Cross-correlation: A Contrast method for studying fetal cardiovascular time series

Stacy Kalisz

Follow this and additional works at: http://scholarworks.rit.edu/theses

Recommended Citation
CROSS-CORRELATION: A Contrast Method for Studying Fetal Cardiovascular Time Series

A Thesis Submitted in Partial Fulfillment of the Requirements for the

MASTER OF SCIENCE

in Mechanical Engineering at Rochester Institute of Technology, 1996

By

Stacy Kalisz

Approvals:

Dr. Mark H. Kempski, Thesis Advisor

Dr. Kevin Kochersberger, Thesis Committee

Dr. Alan Nye, Thesis Committee

Dr. Charles Haines, Department Head
Release

I, Stacy Kalisz, hereby grant permission to the Wallace Memorial Library of the Rochester Institute of Technology to reproduce my Thesis entitled CROSS CORRELATION: A Contrast Method for Studying Fetal Cardiovascular Time Series, in whole or part. Any such reproductions may not be for commercial use or profit.

Signed,

Stacy Kalisz

12/12/96
(Date)
# Table of Contents

Table of Contents i

List of Figures iv

List of Tables ix

Abstract x

1.0 Introduction 1
   1.1 Objectives 2
   1.2 Waveforms Studied 3
   1.3 Cardiovascular Background 6

2.0 Methodology 7
   2.1 Sonography 7
   2.2 Waveform Reconstruction 8
   2.3 Theory 9
   2.4 Cross-correlation 11
   2.5 Test Cases 14
      2.5.1 Composite Sinusoid Example 14
      2.5.2 Examples Containing Noise 21
         2.5.2.1 Noise Case A 21
         2.5.2.2 Noise Case B 27
         2.5.2.3 Summary 32
      2.5.3 Cross-correlation Sequencing 34
   2.6 Processing Performed 38
      2.6.1 Maternal breathing intact versus 38
          maternal stopped breathing study
      2.6.2 Cross Gestational Study 39

3.0 Results 41
   3.1 Maternal breathing intact versus 41
      maternal stopped breathing study
      3.1.1 Band Power Ratio Results 42
         3.1.1.1 MVV Cross-correlated With HRV 42
         3.1.1.2 MVV Cross-correlated With PVV 42
3.1.1.3 HRV Cross-correlated With PVV 45
3.1.2 Band Power Absolute Results 45
  3.1.2.1 MVV Cross-correlated With HRV 45
  3.1.2.2 MVV Cross-correlated With PVV 48
  3.1.2.3 HRV Cross-correlated With PVV 48

3.2 Cross Gestational Study 51
  3.2.1 Band Power Ratio Results 51
    3.2.1.1 MVV Cross-correlated With HRV 51
    3.2.1.2 MVV Cross-correlated With PVV 52
    3.2.1.3 HRV Cross-correlated With PVV 55
  3.2.2 Band Power Absolute Results 55
    3.2.2.1 MVV Cross-correlated With HRV 55
    3.2.2.2 MVV Cross-correlated With PVV 58
    3.2.2.3 HRV Cross-correlated With PVV 58
  3.2.3 Other Cross Gestational Observations 61

3.3 General Observations 61

4.0 Discussion 63
  4.1 Test Cases 63
  4.2 Maternal breathing intact versus maternal stopped breathing study 65
  4.3 Cross Gestational Study 66

5.0 Future Research and Applications 70

References 72

Appendix A SK ac/cc processing.VI 75
  A.1 SK ac/cc processing.VI 75
  A.2 Default Values 76

Appendix B Sub-VI’s 78
  B.1 Separate Data.vi 78
  B.2 Cross Correlates.vi 78
  B.3 Case Struc for Divisions.vi 79

Appendix C User’s Guide 80
Appendix D  Other potential algorithm uses  82

Appendix E  Abstract - Ursem et. al.  83
## List of Figures

<table>
<thead>
<tr>
<th>Figure</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Section 1</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-1</td>
<td>Umbilical Artery Velocity Profile</td>
<td>3</td>
</tr>
<tr>
<td>1-2</td>
<td>Variability Time Series Construction</td>
<td>5</td>
</tr>
<tr>
<td>a</td>
<td>Heart Rate Variability</td>
<td></td>
</tr>
<tr>
<td>b</td>
<td>Peak Velocity Variability</td>
<td></td>
</tr>
<tr>
<td>c</td>
<td>Mean Velocity Variability</td>
<td></td>
</tr>
<tr>
<td><strong>Section 2</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2-1</td>
<td>Composite Sinusoid Y</td>
<td>16</td>
</tr>
<tr>
<td>2-2</td>
<td>Power Density Spectrum $\left(\text{Vrms}\right)^2/\text{Hz}$ of Composite Sinusoid Y</td>
<td>16</td>
</tr>
<tr>
<td>2-3</td>
<td>Composite Sinusoid Z</td>
<td>17</td>
</tr>
<tr>
<td>2-4</td>
<td>Power Density Spectrum $\left(\text{Vrms}\right)^2/\text{Hz}$ of Composite Sinusoid Z</td>
<td>17</td>
</tr>
<tr>
<td>2-5</td>
<td>Single-sided Cross-correlation of the Composite Sinusoids</td>
<td>19</td>
</tr>
<tr>
<td>2-6</td>
<td>Single-sided Cross-spectral Amplitude Spectrum of the Composite Sinusoids $\left(\text{Vrms}\right)^2/\text{Hz}$</td>
<td>19</td>
</tr>
<tr>
<td>2-7</td>
<td>Band Power Representation of the Composite Sinusoid Cross-correlation Results</td>
<td>20</td>
</tr>
<tr>
<td>2-8</td>
<td>Composite Sinusoid Y with noise (amplitude 2.32) added</td>
<td>22</td>
</tr>
<tr>
<td>2-9</td>
<td>Power Density Spectrum $\left(\text{Vrms}\right)^2/\text{Hz}$ of Composite Sinusoid Y- noise (amplitude 2.32) added</td>
<td>22</td>
</tr>
<tr>
<td>2-10</td>
<td>Composite Sinusoid Z with noise (amplitude 2.32) added</td>
<td>23</td>
</tr>
<tr>
<td>2-11</td>
<td>Power Density Spectrum $\left(\text{Vrms}\right)^2/\text{Hz}$ of Composite Sinusoid Z with noise (amplitude 2.32) added</td>
<td>23</td>
</tr>
<tr>
<td>Figure</td>
<td>Description</td>
<td>Page</td>
</tr>
<tr>
<td>--------</td>
<td>------------------------------------------------------------------------------</td>
<td>------</td>
</tr>
<tr>
<td>2-12</td>
<td>Single-sided Cross-correlation of the Composite Sinusoids with noise (amplitude 2.32) added</td>
<td>25</td>
</tr>
<tr>
<td>2-13</td>
<td>Single-sided Cross-spectral Amplitude Spectrum of the Composite Sinusoids with noise (amplitude 2.32) added [(V_{rms})^2/Hz]</td>
<td>25</td>
</tr>
<tr>
<td>2-14</td>
<td>Band Power Representation of the Composite Sinusoid Cross-correlation Results with noise (amplitude 2.32) added</td>
<td>26</td>
</tr>
<tr>
<td>2-15</td>
<td>Band Power Results with noise (amplitude 2.32) added and averaged 10 times</td>
<td>26</td>
</tr>
<tr>
<td>2-16</td>
<td>Composite Sinusoid Y with noise (amplitude 7) added</td>
<td>28</td>
</tr>
<tr>
<td>2-17</td>
<td>Power Density Spectrum [(V_{rms})^2/Hz] of Composite Sinusoid Y with noise (amplitude 7) added</td>
<td>28</td>
</tr>
<tr>
<td>2-18</td>
<td>Composite Sinusoid Z with noise (amplitude 7) added</td>
<td>29</td>
</tr>
<tr>
<td>2-19</td>
<td>Power Density Spectrum [(V_{rms})^2/Hz] of Composite Sinusoid Z with noise (amplitude 7) added</td>
<td>29</td>
</tr>
<tr>
<td>2-20</td>
<td>Single-sided Cross-correlation of the Composite Sinusoids with noise (amplitude 7) added</td>
<td>30</td>
</tr>
<tr>
<td>2-21</td>
<td>Single-sided Cross-spectral Amplitude Spectrum of the Composite Sinusoids with noise (amplitude 7) added [(V_{rms})^2/Hz]</td>
<td>30</td>
</tr>
<tr>
<td>2-22</td>
<td>Band Power Representation of the Composite Sinusoid Cross-correlation Results with noise (amplitude 7) added</td>
<td>31</td>
</tr>
<tr>
<td>2-23</td>
<td>Band Power Results with noise (amplitude 7) added and averaged 10 times</td>
<td>31</td>
</tr>
<tr>
<td>2-24</td>
<td>Composite Sinusoid Z</td>
<td>35</td>
</tr>
<tr>
<td>2-25</td>
<td>Power Density Spectrum [(V_{rms})^2/Hz] of Composite Sinusoid Z</td>
<td>35</td>
</tr>
<tr>
<td>2-26</td>
<td>Composite Sinusoid Y</td>
<td>36</td>
</tr>
<tr>
<td>Figure</td>
<td>Description</td>
<td>Page</td>
</tr>
<tr>
<td>--------</td>
<td>-----------------------------------------------------------------------------</td>
<td>------</td>
</tr>
<tr>
<td>2-27</td>
<td>Power Density Spectrum ((V_{rms})^2/Hz) of Composite Sinusoid Y</td>
<td>36</td>
</tr>
<tr>
<td>2-28</td>
<td>Single-sided Cross-correlation of the Composite Sinusoids</td>
<td>37</td>
</tr>
<tr>
<td>2-29</td>
<td>Single-sided Cross-spectral Amplitude Spectrum of the Composite Sinusoids ([(V_{rms})^2/Hz])</td>
<td>37</td>
</tr>
</tbody>
</table>

**Section 3**

| 3-1    | Maternal Breathing versus Stop Breathing Study-Results of Mean Velocity Variability and Heart Rate Variability Cross-correlation Band Power Ratio 0-1 Hertz | 43   |
| 3-2    | Maternal Breathing versus Stop Breathing Study-Results of Mean Velocity Variability and Heart Rate Variability Cross-correlation Band Power Ratio 1-2 Hertz | 43   |
| 3-3    | Maternal Breathing versus Stop Breathing Study-Results of Mean Velocity Variability and Peak Velocity Variability Cross-correlation Band Power Ratio 0-1 Hertz | 44   |
| 3-4    | Maternal Breathing versus Stop Breathing Study-Results of Mean Velocity Variability and Peak Velocity Variability Cross-correlation Band Power Ratio 1-2 Hertz | 44   |
| 3-5    | Maternal Breathing versus Stop Breathing Study-Results of Heart Rate Variability and Peak Velocity Variability Cross-correlation Band Power Ratio 0-1 Hertz | 46   |
| 3-6    | Maternal Breathing versus Stop Breathing Study-Results of Heart Rate Variability and Peak Velocity Variability Cross-correlation Band Power Ratio 1-2 Hertz | 46   |
| 3-7    | Maternal Breathing versus Stop Breathing Study-Results of Mean Velocity Variability and Heart Rate Variability Cross-correlation Band Power 0-1 Hertz (Absolute) | 47   |
Table of Figure Descriptions:

<table>
<thead>
<tr>
<th>Figure</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>3-8</td>
<td>Maternal Breathing versus Stop Breathing Study- Results of Mean Velocity Variability and Heart Rate Variability Cross-correlation Band Power 1-2 Hertz (Absolute)</td>
<td>47</td>
</tr>
<tr>
<td>3-9</td>
<td>Maternal Breathing versus Stop Breathing Study- Results of Mean Velocity Variability and Peak Velocity Variability Cross-correlation Band Power 0-1 Hertz (Absolute)</td>
<td>49</td>
</tr>
<tr>
<td>3-10</td>
<td>Maternal Breathing versus Stop Breathing Study- Results of Mean Velocity Variability and Peak Velocity Variability Cross-correlation Band Power 1-2 Hertz (Absolute)</td>
<td>49</td>
</tr>
<tr>
<td>3-11</td>
<td>Maternal Breathing versus Stop Breathing Study- Results of Heart Rate Variability and Peak Velocity Variability Cross-correlation Band Power 0-1 Hertz (Absolute)</td>
<td>50</td>
</tr>
<tr>
<td>3-12</td>
<td>Maternal Breathing versus Stop Breathing Study- Results of Heart Rate Variability and Peak Velocity Variability Cross-correlation Band Power 1-2 Hertz (Absolute)</td>
<td>50</td>
</tr>
<tr>
<td>3-13</td>
<td>Cross Gestational Study- Results of Mean Velocity Variability and Heart Rate Variability Cross-correlation Band Power Ratio 0-1 Hertz</td>
<td>53</td>
</tr>
<tr>
<td>3-14</td>
<td>Cross Gestational Study- Results of Mean Velocity Variability and Heart Rate Variability Cross-correlation Band Power Ratio 1-2 Hertz</td>
<td>53</td>
</tr>
<tr>
<td>3-15</td>
<td>Cross Gestational Study- Results of Mean Velocity Variability and Peak Velocity Variability Cross-correlation Band Power Ratio 0-1 Hertz</td>
<td>54</td>
</tr>
<tr>
<td>3-16</td>
<td>Cross Gestational Study- Results of Mean Velocity Variability and Peak Velocity Variability Cross-correlation Band Power Ratio 1-2 Hertz</td>
<td>54</td>
</tr>
<tr>
<td>Figure</td>
<td>Description</td>
<td>Page</td>
</tr>
<tr>
<td>----------</td>
<td>-----------------------------------------------------------------------------</td>
<td>------</td>
</tr>
<tr>
<td>3-17</td>
<td>Cross Gestational Study- Results of Heart Rate Variability and Peak Velocity Variability Cross-correlation Band Power Ratio 0-1 Hertz</td>
<td>56</td>
</tr>
<tr>
<td>3-18</td>
<td>Cross Gestational Study- Results of Heart Rate Variability and Peak Velocity Variability Cross-correlation Band Power Ratio 1-2 Hertz</td>
<td>56</td>
</tr>
<tr>
<td>3-19</td>
<td>Cross Gestational Study- Results of Mean Velocity Variability and Heart Rate Variability Cross-correlation Band Power 0-1 Hertz (Absolute)</td>
<td>57</td>
</tr>
<tr>
<td>3-20</td>
<td>Cross Gestational Study- Results of Mean Velocity Variability and Heart Rate Variability Cross-correlation Band Power 1-2 Hertz (Absolute)</td>
<td>57</td>
</tr>
<tr>
<td>3-21</td>
<td>Cross Gestational Study- Results of Mean Velocity Variability and Peak Velocity Variability Cross-correlation Band Power 0-1 Hertz (Absolute)</td>
<td>59</td>
</tr>
<tr>
<td>3-22</td>
<td>Cross Gestational Study- Results of Mean Velocity Variability and Peak Velocity Variability Cross-correlation Band Power 1-2 Hertz (Absolute)</td>
<td>59</td>
</tr>
<tr>
<td>3-23</td>
<td>Cross Gestational Study- Results of Heart Rate Variability and Peak Velocity Variability Cross-correlation Band Power 0-1 Hertz (Absolute)</td>
<td>60</td>
</tr>
<tr>
<td>3-24</td>
<td>Cross Gestational Study- Results of Heart Rate Variability and Peak Velocity Variability Cross-correlation Band Power 1-2 Hertz (Absolute)</td>
<td>60</td>
</tr>
</tbody>
</table>

**Appendix A**

| A-1       | Overlap Example                                                             | 76   |
| A-2       | Representation of Default Sub-signal Correlation                           | 77   |
## List of Tables

<table>
<thead>
<tr>
<th>Table</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Table 2-1</td>
<td>Noisy Composite Sinusoid Band Power and Frequency Results</td>
<td>32</td>
</tr>
<tr>
<td>Table 2-2</td>
<td>Averaged Noisy Composite Sinusoid Band Power and Frequency Results</td>
<td>33</td>
</tr>
</tbody>
</table>
Abstract

Congenital cardiac malformations are a serious health concern affecting the development of the fetal cardiovascular system. Identification of a fetus with abnormalities early in pregnancy, 10-20 weeks gestation, could assist in clinical diagnosis and be a great asset in health care. This thesis is a continuation of, and works in concert with, other research efforts conducted at Rochester Institute of Technology (RIT) aimed at characterizing fetal cardiovascular health through applied signal processing.

This thesis utilizes cross-correlation as a technique for analyzing the cyclic variations and assessing commonalities of individual parts of fetal umbilical artery time series data. These time series include heart rate variability, peak velocity variability, and mean velocity variability. Here, common frequency components of cross-correlated signals are evident and unique frequency components of an individual signal are attenuated.

Specifically, the studies conducted herein contain analysis of two data types. A study of maternal breathing intact versus maternal stop breathing was performed. This study evaluates the cyclic variations associated with fetal umbilical artery data taken during maternal breathing and stop breathing states. Additionally, an analysis of a cross gestational data group was done. The cross gestational study is a cross sectional study containing three gestational ages (10-12, 13-16, 17-20 weeks). This study was done to analyze the commonalities and differences in fetal umbilical artery blood velocity variability data obtained during the different gestational periods. Frequency consistencies and differences were discovered in both studies and are discussed.
1.0 Introduction

Congenital cardiac malformations are a serious health concern affecting the development of the fetal cardiovascular system. Current diagnostic tools allow assessment of fetal cardiovascular health during the latter half of pregnancy, but are not applicable prior to 20 weeks gestation (Wladimiroff 1992). Identification of a fetus with functional abnormalities early in pregnancy, 10-20 weeks gestation, could assist clinical diagnosis and be a great asset in health care. This thesis is a continuation of, and works in concert with, other research efforts conducted at Rochester Institute of Technology (RIT) aimed at characterizing fetal cardiovascular health. The application of signal processing techniques to analyze blood velocity waveforms has been the mainstage of this effort.

The fetal cardiovascular system is often monitored clinically using Doppler ultrasound imaging and pulsed-wave (PW) Doppler velocimetry. These methods are popular because of their non-invasive nature and pose low observation induced risks to both mother and fetus (Huhta 1989). The data analyzed in this thesis were obtained from PW Doppler velocimetry of human fetal blood vessels. It is important to note that all data used in this study was taken with full maternal consent before any fetal data was acquired. The data was gathered by clinical research colleagues in the Netherlands using a Toshiba SSH-140 (Toshiba Corporation, Medical Systems Division, Tokyo, Japan) clinical Doppler ultrasound machine. This data was then supplied to RIT for analysis. Analysis was done using custom algorithms programmed at RIT to generate and analyze time series data.
The remainder of this section describes the long term and short term objectives of this project. The time series waveforms studied within this thesis will be introduced. Finally, the developmental aspects of the cardiovascular development will be discussed.

1.1 Objectives

The research project with which this thesis is associated has both long term and short term goals. The long term goals include the development of a non-invasive measure of the fetal cardiovascular well-being, and to define operational norms for fetal cardiovascular function. Several short term goals are associated with effective application of various signal processing techniques to achieve the long term objectives. This thesis supports the long term project objectives with its primary short term goal being to use cross-correlation as a qualitative method of representing the cyclic variations and commonalities of individual parts of fetal umbilical artery data. This evaluation will be done by analyzing the frequency domain “signature” of fetal blood velocity variability time series. The overall study contains two data cases to be analyzed. The first case investigates whether maternal breathing versus maternal stop breathing influences variability time series frequency content. The second case investigates variability time series obtained as gestation progressed in a cross sectional study containing three gestational age groups 10-12, 13-16, 17-20 weeks, respectively. This study was done to analyze the commonalities and differences in the fetal umbilical artery velocity variability data obtained during the different gestational periods.
1.2 Waveforms Studied

The time series data studied herein contain cross-correlated comparisons of: the mean velocity variability (MVV) with heart rate variability (HRV) time series, the mean velocity variability (MVV) with peak velocity variability (PVV) time series, and the heart rate variability (HRV) with the peak velocity variability (PVV) time series. It is hypothesized that these data series are indicative of intrinsic hemodynamic control mechanisms during fetal development.

Figure 1-1 represents a velocity profile as derived from the analysis processes developed at RIT (Gallagher 1995). The peak velocity, threshold and mean pulse velocity values are all depicted in Figure 1-1. These entities are then used to create the velocity time series data used herein, as described in the rest of this section.

Figure 1-1:
The HRV time series is a standard waveform for assessing cardiovascular and central nervous system function in late gestational fetuses, neonates, and adults (van Ravenswaaij-Arts 1993, Karin 1993, Saul 1991, Breborowicz 1988). The HRV data series is a long-duration measure of the beat-to-beat changes in the timing of the cardiac contraction. In our study, the periodicity of cardiac contractions is measured using an event marker. Here, a velocity threshold is set proportional to the overall (i.e. ‘global’) mean velocity. An event mark is ‘set’ whenever the rising edge of a velocity pulse crosses the threshold, and the time difference between event marks identifies the beat-to-beat periodicity. The beat-to-beat periodicity is inverted to obtain the instantaneous heart rate. HRV is obtained by subtracting the global mean heart rate from the instantaneous heart rate (Figure 1-2 a).

The peak velocity (PV) in each cardiac pulse (i.e. between event markers) is identified and recorded for each cardiac cycle in the umbilical artery blood velocity waveform. The PVV is the variance about the average peak velocity value. The PVV is used to make embedded rhythms more evident (Kempski 1993, 1995) (Figure 1-2 b).

The area under the velocity curve between event markers is the mean velocity (MV) for a cardiac cycle. The MVV is the variance about the average value of the mean velocity for the recorded waveform. The MVV is a standard waveform used to study beat-to-beat changes within a velocity time series (Figure 1-2 c).
Figure 1-2:

**Figure 1-2 (a):**

- **Instantaneous Heart Rate (IHR):**
  - Graph showing heart rate variability (HRV) over time.
  - HRV = IHR - HRbar

**Figure 1-2 (b):**

- **Peak Velocity (PV):**
  - Graph showing peak velocity and average PV over time.
  - PVV = PV - (Average PV)

**Figure 1-2 (c):**

- **Mean Velocity (MV):**
  - Graph showing mean velocity and average MV over time.
  - MVV = MV - (Average MV)
1.3 Cardiovascular Background

The cardiovascular system is the first functioning organ system in the embryo/fetus during gestation. The human heart begins development in utero as two simple tubes. The two tubes then fuse together to form a single heart tube. Morphogenesis (including looping) and growth then transform the heart tube into the mature four chambered heart (Clark and Van Mierop 1989, Marieb 1992). The muscle wrapped heart tube begins beating during the third gestational week (22 ± 1 days) and continues to beat during further development. Structurally the cardiovascular system is in place and there are few changes that occur during middle (9-20 weeks) and late gestation (beyond 20 weeks) (Sissman 1970).

The embryo/fetus behaves as the mature cardiovascular system does in that it is regulated by demand (Kempski 1993 and 1995, Clark 1990). One major difference between the mature system and the embryo/fetus is that during primary cardiovascular development cardiac output early in development is not regulated by the central nervous system. Functional innervation does not appear until after primary cardiac morphogenesis is complete (Pappano 1977). The central nervous system does not begin control until around the 16-17th week of gestation (Walker 1975). The exact mechanism that controls the cardiac output in the embryo/fetus in early development is not yet known.

The fetal/placental vascular bed is transformed from a high flow resistance system to a low flow resistance system between 10-18 weeks of gestation (Wladimiroff 1991). This transformation is essential in maintaining optimum blood flow to a developing fetus throughout the remainder of pregnancy.
2.0 Methodology

The data used in this thesis was originally obtained as part of an international multi-institutional collaboration under National Institutes of Health (NIH) Special Center of Research (SCOR) grant P50 HL51498-01 to the University of Rochester. Clinical data acquisition of the Doppler ultrasound records were performed at Academic University Hospital - Rotterdam, Erasmus University, The Netherlands. All subsequent data analysis was performed at Rochester Institute of Technology (RIT).

The study protocol for use of human fetal data included in this thesis was approved by the institutional review boards at Erasmus University, RIT, and the University of Rochester. It is also important to note that all data used in this study was recorded with full maternal consent. The patients discussed within this thesis were recruited from the normal obstetrical program at the Academic Hospital- Rotterdam.

2.1 Sonography

Clinical blood velocity data was recorded using a Toshiba SHH-140A (Toshiba Corporation, Medical Systems Division, Tokyo, Japan) Doppler ultrasound machine. The system operates at power outputs of less than 100 mW/cm² spatial peak-temporal average in both imaging and Doppler modes by manufacturer’s specifications. The high-pass wall filter was set at 100 Hz or less. The Doppler blood velocity data is recorded in both video and audio formats to sVHS video cassette tapes in PAL format on a Panasonic model AG7350 machine (Matsushita Electric Ind Co, Japan).
Only the data from pregnancies that progressed uneventfully as indicated by the delivery of a normal fetus with a birth weight between the 10th and 90th percentile corrected for maternal parity and fetal sex (Kloosterman 1970) are used in the studies performed within this thesis. The Doppler data was gathered by one examiner (Nicolette T. C. Ursem) with the mother in the semirecumbent position and during fetal apnea, using a transvaginal probe 6 MHz (for 10-12 weeks) or a transabdominal probe 5 MHz (for 13-20 weeks). The gestational age for the fetuses was determined by the date of the last menstrual period and verified using the crown rump length (fetuses between 10-12 weeks gestation) and the biparietal diameter (fetuses between 13-20 weeks gestation). All the data used in the studies described within this thesis are umbilical artery Doppler ultrasound data.

2.2 Waveform Reconstruction

Digital velocity waveform reconstruction was performed at RIT. The analog Doppler audio waveforms were digitized at 44kHz for greater than 16 second intervals using a Gateway 2000 P5-90 personal computer. The analog-to-digital conversion was accomplished in the computer using LabPC+ and BNC-2081 data acquisition boards (National Instruments, Austin, Texas). The flow velocity waveforms were reconstructed from the Doppler audio data using the ‘DopV’ collection of computer algorithms (Gallagher 1995, Kettles 1995) created at RIT using LabVIEW® software (National Instruments, Austin, Texas).
The 'DopV' software (RIT) constructs three time series waveforms from each blood velocity waveform scrutinized herein. The three time series are the respective time courses of heart rate variability (HRV), peak velocity variability (PVV) and mean velocity variability (MVV). HRV measures the beat-to-beat variance in heart rate about an average value. PVV is the variance about the average peak velocity value. The MVV is the variance about the average value of the mean velocity for the recorded waveform.

Each of the data time series undergoes a uniform linear interpolation to yield new data sets that have N number of points with uniform spacing with respect to time where N=512 for this thesis. If a trend exists in the variability data series, the data is detrended via low-order polynomial fit to remove DC drift.

The primary analysis tools for the purpose of this thesis are the cross-correlation, fast Fourier transform (FFT), and power density spectrum. These signal processing methodologies are introduced in the Section 2.3.

2.3 Theory

Time series convolution can be used to study the time/frequency signature of a signal, depending on the processing methodology (Press 1992, Proakis 1988). Convolution techniques increase the frequency resolution in the signal analysis since the combination of the signals increases the number of data points. That is, if a signal \( f(t) \) and another signal \( g(t) \) are both discrete time series of length \( N \), then the output generated by convolving \( f(t) \) with \( g(t) \) is the function \( R(\tau) \) of length \( 2N-1 \). Autocorrelation and cross-
correlation are special cases of convolution, where correlation is the measure of the similarity of two quantities (Hewlett Packard 1985).

The autocorrelation function is widely used in signal analysis to identify trends in data samples (Stremler 1990). It can be obtained by taking the inverse Fourier transform of the power spectral density. Therefore, taking the Fourier transform of the autocorrelation function yields the power spectral density (Stremler 1990, Baselli 1987, Hewlett Packard 1985, Zetterberg 1970). Autocorrelation essentially compares the frequency content of a given signal with itself (Press 1992, Stremler 1990, Proakis 1988, Hewlett Packard 1985).

The cross-correlation function measures the similarity of a signal \( f(t) \) with another signal \( g(t) \) (Press 1992, Stremler 1990, Proakis 1988, Hewlett Packard 1985):

\[
R_{fg}(\tau) = \lim_{T \to \infty} \frac{1}{T} \int_{-T/2}^{T/2} f^*(t) g(t + \tau) dt
\]

(Equation 2-1).

where \( * \) represents the complex conjugate

Here noise from either input signal \( f(t) \) or \( g(t) \) is attenuated in the cross-correlation function \( R_{fg}(\tau) \). This arises from the fact that if \( f(t) \) and \( g(t) \) are orthogonal or statistically independent they are uncorrelated and \( R_{fg}(\tau)=0 \). Therefore, if the noise which contaminates either \( f(t) \) or \( g(t) \) is ‘white’ or ‘gaussian’ then it will be uncorrelated and attenuated in the cross-correlation function (Stremler 1990, Proakis 1988, Hewlett Packard 1985).
Power spectral analysis has become a very powerful tool in recent years for evaluating different characteristics associated with the cardiovascular development of the human fetus, as well as animal models of embryonic and fetal development (Kempski 1995, 1992). This methodology applies the Fourier transform exclusively. The issue addressed within this thesis is to approach the spectral analysis in a different way. Here, the cross power spectral density of the function is obtained by taking the fast Fourier transform (FFT) of the cross-correlation resultant, $R_{fg}(\tau)$.

The intent of this thesis is to apply cross-correlation to variability time series data obtained from fetal blood velocity waveforms in order to identify common variability trends. Power spectral analysis of the cross-correlated results will then be used to explore similarities and differences in the frequency content of the variability time series.

2.4 Cross-correlation

To perform the required cross-correlations, algorithms were created at RIT by the author which supplement the afore mentioned ‘DopV’ custom software algorithms. These new cross-correlation algorithms are contained in $SK\ ac/cc\ processing.VI$ which were written using the LabVIEW® (National Instruments, Austin, Texas) software language. The algorithm $SK\ ac/cc\ processing.VI$ utilizes cross-correlation (Equation 2-2, derived from Equation 2-1) as a method of analyzing variability in the given fetal cardiovascular time series data.
\[ R_f(\tau) = \sum_{k=1}^{n} f^*(t_k)g(t_k + \tau) \]  
(Equation 2-2)

where \( * \) represents the complex conjugate

Upon opening the algorithm the default values enable the cross-correlated time series as well as the amplitude spectrum of the cross-correlated signals to be sent to a spreadsheet. There are several other capabilities built into this algorithm that may be useful in further studies and will be discussed in full detail in Appendix A.

The amplitude spectrum of \( R_{fg}(\tau) \) contains the power density associated with the cross-correlation of the time series, \( f(t) \) and \( g(t) \) and provides a format for comparison of these different signals. It also is a form that can utilize previously developed ‘Post Processing’ algorithms (Kettes 1995) which provide a streamline data reduction scheme, suitable for comparative data analysis.

Recall, the three variability time series being analyzed are HRV, PVV, and MVV. These three variability time series files comprise a “data set” for one fetus. The full analysis of one fetal “data set” by the \( SK \ ac/cc \ processing: \) \( VI \) algorithm requires that the algorithm be run three times. Each permutation of the algorithm will cross-correlate two different variability time series. The result is the cross-correlation of the MVV with HRV, MVV with PVV, and HRV with PVV.

The properties of the cross-correlation analysis (see Section 2.5 Test Cases) clearly shows that the order in which data files are entered into the cross-correlation operation is not important. Hence, for ease of processing consistency the order of signal correlation mentioned above was adopted throughout this thesis.
The primary step in post-processing cardiovascular spectra for comparison is to ‘group’ the embryonic/fetal spectra in terms of gestational age, treatment protocols, etc. as determined by the study. Representative group averages can then be obtained for further processing and comparison. Therefore, after utilizing the SK ac/cc processing.VI the Spectral Post Processing.VI (Kettles 1995) algorithm is used to generate a ‘common’ spectrum by averaging the individual spectra across each discrete frequency. The results are sent to a spreadsheet.

The spectral files are then sent to the Band Power Calculation (10 Bands).VI (Kettles 1995). This algorithm calculates the associated power in ten specified frequency bands (i.e. area under the curve in the specified frequency range). This division into specified frequency bands for spectral power computation is consistent with HRV studies available in the literature (van Ravenswaaij-Arts 1993, Karin 1993, Saul 1991, Breborowicz 1988). In these studies, the band power data provides a ‘tailored’ view of the spectrum, and certain HRV frequency axis bands have been indicative of parasympathetic and sympathetic neural control (van Ravenswaaij-Arts 1993). The study of early (10-20 weeks) fetal HRV, PVV, and MVV is yet undefined from the band power perspective. Hence, our use of these measures is both exploratory and descriptive.

The output from the Band Power Calculation (10 Bands).VI (Kettles 1995) contains signal power calculated in each band (i.e. absolute band power) and a ratio of the power in each band to the total spectrum power (i.e. ‘band-power-ratio’). The band-power-ratio is an alternative way to display the spectral power distribution as a percentage of the total spectral power (Kettles 1995). Essentially the band-power-ratio is the spectral
band power content normalized by the power in the entire spectrum. These absolute band power and band-power-ratio data are used to create a histogram for comparison between control and test groups (i.e. maternal intact breathing versus maternal stop breathing).

For the data reported in this thesis most power spectral activity occurs between 0-2 Hz which is below nominal fetal heart rate. The band power calculations were divided into 0.0-0.1 Hz frequency bins. The *Band Power Calculation (10 Bands)* is limited to 10 bands, hence two distinct ranges are calculated. Specifically, the band power analysis as well as the statistical analysis was done for each data set from 0-1 Hz as well as 1-2 Hz.

### 2.5 Test Cases

For the purpose of evaluating the accuracy of the algorithms generated for this thesis several test cases were done. This section contains sinusoid test cases which demonstrate, verify, and evaluate the algorithms created herein. The application of these algorithms to fetal variability waveforms is outlined in Section 2.6.

#### 2.5.1 Composite Sinusoid Example

Composite Sinusoid Y, (Figure 2-1) can be represented by Equation 2-3 where $\omega$ is frequency in Hertz (Hz), $f$ is the frequency conversion from cycles to radians, $t$ is in seconds, and $A$ is amplitude in arbitrary units. The associated power density spectrum is shown in Figure 2-2.
\[ Y = A_1 \sin(\omega_1 ft) + A_2 \sin(\omega_2 ft) + A_3 \sin(\omega_3 ft) \]  
\[ \text{Equation 2-3} \]

where:

\[ A_1 = 3 \quad \omega_1 = 2 \quad f = 2\pi \]
\[ A_2 = 5 \quad \omega_2 = 3 \quad t = 0 \rightarrow 20 \]
\[ A_3 = 7 \quad \omega_3 = 5 \]

note: initial 500 (of 1024) data points plotted for clarity

The time series of the component sinusoid generated by Equation 2-3 is shown in Figure 2-1 and appears in the frequency domain (Figure 2-2) as distinct spikes. In this single-sided spectral representation spikes occur at frequencies which correspond to \( \omega_1 \), \( \omega_2 \) and \( \omega_3 \) of Equation 2-3. The amplitudes of the component sinusoids \((A_1, A_2, A_3)\) appear in Figure 2-2 as corresponding power density values \(\frac{(\text{Amplitude})^2}{\text{df}}\) for the single-sided spectrum depicted.

Composite Sinusoid \(Z\), (Figure 2-3) can be represented by Equation 2-4 where \(\phi\) is frequency in Hertz (Hz), \(f\) is the frequency conversion from cycles to radians, \(t\) is in seconds, and \(B\) is amplitude in arbitrary units. The associated power density spectrum is shown in Figure 2-4.

\[ Z = B_1 \sin(\phi_1 ft) + B_2 \sin(\phi_2 ft) \]  
\[ \text{Equation 2-4} \]

where:

\[ B_1 = 10 \quad \phi_1 = 2 \quad f = 2\pi \]
\[ B_2 = 2 \quad \phi_2 = 3 \quad t = 0 \rightarrow 20 \]

note: initial 500 (of 1024) data points plotted for clarity
Figure 2-1:

Composite Sinusoid Y

Figure 2-2:

Power Density Spectrum (Vrms)²/Hz of Composite Sinusoid Y
Figure 2-3:

Composite Sinusoid Z

Figure 2-4:

Power Density Spectrum (Vrms)^2/Hz of Composite Sinusoid Z
Cross-correlating these two sinusoids \( f(t) = Y \) and \( g(t) = Z \) (Equation 2-2) using SK ac/cc processing. This yields Figure 2-5.

One of the goals of this thesis is to determine if the cross-correlation can be used as an accurate method of representing the common frequency contents of fetal umbilical artery time series data (specifically HRV, PVV, and MVV). Here, the common frequency components in each individual time series should appear in the cross-correlation.

Looking at the composite sinusoid example, it is easy to see that \( Y \) and \( Z \) have frequencies in common since \( \omega_1 = \phi_1 = 2 \) Hz and \( \omega_2 = \phi_2 = 3 \) Hz. Since amplitude \( B_1 = 10 \) at frequency \( \phi_1 = 2 \) Hz, there is a high peak on the amplitude spectrum at frequency \( \omega_1 = \phi_1 = 2 \) Hz (Figure 2-6). Notice that at frequency \( \omega_2 = \phi_2 = 3 \) Hz the peak in the amplitude spectrum (Figure 2-6) is not very large by comparison to that of the peak at \( \omega_1 = \phi_1 = 2 \) Hz. Both signals have this frequency (\( \omega_2 = \phi_2 = 3 \) Hz) in common, however due to smaller amplitudes (\( A_2 = 5, B_2 = 2 \)) at this frequency there is a smaller cross correlation spectral peak. Further, \( \omega_3 = 5 \) Hz, has no corresponding frequency at \( \phi_3 \) nor harmonics at \( \phi_1 \) or \( \phi_2 \) and therefore is attenuated and not apparent in the amplitude spectrum of the cross-correlation (Figure 2-6).

The spectral results of the composite sinusoid cross-correlation were then processed using Spectra Post Processing (Kettles 1995) and Band Power Calculation (5 Bands) (Kettles 1995). The resulting band power values were used to create the histogram as shown in Figure 2-7. It is expected that the band power computed at the frequencies \( \omega_1 = \phi_1 = 2 \) Hz appear relatively high, while the band power associated with frequencies \( \omega_2 = \phi_2 = 3 \) Hz appear diminished in power by comparison. We also expect
Figure 2-5:

Single-sided Cross Correlation of the Composite Sinusoids

Figure 2-6:

Single-sided Cross-spectral Amplitude Spectrum of the Composite Sinusoids [(Vrms)^2/Hz]
Figure 2-7:

Band Power Representation of the Composite Sinusoid Cross Correlation Results
band power at \( \omega_3 = 5 \) Hz to be small since correlation at this frequency is low. Band one (0.0-1.5 Hz) shows a small power value, this is due to spectral leakage from the peak located at 2 Hz (not evident in Figure 2-6 due to the vertical axis scaling). Please note that \( f(t) \) and \( g(t) \) and hence \( R_{fg}(\tau) \) are zero-mean. As shown in Figure 2-7 the Band Power results are consistent with the original spectral distribution shown in Figure 2-6.

### 2.5.2 Examples Containing Noise

The analysis was repeated adding noise to the composite sinusoids \( Y \) (Equation 2-3) and \( Z \) (Equation 2-4).

#### 2.5.2.1 Noise Case A

Random ‘white’ noise with an amplitude differing from any sinusoid amplitude and associated harmonics (noise amplitude 2.32) was used (Figures 2-8 and 2-10). The noise amplitude was chosen such that it will avoid erroneous correlation of the noise with associated harmonics of the sinusoid. The associated power density spectrum plots are found in Figures 2-9 and 2-11. The noise appears attenuated in the frequency domain including the power density spectrum results.

Cross-correlating the noisy composite sinusoids yields Figure 2-12. Looking at the cross-correlation plot, the noise signature is not visually evident, as it was in Figures 2-8 and 2-10.
Figure 2-8:

Composite Sinusoid Y - noise (amplitude 2.32) added

Figure 2-9:

Power Density Spectrum (Vrms)^2/Hz of Composite Sinusoid Y with noise (amplitude 2.32) added
Figure 2-10:

Composite Sinusoid Z- noise (amplitude 2.32) added

Figure 2-11:

Power Density Spectrum (Vrms)^2/Hz of Composite Sinusoid Z with noise (amplitude 2.32) added
The amplitude spectrum resulting from SK ac/cc processing is shown in Figure 2-13. The signature of the noise is not evident. This result is as expected, since the cross-correlation technique decreases the noise signature on output (Stremler 1990, Proakis 1988, Hewlett Packard 1985).

The band power results of the noisy composite sinusoid (noise amplitude 2.32) are shown in Figure 2-14. The band power results indicate that the signature of the frequencies at $\omega_1 = \phi_1 = 2$ Hz and $\omega_2 = \phi_2 = 3$ Hz remain intact and are consistent with those represented in Figure 2-7, where no noise was added to the composite sinusoid. The 4.5-5.5 band (Figure 2-14) shows a higher power then in the initial 'noise-free' case. Since the added noise is broad-band, the potential exists for 'weaker' signals to show more affects from the noise.

Averaging the composite sinusoid ten times with noise amplitude 2.32 yields Figure 2-15. Averaging is done with a Labview® algorithm. Two composite sinusoids are created. Noise is added to the sinusoids. The sinusoids are then cross correlated. This is repeated ten times. The ten cross correlated results are all added and divided by ten to yield the average cross correlation. The spectral post processing and other steps then follow. The noise is generated at random by an existing Labview® algorithm, therefore affecting the sinusoid differently each iteration.
Figure 2-12:

**Single-sided Cross Correlation of the Composite Sinusoids with noise added (amplitude 2.32)**

![Graph](image_url)

- **Time (seconds)**
- **Amplitude (V)**

Figure 2-13:

**Single-sided Cross-spectral Amplitude Spectrum of the Composite Sinusoids with noise added (amplitude 2.32) \[(V_{rms})^2/Hz\]**

![Graph](image_url)

- **Frequency (Hertz)**
- **Amplitude (V_{rms})^2/Hz**
Figure 2-14:

Band Power Representation of the Composite Sinusoid Cross Correlation Results with noise (amplitude 2.32) added

Figure 2-15:

Band Power Results with noise (amplitude 2.32) added and averaged 10 times
2.5.2.2 Noise Case B

Another test case with a noise amplitude of 7.0 (recall, the highest sinusoid amplitude in Equations 2-3 and 2-4 is $B_1 = 10$) was done. The composite sinusoids with noise amplitude of 7.0 are shown in Figures 2-16 and 2-18. The associated power density spectrum plots are found in Figures 2-17 and 2-19. The noise appears attenuated in the power density spectrum results. There is representation of the noise at amplitudes $<4.0 \ (\text{Vrms})^2/\text{Hz}$ and the spikes are slightly broader than the 'noise-free' case.

Cross-correlating the noisy composite sinusoids yields Figure 2-20. Looking at the cross-correlation plot, the noise signature is not as visually evident as it was in Figures 2-16 and 2-18.

The amplitude spectrum resulting from SK ac/cc processing.VI is shown in Figure 2-21. The signature of the noise is evident at values $<3.0 \ (\text{Vrms})^2/\text{Hz}$ and the spikes are slightly broader then the 'noise-free' case (Figure 2-6).

The band power results of the noisy composite sinusoid (noise amplitude 7.0) are shown in Figure 2-22. The band power results indicate that the signature of the frequencies at $\omega_1 = \phi_1 = 2 \ \text{Hz}$ and $\omega_2 = \phi_2 = 3 \ \text{Hz}$ remain intact and are consistent with those represented in Figure 2-7, where no noise was added to the composite sinusoid. The 4.5-5.5 band (Figure 2-22) shows a higher power than the initial 'noise-free' case (Figure 2-6).
Figure 2-16:

Composite Sinusoid Y-noise (amplitude 7) added

Figure 2-17:

Power Density Spectrum \((V_{\text{rms}})^2/\text{Hz}\) of Composite Sinusoid Y with noise (amplitude 7) added
Figure 2-18:

Composite Sinusoid Z- noise (amplitude 7) added

Figure 2-19:

Power Density Spectrum (Vrms)^2/Hz of Composite Sinusoid Z with noise (amplitude 7) added
Figure 2-20:

Single-sided Cross Correlation of the Composite Sinusoids with noise added (amplitude 7)

Figure 2-21:

Single-sided Cross-spectral Amplitude Spectrum of the Composite Sinusoids with noise added (amplitude 7) [(Vrms)^2/Hz]
Figure 2-22:

Averaging the composite sinusoid ten times with noise amplitude 7 yields Figure 2-23.

Figure 2-23:
2.5.2.3 Summary

Recall, the ‘noise free’ band power histogram (Figure 2-7) for the cross-correlated composite sinusoids Y and Z showed frequencies $\omega_1 = \phi_1 = 2$ Hz appear relatively high, $\omega_2 = \phi_2 = 3$ Hz appear medium in power by comparison and $\omega_3 = 5$ Hz is barely represented. Since cross-correlation is a technique used to decrease the signature of noise in an output, adding noise to the sinusoids should not greatly affect the resulting band power histogram (Stremler 1990, Proakis 1988, Hewlett Packard 1985). Table 2-1 contains the band power results obtained from the noise examples.

Table 2-1:

<table>
<thead>
<tr>
<th>Frequency Band</th>
<th>Band Power Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>#</td>
<td>(Hertz)</td>
</tr>
<tr>
<td>1</td>
<td>0.0-1.5</td>
</tr>
<tr>
<td>2</td>
<td>1.5-2.5</td>
</tr>
<tr>
<td>3</td>
<td>2.5-3.5</td>
</tr>
<tr>
<td>4</td>
<td>3.5-4.5</td>
</tr>
<tr>
<td>5</td>
<td>4.5-5.5</td>
</tr>
</tbody>
</table>

Looking at Table 2-1 it can be seen that frequency bands 2 and 3 appear consistent even though noise is added. Adding a noise amplitude of 2.32 causes a 3.63% and 3.36% difference in the two bands respectively. Adding a noise amplitude of 7.0 causes a 9.56% and 16.81% difference in these two bands. Hence, the values are not affected greatly, as expected. This demonstration is helpful in knowing that noise will not play a significant role in the analysis of data where common frequencies occur. Note, the higher the value of noise, the more it will appear in the cross-correlated results.
Frequency bands 1, 2 and 5 experience an increase in band power value. Notice, the value increases as the noise amplitude increases in these cases as well. The amount of increase is larger in these bands (>100%). This is attributed to the fact that the power band values are small in the 'noise free' case, therefore a small increase equates to a larger percent difference. Also, it appears that the noise is indeed affecting signals which are not strongly correlated.

Noise effects on a signal can be reduced by averaging the cross correlated results. Looking at Figure 2-15 and Figure 2-23, it can be seen that the amplitudes affected by adding noise shown in the band power results (Figures 2-14 and 2-22) were consistent, Table 2-2. Recall that frequency bands 2 and 3 had a 3.63% and 3.36% difference after adding a noise amplitude of 2.32 and a 9.56% and 16.81% difference with a noise amplitude of 7.0 added (Table 2-1). The differences between the noise free and the noise averaged (Table 2-2) percent differences in bands 2 and 3 respectively are reduced to 0.14% and 2.67% for the 2.32 amplitude and 3.41% and 2.75% for the amplitude of 7.0. Notice that for a noise amplitude of 7.0, more than a ten-fold averaging may be required to effectively reduce the influence of this large amplitude noise on the cross-correlation (Table 2-2).

Table 2-2:

<table>
<thead>
<tr>
<th>Frequency Band</th>
<th>Band Power Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>#</td>
<td>'Noise Free'</td>
</tr>
<tr>
<td>1</td>
<td>0.0-1.5</td>
</tr>
<tr>
<td>2</td>
<td>1.5-2.5</td>
</tr>
<tr>
<td>3</td>
<td>2.5-3.5</td>
</tr>
<tr>
<td>4</td>
<td>3.5-4.5</td>
</tr>
<tr>
<td>5</td>
<td>4.5-5.5</td>
</tr>
</tbody>
</table>
2.5.3 Cross-correlation Sequencing

Another important demonstration is that the order in which two signals are cross-correlated does not matter. Recall, the definition of the cross-correlation function (Press 1992, Stremler 1990, Proakis 1988, Hewlett Packard 1985):

\[ R_{fg}(\tau) = \lim_{T \to \infty} \frac{1}{T} \int_{-T/2}^{T/2} f(t)g(t+\tau)dt \] (Equation 2-1 repeated).

From the example in Section 2.5.1 (Composite Sinusoid Example) recall, \( f(t)=Y \) and \( g(t)=Z \) where \( Y \) (Equation 2-3) and \( Z \) (Equation 2-4) are repeated below for clarity.

\[ Y = A_1 \sin(\omega_1 t) + A_2 \sin(\omega_2 t) + A_3 \sin(\omega_3 t) \] (Equation 2-3 repeated)

\[ A_1 = 3 \quad \omega_1 = 2 \quad f = 2\pi \]
where:
\[ A_2 = 5 \quad \omega_2 = 3 \quad t = 0 \rightarrow 20 \]
\[ A_3 = 7 \quad \omega_3 = 5 \]

note: initial 500 (of 1024) data points plotted for clarity

and

\[ Z = B_1 \sin(\phi_1 t) + B_2 \sin(\phi_2 t) \] (Equation 2-4 repeated)

where:
\[ B_1 = 10 \quad \phi_1 = 2 \quad f = 2\pi \]
\[ B_2 = 2 \quad \phi_2 = 3 \quad t = 0 \rightarrow 20 \]

note: initial 500 (of 1024) data points plotted for clarity

To illustrate that the cross-correlation yields the same results regardless of the signal order, the following example will define \( f(t)=Z \) (Figure 2-24) and \( g(t)=Y \) (Figure 2-26). The respective power spectral density plots are shown in Figures 2-25 and 2-27.
Figure 2-24:

Composite Sinusoid Z

Figure 2-25:

Power Density Spectrum \((V_{rms})^2/Hz\) of Composite Sinusoid Z
Figure 2-26:

Composite Sinusoid Y

Figure 2-27:

Power Density Spectrum \((V_{\text{rms}})^2/\text{Hz}\) of Composite Sinusoid Y
Cross-correlating the two sinusoids (as done using SK ac/cc processing) yields Figure 2-28. The associated amplitude spectrum is shown in Figure 2-29.

**Figure 2-28:**

![Single-sided Cross Correlation of the Composite Sinusoids](image)

**Figure 2-29:**

![Single-sided Cross-spectral Amplitude Spectrum of the Composite Sinusoids](image)
Comparing the cross-correlation plots, Figures 2-5 and 2-28, and the amplitude spectrum plots Figures 2-6 and 2-29, it is evident that reversing the sequence of the signals produces the same results. Hence,

\[ R_{fg}(\tau) = \lim_{T \to \infty} \frac{1}{T} \int_{-T/2}^{T/2} f^*(t)g(t + \tau)dt = \lim_{T \to \infty} \frac{1}{T} \int_{-T/2}^{T/2} g^*(t)f(t + \tau)dt \]  

(Equation 2-5).

2.6 Processing Performed

The analysis sequence described above was performed for two different data types for the purposes of this thesis:

- Maternal breathing intact versus maternal stopped breathing study
- Cross Gestational Study

2.6.1 Maternal breathing intact versus maternal stopped breathing study:

Fetal umbilical artery velocity data is obtained from PW Doppler ultrasound examination of fetuses during 10-12 weeks gestation using the transvaginal probe exclusively. This study includes 10 “data sets” (HRV, PVV, and MVV) taken from fetuses with the maternal breathing intact and compared those results to 10 “data sets” taken from the same fetuses with maternal breathing stopped. The HRV, PVV, and MVV time series data is used in this study. Paired “data sets” from ten fetuses were used where data records with spontaneous maternal breathing are ‘matched’ with the respective
maternal stop breathing case for each of the 10 patients. Hence the band power data comparison histograms have two bars.

The statistical analysis was done using the SPSS® Version 6.1 for Windows software. A comparison of the means and variance was done. Equal sample variance did not occur, therefore a non-parametric Kruskal-Wallis test was done. The significance level was set at p<0.1 since the number of “data sets” was small (10). The statistical analysis of these data does not require the one way ANOVA Scheffe test. The Scheffe test is strictly for multiple comparisons associated with comparing more then two data series and is introduced in the study outlined in Section 2.6.2.

2.6.2 Cross Gestational Study:

This study includes fetal umbilical artery velocity time series data (HRV, PVV, MVV) from 107 patients. The maternal age varied between 14 and 46 years (median 28 years). Of the fetal data for this study 42 patients are from the 10-12 week gestational age, 41 are from the 13-16 week gestational age and 24 are from the 17-20 week gestational age. The velocity data obtained from Doppler ultrasound of fetuses during 10-12 weeks gestation utilized the transvaginal probe. The velocity data obtained from Doppler ultrasound of fetuses during 13-20 weeks gestation utilized the transabdominal probe.

Three groupings were designated during the study as follows: Group 1: 10-12 weeks gestation, Group 2: 13-16 weeks gestation and Group 3: 17-20 weeks gestation. Hence for this study, band power histogram comparison charts have three bars, one for
each group. The statistical analysis was done using the SPSS® Version 6.1 for Windows software. A comparison of the means and variance was done. Unequal variances occurred, therefore a non-parametric Kruskal-Wallis test was done. The significance level was set at $p<0.05$. The statistical analysis of this data requires the one way ANOVA Scheffe test. The Scheffe test is strictly for multiple comparisons associated with comparing more than two data series.
3.0 **Results**

The two studies conducted in this thesis approach different data and analysis interests and will be treated individually. Both studies were conducted using heart rate variability (HRV), peak velocity variability (PVV) and mean velocity variability (MVV) time series data, each data packet is 512 points long and between 20-30 seconds in duration. The analysis format (as described in Section 2.0) is consistent for both studies. The analysis performed on the data is repeated three times: first cross-correlating the MVV with HRV, second cross-correlating MVV with PVV, and third cross-correlating HRV with PVV. Individual band power calculations for 0-1 Hz as well as 1-2 Hz were computed for the two studies and statistical tests were performed as described in Section 2.6.

3.1 **Maternal breathing intact versus maternal stopped breathing study:**

Figures 3-1 to 3-12 represents the band power results from the maternal breathing versus maternal stop breathing study. During the analysis itself, four charts for each cross-correlation processing permutation are created. The charts show the band-power-ratio data (i.e. the fractional contribution of band power to total spectral power) and the absolute band power data for the analysis of 0-1 Hz as well as 1-2 Hz. The statistical significance of the results shown in the histograms was then calculated as described previously to the p<0.1 level. In each histogram plot the data depicted are sample means. The error bars show the standard error of the mean (SEM).
3.1.1 Band Power Ratio Results:

3.1.1.1 MVV Cross-correlated With HRV

The results of the MVV and HRV time series cross-correlation of the spontaneous maternal breathing versus the maternal stop breathing cases can be seen in Figure 3-1 and Figure 3-2. While there are histogram differences between the two cases, they did not prove to differ statistically (p<0.1) in most power bands. Band one (0.0-0.1 Hz) and band eight (0.7-0.8 Hz) for the 0-1 Hz frequency range (Figure 3-1) and band two (1.1-1.2 Hz) and three (1.2-1.3 Hz) for the 1-2 Hz frequency range (Figure 3-2) possessed variances which were statistically significant (*).

3.1.1.2 MVV Cross-correlated With PVV

The results of the MVV and PVV time series cross-correlation of the spontaneous maternal breathing versus the maternal stop breathing cases can be seen in Figure 3-3 and Figure 3-4. While there are histogram differences between the two cases, they did not prove to differ statistically (p<0.1) in most power bands. Band one (0.0-0.1 Hz) for the 0-1 Hz frequency range (Figure 3-3) and bands one (1.0-1.1 Hz), three (1.2-1.3 Hz) and six (1.5-1.6 Hz) for the 1-2 Hz frequency range (Figure 3-4) possessed variances which were statistically significant (*).
Figure 3-1:

Results of Mean Velocity Variability and Heart Rate Variability Cross Correlation Band Power Ratio

0-1 Hertz

![Graph showing results](image)

Note: Only the top half (+) of the error bars (SEM) are represented (repeated throughout).

Figure 3-2:

Results of Mean Velocity Variability and Heart Rate Variability Cross Correlation Band Power Ratio

1-2 Hertz

![Graph showing results](image)

...
Figure 3-3:

Results of Mean Velocity Variability and Peak Velocity Variability Cross Correlation Band Power Ratio

0-1 Hertz

Figure 3-4:

Results of Mean Velocity Variability and Peak Velocity Variability Cross Correlation Band Power Ratio

1-2 Hertz
3.1.1.3 HRV Cross-correlated With PVV

The results of the HRV and PVV time series cross-correlation of the spontaneous maternal breathing versus the maternal stop breathing cases can be seen in Figure 3-5 and Figure 3-6. While there are histogram differences between the two cases, they did not prove to differ statistically (p<0.1) in most power bands. Band one (0.0-0.1 Hz) for the 0-1 Hz frequency range (Figure 3-5) and none of the 1-2 Hz (Figure 3-6) frequency range possessed variances which were statistically significant (*).

3.1.2 Band Power Absolute Results:

3.1.2.1 MVV Cross-correlated With HRV

The results of the MVV and HRV time series cross-correlation of the spontaneous maternal breathing versus the maternal stop breathing cases can be seen in Figure 3-7 and Figure 3-8. While there are histogram differences between the two cases, they did not prove to differ statistically (p<0.1) in most power bands. Band one (0.0-0.1 Hz), two (0.1-0.2 Hz), and eight (0.7-0.8 Hz) for the 0-1 Hz frequency range (Figure 3-7) and band three (1.2-1.3 Hz) for the 1-2 Hz frequency range (Figure 3-8) possessed variances which were statistically significant (*).
Figure 3-5:

Results of Heart Rate Variability and Peak Velocity Variability Cross Correlation Band Power Ratio
0-1 Hertz

Breathing
Nonbreathing

Figure 3-6:

Results of Heart Rate Variability and Peak Velocity Variability Cross Correlation Band Power Ratio
1-2 Hertz

Breathing
Nonbreathing
Figure 3-7:

Results of Mean Velocity Variability and Heart Rate Variability Cross Correlation Band Power (Absolute)
0-1 Hertz

Figure 3-8:

Results of Mean Velocity Variability and Heart Rate Variability Cross Correlation Band Power
1-2 Hertz (Absolute)
3.1.2.2 MVV Cross-correlated With PVV

The results of the MVV and PVV time series cross-correlation of the spontaneous maternal breathing versus the maternal stop breathing cases can be seen Figure 3-9 and Figure 3-10. While there are histogram differences in the two cases, they did not prove to differ statistically (p<0.1) in most power bands. Band one (0.0-0.1 Hz) for the 0-1 Hz frequency range (Figure 3-9) and three (1.2-1.3 Hz) for the 1-2 Hz frequency range (Figure 3-10) possessed variances which were statistically significant (*).

3.1.2.3 HRV Cross-correlated With PVV

The results of the HRV and PVV time series cross-correlation of the spontaneous maternal breathing versus the maternal stop breathing cases can be seen Figure 3-11 and Figure 3-12. While there are histogram differences in the two cases, they did not prove to differ statistically (p<0.1) in most power bands. Band one (0.0-0.1 Hz) for the 0-1 Hz frequency range (Figure 3-11) and none of the 1-2 Hz (Figure 3-12) frequency range possessed variances which were statistically significant (*).
Figure 3-9:

Results of Mean Velocity Variability and Peak Velocity Variability Cross Correlation Band Power (Absolute)

0-1 Hertz

Figure 3-10:

Results of Mean Velocity Variability and Peak Velocity Variability Cross Correlation Band Power

1-2 Hertz (Absolute)
Figure 3-11:

Results of Heart Rate Variability and Peak Velocity Variability Cross Correlation Band Power (Absolute) 0-1 Hertz

Figure 3-12:

Results of Heart Rate Variability and Peak Velocity Variability Cross Correlation Band Power 1-2 Hertz (Absolute)
3.2 Cross Gestational Study:

Figures 3-13 to 3-24 represents the band power results from the cross gestational study. During the analysis itself, four charts for each cross-correlation processing permutation are created. The charts show the band-power-ratio data (i.e. the fractional contribution of band power to total spectral power) and the absolute band power data for the analysis of 0-1 Hz as well as 1-2 Hz. The statistical significance of the results shown in the plots was then calculated as described previously to the p<0.05 level. In each histogram plot the data depicted are sample means. The error bars show the standard error of the mean (SEM).

3.2.1 Band Power Ratio Results:

3.2.1.1 MVV Cross-correlated With HRV

The results of the MVV and HRV time series cross-correlation of the cross gestational data can be seen in Figure 3-13 and Figure 3-14. For bands one (0.0-0.1 Hz), two (0.1-0.2 Hz), three (0.2-0.3 Hz), four (0.3-0.4 Hz), six (0.5-0.6 Hz), and seven (0.6-0.7 Hz) there is a statistically significant (p<0.05) difference between the 10-12 week gestation age and both the 13-16 week and 17-20 week groups (*) for the 0-1 Hz frequency range (Figure 3-13). Also, for the 0-1 Hz frequency range, a statistically significant difference is shown in band five (0.4-0.5 Hz) between the 10-12 week
gestational age and the 13-16 week (†), and in band eight (0.7-0.8 Hz) between the 10-12 week gestational age and the 17-20 week (ζ). For the 1-2 Hz frequency range (Figure 3-14), with the exception of band one (1.0-1.1 Hz) there is a statistical significance demonstrated within all of the bands (1.1-2.0 Hz) between the 10-12 week gestation and both the 13-16 and 17-20 week gestational age (*).

3.2.1.2 MVV Cross-correlated With PVV

The results of the MVV and PVV time series cross-correlation of the cross gestational data can be seen in Figure 3-15 and Figure 3-16. For bands two (0.1-0.2 Hz), three (0.2-0.3 Hz), and four (0.3-0.4 Hz) there is a statistically significant (p<0.05) difference between the 10-12 week gestation age and both the 13-16 week and 17-20 week groups (*) for the 0-1 Hz frequency range (Figure 3-15). Also, for the 0-1 Hz frequency range, a statistically significant difference is shown in band one (0.0-0.1 Hz) between the 10-12 week gestational age and the 13-16 week (†). For the 1-2 Hz frequency range (Figure 3-16) there is a statistical significance demonstrated within all of the bands (1.0-2.0 Hz) between the 10-12 week gestation and both the 13-16 and 17-20 week gestational age (*).
Figure 3-13:

Cross Gestational Study - Results of Mean Velocity Variability and Heart Rate Variability Cross Correlation Band Power Ratio
0-1 Hertz

Figure 3-14:

Cross Gestational Study - Results of Mean Velocity Variability and Heart Rate Variability Cross Correlation Band Power Ratio 1-2 Hertz
Figure 3-15:

Cross Gestational Study - Results of Mean Velocity Variability and Peak Velocity Variability Cross Correlation Band Power Ratio 0-1 Hertz

Figure 3-16:

Cross Gestational Study - Results of Mean Velocity Variability and Peak Velocity Variability Cross Correlation Band Power Ratio 1-2 Hertz
3.2.1.3 HRV Cross-correlated With PVV

The results of the HRV and PVV time series cross-correlation of the cross gestational data can be seen in Figure 3-17 and Figure 3-18. For all bands (0.0-0.8 Hz) except bands nine (0.8-0.9 Hz) and ten (0.9-1.0 Hz) there is a statistically significant (p<0.05) difference between the 10-12 week gestation age and both the 13-16 week and 17-20 week groups (*) for the 0-1 Hz frequency range (Figure 3-17). For the 1-2 Hz frequency range for all bands (1.2-2.0 Hz) except bands one (1.0-1.1 Hz) and two (1.1-1.2 Hz) there is a statistically significant variance between the 10-12 week gestation age and both the 13-16 week and 17-20 week groups (*).

3.2.2 Band Power Absolute Results:

3.2.2.1 MVV Cross-correlated With HRV

The results of the MVV and HRV time series cross-correlation of the cross gestational data can be seen in Figure 3-19 and Figure 3-20. For bands one through four (0.0-0.4 Hz) there is a statistically significant (p<0.05) difference between the 10-12 week gestation age and the 17-20 week group (ζ) for the 0-1 Hz frequency range (Figure 3-19). For the 1-2 Hz frequency range (Figure 3-20) it can be seen that for band three (1.2-1.3 Hz) and bands five through ten (1.4-2.0 Hz) there is a statistically significant difference demonstrated within all of the bands between the 10-12 week gestation and both the 13-16 and 17-20 week gestational age (*). Also, band two (1.1-1.2 Hz) demonstrates a statistical difference between the 10-12 week gestation and 13-16 week gestational age (†).
Figure 3-17:

Cross Gestational Study - Results of Heart Rate Variability and Peak Velocity Variability Cross Correlation Band Power Ratio

0-1 Hertz

Figure 3-18:

Cross Gestational Study - Results of Heart Rate Variability and Peak Velocity Variability Cross Correlation Band Power Ratio 1-2 Hertz
Figure 3-19:

Cross Gestational Study - Results of Mean Velocity Variability and Heart Rate Variability Cross Correlation Band Power (Absolute) 0-1 Hertz

Figure 3-20:

Cross Gestational Study - Results of Mean Velocity Variability and Heart Rate Variability Cross Correlation Band Power 1-2 Hertz (Absolute)
3.2.2.2 MW Cross-correlated With PVV

The results of the MVV and PVV time series cross-correlation of the cross gestational data can be seen in Figure 3-21 and Figure 3-22. For bands three (0.2-0.3 Hz) and four (0.3-0.4 Hz) there is a statistically significant (p<0.05) difference between the 10-12 week gestation age and the 17-20 week group (C) for the 0-1 Hz frequency range (Figure 3-21). For the 1-2 Hz frequency range (Figure 3-22), with the exception of band one (1.0-1.1 Hz) there is a statistically significant difference demonstrated within all of the bands (1.1-2.0 Hz) between the 10-12 week gestation and both the 13-16 and 17-20 week gestational age (*).

3.2.2.3 HRV Cross-correlated With PVV

The results of the MVV and HRV time series cross-correlation of the cross gestational data can be seen in Figure 3-23 and Figure 3-24. For bands two (0.1-0.2 Hz), three (0.2-0.3 Hz), and four (0.3-0.4 Hz) there is a statistically significant (p<0.05) difference between the 10-12 week gestation age and the 17-20 week group (C) for the 0-1 Hz frequency range (Figure 3-23). For the 1-2 Hz frequency range (Figure 3-24), with the exception of band one (1.0-1.1 Hz) and band four (1.3-1.4 Hz) there is a statistically significant difference demonstrated within all of the bands (1.1-1.3, 1.4-2.0 Hz) between the 10-12 week gestation and both the 13-16 and 17-20 week gestational age (*). Band four (1.3-1.4 Hz) possesses a variance which is statistically significant between the 10-12 week gestation and the 13-16 week gestation (†).
Figure 3-21:

Cross Gestational Study - Results of Mean Velocity Variability and Peak Velocity Variability Cross Correlation Band Power (Absolute) 0-1 Hertz

Figure 3-22:

Cross Gestational Study - Results of Mean Velocity Variability and Peak Velocity Variability Cross Correlation Band Power 1-2 Hertz (Absolute)
**Figure 3-23:**

Cross Gestational Study - Results of Heart Rate Variability and Peak Velocity Variability Cross Correlation Band Power (Absolute) 0-1 Hertz

**Figure 3-24:**

Cross Gestational Study - Results of Heart Rate Variability and Peak Velocity Variability Cross Correlation Band Power 1-2 Hertz (Absolute)
3.2.3 Other Cross Gestational Observations

Looking at the three cases explored in Section 3.2 it can be seen that the 10-12 week gestational data shows a broad spectrum in the 1-2 Hz range whereas the other cases (13-16 and 17-20 weeks) appear to be diminishing. Finally, in looking at the results above, the 13-16 week gestation group is not statistically different from the 17-20 week gestation group in any of the comparative results.

3.3 General Observations

As shown in Section 3.1 and Section 3.2 results of the absolute band power and band-power-ratio were obtained and used for spectral comparison. Comparing the absolute band power and band-power-ratio histograms, differences in amplitude can be seen. This difference can be attributed to the nature of the ratio data. The ratio data is normalized in such a way that it represents the fractional contribution of band power to total spectral power. The results of the statistical analysis using the absolute band power and band-power-ratio data did have differences. However, the quantitative magnitude differences between spectra did not effect the qualitative conclusions based on the spectral comparisons.
The data used in the two studies discussed herein do not have the ability to be averaged. The data file lengths are not long enough to divide the time series into sub-parts in order to provide a means for averaging. Also, the nature of the data (i.e. velocity time series) does not lend itself to multiple averaging based on the limited acquisition runs performed per patient.
4.0 Discussion

Congenital cardiac malformations are a serious health concern affecting the development of the fetal cardiovascular system. Currently diagnostic tools that allow assessment of fetal cardiovascular health early in pregnancy are not applicable prior to 20 weeks gestation (Wladimiroff 1992). Identification of a fetus with abnormalities early in pregnancy, 10-20 weeks gestation, could assist in diagnosis and be a great asset in health care. This thesis is a continuation of, and works in concert with, other research efforts conducted at Rochester Institute of Technology (RIT) aimed at characterizing fetal cardiovascular health (Gallagher 1995, Kettles 1995).

4.1 Test Cases:

One of the goals of this thesis was to determine if the cross-correlation can be used as an accurate method of representing the frequency content of individual parts of fetal umbilical artery time series data (specifically HRV, PVV, and MVV). If this is possible, then the major frequency components in each individual signal should appear in the cross-correlation and respective power density. The test cases performed demonstrated that the common frequency components of the signals are evident in the cross-correlated data (Section 2.5). Frequency components not in common to both signals, or with low amplitudes, were attenuated. Hence, individual frequency components from respective input signals are evident in the cross-correlated data and the corresponding power
spectrum. Therefore, the cross-correlation technique can be useful in studying frequency commonalities and variability.

Cross-correlation is a technique used to decrease the noise signature in correlated output (Stremler 1990, Proakis 1988, Hewlett Packard 1985). Two examples of noise addition were demonstrated (Section 2.5.2). It was evident from these examples that noise does not qualitatively affect the results, since the noise is attenuated. This demonstration is helpful in knowing that noise may not play a significant role in the analysis of data where common frequencies occur. However, if the noise magnitude relative to signal magnitude is large, the noise may affect cross-correlated results. Noise is broad band and hence could have the tendency to affect ‘weaker’ signals. In areas with no significant frequency correlation, the test data indicate (Section 2.5) that a strong noise signal affects the results more so then a weaker noise signal (Figures 2-14 and 2-22). The influence of noise is substantially reduced by successive signal correlation and averaging (Table 2-2).

Another important demonstration is that the order in which two signals are cross-correlated does not matter. As demonstrated, in Section 2.5.3, it is evident that reversing the sequence of the signals produces the same results.
4.2 Maternal breathing intact versus maternal stopped breathing study:

Maternal breathing may bias HRV, MVV, and PVV data interpretation, therefore a study evaluating the effects of maternal breathing on fetal ultrasound data analysis is necessary. Hence, the main goal of this study is to use cross-correlation to evaluate the cyclic variations and commonalities of the fetal umbilical artery data for the maternal breathing versus non-breathing condition.

Normal adult maternal breathing occurs at a rate of 15-16 breaths per minute. This equates to a maternal breathing frequency of approximately 0.26 Hz, this will fall within band three (0.2-0.3 Hz) of the spectral plots depicted in Section 3.1. Looking at the cross-correlation results (Section 3.1) of both the band-power-ratio (Figure 3-1 to Figure 3-6) and absolute band power (Figure 3-7 to Figure 3-12) data, common frequencies exist in the HRV, PVV and MVV time series (i.e. no statistical significant difference in the data). This ‘common variability’ occurred in the normal maternal breathing range (0.2-0.3 Hz) and most other ranges. However, there is a consistent difference that occurs in band one (0.0-0.1 Hz), that is statistically significant. Detrending of the HRV, PVV, and MVV data is designed to yield zero-mean variability time series. Hence, band powers occurring in the 0.0-0.1 Hz frequency range are not due to mean value (i.e. DC) cross-correlation. As discussed above, normal maternal breathing occurs at a higher frequency then this band (nominally 0.2-0.3 Hz), therefore the spectral signature at 0.0-0.1 Hz should not be directly due to maternal breathing affects. Whether this observation has a physiologic interpretation is unclear. Further, whether or not the
0.0-0.1 Hz band is meaningful in and of itself is unclear. The amount of data transformation that occurs and the fact that a single cycle of data is being analyzed could suggest that this frequency band (0.0-0.1 Hz) is insignificant.

Evaluating the results obtained in the 1-2 Hz frequency range, there are instances where band one (1.0-1.1 Hz), band two (1.1-1.2 Hz) and band three (1.2-1.3 Hz) appear to have differences that are statistically significant between breathing intact and stop breathing conditions. These differences may be due to maternal heart rate influences on placental hemodynamics during intact versus stop breathing conditions. For the maternal heart rates recorded, the average heart rate is 69.3 ± 3.8 beats per minute or 1.15 ± 0.064 Hz. The 1.15 Hz average maternal heart rate is situated near the frequency bands which show statistical variances (i.e. 1.0-1.1 Hz, 1.1-1.2 Hz, 1.2-1.3 Hz, respectfully). Unfortunately, maternal heart rate data was recorded for only a few fetal records during the ultrasound data acquisition. Therefore, it is possible to speculate that maternal circulation hemodynamics are affecting the fetal variability time series data cross-correlation results.

4.3 Cross Gestational Study:

The cardiovascular system in the embryo/fetus behaves as the mature cardiovascular system does in that it is regulated by demand (Kempski 1993 and 1995, Clark 1990). One major difference between the mature system and the embryo/fetus is that during primary cardiovascular development cardiac output is not regulated by the central nervous system. Functional innervation appears after primary cardiac morphogenesis is
complete (Pappano 1977). The human fetal central nervous system begins functional hemodynamic control around the 16-17th week of gestation (Walker 1975). The exact mechanism that controls the cardiac output in the embryo/fetus in early development is not yet known.

The fetal/placental vascular bed is transformed from a high resistance flow system to a low flow resistance system between 10-18 weeks of gestation (Wladimiroff 1991). This transformation is essential in maintaining optimum blood flow to the developing fetus throughout the remainder of pregnancy.

Looking at the results obtained using cross-correlation to compare time series waveform frequency content during gestation, several observations can be made (Section 3.2). Band-power-ratio (Figures 3-13 to 3-18) and absolute band power (Figures 3-19 to 3-24) data show that there are several power bands that appear to be statistically different (p<0.05) between the 10-12 week and both the 13-16 and 17-20 week gestation groups. It is important to note that in these findings that there is no significant difference in any band power between the 13-16 week gestation group and the 17-20 week gestation group.

Comparing the band-power-ratios of the three cross-correlations, the MVV and PVV time series demonstrate the strongest correlation. The HRV showed weaker correlation with the velocity data (PVV, MVV). In general, the overall shape distribution of the spectral power changes with gestation. For example, Figure 3-15 and Figure 3-16 show that early gestational data correlations (10-12 weeks) have broad spectral content which becomes more focused to the sub-one Hz frequencies as gestation progresses.
These observations may suggest a partial coupling between these time series data that shifts with gestational age.

These results suggest that the regulation mechanism of fetal cardiovascular function is different in the 10-12 week gestational period then that of the 13-20 week gestational period. The transition between the 10-12 week and the later gestational age (13-20 weeks) is substantial in the cross-correlation result histograms. The increased correlation in the later gestational periods (13-16 and 17-20 weeks) may be due to a transition from biochemical hemodynamic regulation during early fetal development to central nervous system based regulation late in development. Another possibility is that there is better correlation between HRV and velocity variability (MVV, PVV) time series due to coincident regulation by parasympathetic neural control mechanisms. Also, placental mechanics change dramatically during this time period and could affect the variability time series due to changes in umbilical artery afterload mechanics. The placental circulation changes from high resistance, low capacitance to low resistance, high capacitance around the 12-14 week gestation age (Jauniaux 1991).

The gestational periods that were compared in this study (10-12, 13-16, 17-20 weeks), show statistically significant differences in cross-correlation spectra between the 10-12 week and the 13-16 and 17-20 week groups. Recall that the 10-12 week ultrasound was done using a transvaginal transducer and the 13-20 week ultrasound examinations were done using a transabdominal transducer. In addition, a statistical significant difference between the 13-16 and 17-20 week fetus results were not observed throughout this study. This evidence suggests that there may be a consistency among the
transabdominal recordings. Hence, the possible influence of transabdominal versus transvaginal transducer bias may exist in these data. Here, transabdominal measurements may be affected by maternal abdomen movement during breathing or by inherent differences in technique when using the two devices. Indeed Jaffa (Jaffa 1995) has suggested that the transabdominal flow velocity waveform recordings are attenuated from those obtained transvaginally. While spectra derived from maternal breathing does not influence transvaginal recordings (Ursem et. al. 1996- Appendix E), no evaluation has yet occurred for transabdominal recordings.
5.0 Future Research and Applications

Analysis of amplitude modulation, frequency modulation, heart rate variability (HRV) analysis, and commonalities in frequency are but a few interesting aspects of recent studies in regards to cardiovascular data (Gallagher 1995, Kettes 1995, Kempski 1995, van Ravenswaaij-Arts 1993, Karin 1993, Saul 1991, Breborowicz 1988). The long term goals of this research include the development of a non-invasive measure of the fetal cardiovascular well-being, and to define operational norms for fetal cardiovascular function. Several aspects of the algorithms created for the purpose of this thesis, both explored and unexplored, could assist in the continuing search for the solution and conclusion of these goals. The hope is that someday the algorithms herein could work in concert with others created at Rochester Institute of Technology (RIT) (Gallagher 1995, Kettes 1995) to serve as clinical diagnostic tools for fetal cardiovascular malformations.

Several aspects of the algorithms created herein could be useful in time frequency analysis and stationarity concerns. Specifically, assessing self-consistency within a signal could be useful in evaluating the frequency domain sub-components of that signal over time (i.e. time-frequency analysis). Looking at the relationship of smaller parts of one signal compared with smaller parts of another signal could also prove beneficial in the study of time-dependent consistencies between the signals being scrutinized.

Maternal heart rate data was recorded for only a few patients during the ultrasound data acquisition for the maternal breathing versus stop breathing study and for none of the patients in the cross gestational study. This lapse in maternal heart rate documentation was not within the control of RIT personnel. However, if we observe the
maternal heart rates which were recorded, it can be seen that the average heart rate is 69.3 ± 3.8 beats per minute or 1.15 ± 0.064 Hz. The 1.15 Hz average maternal heart rate is near the frequency bands with statistical variances as found in the maternal breathing versus stop breathing study (Section 3.1). It is possible that maternal circulation hemodynamics, perhaps mediated in the placental circulation, is affecting the velocity time series data cross-correlation results. However such a claim is speculative at this juncture. Therefore, future ultrasound data acquisition with the maternal heart rate and respiration rate recorded simultaneously would easily create the data to perform such an analysis.

The apparent difference between the 10-12 week and 13-20 week gestational data band power histogram (Section 3.2) brings up an interesting speculation with regards to the transvaginal versus the transabdominal probes. The transvaginal probe is used during the 10-12 week gestation because the fetus is small and difficult to analyze using the transabdominal probe. The transabdominal probe is often used during the 13-16 and 17-20 week gestation periods to gather data, due to maternal comfort with this technique, as opposed to the transvaginal probe. It would be valuable to evaluate the use of the two different probes in future studies to see if the appearance of the differing power in the 10-12 week gestational data can be attributed to the use of the transvaginal probe. The impact of maternal breathing on transvaginal probe ultrasound recordings shows no significant difference (Ursem et. al. 1996- Appendix E), but no check on the transabdominal probe with or without maternal breathing has yet been recorded. A study to evaluate the effects of maternal breathing on the transabdominal probe ultrasound recordings would be valuable.
References


Appendix A:  

**SK ac/cc processing.VI**

A.1 **SK ac/cc processing.VI**

This algorithm is composed of the sub-vi’s *Case Struc for Divisions.vi, Cross Correlates.vi,* and *Separate Data.vi,* which are discussed in Appendix B. For the purpose of this thesis, the main function of this algorithm is to import two signals, cross-correlate them, and compute the power contents in the individual and cross-correlated signals. All of the power spectra and cross-correlations are depicted as ‘single-sided’. It is important to note that a cross-correlation of a signal with itself is an autocorrelation.

For purposes of post analysis and consistency all power plots are depicted with the y-axis in power density units (Vrms)²/Hz and the x-axis in frequency units (Hz). The peak power values for all power spectrum results within the algorithm are calculated and displayed. The differential time ‘dt’ and differential frequency ‘df’ values for the respective time series and spectral density plots are calculated and displayed. The number of points plotted within a particular graph is also computed and displayed.

As mentioned above, the algorithm imports two signals. Each signal can be divided into as many as 8 sub-signals. The sub-portions of the first signal can then be cross-correlated with sub-portions of the second signal. Plots of the cross-correlation and the power density spectra of the sub-signal cross-correlations are shown as single-sided representations. All power density spectrum calculations are done using the dual-sided correlation function.

The *SK ac/cc processing.VI* algorithm has the capability to input and calculate the cross-correlation/amplitude spectrum of sub-signals with overlap. The user specifies the
overlap as a percentage of the number of points in the signal and toggles the overlap option to ‘On’. For example (Figure A-1), an original signal containing 1024 data points with a division of 2 is specified. If a percent overlap of 50% is requested, the first of the two sub-signals will contain data points 1-512 and the second sub-signal will contain data points 257-768. When overlapping, if a data record is not divided evenly with divisions and the specified overlap, the data will be truncated.

**Figure A-1:**

Original Signal: contains 1024 data points

1-1024

Original Signal with 2 divisions and 50% overlap:

1-512

257-768

50%

513-1024

A.2 Default Values

For this thesis, the algorithm SK ac/cc processing VI was used to analyze all data sets reported. Upon opening the algorithm the front panel (user interface) is set with certain default values for the user inputs. The default values (as shown upon opening the
algorithm) were those utilized in the performance of this thesis. The overlap was set to
'Off' and to 0\% and the number of divisions was set to 2. The sub-correlations were
therefore of the first half of the two signals, the second half of the two signals, the first
half of the first signal with the second half of the second signal, and the second half of the
first signal with the first half of the second signal (Displayed below in Figure A-2).

Figure A-2:

<table>
<thead>
<tr>
<th>Signal 1: 512 points</th>
<th>Signal 2: 512 points</th>
</tr>
</thead>
</table>

2 Divisions Specified:

<table>
<thead>
<tr>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
</tr>
</thead>
<tbody>
<tr>
<td>A: Signal 1, from 0 - 256</td>
<td>B: Signal 1, from 257-512</td>
<td>C: Signal 2, from 0 - 256</td>
<td>D: Signal 2, from 257-512</td>
</tr>
</tbody>
</table>

Defaults Cross-correlations Performed:

<table>
<thead>
<tr>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
</tr>
</thead>
<tbody>
<tr>
<td>&amp;</td>
<td>&amp;</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>&amp;</td>
<td>&amp;</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>&amp;</td>
<td>&amp;</td>
</tr>
</tbody>
</table>

The 'Save' option for creating spreadsheet files is also default, this will save the cross-
correlation and amplitude spectrum obtained from the two original signals.
Appendix B: Sub-VI’s

B.1 Separate Data.vi

It is assumed that the user knows the content of the data that s/he wishes to process. Under this assumption the algorithms constructed for the purpose of this thesis anticipate two columns of data. Hence the left is time, while the right column is measured data. The function of this sub-vi is to import data and to split it into two separate columns. The data is transposed within the algorithm to convert from the spreadsheet column-dominant format to the row-dominant LabVIEW® format.

B.2 Cross Correlates.vi

This algorithm uses the data brought in via Separate Data.vi. Two data files are imported and the measured data columns are sent into the ‘Cross Correlate’ operation (contained within LabVIEW®). The time increment ‘dt’ is calculated using the time column. The ‘cross correlate’ results along with the original time data are plotted in single-sided format.

Since the cross-correlation is an operation performed in the time domain, the data is translated to the frequency domain as follows. The ‘Auto Power Spectrum’ signal processing operation (within LabVIEW®) is used to obtain the power density spectrums \((\text{Vrms})^2/\text{Hz}\) for the two individual original data files (measurement column) that were initially imported. The ‘dt’ value and the signal duration are used to calculate the frequency axis increment ‘df’. The frequency axis against which the power representation
is plotted is determined based on the sampling frequency and Nyquist criterion. The important focus for the purposes of this thesis is the amplitude spectrum $((V_{rms})^2/\text{Hz})$ of the cross-correlation of the two original signals that were imported. All power spectrums are plotted as single-sided spectrums. For the purpose of calculations, the power calculations are done using the dual-sided cross-correlation functions.

The algorithm also has the capability to save the cross-correlation and the cross-correlated amplitude spectrum to a spreadsheet. In addition, the peak values for the power representations are obtained.

B.3 Case Struc for Divisions.vi

Two signals are imported into this sub-vi. Each signal can then be divided into sub-signals. Sub-signals of each original signal can then be cross-correlated with each other, as specified by the user. The number of divisions is specified by the user. The algorithm is programmed so the division can be anywhere from 1 to 8 divisions. If the user specifies 1 division, the signal will be processed as imported.

This sub-vi cross-correlates the sub-signals, as specified by the user, and computes the amplitude spectrum (using the ‘MHK Amplitude Spectrum’ algorithm written by Dr. Mark Kempski using LabVIEW®). While the graphs are represented as single-sided, calculations are done using the entire data set. The values for ‘dt’ and the peak power value are also calculated.
Appendix C: User’s Guide

User’s Guide

Upon opening LabVIEW®, a front panel (user interface) appears. The user interface is equipped with several options and mechanisms to change the performance of an algorithm. The algorithm SK ac/cc processing.VI which was constructed for the purpose of this thesis has several user interface options (as discussed Appendix A and Appendix B). This section provides an easy guide to running the algorithm. Each user interface option is hi-lighted within this section with a brief synopsis of the function.

File Name 1: Type the name of the first file to be imported in this box. (If the algorithm is run with no file name written here, a directory prompt will result and a file can be selected in that manner).

File Name 2: Type the name of the second file to be imported in this box. (If the algorithm is run with no file name written here, a directory prompt will result and a file can be selected in that manner).

# divisions: A signal can be divided into 1 (itself) to 8 sub-divisions. The user specifies the number of divisions desired here.
**Overlapping?** The indicator should be in the ‘On’ position if overlap of the signal is desired and the ‘Off’ position if no overlapping is desired (See Figure A-1).

**% overlap** Identify the percentage of overlap. If a percentage is identified with the ‘Overlapping?’ indicator in the ‘Off’ position, no overlapping will occur (See Figure A-1).

**Save to spreadsheet?** Select ‘Save’ if it is desired to output the cross-correlation and amplitude spectrum of the two original signals to a spreadsheet. Select ‘Not Save’ if no spreadsheet output is desired.
Appendix D: Other potential algorithm uses

The algorithm *sk processing.vi* was also created during the research and development associated with this thesis. The differences between the *sk processing.vi* algorithm and *SK ac/cc processing.VI* is that the former (*sk processing.vi*) produces sub-signals which can be autocorrelated with themselves, while the latter (*SK ac/cc processing.VI*) allows the cross-correlation of sub-signals from two different imported signals.

The sub-signal capabilities built into the algorithm *sk processing.vi* provides an easy analysis of self consistencies within signals. This could be helpful and beneficial in analyzing the periodicity of a velocity signal or a variability time series data set. The overlapping capability built into the algorithm could be used to increase resolution of the signal as well as evaluate self consistencies within the signal.

*SK ac/cc processing.VI* has the potential to use sub-signaling to evaluate consistencies within the different parts of a signal. Again, overlapping could be used to increase the resolution.
Appendix E: Abstract presented at the Weinstein Cardiovascular Conference, Philadelphia, PA 1996

POWER SPECTRAL ANALYSIS OF UMBILICAL ARTERY BLOOD FLOW VELOCITY IN THE WEEK 10 TO 12 HUMAN FETUS


Department of Obstetrics and Gynecology, Academic Hospital Dijkzigt, Erasmus University Rotterdam, The Netherlands; *Department of Mechanical Engineering, Rochester Institute of Technology; SCOR Pediatric Cardiovascular Diseases, *Division of Pediatric Cardiology, University of Rochester.

The fetal cardiovascular system is precisely regulated during development. We used power spectral analysis to define heart rate variability and peak velocity amplitude variability in the human fetus during conditions of maternal spontaneous and stop breathing. Doppler recordings were made from the free floating loop of the umbilical artery using a transvaginal probe. Separate matched velocity time series were recorded during spontaneous maternal breathing and during stop breathing at weeks 10 (n=1), 11 (n=3), and 12 (n=6). Peak velocity, mean velocity, and instantaneous heart rate (via velocity rising edge threshold detection) were determined for each velocity time series. Peak velocity variability and heart rate variability time series were determined, de-trended via low-order polynomial fit to remove DC-drift, and subject to power spectral decomposition using FFT. To compensate for mean heart rate differences between fetuses, we normalized spectral frequency axes for each fetus by the respective heart rate. For comparison purposes, the unitless normalized frequency axes ranged from zero (DC) to 1 (heart rate).

To compensate for mean-velocity (or mean heart rate) differences between fetuses, we computed the ratio of spectral power in 10 pre-set bands (0.1 increments of normalized frequency) to total spectral power. The average power ratios for heart rate variability during stop breathing were 4%, 16%, 25%, 25%, 17%, 8%, 3%, <1%,<1%, and <1%, respectively, in each band. During spontaneous maternal breathing these ratios changed to 4%, 14%, 25%, 29%, 14%, 8%, 3%, 1%,<1%, and <1%, respectively. The average power ratios for peak-velocity variability during stop breathing were 25%, 26%, 20%,
13%, 9%, 4%, 1%, 1%, <1%, and <1%, respectively. During spontaneous maternal breathing these ratios changed to 28%, 30%, 16%, 11%, 9%, 4%, 1%, <1%, <1%, and <1%, respectively. Paired statistical comparison of data from spontaneous and stop breathing conditions using student's t-test showed no difference in spectral power distribution attributable to maternal breathing. Thus, measures of fetal heart rate variability and peak-velocity amplitude variability using power spectral analysis are new tools for the analysis of homeostasis of the early human fetus. We speculate that cardiovascular alterations associated with maternal and fetal pathology will lead to earlier clinical diagnosis and therapy.