering (cut-off 0.5Hz) to avoid aliasing.

A subset of 9 meditation subjects further performed an experiment in which they were cued to inhale and exhale in the exact pattern as during a previous meditation period (paced breathing), but without employing any meditation techniques. This was done in order to evaluate the intrinsic effects of meditation as opposed to the effects of ‘meditative’ breathing. External visual stimuli were used to cue the subjects to reproduce the same breathing patterns as in a previous meditation session. Both protocols were approved by the Institutional Review Board of Massachusetts General Hospital, Boston, MA, USA. Written informed consent was obtained from all study participants, and they were compensated for completion of assessment procedures.

5.3 Instantaneous PI and HRV Estimation

First, optimal values for regression orders of the bivariate model $p$ and $q$, local maximum likelihood interval $l$, and weighting time constant $\alpha$ are obtained by minimizing the AIC for maximum likelihood estimation, as well as the KS distance on the KS plot. This empirical optimization yields to $p = 4$, $q = 6$, $l = 90s$, and $\alpha = 0.98$. The proposed maximum likelihood point process model is then applied to both meditating and control subjects with these optimal model parameters. The instantaneous mean PI estimate $\mu_{PI}(t)$, PI variance $\sigma_{PI}^2(t)$, mean heart rate $\mu_{HR}(t)$, and HRV index $\sigma_{HR}^2(t)$ are updated every $\Delta = 5ms$.

The estimated instantaneous HRV indices for two representative subjects, one from each group, are shown in Figures 5.1 and 5.2, respectively. In particular, sudden variations can be observed in the estimated mean PI of the experienced meditator. These distinctive contractions are not classifiable as ectopic beats, but could be attributed to fast tachycardic or bradycardic events, possibly due
5.4 Model Goodness-of-Fit

The goodness-of-fit of the model is tested against the experimental data using KS plots and transformed quantiles' autocorrelation functions for each subject, as shown in Figure 5.3 for the two representative subjects. For all 23 subjects considered, the KS plots approximately follow the cumulative distribution function (cdf) of the uniform distribution (the ideal fit), and mostly stay within the

Figure 5.1: From top to bottom, instantaneous mean PI, PI variance, mean HR, and HRV indices estimated by the point process algorithm for an expert meditator subject.

to sharp shifts in the sympathovagal balance. Sharp increases in the HRV index are consequently observed at corresponding timings. Of note, similar transients are less frequent in the mean PI of the control subject.
95% confidence interval. The reportedly small KS distances further indicate that the model fits well with the original data.

Additionally, transformed quantiles’ autocorrelation plots are also generated for up to 60 lags (approximately 1 minute), and we observe a low autocorrelation for all the subjects. Very high number of points stay within the 95% confidence interval, which indicates that the model has successfully extracted all the dynamic structure from the original data.

5.5 Time-Frequency Analysis of PI and RP

After validating the model, time-frequency analysis of PI, RP, and coherence between PIs and RP is performed for each subject in order to identify the dynamic
respiratory frequency $\omega_{RP}(t)$, and the dynamic frequency where maximum coherence occurs $\omega_{coh}(t)$, as a preliminary step for evaluating dynamic RSA. The time-varying bivariate AR model is used to estimate the dynamic auto-spectra of PI and RP, as well as the cross-spectrum between the two. These time-frequency plots are shown in Figure 5.4 for the two representative subjects. From the time-frequency distributions of RP and coherence, it is evident that frequency of maximum coherence ($\omega_{coh}(t)$) closely matches with the respiratory frequency ($\omega_{RP}(t)$), confirming the mentioned assumption that the highest correlation between PIs and RP generally occurs at the predominant respiratory frequency.

For the meditation subject, a notable drop in the predominant respiratory frequency is observed during meditation. During baseline and number generation phases, the subject breaths at around 0.25Hz, whereas respiratory frequency
falls to around 0.2Hz during meditation (even slower in early meditation). Of note, each expert meditator exhibits different trends in respiration, likely due to individual differences in the ability to sustain a deep meditative state. Therefore, a reliable method for autonomic control assessment should be able to account for a wide range of respiratory dynamic changes. As the proposed method relies on estimates of instantaneous respiratory frequency to compute the RSA gain, it is possible to follow such variations in breathing. As we shall see in the later analysis, measures based on the standard subdivision of frequency bands are not able to account for such changes.

5.6 Instantaneous RSA Estimation

5.6.1 Respiration and Coherence based RSA Estimations

Next, the bivariate model for RSA introduced in Chapter 4, together with the time-frequency spectral characterization, is used to estimate the instantaneous RSA. As applied to the considered experimental data, the first important finding was that both $RSA_a^{gain}(t)$ (respiration based) and $RSA_b^{gain}(t)$ (coherence based) give very similar RSA estimates in all the subjects considered. As previously noted, this finding was somehow expected, as PIs are often highly correlated with respiration activity at the main respiratory frequency, indicating both $RSA_a^{gain}(t)$ and $RSA_b^{gain}(t)$ as reliable estimates of instantaneous RSA. Results are shown in Figures 5.5 and 5.6 for one experienced meditator, and for a control subject, respectively. For both subjects a high coherence (> 0.8) is generally observed, with only one evident exception in the experienced meditator where coherence drops below 0.8 at the timings corresponding to some of the fast transients in the heart beat dynamics.

A significant increase in RSA gain is clearly noticeable during meditation, whereas in the control subject RSA gain seems to fluctuate around baseline levels along the entire experiment. Of note, for a fair comparison across subjects, the RSA gain is normalized by the standard deviation of the corresponding RP. The significant increase in RSA during meditation practice is an important finding, and we further provide evidence to support this statement in the following
Figure 5.4: Time-frequency distributions of PI power (top), RP power (middle), and coherence between PI and RP (bottom) for the expert meditator (left) and the control subject (right).
Figure 5.5: Dynamic frequencies where maximum RP power is observed ($f_{RP}$) and coherence between PIs and RP is maximum ($f_{coh}$) (top), coherence at $f_{RP}$ and maximum coherence (middle), RSA gain estimated at $f_{RP}$ and $f_{coh}$ by the point process model (bottom) for the expert meditation subject (nrpu=normalized respiratory units).

Figure 5.6: Dynamic frequencies where maximum RP power is observed ($f_{RP}$) and coherence between PIs and RP is maximum ($f_{coh}$) (top), coherence at $f_{RP}$ and maximum coherence (middle), RSA gain estimated at $f_{RP}$ and $f_{coh}$ by the point process model (bottom) for the control subject.
5.6 Instantaneous RSA Estimation

Sections, including a detailed statistical analysis.

5.6.2 Dynamic and Static RSA Estimations

As the RSA transfer function exhibits low-pass characteristics [123], it could be argued that increases in RSA during meditation are not a result of meditation itself, but are only a result of the drop in breathing frequency. In order to account for such argument, we estimate the RSA gain at a fixed frequency. Figure 5.7 shows the comparison between two RSA estimates, one at the dynamic respiratory frequency, and one at a fixed frequency all along the experiment ($f_{fix} = 0.223$Hz for the particular meditation subject). The fixed frequency $f_{fix}$ was chosen so that, on average, the highest RP power was observed at $f_{fix}$ during the entire experiment. We refer to this fixed frequency based RSA estimation as static evaluation as opposed to the dynamic evaluations, $RSA^{a}_{gain}(t)$ and $RSA^{b}_{gain}(t)$, described in this thesis. Higher RSA is found during meditation regardless of whether the static or dynamic evaluation method was used, thus indicating that meditation yields higher RSA independently of changes in respiration. For the RSA estimation based on static frequency, drops in coherence are observed more frequently, especially during the early meditation epoch. Thus, the proposed dynamic RSA estimation based on time-varying respiration relies on higher values of coherence to provide more accurate results on the linear interactions associated with cardiorespiratory coupling.

It is important to highlight that the static evaluation requires observing the entire data segments in order to estimate the mean respiratory frequency, and as such could not be implemented in an on-line fashion for prospective real-time monitoring use. Furthermore, our dynamic evaluations add in flexibility, and overcome at the same time the problems associated with a rigid subdivision in frequency bands [93]. A more comprehensive statistical analysis as applied to the two groups considered is presented in Section 5.8.

5.6.3 Flow and Belt Respiration

We compare RSA estimates obtained by using two distinct acquisition methods for the respiration signals. The first method measures the air flow through the
subject’s airways (flow RP), whereas the second method measures the lung volume from the expansion and contraction of the abdomen using a respiration belt (belt RP). Even though both signals give similar respiratory frequencies, the amplitudes are incomparable, thus they were normalized by the standard deviation of each RP signal in each single experiment. Figure 5.8 shows a comparison of the instantaneous RSA estimations obtained using flow and belt respiration signals for the previously shown expert meditator subject. The correlation between RP frequencies estimated for two signals is 0.96, whereas the corresponding RSA estimates have a correlation of 0.83. Such high correlation indicates that regardless of the respiration measuring method, both flow and belt RP signals lead to a similar and consistent estimation of RSA. Deviations from a correlation of 1.0 can be reasonably attributed to experimental noise.

5.7 Standard LF/HF Spectral Analysis

We here compare the standard frequency domain indices [93] with the proposed RSA measures. Figure 5.9 shows the PI power in the LF (0.04 – 0.15Hz) and
5.7 Standard LF/HF Spectral Analysis

Figure 5.8: Comparison of RSA estimations obtained using flow RP and belt RP signals for the expert meditator subject.

Figure 5.9: From top to bottom, PI power in the LF band, PI power in the HF band, LF/HF ratio, and percentage RP power in the LF band for the expert meditator subject.
HF (0.15 – 0.5Hz) bands, the LF/HF ratio, and the percentage of RP power in the LF band for an exemplary meditation subject. It is interesting to note that for the considered subject, the average respiratory frequency was found to be 0.146Hz, which is at the borderline between the LF and HF bands. As shown in Figure 5.9, on average 47.3% of RP power falls in the LF band. This means that the respiratory-driven autonomic control on HRV is now present in both frequency bands, thus causing a bias in the LF/HF ratio as an indicator of the sympathovagal balance.

A slight increase in HF power is observed during the middle and late meditation epochs possibly due to the effects of meditation, but those changes are also mirrored in LF. Therefore the LF/HF ratio fails to capture the corresponding autonomic dynamics happening during meditation sessions, where slow breathing cycles are usually observed. In contrast (Figure 5.5), the proposed RSA estimates show an increase in RSA during practice epochs as a result of meditation influence, as would be expected from self-reports of increasing relaxation over the course of a typical meditation session.

5.8 Statistical Analysis

5.8.1 Time Domain Indices

In this Section, we present a statistical comparison of both meditation and control groups in terms of time domain indices. A summary of average PIs, heart rates, and their variances estimated by the point process model, and standard SDNN and pNN50 estimates for the two groups are shown in Table 5.1. On average, the control group exhibits a lower heart rate when compared to the expert meditator group, although with no statistically significant differences between the two groups. Of note, in Figure 5.2, the control subject exhibits a higher heart rate compared to the expert meditator, which is in disagreement with the mean statistics, possibly due to large variations in heart rate within each group. For both groups no significant changes in mean heart rate were observed during practice or number generation epochs compared to the baseline.
Table 5.1: Statistical comparison of point process heart beat indices between meditation and control groups, along with the standard time domain indices [93] (mean ± sd)

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Practice (Early)</th>
<th>Practice (Middle)</th>
<th>Practice (Late)</th>
<th>Numbers</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\mu_{PI}$ (ms)</td>
<td>Meditation</td>
<td>978 ± 115</td>
<td>1049 ± 168</td>
<td>992 ± 133</td>
<td>961 ± 105</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>1052 ± 176</td>
<td>1084 ± 178</td>
<td>1083 ± 172</td>
<td>1050 ± 160</td>
</tr>
<tr>
<td>$\mu_{HR}$ (bpm)</td>
<td>Meditation</td>
<td>62.4 ± 7.2</td>
<td>58.7 ± 9.3</td>
<td>61.8 ± 8.3</td>
<td>62.5 ± 9.6</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>62.4 ± 7.5</td>
<td>58.8 ± 9.6</td>
<td>57.0 ± 9.1</td>
<td>57.0 ± 8.8</td>
</tr>
<tr>
<td>$\sigma_{PI}$ (ms)</td>
<td>Meditation</td>
<td>27.1 ± 18.6</td>
<td>30.0 ± 19.1</td>
<td>29.1 ± 17.6</td>
<td>32.5 ± 20.6</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>26.2 ± 15.5</td>
<td>33.8 ± 23.9</td>
<td>35.7 ± 23.4</td>
<td>39.4 ± 27.0</td>
</tr>
<tr>
<td>$\sigma_{HR}$ (bpm)</td>
<td>Meditation</td>
<td>1.7 ± 1.2</td>
<td>1.8 ± 1.2</td>
<td>1.9 ± 1.2</td>
<td>2.4 ± 2.0</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>1.6 ± 0.8</td>
<td>1.8 ± 1.0</td>
<td>1.8 ± 1.0</td>
<td>1.9 ± 1.1</td>
</tr>
<tr>
<td>$SDNN$ (ms)</td>
<td>Meditation</td>
<td>56.7 ± 27.8</td>
<td>61.1 ± 23.2</td>
<td>65.4 ± 26.9</td>
<td>68.4 ± 32.1</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>68.5 ± 28.6</td>
<td>74.4 ± 32.9</td>
<td>78.7 ± 37.7</td>
<td>77.9 ± 37.5</td>
</tr>
<tr>
<td>$pNN50$ (%)</td>
<td>Meditation</td>
<td>24.0 ± 23.6</td>
<td>26.6 ± 19.8</td>
<td>27.9 ± 22.2</td>
<td>30.3 ± 25.0</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>35.9 ± 25.8</td>
<td>35.9 ± 25.6</td>
<td>38.6 ± 25.7</td>
<td>40.7 ± 23.5</td>
</tr>
</tbody>
</table>

[93] Refer to the cited reference for detailed methodology and data analysis.
Standard time domain measures SDNN and pNN50, as described in Chapter 4, also fail to show statistical significance between the two groups during practice epochs, although on average both SDNN and pNN50 are somewhat higher for the control group. For both groups a general increase in SDNN is observed during practice epochs compared to baseline or number generation epochs. In summary, standard time domain measures of HRV are not able to report any significant changes distinguishing meditation practice from very relaxing states.

5.8.2 Frequency Domain Indices

Average RSA statistics estimated by the proposed point process algorithm along with respiration and coherence statistics are shown in Table 5.2. We also compare the proposed RSA estimations with standard frequency domain HRV measures, and RSA measures computed within the HF band. PI power in HF increases (no statistical significance) in expert meditators during meditation practice, suggesting an improved vagal tone during meditation. We do not observe statistically significant changes in LF/HF as well, possibly due to the considerable transient presence of respiration within the LF band during meditation practice. Conversely, RSA gain estimated at instantaneous respiratory frequency using the proposed point process model does reveal significant differences between the baseline and meditation condition for the meditators. In fact, all three meditation epochs show a significant increase in RSA ($p \leq 0.01$), where increment is between 29% and 44% compared to the baseline. No such difference is found in the control group. In addition, coherence between PIs and RP remains high, between 0.86 and 0.96, at the respiratory frequency for both groups.

Within the meditation group, meditation epochs result in decrease in respiratory frequency as well as respiratory power, though changes are not significant. Previously it has been reported that the change in respiratory rate during meditation compared to baseline is highly correlated with meditation practice [84], suggesting that changes in respiration reflect increasing mastery of the meditation technique. Respiratory rate increases slightly during number generation phase for both groups compared to baseline, also without statistically significant differences.
In order to show that RSA statistics are not biased by lower predominant respiratory frequencies during meditation, we compute the RSA gains at fixed frequencies where (on average) maximum respiration is observed. We still found mean values comparable to the dynamic assessment (i.e., higher RSA during meditation which is not evident in control subjects), although with higher standard error, lower significance levels, and lower coherence values at constant frequencies. This important outcome indicates that RSA gains estimated accounting for dynamic respiratory frequencies provide a more accurate linear assessment, and consequently yield lower variability of the estimates and less identification uncertainty. During the silent random number generation phase, RSA values are statistically comparable to baseline levels in both groups.

Previous frequency domain methods estimated RSA within the HF band to disentangle effects from the baroreflex loop [11]. The proposed method is independent of such a frequency division, as it is based on time-varying instantaneous respiratory parameters. In order to explore frequency band biases, we have applied our proposed method singularly within the HF band and LF band (also in Table 5.2). Mean respiration power in HF decreases during meditation due to the shift in breathing rate to lower frequencies, then increasing back to baseline levels in the random number generation epoch. A similar trend is noticeable in the control group as well, but it is less significant. As expected, we observe an increase in RSA during meditation, but all the increments are less significant compared to the proposed dynamic RSA estimation where the entire spectrum was accounted for in the analysis. Interestingly, HF band based estimation fails to show a significant RSA increase ($p > 0.1$) for the third meditation epoch, compared to the highly significant results given by our dynamic RSA estimation ($p = 0.005$).

In the LF band, respiration power increases considerably during meditation. It is interesting to note that high coherence ($\geq 0.74$) is observed during meditation epochs between respiration and PIs even in this range. This is possibly due to the ‘leakage’ of RP power into LF during meditation, consequently increasing respiratory driven effects in the LF band within the baroreflex control loop, and biasing the LF/HF ratio as a measure of sympathovagal balance. Importantly, results from the control group do not evidence a similar effect.
Table 5.2: Statistical comparison of RP, coherence, and estimated RSA indices between meditation and control groups, along with the standard frequency domain HRV measures (mean ± sd)

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Practice (Early)</th>
<th>Practice (Middle)</th>
<th>Practice (Late)</th>
<th>Numbers</th>
</tr>
</thead>
<tbody>
<tr>
<td>PI power in LF (10^{-3}ms²)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meditation</td>
<td>2.23 ± 0.75</td>
<td>2.22 ± 0.54</td>
<td>2.18 ± 0.57</td>
<td>2.45 ± 0.71</td>
<td>1.86 ± 0.39</td>
</tr>
<tr>
<td>Control</td>
<td>1.98 ± 0.50</td>
<td>2.26 ± 0.70</td>
<td>2.22 ± 0.90</td>
<td>2.29 ± 0.72</td>
<td>1.56 ± 0.48</td>
</tr>
<tr>
<td>PI power in HF (10^{-3}ms²)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meditation</td>
<td>1.96 ± 0.56</td>
<td>2.75 ± 0.96</td>
<td>2.90 ± 0.94</td>
<td>2.70 ± 0.70</td>
<td>2.42 ± 0.84</td>
</tr>
<tr>
<td>Control</td>
<td>1.87 ± 0.64</td>
<td>1.89 ± 0.64</td>
<td>2.26 ± 0.76</td>
<td>2.39 ± 0.80</td>
<td>2.20 ± 0.92</td>
</tr>
<tr>
<td>LF/HF</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meditation</td>
<td>1.68 ± 0.26</td>
<td>1.93 ± 0.41</td>
<td>1.67 ± 0.28</td>
<td>1.61 ± 0.27</td>
<td>1.73 ± 0.36</td>
</tr>
<tr>
<td>Control</td>
<td>1.48 ± 0.40</td>
<td>1.27 ± 0.14</td>
<td>1.35 ± 0.27</td>
<td>1.40 ± 0.28</td>
<td>1.25 ± 0.27</td>
</tr>
<tr>
<td>RSA at dynamic $f_{RP}$ (ms/nrpu)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meditation</td>
<td>33.3 ± 5.6</td>
<td><strong>47.7 ± 6.9</strong></td>
<td><strong>43.1 ± 6.9</strong></td>
<td><strong>47.8 ± 7.3</strong></td>
<td>27.6 ± 4.9</td>
</tr>
<tr>
<td>Control</td>
<td>29.0 ± 6.2</td>
<td>23.8 ± 7.2</td>
<td>24.2 ± 7.5</td>
<td>25.2 ± 6.3</td>
<td>26.7 ± 5.5</td>
</tr>
<tr>
<td>$f_{RP}$ (Hz)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meditation</td>
<td>0.20 ± 0.07</td>
<td>0.16 ± 0.03</td>
<td>0.17 ± 0.04</td>
<td>0.17 ± 0.05</td>
<td>0.22 ± 0.05</td>
</tr>
<tr>
<td>Control</td>
<td>0.23 ± 0.08</td>
<td>0.24 ± 0.08</td>
<td>0.25 ± 0.07</td>
<td>0.25 ± 0.07</td>
<td>0.25 ± 0.05</td>
</tr>
<tr>
<td>Coherence at dynamic $f_{RP}$</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meditation</td>
<td>0.89 ± 0.11</td>
<td>0.93 ± 0.04</td>
<td>0.89 ± 0.09</td>
<td>0.89 ± 0.10</td>
<td>0.86 ± 0.14</td>
</tr>
<tr>
<td>Control</td>
<td>0.96 ± 0.03</td>
<td>0.92 ± 0.08</td>
<td>0.95 ± 0.05</td>
<td>0.92 ± 0.09</td>
<td>0.92 ± 0.06</td>
</tr>
<tr>
<td>RSA at fixed freq. (ms/nrpu)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meditation</td>
<td>30.3 ± 6.5</td>
<td><strong>46.6 ± 8.0</strong></td>
<td><strong>41.5 ± 8.7</strong></td>
<td><strong>45.4 ± 10.9</strong></td>
<td>28.3 ± 9.6</td>
</tr>
<tr>
<td>Control</td>
<td>29.8 ± 6.6</td>
<td>24.2 ± 7.7</td>
<td>25.2 ± 8.5</td>
<td>25.5 ± 7.1</td>
<td>27.1 ± 6.8</td>
</tr>
<tr>
<td>Coherence at fixed freq.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meditation</td>
<td>0.63 ± 0.25</td>
<td>0.81 ± 0.09</td>
<td>0.75 ± 0.14</td>
<td>0.78 ± 0.11</td>
<td>0.62 ± 0.21</td>
</tr>
<tr>
<td>Control</td>
<td>0.79 ± 0.15</td>
<td>0.84 ± 0.13</td>
<td>0.88 ± 0.09</td>
<td>0.88 ± 0.10</td>
<td>0.73 ± 0.19</td>
</tr>
</tbody>
</table>

*Continue on next page*
Continued from previous page

Statistical comparison of RP, coherence, and estimated RSA indices between meditation and control groups, along with the standard frequency domain HRV measures (mean ± sd)

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Practice (Early)</th>
<th>Practice (Middle)</th>
<th>Practice (Late)</th>
<th>Numbers</th>
</tr>
</thead>
<tbody>
<tr>
<td>RP power in HF (10^{-4} rpu²)</td>
<td>Meditation</td>
<td>1.93 ± 0.40</td>
<td>1.27 ± 0.27</td>
<td>1.43 ± 0.27</td>
<td>1.37 ± 0.27</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>2.91 ± 0.79</td>
<td>2.88 ± 0.72</td>
<td>2.74 ± 0.69</td>
<td>2.88 ± 0.70</td>
</tr>
<tr>
<td>RSA at max. coh. in HF (ms/nrpu)</td>
<td>Meditation</td>
<td>32.7 ± 5.1</td>
<td><strong>43.1 ± 8.0</strong></td>
<td><strong>39.2 ± 8.9</strong></td>
<td>38.6 ± 9.3</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>30.9 ± 6.5</td>
<td>27.7 ± 5.3</td>
<td>26.6 ± 7.6</td>
<td>27.7 ± 7.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(p &gt; 0.1)</td>
<td>(p &gt; 0.1)</td>
<td>(p &gt; 0.1)</td>
<td>(p &gt; 0.1)</td>
</tr>
<tr>
<td>freq. of max. coh. in HF (Hz)</td>
<td>Meditation</td>
<td>0.22 ± 0.04</td>
<td>0.19 ± 0.02</td>
<td>0.19 ± 0.03</td>
<td>0.20 ± 0.03</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>0.25 ± 0.05</td>
<td>0.26 ± 0.07</td>
<td>0.26 ± 0.06</td>
<td>0.26 ± 0.06</td>
</tr>
<tr>
<td>max. coh. in HF</td>
<td>Meditation</td>
<td>0.86 ± 0.11</td>
<td>0.84 ± 0.14</td>
<td>0.86 ± 0.09</td>
<td>0.83 ± 0.15</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>0.92 ± 0.07</td>
<td>0.92 ± 0.06</td>
<td>0.93 ± 0.05</td>
<td>0.92 ± 0.07</td>
</tr>
<tr>
<td>RP power in LF (10^{-4} rpu²)</td>
<td>Meditation</td>
<td>0.42 ± 0.18</td>
<td>0.70 ± 0.19</td>
<td>0.53 ± 0.14</td>
<td>0.53 ± 0.18</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>0.19 ± 0.05</td>
<td>0.15 ± 0.06</td>
<td>0.17 ± 0.07</td>
<td>0.17 ± 0.06</td>
</tr>
<tr>
<td>RSA at max. coh. in LF (ms/nrpu)</td>
<td>Meditation</td>
<td>33.6 ± 6.4</td>
<td>26.7 ± 5.0</td>
<td>29.8 ± 6.5</td>
<td>33.6 ± 6.7</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>32.6 ± 6.3</td>
<td>34.6 ± 7.1</td>
<td>29.2 ± 7.2</td>
<td>33.9 ± 5.8</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(p &gt; 0.1)</td>
<td>(p &gt; 0.1)</td>
<td>(p &gt; 0.1)</td>
<td>(p &gt; 0.1)</td>
</tr>
<tr>
<td>freq. of max. coh. in LF (Hz)</td>
<td>Meditation</td>
<td>0.12 ± 0.02</td>
<td>0.13 ± 0.02</td>
<td>0.13 ± 0.01</td>
<td>0.13 ± 0.01</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>0.12 ± 0.02</td>
<td>0.12 ± 0.02</td>
<td>0.13 ± 0.02</td>
<td>0.13 ± 0.02</td>
</tr>
<tr>
<td>max. coh. in LF</td>
<td>Meditation</td>
<td>0.64 ± 0.21</td>
<td>0.82 ± 0.12</td>
<td>0.79 ± 0.16</td>
<td>0.74 ± 0.19</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>0.59 ± 0.22</td>
<td>0.61 ± 0.21</td>
<td>0.58 ± 0.19</td>
<td>0.60 ± 0.16</td>
</tr>
</tbody>
</table>
Figure 5.10: Mean values and standard errors of dynamic RSA estimates for meditator and control groups during rest, practice, and number generation phases.

Figure 5.10 shows the mean RSA as estimated by the proposed point process model for the two groups, along different epochs in the experiment. Again, ‘practice’ epochs implicate engaging in meditation for the meditator group, while ‘practice’ refers to relaxation for the control group. The expert meditator group has a significantly high RSA gain during meditation, while the control group does not show significant changes compared to the baseline epoch. Expectedly, both dynamic RSA measures proposed in this thesis, respiration based and coherence based, give similar statistics for RSA estimates.

5.8.3 Paced Breathing

Finally, we further compare the RSA statistics of the meditation group during the paced breathing experiment with the meditation experiment. As expected, paced breathing successfully reproduces respiration characteristics as during meditation, with undistinguished mean respiratory frequencies \( f_{RP} = 0.17 \pm 0.06\text{Hz} \) paced vs. \( 0.17 \pm 0.04\text{Hz} \) meditation). As we compare results from the respective respiration dynamics within each subject, it is reasonable to assume that the dif-
Figure 5.11: Paced breathing: middle epoch reproduces slow breathing pattern as in meditation, but no significant changes in RSA were found compared to the baseline epoch.

ferences between the two experiments solely represent the effects of meditation. On average, at dynamic respiratory frequency, mean coherence was found to be $0.91 \pm 0.07$ ($0.89 \pm 0.09$ with meditation), and at the fixed frequency it dropped to $0.80 \pm 0.08$ ($0.75 \pm 0.14$ with meditation).

Figure 5.11 shows dynamic RSA estimates during paced breathing for one representative subject. Overall, even in the presence of slower respiratory frequencies, RSA estimation does not alter significantly during paced breathing as compared to the baseline. For the group of subjects considered, no statistical significance ($p = 0.10$) was found between baseline and paced breathing, as opposed to the high significance ($p = 0.0005$) obtained during meditation. This result further supports the finding that changes in RSA during meditation are not simply due to changes in respiratory rate, but effectively associated to meditation practice.
5.9 Discussion of Meditation Results

The maximum likelihood point process model introduced in Chapter 4 is applied for instantaneous estimation of a set of HRV and RSA measures in a meditation protocol under dynamic respiration characteristics. Within the point process model, the mean PI is modeled as a bivariate regression of both previous PIs and respiration values. We termed the feed-forward dependency of the PIs on respiration as RSA, and a transfer function approach is used to quantify the instantaneous RSA estimates. The model is validated statistically using KS goodness-of-fit tests and independence tests.

Obviating any artificial subdivision in frequency bands, our proposed method is robust to variations in respiration patterns observed during meditation practice, and relies on the instantaneous respiratory spectral power distribution and the dynamic coherence between respiration and PIs. As a further proof that RSA gains are not considerably biased by possible shifts in predominant respiratory frequency, we have computed similar indices at pre-estimated fixed frequencies where coherence is highest on average along each experiment, and verified that average statistics using fixed frequency based estimates corroborate the results from the proposed method. We have also demonstrated that considering the entire spectrum instead of designated frequency intervals leads to more reliable and less variable estimates.

Statistical analysis further reports a significant increase of RSA during meditation for the expert meditator group, while no relevant difference and no statistical significance was found for the control group, or during paced breathing. While traditional HRV indices confirm previous findings pointing at an autonomic assessment not necessarily reflective of quiescent cardiac dynamics [106], and possibly biased by altered breathing patterns [85], our statistical RSA appraisal substantiates previous reports of a marked increase of RSA during meditation [44], and further indicates that these changes are not simply due to changes in respiration. Although unlikely, it is possible that mental effort of following the visual cues during the paced breathing condition may have contributed to the observed differences in RSA between this condition and the meditative state. However, the meditative state also requires some mental effort to remain focused,
5.10 Summary and Contributions

and so differences in cognitive load between the conditions is likely minimal.

Our findings are further substantiated by the absence of an increase in RSA during an experiment in which respiratory dynamics similar to those in meditation were reproduced without effective meditation practice. Comparison between the two protocols allows for isolation of the physiological effects of meditation, thus removing possible additional biases in parameter estimation due to systematic changes in respiration characteristics, and it helps in identifying important changes in cardiorespiratory coupling in the presence of dynamic breathing patterns. Therefore, our overall results support the hypothesis that increased RSA during mindfulness meditation performed by experienced practitioners may reflect adaptive properties of the central-autonomic nervous system to this practice, that are not related to any ‘voluntary intention’ towards the breathing process.

Future research will be required to identify physiological and psychological causes of increased RSA during meditation. As some studies suggest, meditation-based clinical interventions can impact physiological recovery during emotional challenges [53, 103]. These RSA measures may provide useful novel applications in dynamic instantaneous impact of meditation and other behavioral interventions on autonomic functioning. Future studies may address whether these methods can also be used to determine an objective measure of meditative states. Such research may lead to finding how meditation practice is capable of positively influencing mood and decreasing arousal with targeted changes to the vagal tone.

5.10 Summary and Contributions

1. The maximum likelihood point process algorithm is applied to subjects practicing meditation who had prior meditation experience, and a control group who were asked to relax under equal conditions. Results show a significant increase in RSA during meditation practice, which is not evident in the control group, providing interesting insights into the effects of meditation on cardiorespiratory function. The results encourage further investigation into the potential benefits of meditation on cardiovascular health.
2. The point process RSA estimation applied on a second experiment, i.e., a paced breathing experiment, further complements the results obtained in the meditation protocol by removing possible biases in the parameter estimation due to systematic changes in respiration characteristics. Lack of RSA changes during paced breathing demonstrates that RSA increase is due to the intrinsic effects of the meditation.

3. A detailed statistical analysis show that proposed dynamic RSA estimation methods generate indices with statistically significant results in the meditation protocol, compared to the standard HRV measures or fixed frequency based RSA estimates.

4. For all meditation and control subjects considered KS plots and transformed quantiles autocorrelation functions mostly stay between 95% confidence intervals, indicating that novel point process based RSA estimation methods are highly suitable for assessing cardiorespiratory dynamics in experimental protocols where significant variation in the respiration is observed.
Chapter 6

Conclusions and Future Directions

6.1 Conclusions

This thesis presents novel signal processing algorithms for cardiac arrhythmia analysis and cardiorespiratory control. We investigate atrial fibrillation arrhythmia, which is the most common cardiac arrhythmia condition found in clinical practice, associated with an increased risk of stroke. The algorithms we develop for analyzing atrial fibrillation from ECG recordings are capable of monitoring the fibrillatory rate accurately and dynamically, thus facilitate characterizing atrial fibrillation episodes into paroxysmal and persistent types. These results could be further developed into aiding tailored treatment methods for atrial fibrillation in clinical practice. In this study, we develop a new class of time-frequency distributions, which is capable of achieving good time and frequency resolutions with reduced cross-terms. These new time-frequency distributions and the novel framework for developing them have many applications in analyzing various multi-component signals beyond the applications shown in this thesis.

Heart rate variability and respiratory sinus arrhythmia are important indicators of cardiovascular health of a subject. These measures provide vital information on autonomic nervous system functions and cardiorespiratory coupling. The second half of the thesis introduces a maximum likelihood inverse Gaussian
point process model for instantaneous estimations of heart rate variability and respiratory sinus arrhythmia. Most of the existing estimation methods do not take into account the dynamic changes in respiration and autonomic inputs, rely on interpolation of heart beat intervals which conflicts with underlying physiology, and fail to provide instantaneous estimates. Our model overcomes these shortcomings, and provides dynamic and instantaneous estimates of heart rate variability and respiratory sinus arrhythmia. Further, we give statistical evidence to the accuracy of the model by model goodness-of-fit tests. We apply the proposed model in two experimental protocols which exhibit distinctive psychophysiological states, acute pain and meditation, to characterize important changes in respiratory sinus arrhythmia during these experiments. Below we describe the main findings and conclusions of the thesis in more detail.

In Chapter 2, we introduce a framework for deriving kernel functions for the Cohen class of quadratic time-frequency distributions based on multi-dimensional Fourier transform of a radially symmetric function. The framework generates highly structured kernels with desirable properties and distinctive characteristics. Our framework generalizes and improves the existing reduced interference distribution framework. Then, the framework was used for a radial-$\delta$ function to derive a generalized kernel formula, which subsumes existing and well known kernels of Margenau-Hill, Born-Jordan, and Bessel distributions. Though these distributions were introduced in the literature independently, our results show the relationship between them, containing them into a single formula. The higher order radial-$\delta$ kernels are shown to be more effective in time-frequency analysis of multi-component signals, as they are capable of reducing interference terms in the time-frequency plane while achieving good time and frequency resolutions. Finally, we present a novel sinh-$\delta$ kernel which generates a Kaiser window based time-frequency distribution. The higher order radial-$\delta$ kernels and the sinh-$\delta$ kernel which show superior characteristics in time-frequency analysis of multi-component signals are new revelations in this thesis.

In Chapter 3, we analyze atrial fibrillation cardiac arrhythmia condition from ECG recordings using new algorithms, which include the new time-frequency distributions presented. First, we introduce a regularized orthonormal basis function based interpolation method for atrial activity extraction from atrial
fibrillation ECGs. We show that the proposed method cancels out the dominant ventricular components successfully, and extracts atrial activity preserving morphological features, compared to the widely used average beat subtraction method. Then, several time-frequency distributions including new radial-δ kernel based distributions are applied on the extracted atrial signal to estimate the time-varying dominant atrial fibrillation frequency. We show that higher order radial-δ kernel based distributions estimate the dynamic atrial fibrillation frequency more accurately, with better time and frequency resolutions and less cross-terms. Furthermore, atrial activity extraction and subsequent fibrillatory frequency tracking have been combined into a single algorithm for efficient computation. Such a direct analysis may assist real-time monitoring of atrial fibrillation. The proposed algorithms are tested on simulated as well as real ECGs with atrial fibrillation episodes. Results show accurate tracking of fibrillatory frequencies, which enable identification of different types of atrial fibrillation episodes.

We introduce a maximum likelihood point process model for estimation of heart rate variability and respiratory sinus arrhythmia in Chapter 4. Our model based on inverse Gaussian point process represents the underlying physiology of heart beat generation process accurately. We estimate heart rate variability and respiratory sinus arrhythmia dynamically, based on instantaneous respiratory frequency and frequency where maximum coherence between heart beat intervals and respiration is observed. Thus, our method is robust to fast dynamic changes in respiration and autonomic inputs compared to the existing methods. The algorithm utilizes time-frequency analysis of heart beat intervals and respiratory signal, thus provides a better characterization of cardiorespiratory control compared to the standard time or frequency domain methods. It also overcomes nonstationarity problems associated with the traditional subdivision of fixed frequency bands for heart rate variability estimation by computing the estimations centered around instantaneous respiratory frequency. Our simulation results demonstrate the ability of the proposed algorithm to estimate respiratory sinus arrhythmia accurately even when autonomic and respiratory parameters are fast changing.

The proposed point process algorithm is applied to two experimental proto-
cols which show distinctive psychophysiological characteristics. The first protocol consisted of subjects experiencing controlled acute pain at a range of intensity levels. The results indicate reduced respiratory sinus arrhythmia during pain experience. Further, we found a strong inverse correlation between pain intensity level and respiratory sinus arrhythmia estimations. Our results motivate further investigation into application of respiratory sinus arrhythmia estimation as an indicator of the acute pain level. In the second experiment we investigate the effects of meditation techniques on cardiorespiratory control by applying the point process model. The chosen protocol consisted of subjects who has considerable prior meditation experience practicing ‘insight’ meditation, and a control group who were asked to relax under equal conditions. Our results indicate a significant increase in respiratory sinus arrhythmia during meditation practice, which is not evident in the control group, providing interesting insights into the benefits of meditation on cardiorespiratory function. Additionally, a further analysis is conducted on a paced breathing experiment where meditation subjects experience similar respiration characteristics as in meditation, but without performing meditation in order to differentiate the physiological effects of meditation from the respiratory rate driven autonomic changes. The results further confirm that meditation results in increased vagal tone, and thus may have positive influence on cardiovascular health. In both experiments, model goodness-of-fit tests and detailed statistical analysis provide the validity and the significance of the results.

6.2 Future Research Directions

The results presented in this thesis give rise to number of new directions for future research:

1. The generic framework for kernel function design based on multi-dimensional Fourier transform of a radial function can be further utilized for generating highly structured kernels for quadratic time-frequency distributions. Though we derive a class of kernels based on a radial-$\delta$ function, carefully chosen other functions may also yield to kernels with desirable characteristics for time-frequency analysis of various nonstationary signals.
2. The algorithms presented in this thesis are capable of accurate identification and tracking of fibrillatory frequencies of atrial fibrillation from ECG recordings. A fibrillatory frequency based discrimination analysis could be further employed for characterizing atrial fibrillation episodes into paroxysmal and persistent types. Thus, treatment methods such as direct current cardioversion or pharmaceutical therapy can be tailored accordingly.

3. The maximum likelihood point process model could be further improved by introducing additional variables to the model. For example, arterial blood pressure could be added as a covariate to the multivariate model of respiratory sinus arrhythmia estimation. Having arterial blood pressure in the model will enable differentiating closed-loop blood pressure control dynamics from the respiratory driven effects. Also, nonlinear interactions between heart beat intervals and respiration could be modeled by carefully introducing additional terms to the model which capture the nonlinear dynamics. These additions may lead to more accurate heart rate variability and respiratory sinus arrhythmia estimates. Further, a vagal filter may be applied to the proposed model, which would enable obtaining more direct estimates of vagal control of the autonomic nervous system.

4. Furthering the results presented on the meditation protocol, future research is required to identify physiological and psychological causes of increased respiratory sinus arrhythmia during meditation. Future studies may address whether the proposed respiratory sinus arrhythmia estimation methods can also be used to determine an objective measure of meditative states. It may also lead to finding how meditation practice is capable of positively influencing mood and decreasing arousal with targeted changes to the parasympathetic tone.

5. Sympathetic and parasympathetic tones as well as the sympathovagal balance are important predictors of atrial fibrillation episodes [52]. Thus, proposed point process based heart rate variability and respiratory sinus arrhythmia estimation algorithms could be employed for further analysis of atrial fibrillation. Combining the point process algorithms to estimate the
autonomic tone with the proposed time-frequency analysis of atrial fibrillation may result in improved understanding of paroxysmal and persistent atrial fibrillation conditions.

As final note, the overall results achieved during the course of the presented thesis work constitute a pertinent advancement in the analysis and modeling of cardiac arrhythmia and cardiorespiratory control, and they point at several long-term research goals and directions. In particular, the fibrillatory frequency estimation methods we have developed encourage a better understanding of the wavefront propagation mechanisms in cardiac tissues of the human heart, whereas findings of improved vagal tone during meditation practice encourage further investigation into permanent alterations in the brain structure and the nervous system which may occur due to long-term meditation. Finally, as acute pain is a major symptom in many medical conditions, the relationships we established between pain and respiratory sinus arrhythmia promotes further research on the use of cardiorespiratory estimates as an early diagnosing tool for central-autonomic neurological disorders.
Bibliography


