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FUNCTIONAL EVALUATION OF PROSTHETIC HEART-VALVES THROUGH ACOUSTIC ANALYSIS

submitted by

JEFFREY P. LARIVIERE, B.Eng

A thesis submitted to

the Faculty of Graduate Studies and Research

in partial fulfillment of

the requirements for the degree of

Master of Engineering

Ottawa-Carleton Institute for Electrical Engineering

Faculty of Engineering

Department of Systems and Computer Engineering

Carleton University

Ottawa, Ontario, Canada, K1S 5B6

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Functional Evaluation of Prosthetic Heart-Valves

Name through Acoustic Analysis

by JEFFREY P. LARIVIER

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**FUNCTIONAL EVALUATION OF
PROSTHETIC HEART-VALVES
THROUGH ACOUSTIC ANALYSIS**

by: Jeffrey P. Lariviere

September 1995

DSP	Digital Signal Processor
DWT	Discrete Wavelet Transform
FT	Fourier Transform
Hz	Hertz (cycles per second)
NMF	Normalized Maximal Frequency
P-P plot	Probability-Probability plot
S1	first heart sound (accompanies the beginning of systole)
S2	second heart sound (accompanies the end of systole, beginning of diastole)
SNR	Signal to Noise Ratio
SSA	sound spectral analysis
STFT	Short Time Fourier Transform

ABSTRACT

Noninvasive medical diagnostic tests based on acoustic signal analysis have become more reliable and prevalent during the last decade due to advances in signal processing techniques and computer processing power. The monitoring of changes in sounds of artificial heart-valves has been useful in the early detection of valve malfunction in both mechanical valves and bioprosthetic valves. This thesis examines the acoustic features of mechanical heart-valves subject to thrombosis, the major cause of mechanical heart valve failure.

Thrombus simulants were attached to the inflow valve housing and *in-vitro* sound recordings were made of mechanical aortic valves in a mock circulatory loop driven by a pulsatile artificial heart. *In vivo* sound recordings were also made of an unobstructed valve shortly after surgical implantation in a Holstein calf. Significantly, in this study the thrombus simulants did not impede the mechanical valve's occluder movement, rather they were attached upstream from the valve and only affected the volume flow rate and shape.

Features of the acoustic signal were compared in the time domain and frequency domain. Spectral estimators, including the Fourier Transform, Pole-Zero modelling, Filter Banks and Wavelet Transforms were compared and evaluated in terms of their ability to distinguish obstructed valves from unobstructed valves. Results indicate that FFT analysis of the flow noise during maximum flow rate gave the highest amount of correlation (0.94) with the amount of obstruction present. In terms of the number of factors produced by each spectral analysis method which showed good correlation (> 0.70), the Pole-Zero analysis method provided the best results, with 15 significant indicators of obstruction.

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Finally, a special thanks to my family for their unwavering support, enthusiasm and motivation. This work is dedicated to them and to the memory of David Q. Conibear.

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LIST OF SYMBOLS

Symbols and Abbreviations:

$m(t)$	measured waveform
$\hat{m}(t)$	coherently averaged waveform
$d(t)$	deterministic component of measured waveform
$n(t)$	noise component of measured waveform
T	period of pump cycle
Δt_{oc}	time between opening and closing peaks
Δt_{eo}	time between start of ejection phase and opening peak
Δt_{fc}	time between start of fill phase and closing peak
$Z(f)$	Frequency response of equivalent jitter filter
$l(n)$	low pass filter impulse response
$h(n)$	high pass filter impulse response
$x(n)$	original discrete time signal
$a_i(n)$	approximation output
$d_i(n)$	detailed output
$\textcircled{2\downarrow}$	downsampling by 2
ANOVA	Analysis of Variance
ARMA	Autoregressive Moving Average
CWT	Continuous Wavelet Transform
DAT	Digital Audio Tape

DSP	Digital Signal Processor
DWT	Discrete Wavelet Transform
FT	Fourier Transform
Hz	Hertz (cycles per second)
NMF	Normalized Maximal Frequency
P-P plot	Probability-Probability plot
S1	first heart sound (accompanies the beginning of systole)
S2	second heart sound (accompanies the end of systole, beginning of diastole)
SNR	Signal to Noise Ratio
SSA	sound spectral analysis
STFT	Short Time Fourier Transform

1.0 Introduction

One of the most prevalent diagnostic tools available to physicians is the stethoscope. Its widespread use confirms the value of acoustic information in making preliminary diagnoses regarding the physiology of cardiovascular and respiratory systems. Signal processing engineering techniques offer the potential of improving the signal to noise ratio (SNR) of these signals as well as aiding the clinician in diagnosing disease-states of natural organs and malfunctionings of prostheses¹ [1][21][22].

In the case of the heart, the detection and classification of disease-states or malfunctions using phonocardiograms² has an important economic and safety benefit, due mainly to the non-invasive nature of the procedure. In addition, with the increased storage and computational abilities of today's digital signal processors (DSPs), twenty-four hour, portable inexpensive monitoring devices are feasible although the design of such devices must take into account the chest-thorax nonhomogeneous and time-varying transmission medium [13].

Thrombus formation is one of the major complications associated with blood-conducting systems such as arteries, natural and prosthetic valves, ventricular assist devices and total artificial hearts [31]. Thrombus formations occur when components of the blood, platelets, contact wettable or rough surfaces. When this happens, they tend to disintegrate, releasing

-
1. Artificial limbs or organs.
 2. Recordings of heart sounds.

granules of a substance known as *platelet factor 3*. Platelet factor 3 then reacts with several blood proteins and calcium ions to form prothrombinase, which in turn, reacts with other proteins to form fibrous formations, referred to as clots [4].

Thrombus formations are the major complication associated with mechanical heart-valves. Thrombotic occlusion and thromboemboli (thrombus deposits which break free from the site of formation) occur at a rate of 1-4% per patient-year [31].

The detection of thrombosis of prosthetic valves through sound analysis is essentially a problem in classification, where valves are classified as either obstructed or unobstructed based on some feature of their produced sound. In general, classifiers make decisions based on the joint distributions of feature vectors¹ within the feature space [20]. With regard to acoustical data, features may be generated from the time domain, or after a suitable spectral estimation transformation, from the frequency domain [6].

Accurate spectral estimation is an important component of many of the classification techniques², since the power distribution of the auditory signal will exhibit changes correlated

-
1. Feature vectors are sets of features extracted from a data set. For example, if one was looking at the combined characteristics of height and body weight, a feature vector would be comprised of a weight value and a height value. The feature space would therefore consist of all possible combinations of these values.
 2. Classification techniques in general attempt to assign group membership to an object based on a set of observed properties of the object. The observed properties may be taken from the frequency domain, in which case the choice of the spectral estimation method is a fundamental consideration.

to changes in the physical components generating the signal. For instance, diseases which cause occlusions in the coronary arteries may produce turbulence in the blood flow, contributing to a sound with a higher frequency component than sound produced by smooth flowing blood [2][3][32].

The detection of malfunctioning cardiac related prostheses can likewise benefit from spectral estimation methods. For example, the degradation of bioprosthetic heart valves due to calcification and stiffening causes shifts of the dominant peaks of the power spectrum towards the higher frequencies [12].

1.1 THESIS OBJECTIVES

This thesis examines the correlation between time-domain features of phonocardiograms, their frequency domain counterparts and the state of the valves contributing to the received sounds. A variety of spectral estimation techniques are examined, including the Fast Fourier Transform (FFT), pole-zero modelling, filter bank analysis and a class of wavelet transforms. These techniques are evaluated in terms of their ability to generate appropriate feature vectors, i.e. well separated clusters as determined by analysis of variance (ANOVA) tests.

1.2 THESIS ORGANIZATION

Chapter 2 provides physiological information about the heart and the work done by past researchers to determine the condition of prosthetic valves through the use of sound analysis. Chapter 3 describes the experimental setups used for the collection of data as well as

the signal processing steps taken. Chapter 4 examines the data in the time-domain and frequency-domain with the objective of determining correlations between the recorded sounds and the amount of thrombus simulants¹ present in the flow. It evaluates a number of spectral estimators for their ability to generate variables with strong correlations. Chapter 5 examines recordings taken during a calf-implant operation of a correctly functioning ventricular assist device and its prosthetic valves. Chapter 6 concludes with a discussion of the previous chapters' results and heart valve function classification is discussed in terms of the generated feature vectors and application constraints.

1. Silicon medical adhesive was used to simulate the thrombus formations.

2.0 Historical Perspective

2.1 BACKGROUND PHYSIOLOGY

The heart is comprised of left and right halves, with each half divided into blood receiving and blood pumping chambers, known as the atria and ventricles respectively. The atria collect blood from the lungs (left atrium) and the rest of the body (right atrium) in preparation for the ventricles. The ventricles in turn pump the blood to the lungs (right ventricle) and the rest of the body (left ventricle) through the aorta. The contraction of the chambers is referred to as *systole*. The relaxation and filling of the chambers is termed *diastole*. Diastole normally lasts longer than systole and the systolic-diastolic cycle gives rise to the familiar "lub-dub" sound of the heart, where the "lub" is termed the first heart sound (S1) and the "dub" is the second heart sound (S2).

The heart has four valves, separating the chambers and controlling the direction of blood flow. Within the heart, the *Tricuspid* valve separates the right atrium from the right ventricle, the *Mitral* valve separates the left atrium from the left ventricle. Controlling blood flow out of the heart, the *Pulmonary* valve separates the right ventricle from the pulmonary artery, leading to the lungs, while the *Aortic* valve separates the left ventricle from the aorta, which is the main supply artery to the rest of the body. Figure 1 shows a schematic of a cross-section of the interior of the heart. Notice that the left ventricle will eject the blood through the aortic valve and in this figure the blood would be passed *behind* the right ventricle.

A cardiac cycle starts with an electrical excitatory impulse being generated within the

heart. This impulse causes the atria and ventricles to contract. When the ventricular pressure exceeds that of the atrial pressure, the tricuspid and mitral valves close, producing S1. The ventricular pressure continues to rise until it exceeds the aortic (left ventricle) and pulmonic (right ventricle) pressures. The aortic and pulmonic valves then open and the ventricles eject the blood. The ventricles then relax and the pressure within them decreases rapidly.

FIGURE 1. Schematic of the interior of the heart showing the four valves

When the ventricular pressure drops below the aortic and pulmonic pressure, the aortic and pulmonic valves close, producing S2. The ventricular pressure continues to drop until just below the atrial pressure, at which point the tricuspid and mitral valves open, allowing the ventricles to fill with blood [4][19]. S1 and S2 are not solely due to the closing and opening of the valves. Other factors such as the deceleration of the blood, characteristics of the vessel and chamber walls and turbulence of the flow are all recognized to contribute

to the final sound [37].

2.2 SOUND ANALYSIS OF PROSTHETIC VALVES

The first total valvular replacement was performed by Starr and Edwards in 1961. Their mitral valve prostheses consisted of a caged ball design and for the next 10 years was used extensively in the treatment of advanced mitral, aortic and/or tricuspid dysfunction [10]. Phonocardiography was first applied to the analysis of mitral valves in 1965 [17] where timing durations between the Q component of the QRS wave¹ and the prosthetic mitral valve's closing click as well as the duration between the natural aortic valve opening and the prosthetic valve's opening click were examined. They concluded that timing durations may give indirect information about valvular malfunction. Significantly, all of their analysis was based on time domain inter-event durations and no spectral characteristics were examined.

The major complication associated with mechanical valves is thrombus formation and the resulting danger of emboli² [31][41]. Depending on their location of formation, thrombus deposits may also result in valve movement obstruction. In 1970, Demany [10] reported the absence of the opening click of a mitral disc-valve to be an important diagnostic indicator of valve dysfunction due to occluder movement obstruction. During this same time,

-
1. The QRS wave complex is the electrical excitation pulse that propagates across the heart and causes the ventricles to contract. The Q component of the QRS wave complex is the local minimum of the waveform immediately preceding the global maximum (the R component).
 2. Emboli refers to thrombus formations which break away from the source of formation.

spectral-based analysis was being performed by Hylen and associates [18] for the detection of cage-ball valve ball variance¹. Their observations showed that peak frequencies below 1300Hz during the aortic valve opening sound, as determined through sound spectral analysis (SSA), was a strong indication of ball variance. They further concluded that SSA was particularly effective with patients with multiple valve replacements, as clinical assessment was difficult due to the close proximity of mitral closing sounds and aortic opening sounds and auscultation² techniques in some cases were incapable of resolving the missing high frequencies of the aortic valve opening sounds - an indication of ball variance.

During this same period, a real-time spectroanalyzer was developed by Kagawa and associates to aid in clinical diagnoses of thrombosed disc valves [22]. Kagawa *et al.* developed an algorithm for classification based on a standard parameter obtained from the spectrum of the closing sound and termed the normalized maximal frequency (NMF). The NMF is defined as the maximum frequency at the -30dB level after the spectrum has been normalized to 36dB. They observed the evolution of the NMF of patients over a ten year period and showed the correlation between a decrease in NMF and the formation of thrombi on the disc-contacting surfaces of valves.

In an effort to reduce the thromboembolic complications arising with the use of mechani-

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1. In this context, variance refers to diameter changes, grooving, cracking, etc.
 2. Listening to sounds produced by the body with a stethoscope.

cal valves, researchers have turned towards bioprosthetic valves, typically porcine, as a possible solution. These valves offer better resistance to thrombosis, but suffer from inevitable tissue degeneration, with a median failure-free lifetime of approximately 13 years [34]. Tissue degeneration of the valve leaflets is most often due to the accumulation of calcium deposits which results in stenosis, fibrosis and stiffening [15]. These effects contribute to a shifting of the peaks of the spectra of the closing sounds towards the higher frequencies

In order to improve the performance of classifiers based on features of the spectra, researchers have focused on improving spectral estimation techniques [16][38][40]. In some cases, when the area of interest within the phonocardiogram signal is small e.g. 20ms or less, FFT methods may not provide enough frequency resolution due to their inherent trade-off between window size and frequency resolution. In 1983, Joo *et al.* investigated pole-zero modelling as an alternative method of spectral estimation of the closing sounds of an aortic bioprosthetic valve. In their study, 8 poles and 8 zeroes were used for the model and the two dominant peaks of the spectra were used as a heuristic feature vector for a Gaussian classifier [21]. Since then, other researchers have explored the optimum number of poles and zeros by minimizing the difference in a mean square sense between the impulse response of modelled waveforms and the true waveform shape and evaluating the effect of the number of poles and zeros in the model when the signal has been truncated or has had noise added to it [7].

Previous studies have shown that thrombi may occur at different sites relative to a valve [31]. When the site of formation directly impedes valve occluder movement, for example, the disc-contacting surface of a strut, sound spectral analysis of the contact "click" is an effective method of detection [30]. When the thrombus does not directly impede occluder movement but is of sufficient size relative to the cross-sectional flow area, turbulence in the flow may be produced, causing a change in spectral features. This is an approach of Semmlow and associates in the detection of coronary artery disease [33] and is the main question explored in this thesis. That is, how well can different analysis methods detect thrombus simulants when they do not directly impede the valve's occluder movement.

2.3 METHOD OF EVALUATION

Each of the analysis methods examined resulted in large sets of computed data values. The purpose of the evaluation criterion was to rate the ability of the statistics of these computed values to predict the state of valves being examined. As will be shown, the reduction in the number of generated values was possible through factor analysis, since there was often a high degree of correlation among the computed variables. The reduction in variables was desirable for computational purposes. After reducing the number of variables, the next step involved omitting the variables which did not show a large difference in value when comparing obstructed valve sounds with nonobstructed valve sounds. For instance, if the power level at 350 Hz was more or less constant whether the sound was generated from a obstructed valve or a nonobstructed valve, this variable would be eliminated from

further consideration as a "good" predictor of blockage. The basis for making the determination of omitting or retaining each variable was an analysis of variance test. Since groups of variables were being considered, the groups statistics were used as final indicators of blockage and so the mean, the variance, the skew and the kurtosis were computed for each set of variables. Finally, for each of these four statistical measures, a correlation coefficient was calculated indicating how well each of these measures correlated with the amount of obstruction in the original recordings. Measures which correlated well (> 0.7) were considered as "high score" measures. The number of high scores obtained and the average high score values were retained as a final evaluator of each individual method of analysis.

3.0 Experimental Setup

3.1 *IN VITRO* SETUP

A mock circulation loop was set up with a semi-anechoic chamber isolating the outflow valve from the artificial heart as shown in the diagram of figure 2 and in the photograph of figure 3. Pressure transducers (Foxboro/ICT, model 1125-03G-C54) were located five cm.

FIGURE 2. Schematic of mock circulatory loop

upstream from the valve and seven cm. downstream from the valve, inside the semi-anechoic chamber. Immediately downstream from the valve, a ninety degree glass elbow was used and a video camera was mounted such that a clear view looking into the valve was obtained. Two microphones (Audio-Technica, model AT31B) were positioned within the chamber, approximately 4 cm. from the valve.

FIGURE 3 Photograph of experimental setup showing artificial heart (center), anechoic chamber (left) and reservoir (far left)

One microphone was fed to a Sony digital audio tape (DAT) recorder (model TCD-D7), the other to a TEAC DAT recorder (model DA-P20). The record level for the TEAC was set such that the loudest component of the cycle occurred at -6 dB (the dynamic recording range for both recorders is -90 dB to 0 dB), whereas the record level for the Sony was set much higher, allowing the quieter components of the cycle to be recorded at approximately -12 dB. Both sound recording machines recorded with a sampling frequency of 48 kHz. All microphones used had a flat (± 3 dB) frequency response from 20 Hz to 20 kHz. The pressure transducers were sampled at 100 Hz using an analog to digital data capture board (Analog Devices Inc. model AD1000), as was the heart motor current and voltage supply levels. In order to synchronize the DAT recordings with the AD1000 recordings, a simple pulse emitter circuit was constructed that allowed the author to send a high-frequency pulse to a separate channel of the AD1000 board as well as to a speaker located close to the microphones in the anechoic chamber. The pulse emitter also triggered a stopwatch which was video recorded in the field of view along with the valve movement.

The valve used in all recordings was a 25 mm internal diameter Medtronic-Hall mechanical valve. In order to simulate the effects of an attached thrombus, silicon medical adhesive cured at 50° C for 20 minutes was applied at different sites around the valve, at the interface between the valve housing and the cannula. This site was chosen after consultation with an expert in the field (Dr. T. Mussivand, Director of the Cardiovascular Devices Division of the University of Ottawa Heart Institute) familiar with the problem of throm-

bus deposits on mechanical heart-valves. Figure 4 shows a schematic view of the location of the thrombus simulant, while figure 5 shows photographs taken of valves with 40% obstruction and no obstruction. For each thrombus trial, one minute recordings were made at each of 11 different mean aortic pressure settings, ranging from 70 mmHg to 170 mmHg in steps of 10 mmHg. For each trial the mean flow rate was recorded using an

FIGURE 4. Transparent schematic view of valve within cannula showing location of thrombus simulant

Omega meter (model FPM-700A). During a second series of trials, the local flow rate was recorded using an ultrasonic flowmeter (Transonic Systems Inc., model T101) located immediately downstream from the second pressure tap (downstream from the valve). All trials were conducted with the artificial heart controller operating in "fixed rate" mode at 70 cycles per minute (mean beat duration of 857 ms), 35% (300 ms per beat) was systolic, 65% (557 ms per beat) was diastolic.

3.2 *IN VIVO* SETUP

A male Holstein calf weighing approximately 90-100 Kg was implanted with an Electro-Hydraulic Ventricular Assist Device (EHVAD) according to the standard protocol as

FIGURE 5

Interior view of valves with 40% obstruction (trial 28-3) and 0% obstruction (trial 28-4). Objects to the left of the valves are Canadian pennies.

described in [25]. Immediately after surgery, sound recordings were made in the operating room using a TEAC DAT recorder (model DA-P20), fed through two microphones (Audio-Technica, model AT31B) inserted into two stethoscope heads (Premier, model 108-210). Two series of recordings were made, the first at 80 cycles per minute, the second at 60 cycles per minute. In each series, 7 recording sites were selected, based on the location of the EHVAD, the inflow valve and the outflow valve.

3.3 PROCESSING STEPS

The main goal of the processing steps described in this section is to extract segments of waveforms from each cycle at a common point within the cycle. Simply using a time offset from the beginning of the captured data recording will not suffice, since there are deviations in the pump cycle's periods that occur in a random fashion.

Each heart sound recording consists of one minute of uninterrupted acoustical data capture. A one minute recording sequence contains between 55 and 75 pump cycles. This section describes the processing steps taken to identify each individual pump cycle and the

method of aligning cycle segments for purposes of *coherent averaging* in the time domain.

FIGURE 6. Three cycles with threshold level of 0.5

Coherent averaging is a method of maximizing the SNR of repetitive signals imbedded in random noise. Fundamental to the method is the requirement that each repeated segment is aligned at a common point [29]. As a first step, the peak associated with S2 is used as a “cycle locator” and identified using a threshold value. See figure 6. (All portions of the waveform above this value are selected as S2 peak candidates.) Since only one peak is desired from each cycle, the S2 peak candidates are disqualified if they occur within 300 ms of any previously occurring S2 peak. Once a peak from each cycle is identified a rectangular window of length 250 ms is positioned 425 ms to the left of each peak and that

portion of the waveform is extracted for further processing. See figure 7.

FIGURE 7. Extracted portions of waveform corresponding to valve opening sounds

Each extracted segment is then aligned by using the first segment as a "template" and shifting the subsequent segments until their cross-correlations are maximized. An example of 8 aligned segments is shown in figure 8. Once all the segments are aligned, an ensemble average is computed and saved as the "first pass average". Each segment is then compared to the first pass average and a closeness of fit value, C , is computed as follows:

$C = (\phi_{xy}[0]) / (\phi_{xx}[0])$, where $\phi_{xy}[0]$ is the zeroth lag cross-correlation between the first pass average and the particular segment and $\phi_{xx}[0]$ is the zeroth lag auto-correlation

of the first-pass average.

FIGURE 8. Aligned segments corresponding to valve opening sounds

The 25 segments with the highest closeness of fit values are retained and used to compute a new ensemble average, the "second-pass average". A typical second-pass average is shown in figure 9. The purpose of this ensemble average is solely for the improvement of

FIGURE 9. "Pass two" average of valve opening sounds

the SNR of the valve opening sound.

Finally, the locations of the start of each of the original 55-75 cycles are retained for all subsequent processing.

4.0 Sound Analysis

4.1 INTRODUCTION

There are four main stages of mechanical heart valve function that occur during each circulatory cycle: closing, fully closed, opening and fully opened. These stages occur due to changes in pressure gradients across the valve. While fully closed, the valve occluder does not move and there is little or no fluid flow, hence no sound produced. While fully open, the noise produced is due to the fluid flow and can be considered a stochastic signal with spectral properties indicative of the underlying physical system that generated the flow [24]. This approach is covered below in the section *Frequency Domain Techniques*, where different spectral estimation methods are evaluated for their ability to distinguish obstructed flow sounds versus unobstructed flow sounds.

The loudest events occur during opening and closing, with the closing click dominating the acoustic waveform, approximately 10 dB louder than the opening click and 18 dB louder than the background flow noise. Opening and closing click waveforms can be considered as deterministic waveforms and may be enhanced by improving the signal to noise ratio through the use of coherent averaging [29] which is covered in section 4.2.1.

Although the acoustic monitoring of prosthetic heart-valves when driven by an artificial heart has some added difficulties due to the ever present pump component sounds, it does allow the heart to operate in a fixed-rate mode. In this mode, the artificial heart will fill and eject at a constant rate of time over multiple cycles. This allows for the monitoring

and comparison of timing delays in the opening and closing of the valves which must therefore be due to other factors such as flow disturbances caused by flow obstructions. The statistical distribution of timing delays and their correlation to underlying physical changes is covered in section 4.2.2, "*Jitter characteristics and thrombus simulants*".

The most noticeable waveform features are the peaks due to opening and closing. This is due to the valve occluder making contact with the housing struts, which arrest the occluder's movement and cause the occluder to bounce once or twice [39]. Multiple peaks can occur in cases of excessive occluder bounce, which may indicate unusual fluid flow. This correlation is discussed in section 4.2.3, "*Bounce features and thrombus simulants*".

4.2 TIME DOMAIN TECHNIQUES

4.2.1 Coherent Averaging

Since the circulatory cycles are sequential in time, a method of aligning and extracting each cycle is needed before the averaging process can be initiated. The method used is covered in chapter 3. The increase in signal to noise ratio can be calculated in the following manner: Let $m(t)$ represent the measured waveform for a portion of each cycle.

$m(t)$ is comprised of a deterministic portion, $d(t)$ and a noise component, $n(t)$ such that

$$m(t) = d(t) + n(t) \quad (\text{EQ 1})$$

If the period between cycles is T , then the measured waveform after k periods will be

$$m(t + kT) = d(t + kT) + n(t + kT) \quad (\text{EQ 2})$$

The coherent averaged signal, $\hat{m}(t)$, using N cycles will therefore be

$$\begin{aligned} \hat{m}(t) &= \frac{1}{N} \sum_{k=0}^{N-1} [d(t + kT) + n(t + kT)] \\ &= d(t) + \frac{1}{N} \sum_{k=0}^{N-1} n(t + kT) \end{aligned} \quad (\text{EQ 3})$$

assuming that $d(t)$ is time invariant.

Examining the SNR of $m(t)$, we have:

$$SNR(m(t)) = \frac{\text{var}(d(t))}{\text{var}(n(t))} \quad (\text{EQ 4})$$

where $\text{var}(x)$ represents the variance of x . The SNR of $\hat{m}(t)$ is:

$$\begin{aligned} SNR(\hat{m}(t)) &= \frac{\text{var}(d(t))}{\text{var}\left[\frac{1}{N} \sum_{k=0}^{N-1} n(t + kT)\right]} \\ &= \frac{\text{var}(d(t))}{\frac{1}{N^2} \sum_{k=0}^{N-1} \text{var}[n(t + kT)]} \end{aligned} \quad (\text{EQ 5})$$

And assuming that $n(t + kT)$ is uncorrelated with $n(t + jT)$, $j \neq k$, this can be simplified to:

$$= N \frac{\text{var}(d(t))}{\text{var}(n(t))} \quad (\text{EQ } 6)$$

The improvement in SNR due to coherent averaging can therefore be shown as:

$$\begin{aligned} \frac{SNR(\hat{m}(t))}{SNR(m(t))} &= \frac{\left[N \frac{\text{var}(d(t))}{\text{var}(n(t))} \right]}{\left[\frac{\text{var}(d(t))}{\text{var}(n(t))} \right]} \\ &= N \end{aligned} \quad (\text{EQ } 7)$$

Figure 10 shows a number of opening click waveforms and their coherent averaged counterpart.

FIGURE 10. Opening clicks and their coherent averaged counterpart

4.2.2 Jitter Characteristics and thrombus simulants

It was observed during the averaging process that the distance in time from the opening peak to the closing peak, Δt_{oc} , varied from cycle to cycle. (Δt_{oc} is graphically defined in figure 12 on page 28.) The variation in Δt_{oc} was confirmed by performing a cross-correlation on the opening waveform from cycle to cycle and recording the amount of shifting needed to achieve a maximum cross correlation between each cycle and the first cycle for that particular trial. The changes in Δt_{oc} reflected differences in the times at which the valve's occluder completed its closing or opening movement. The amount of shifting required to best align each cycle is referred to as *jitter* and it was surmised that an obstruction directly upstream from a valve may disturb the flow sufficiently to alter the moment of opening or closing and may lead to a test of obstruction based on the jitter's statistical characteristics. To test this premise, the jitter values for each of nine trials were plotted as box plots¹ (see Figure 11) allowing the distribution of jitter values to be compared across

-
1. Box plots are a standard statistical tool that give a rough idea of the distribution of a set of values. They are sometimes described as histograms viewed from above. The horizontal line in the middle of each box represents the median value. The solid box represents the 1st and 3rd quartiles which are the points midway between the median and the first value and median and last value, respectively. The outer horizontal lines represent the location of values 1.5 times the interquartile distance away from the 1st or 3rd quartiles. Datum values further than the outer horizontal lines are termed *outliers* and are indicated with an O on the plots. Datum values further than 3 times the interquartile distance away from the 1st or 3rd quartiles are termed *extremes* and are indicated with an E on the plot. Both outliers and extremes, when they appear, are followed by a datum identifier number, allowing a researcher to further explore the causes behind the unusual value. The advantage of box plots is that multiple distributions may be shown side by side allowing for easier comparison between groups of variables.

the groups. The trend towards an increase in the variance of the jitter values as the amount of blockage increases is evident.

FIGURE 11. Box plots of jitter values (mean removed) for nine trials. Groups 1,2,3 have no blockage, groups 4,5,6 have >10% and <25% blockage, groups 7 and 8 have >25%, <50% blockage and group 9 has >50% blockage

The decrease in variance of group 7 may be due to differences in the exact position of the thrombus simulant in relation to the valve occluder since the bead of silicon adhesive used to simulate the thrombus was not completely smooth around the inner perimeter of the valve housing. Other factors may also be responsible for the apparent differences within groups as evident in the first three trials, all of which involved no blockage.

Changes in Δt_{oc} due to a thrombus obstruction may be due to changes in the time of valve opening, valve closing, or both. To determine which event was affected most by an

obstruction, an examination of the individual events (opening and closing) was undertaken. Immediately prior to valve opening, the pump changes direction and begins its ejection phase (corresponding to systole in natural hearts). The change in direction is accompanied by an acoustic artifact which can be distinguished from the background sounds. The approximate resemblance of this artifact to a sync wave allows it to be automatically recognized and the time interval between it and the valve opening sound computed and stored as Δt_{eo} . See figure 12.

FIGURE 12. Δt_{oc} , Δt_{eo} and Δt_{fc} during a portion of actual *in vitro* recording.

The distribution of these variables (after their means have been removed) is plotted in figure 13 as box-plots. As can be seen from the figure, the major difference in variance occurs with group 9 (>50% blockage).

FIGURE 13. Box plots of opening jitter values, Δt_{go} (mean removed) for nine trials. Groups 1,2,3 have 0% blockage, groups 4,5,6 have >10% and <25% blockage, groups 7 and 8 have >25%, <50% blockage and group 9 has >50% blockage

The distributions of the opening jitter for unobstructed and obstructed cases are close to normal as can be visually determined in figure 14 with variance equal to 1.274 ms and 1.513 ms respectively. A better test for a normal distribution is a plot which shows an expected cumulative probability versus an observed cumulative probability of the data set [26]. The expected cumulative values are obtained by constructing a normally distributed data set of the same size as the data set being analyzed. If the analyzed data set is indeed normally distributed, the resulting plot should be a simple diagonal. In the probability and statistics literature, this is referred to as a Probability-Probability plot (P-P plot). Figure 15

shows the P-P plots for the unobstructed jitter and the obstructed jitter.

FIGURE 14. Histograms of a) unobstructed trials' jitter and b) obstructed trials' jitter

FIGURE 15. P-P plots of a) unobstructed trials' jitter and b) obstructed trials' jitter.

This brings up an important consideration when averaging the opening sounds based on a window synchronized with a control signal of the artificial heart. As described in [29], uncorrected jitter during coherent averaging will have the equivalent result of the signal being filtered, with the frequency response of the filter equal to the characteristic function of the probability density function of the jitter. For example, for a normally distributed jitter with variance σ^2 , the frequency response will be:

$$Z(f) = \exp(-2(\pi f \sigma)^2) \quad (\text{EQ 8})$$

Figure 16 shows the magnitude of the frequency response of jitter equivalent filters for obstructed and unobstructed trials. In effect, the jitter will result in a low-pass filtering of the opening sounds if no further attempt at alignment is made through the use of maximizing cross-correlation functions, etc.

In a similar manner the closing jitter was computed using the time difference between artifacts appearing in the pump sound and the peak of the closing sound. The distribution of these values is plotted in figure 17 after the mean value from each group was removed.

Although the trend towards greater variance is not as clear as in figure 11, all trials without obstructions have a smaller variance than any trial with obstructions.

FIGURE 16. Magnitude of frequency response of jitter equivalent filters for obstructed and unobstructed trials

FIGURE 17. Box plots of closing jitter values, Δt_{fc} (mean removed) for nine trials. Groups 1,2,3 have no blockage, groups 4,5,6 have >10% and <25% blockage, groups 7 and 8 have >25%, <50% blockage and group 9 has >50% blockage

4.2.3 Bounce features and thrombus simulants

When the occluder disc in a prosthetic heart valve opens or closes, its movement is arrested by a contact strut. The velocity of the occluder at the point of contact with the arresting strut has been studied *in vitro* and shows a tendency for the occluder to bounce two or three times before coming to rest [39]. The amplitude of bounce and the number of bounces may be influenced by the local flow profile. Obstructions giving rise to flow disturbances may therefore produce bounce behaviour which results in acoustically noticeable differences. From examination of recordings made with >50% blockage a difference was observed in the number and amplitude of waveform peaks immediately preceding the contact click peak. See figure 18. These features were most likely due to changes in bounce characteristics although confirmation of this would require further experiments. This section describes the steps taken in order to explore the relationship between the amount of blockage and the wave shape during the opening sound.

FIGURE 18. Typical opening sounds from a) 50% blockage and b) 0% blockage trials

The accurate determination of the time locations and the amplitudes of multiple peaks was difficult due to the problem of multiple peaks often merging into single peaks. A more objective method of extracting features from the waveform was to divide the opening sound into fifteen 5 ms segments and compute the power, f_i , within each segment, e.g.

$$f_i = \sum_{n=0}^9 [x(nT + p + i \times 5ms)]^2, \quad (i = 0, 1, \dots, 14) \quad (\text{EQ 9})$$

where T is the sampling period, (0.5 ms), $x(t)$ is the waveform and p is the time of the initial opening peak for each cycle. This resulted in a 15 dimension feature vector, f , for each opening click.

Using fifteen 5 ms segments was an arbitrary decision that compromised the desire for maximum waveform resolution and a minimum vector dimensionality. In order to compensate for any changes in microphone placement or recording levels, each vector was scaled to achieve unity power. As well, each vector was used to generate a second vector, consisting of the numerical derivative of the first vector. These will be referred to as OPEN_A and OPEN_B.

From examination of the correlation matrix of the OPEN_A feature vectors, it was apparent that there existed some correlation between adjacent segment power levels. Table 1 shows the correlation matrix with shaded cells for values with magnitudes greater than 0.4, an indication of significant correlation between variables [26] which suggested that a reduction in the number of dimensions used to represent each cycle's waveform was feasible through the use of factor analysis¹.

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1. Factor analysis attempts to reduce the dimensionality of a set of variables by creating a new and smaller set of variables (factors) comprised of a linear combination of the original set. The new factors are orthogonal to each other and created in an order of maximum variance. That is, the first factor will account for the largest amount of variance in the sample, the next factor, uncorrelated with the first factor will account for the largest amount of remaining variance in the sample. Each remaining factor accounts for progressively less amounts of the total sample variance. Although it would take as many factors as original variables to uniquely represent the original set, a reduction in dimensions is possible by dropping those factors that do not contribute greatly to the total sample variance.

Table 1: Correlation matrix for 15 segments of opening sounds

	Seg 1	Seg 2	Seg 3	Seg 4	Seg 5	Seg 6	Seg 7	Seg 8
Seg 1	1.000							
Seg 2	.618	1.000						
Seg 3	-.515	-.162	1.000					
Seg 4	.166	.115	-.076	1.000				
Seg 5	-.446	-.628	.406	-.031	1.000			
Seg 6	-.210	-.540	-.196	-.422	.433	1.000		
Seg 7	.308	-.013	-.505	-.256	-.230	.474	1.000	
Seg 8	-.371	-.352	-.166	-.325	.115	.560	.157	1.000
Seg 9	-.316	-.337	-.105	-.270	.039	.485	.306	.757
Seg 10	-.203	.168	.097	-.186	-.118	-.108	-.349	.298
Seg 11	-.013	.055	.053	.018	-.218	-.217	-.120	-.320
Seg 12	-.349	-.176	.204	-.006	-.083	-.154	-.265	-.153
Seg 13	-.305	-.317	.017	-.111	.059	-.220	-.284	-.195
Seg 14	-.011	-.231	-.109	.341	-.008	-.306	-.100	-.332
Seg 15	-.244	-.265	.049	.034	.039	-.273	-.182	-.219
		Seg 9	Seg 10	Seg 11	Seg 12	Seg 13	Seg 14	Seg 15
Seg 9		1.000						
Seg 10		.078	1.000					
Seg 11		-.238	-.060	1.000				
Seg 12		-.213	.163	.396	1.000			
Seg 13		-.273	-.144	.071	.154	1.000		
Seg 14		-.266	-.312	-.185	.119	.381	1.000	
Seg 15		-.165	-.188	-.233	-.002	.586	.570	1.000

The proportion of variance accounted for by the original variables is referred to as the *communality* of the variables. To simplify the calculations, the original variables are expressed in standardized form with a mean of zero and standard deviation of one. For the set of variables, OPEN_A, 15 variables will therefore sum to a total sample variance or communality of 15. Table 2 shows the 15 factors created through the use of principle component analysis and the total amount of variance accounted for by each factor (their eigenvalues). The sum of all the eigenvalues will equal 15, since the original variables were

Table 2: Factor eigenvalues

factor	eigenvalue	% of total variance	cumulative% of total
1	3.506	23.4	23.4
2	3.002	20.0	43.4
3	2.135	14.2	57.6
4	1.373	9.2	66.8
5	1.339	8.9	75.7
6	0.997	6.6	82.3
7	0.689	4.6	86.9
8	0.328	4.3	91.2
9	0.328	2.2	93.4
10	0.307	2.0	95.4
11	0.250	1.7	97.1
12	0.174	1.2	98.2
13	0.142	0.9	99.2
14	0.121	0.8	100
15	0.000	0.0	100
Total	15	100	

scaled such that each had a mean of zero and a variance of 1. By applying factor analysis, we have obtained a new set of variables, some having more variance than others.

The standard criterion for determining the number of factors needed to adequately represent the original variables is to select all factors with eigenvalues greater than 1. In the case of table 2, this would include the first 5 factors and would account for 75.7 percent of the total variance. Table 3 shows the distribution of this reduced variance over the original variables.

Table 3: Distribution of variance of original variables accounted for by first 5 factors

Variable	Communality
Seg_1	0.843
Seg_2	0.880
Seg_3	0.712
Seg_4	0.460
Seg_5	0.862
Seg_6	0.862
Seg_7	0.802
Seg_8	0.835
Seg_9	0.686
Seg_10	0.775
Seg_11	0.784
Seg_12	0.643
Seg_13	0.707
Seg_14	0.709
Seg_15	0.796

At this point, an analysis of variance¹ (ANOVA) was performed on the first five factors, to determine whether they showed a significant difference between groups of obstructed and unobstructed trials. Table 4 shows the resulting *F ratios* and *p values*. From this table it is apparent that the most significant factors (in order) are 3, 1, and 4. A scatterplot of factors 3 and 1 is shown in figure 19.

Table 4: F-ratios, p values from ANOVA test of 5 factors

factor	F-ratio	p value	Significant?
1	109.08	< 0.001	yes
2	0.70	0.40	no
3	360.14	<0.001	yes
4	50.48	<0.001	yes
5	3.02	0.083	no

-
1. ANOVA tests are used to determine the likelihood of two or more groups of samples originating from the same underlying population. A *null hypothesis* is formed which assumes that the two or more groups do indeed come from the same population. A test statistic is calculated, such as the *F-statistic* and based on this value and the number of samples in each group a *p value* is calculated which represents the probability that one would be wrong if one rejected the null hypothesis. In other words, the lower the *p* value the more certain one is that the two or more groups are "different". Equation 9 shows the *F* statistic calculation when only two groups are being compared.

$$F = \frac{(\bar{y}_1 - \bar{y}_2)^2}{S_p^2 \left[\frac{1}{n_1} + \frac{1}{n_2} \right]} \quad (\text{EQ 9})$$

Here, $\bar{y}_i$ represents the mean of the *i* th group, S_p^2 is the pooled sample variance and *n* is the number of samples in each group.

FIGURE 19. 2D Scatterplot of factors 3 and 1, which account for almost 50% of the variance in the original set of variables

By including factor 4 and changing to a 3D scatterplot, additional separation of the two groups is visible. Figure 20 shows a sequence of rotations of the 3D scatterplot.

FIGURE 20 Four sequences of a 3D scatterplot of factors 3, 1, and 4. Note: Colour legend same as in figure 19.

From figure 20 it is clear that the two groups of trials form distinct but overlapping clusters. This suggests that a classifier based on the covariance matrices and means of groups of sufficient size of these three factors could be successful in determining the obstructed or unobstructed state of a valve. Due to the overlapping nature of the clusters, single sample classification would not be accurate enough for medical diagnostic standards.

Additional information can be obtained by subdividing the available trials into 4 groups, 0% blockage, 10-25% blockage, 25-50% blockage and >50% blockage. Figures 21 and 22 show the 2 and 3D scatterplots for these groups. As can be seen from the 3D scatterplot, the greater the blockage, the further away (in factor space) the cluster moves from the zero blockage cluster.

FIGURE 21 2D Scatter plot of factors 3 and 1 for a four group breakdown of trials

FIGURE 22 Four sequences of a 3D scatterplot of factors 3, 1, and 4 for a four group breakdown. Note: Colour legend same as in figure 21

4.3 FREQUENCY DOMAIN TECHNIQUES

This section examines four distinct methods of estimating frequency distributions in terms of their ability to distinguish obstructed versus unobstructed artificial heart-valve sounds. The first of these methods is Fourier analysis, where the best performance of spectral estimation occurs for stationary signals. Signals which change over time, however, result in a smearing of the power spectrum when plotted in the form of a spectrogram [38]. The second method is similar to a spectrogram, but makes use of Pole-Zero modelling at each step. The "Pole-Zero spectrogram" offers the potential of better frequency resolution than a regular spectrogram, but due to the large number of possible combinations of parameters, requires extensive initial computation. The third method makes use of a filter bank of 64 narrow (20 Hz) band pass filters. The signals are passed through these filters, and their squared and summed outputs represent the power at each filter's center frequency. The fourth method is the Discrete Wavelet Transform (DWT) implemented with a pyramidal coding scheme.¹

Each of the above four methods was applied to identical portions of the valve sound waveform, for obstructed and unobstructed valves. As shown in figure 23, the analyzed valve sounds correspond to the portion of the pump cycle during which relatively steady flow is occurring, after the opening click transients have decayed sufficiently and before the closing click transients commence, i.e. a portion 232 ms to 72 ms before the closing click

1. As provided by Carl Taswell's Matlab toolbox, "Wavebox" © copyright 1993

peak.

FIGURE 23. Location of extracted segments within pump cycle.

Each method results in an “image” of the power present in the acoustic signal at a specific frequency and time and must be evaluated in terms of its ability to distinguish amounts of obstruction. The evaluation process is described in section 4.3.2, immediately following the section on Fourier based spectrograms which is used to establish the statistical processing steps taken for each method of spectral estimation.

4.3.1 Fourier Based Spectrograms

Fourier transforms have been widely used in signal processing applications since the development of the Fast Fourier Transform as a computationally efficient algorithm for determining the phase and amplitude of a series of complex exponentials which can be

combined to form any arbitrary sequence. The Discrete Fourier Transform equation pairs are defined as

$$x[n] = \frac{1}{N} \sum_{k=0}^{N-1} X[k] e^{j(2\pi/N)kn} \quad (\text{EQ 10})$$

for synthesis, and

$$X[k] = \sum_{n=0}^{N-1} x[n] e^{-j(2\pi/N)kn} \quad (\text{EQ 11})$$

for analysis, where N is the number of values in the sequence [27].

The $X[k]$ components can be considered as a measure of how well the $x[n]$ sequence resembles each complex exponential. The squared magnitude of the $X[k]$ components therefore represent the power at each frequency harmonic.

For each 160 ms extracted segment, a spectrogram was computed using 7 overlapping 64 ms windows. This gave an overlap of 75% for adjacent windows. The 64 ms segments were multiplied by a hamming window, then amplitude scaled to achieve unity power. The power spectrum was then calculated using the FFT. At a sampling frequency of 2 kHz, this resulted in 65 frequency bins at each of the 7 windows, for a total of 455 values per extracted segment.

The question now is whether this 455 dimension vector establishes distinct clusters based on the amount of blockage present. Since a high degree of correlation is expected between adjacent frequency and time “bins”, factor analysis was used to reduce the dimensionality and uncorrelate the image. Due to computational constraints, all 455 values could not be analyzed at the same time. Instead, two adjacent windows (130 values) were examined at a time and a subsequent comparison of the results was made. For the initial two windows, factor analysis was able to reduce the dimensionality from 130 to 42. The 42 new factors accounted for more than 68% of the total variance of the original 130 variables. By performing an ANOVA test it was possible to determine which of these factors had the most difference across groups and the most similarity within groups, i.e. which factors could be used as a predictor of blockage.

In all 7 windows, the first factor gave the largest F-ratio, an indication of difference between obstructed and unobstructed groups. To verify this difference, a histogram plot of the two groups is shown in figure 24. The obstructed group was comprised of all trials where there was any blockage ($> 10\%$ of the total flow area).

FIGURE 24. Histograms of factor 1 for a) unobstructed trials and b) obstructed trials

Although the variance is different between these two groups, the most noticeable difference is between their means. The difference in height between the two histograms is merely due to the larger number of cycles in the obstructed group ($N=384$ vs. $N=182$). To investigate whether their means are correlated with the amount of blockage present, that is, will the mean increase as a function of amount of obstruction, the second group was broken down into three groups: 10%-25% blockage, 25%-50% blockage and >50%. The histograms of factor 1 for these three groups and the initial 0% blockage group are shown in figure 25. Clearly there is a shift towards higher values of factor 1 as the amount of obstruction increases.

FIGURE 25. Histograms of factor 1 for a) 0% blockage, b) 10%-25% blockage, c) 25%-50% blockage and d) >50% blockage

Having established that factor 1 is correlated with the amount of obstruction, and knowing that factor 1 is comprised of some linear combination of the original variables, it may be useful to examine more closely the weights involved in this linear combination, in order to determine which of the original variables contributes the most towards this correlation. That is, which frequency and time bins could be used as a predictor of obstruction.

The *factor score matrix* shows the linear combination of original variables that make up each of the extracted factors. Table 5 is a subset of this matrix showing only the combination that makes up factor 1.

In table 5, each number from 1 to 130 is one of the original variables as obtained from a two-window spectrogram (two 65 point FFTs) and represents the power in the signal at different frequency and time bins. The weights show the contribution of each of these original variables to calculation of factor 1, that is:

$$\begin{aligned} factor1 = & var1 \times -0.0040 + var2 \times -0.0036 + var3 \times 0.0332 + \dots \\ & + var128 \times -0.0034 + var129 \times -0.0136 + var130 \times -0.0088 \end{aligned} \quad (EQ\ 12)$$

The variables which have a weight of more than 0.1 have been shaded in the table and represent variables which contribute most to factor 1's value and therefore to the overall correlation between factor 1 and the amount of obstruction present. A better appreciation of the relative contribution of each variable to factor 1 can be shown in a plot of the weights, as in figure 26.

Table 5: Weights of original variables comprising factor 1

#	weight	#	weight	#	weight	#	weight	#	weight	#	weight
1	-.0040	23	-.0259	45	.0197	67	-.0109	89	-.0141	111	-.0324
2	-.0036	24	-.0682	46	.0051	68	.0691	90	.0423	112	-.0314
3	.0332	25	-.0007	47	.0282	69	-.0292	91	-.0072	113	.1032
4	-.0528	26	-.0019	48	.1650	70	-.0110	92	-.0254	114	.2263
5	.04666	27	.0142	49	.2111	71	.0073	93	-.0257	115	.2068
6	.02790	28	.0316	50	.2058	72	-.0166	94	-.0041	116	.0522
7	.01693	29	-.0155	51	.0021	73	-.0342	95	.0207	117	-.0476
8	.0109	30	-.0125	52	.0065	74	-.0139	96	-.0042	118	-.0098
9	.0306	31	.0049	53	.0174	75	.0039	97	-.0137	119	.0578
10	.0116	32	-.0033	54	.0248	76	-.0504	98	-.0101	120	-.0094
11	.0049	33	-.0360	55	-.0040	77	-.0165	99	.0157	121	-.0295
12	.0351	34	-.0437	56	.0042	78	-.0018	100	.0261	122	.0002
13	-.0111	35	-.0276	57	.0674	79	-.0135	101	-.0389	123	.1064
14	.0316	36	-.0393	58	-.0174	80	.0360	102	.0203	124	-.0572
15	-.0027	37	-.0009	59	-.0114	81	.0211	103	.0156	125	.0135
16	-.0255	38	.0453	60	-.0333	82	.0351	104	-.0208	126	.0104
17	-.0729	39	-.0212	61	.0168	83	.0257	105	-.0140	127	-.0270
18	-.0411	40	.0021	62	.0011	84	-.0339	106	.0158	128	-.0034
19	.0270	41	.0090	63	-.0200	85	-.0308	107	.0099	129	-.0136
20	.0233	42	.0345	64	-.0033	86	-.0341	108	-.0195	130	-.0088
21	-.0212	43	-.0270	66	-.0048	87	.0306	109	-.0009		
22	-.0324	44	-.0241	67	-.0240	88	.0168	110	.0367

FIGURE 26. Plot of weight values for each variable contributing to factor 1

Clearly, the major contributors to factor 1 are variables 48, 49, 50, 113, 114 and 115. Since for each window, there are 65 frequency bins computed, these variables represent the power at frequencies 738 Hz to 769 Hz over two adjacent windows, with a slight increase in contribution from the second window. (Weight value changes from 0.2111 for variable 49 to 0.2263 for variable 114, both representing the power at 754 Hz, but over adjacent and overlapping time periods.)

4.3.2 Evaluation of spectral estimators

The primary objective of the analysis of the flow sounds is to determine the amount of obstruction that may be present. Therefore, any evaluation of the spectral estimators should be based on this overall requirement, as opposed to other methods of evaluation based on the ability of the estimator to distinguish exact frequency content. For example, the Wigner time-frequency distribution has the generally considered undesirable property

of generating cross-terms when more than one frequency is present in a signal [8]. If the presence of a cross-term strongly correlates with the presence of an obstruction, however, the Wigner distribution may be perfectly acceptable for the application at hand.

The evaluation process used here is based on the amount of correlation between obstruction amounts and factor scores. As explained in the previous section, factor analysis was performed on each of the spectral estimators' images, in order to uncorrelate the image bins. The factors which show the most variance were retained for further analysis, the rest were discarded. The extracted factors were then subjected to analysis of variance tests to determine which factors showed a strong difference across groups and similarity within groups. (Groups were defined in terms of the amount of obstruction present.) The factors which pass these tests have not yet shown a correlation with the amount of obstruction present, they have simply showed that there is a significant difference between the groups. For example, factor J may have the following box plots for each group:

FIGURE 27. Example box plots showing a strong difference between groups, but little correlation with amount of obstruction present.

To rate the correlation between the factors and the amount of obstruction, the first four moments of expectation (the mean, the variance, the skew and the kurtosis) were computed for each factor passing the analysis of variance test. The Pearson Correlation Coefficient [26] was then computed for each moment which gives a value from -1 to 1 indicating the amount of correlation between these values and the amount of obstruction, with 1 being equal to perfect correlation, 0 showing no correlation and -1 showing perfect negative correlation. Since any correlation (negative or positive) is beneficial for prediction purposes, the magnitude of the correlation coefficient was then used as a evaluation "score". Each spectral estimation method resulted in approximately 40 factors, with usually 10 or more passing the analysis of variance test. By evaluating four moments of expectation for each, there were at least 40 scores for each method.

Although correlation coefficients greater than 0.4 are usually considered adequate indicators of commonality between variables [26], a more stringent requirement for values greater than 0.7 was chosen to represent a "high score". The number of high scores and their means were retained as the final evaluation score for each method.

4.3.3 Pole-Zero Spectrograms

In addition to the traditional Fourier method, each windowed segment was pole-zero modelled and the resulting filter's frequency response computed. The Steglitz-McBride iterative method of estimating the filters' weights was used [35] with the filter input consisting of white noise of equivalent length to the extracted segment. In Pole-Zero modeling, the

parameters of a filter are adjusted so that the output of the filter resembles the waveform being analyzed, usually by minimizing the mean squared difference between the two waveforms. Given white noise as an input to the filter, the filter's frequency response must therefore represent the frequencies present in the original waveform. This is achieved by representing the filter's parameters in the Z domain and then evaluating the filter's response along the unit circle, i.e. replacing z with $e^{j\omega}$.

In order to obtain a "spectrogram" based on this method of frequency content analysis, the original waveform is modelled in overlapping and windowed blocks. For each block, a new filter is created, its frequency response computed, and the squared magnitude retained as an estimate of the power at each frequency bin.

Choices for filter model order will affect the ability of this method to correctly estimate the spectral power of the analyzed waveform. In the analysis of the heart sounds a pole-zero model was computed as:

$$H(z) = \frac{\sum_{k=0}^M b_k z^{-k}}{\sum_{k=0}^N a_k z^{-k}} \quad (\text{EQ 13})$$

with $N = M$ = the filter order.

Two model sizes were used, the first model was limited to 14 poles and 14 zeroes in order to match modelling conditions from previous studies [14]. The second model used 20 poles and 20 zeroes. Figure 28 shows four spectrograms computed; two using FFTs, the other two using the first pole-zero model. Both methods used identical segments of unobstructed valve sounds.

FIGURE 28. Spectrograms; a) FFT based single cycle, b) FFT based 60 cycles averaged, c) pole-zero based single cycle, d) pole-zero based 60 cycles averaged

Analyzing each window's power spectrum separately showed that the frequency band from 707 Hz to 723 Hz had the highest F-scores in ANOVA tests when comparing obstructed versus unobstructed trial groups. Figure 29 shows the F-scores for all 7 windows for the frequency band 676 Hz to 738 Hz. It is clear that this difference between groups evolves over time, with the largest difference occurring during the 3rd time-lag window. (The 3rd time-lag window starts 32ms from the beginning of the extracted segments, as identified previously in figure 23 on page 45.)

FIGURE 29. ANOVA F-scores for time-frequency power bins in frequency band 676 Hz to 738 Hz.

Using the peak value of the ANOVA test score surface, a box plot was made of the two groups of trials: group 1 having 0% blockage and group 2 having >10% blockage. These are shown in figure 30 where the predominant difference is the amount of variance in the two groups.

FIGURE 30. Box plots of power at 723 Hz, 0.032 seconds for unobstructed and obstructed groups

To identify whether this apparent difference is due simply to the greater number of cases in the obstructed group, the obstructed trials were further broken down into 3 groups, 10-25% blockage, 25-50% blockage and >50% blockage. The box plots for the resulting four groups are shown in figure 31. In this plot, the means of the four groups have been subtracted from the samples, allowing easier comparison of the groups' variance. As will be evident in the *results* section (4.3.6) this is an example of a variable which satisfies half of the requirements for our definition of a good predictor; that is, it shows an obvious difference across the groups but does not have a strong correlation with the amount of obstruction present.

FIGURE 31. Box plots of power at 723 Hz, 0.032 seconds for increasing blockage groups

It is interesting to note the difference in results obtained with the 20 order vs. the 14 order pole-zero model. Higher model orders are generally assumed to have an upper limit of usefulness since they tend to start modelling the noise in a signal [24]. When the noise is the primary signal of interest however, this may not be undesirable. Figure 32 shows the difference that an increased pole-zero order can make on the modelled waveform. The top waveform shows the original signal, the next shows the output from a 20 order ($P=Q=20$) filter, the next below shows the output from a 14 order ($P=Q=14$) filter and finally, the bottom shows the output from a 7 order ($P=Q=7$) filter. All filter outputs and parameters were generated using white noise as input. Filter orders higher than 25 tended to produce unstable output, while lower order filters did not model the original signal accurately.

FIGURE 32. Original signal, 20 order model output, 14 order model output and 7 order model output

4.3.4 Filter Bank method

Another method of determining the power content of a signal as it evolves over time is through a filter bank. In this method, a series of narrow band pass filters are applied to a segment of the signal based on the position of a window that slides along the time axis. By squaring and summing each filter's output, an estimate of the power content at the filter's center frequency can be obtained. To evaluate the effectiveness of this approach, two filter

banks were constructed. Each bank was comprised of autoregressive moving average (ARMA) filters, the first bank using 2nd order filters ($P=Q=2$), while the second bank used 8th order filters ($P=Q=8$). Figure 33 shows the magnitude response of the band pass filters. The number of filters used was double the number shown in the figure, with adjacent filters overlapping their 3dB bandwidth by 50%.

FIGURE 33. Magnitude response of 64 bandpass filters, 20 Hz bandwidth, a) 2nd order, b) 8th order.

Typical resulting time-frequency power distributions from the two filter banks are shown in figure 34. Figures (a) and (c) show single segments and figures (b) and (d) show the average of 60 segments, where the averaging process was performed in the power distribu-

tion domain. That is, all of the 60 segments had their power distributions computed and the resulting 60 distributions were averaged together. As expected, the higher order filter bank has better frequency resolution. How this affects the correlation between the distribution and the amount of obstruction in a valve is discussed in section 4.3.6. When comparing these figures to figure 28, it should be kept in mind the frequency bins extend from 180 Hz to 840 Hz, whereas in figure 28 the range is from 0 to 1000 Hz.

FIGURE 34.

Filter bank "spectrograms". a) single segment, 2nd order, b) 60 segments averaged, 2nd order, c) single segment, 8th order, d) 60 segments averaged, 8th order.

4.3.5 Wavelet Transform

Background Theory:

In order to overcome the impracticality of integrating from negative infinity to positive infinity as defined in the Fourier Transform (FT), Gabor [28] introduced the Short Time Fourier Transform (STFT) which makes use of a localized sliding window and is defined as

$$STFT(f, \tau) = \int x(t) g^*(t - \tau) e^{-2j\pi ft} dt \quad (EQ 14)$$

In a similar manner, the Continuous Wavelet Transform (CWT) is defined as

$$CWT(a, \tau) = \frac{1}{\sqrt{a}} \int x(t) h^*\left(\frac{t - \tau}{a}\right) dt \quad (EQ 15)$$

Both distributions can be considered as filter banks, with the impulse response of the filters defined by the frequency modulated $g(t)$ in the case of the STFT and the scaled $h(t)$ in the case of the CWT. The most often cited advantage of the wavelet transform arises from this scaled window, since it allows for small time windows at high frequencies and large time windows at low frequencies, thus improving the time-frequency resolution over the STFT. That is, the time-frequency resolution is allowed to change, depending on the components of the signal being examined, by allowing for good time resolution for high frequency signal components and good frequency resolution for low frequency components. In contrast, the STFT uses the same size time window for all signal components.

Pictorially, the resolution of the two transform methods is shown in figure 35.

FIGURE 35. Resolution of a) the STFT and b) the CWT

The term "frequency" is actually a misnomer when discussing the CWT and more properly should be termed "scale". Pragmatically however, large scale corresponds to low frequencies and small scale corresponds to high frequencies.

Since the reconstruction of a signal is often required in applications, it is desirable for the CWT basis functions, $h(t)$ to be orthogonal, as is the case with the FT basis functions.

Since the scale and offset parameters, (a, τ) of $h_{a,\tau}(t)$ vary continuously, this is not the case. Correct reconstruction is possible however by placing conditions on the basis functions, [5] namely that

$$\int h(t) dt = 0 \quad (\text{EQ 16})$$

As described in [28], a natural way to discretize the CWT is to substitute $(a_o)^j$ for a and $k(a_o)^j T$ for τ in $h_{a,\tau}(t)$, giving

$$h_{j,k}(t) = (a_o)^{-j/2} h[(a_o)^{-j} t - kT], \quad (j, k) \in Z \quad (\text{EQ 17})$$

Here, there is a choice for the value of a_o . The closer it is to 1, the more “redundant” the scaled versions become, i.e. high oversampling, whereas when a_o is set equal to 2, critical sampling is achieved but at the expense of more restrictions on $h_{j,k}(t)$, for example, requiring the set to be orthogonal.

Experimental Parameters:

The Discrete Wavelet Transform (DWT) was implemented using a standard pyramid algorithm with Daubechie's compact orthogonal scaling functions corresponding to lowpass and highpass conjugate quadrature filters [9]. Figure 36 shows a schematic of the processing algorithm employed, where $l(n)$ and $h(n)$ represent the low and high-pass filters, respectively. Each filter stage is followed by a subsampling by two and is equivalent to a dilation of the scaling function followed by a filtering of the original signal, $x(n)$. Each lowpass filter section produces an *approximation* output of the incoming signal, $a_i(n)$ and the highpass section produces a *detailed* output, $d_i(n)$. By iterating the procedure on the approximation outputs, the overall result is a series of detailed outputs at successively

larger scales, followed by a single approximation output.

FIGURE 36. DWT processing schematic

In all trials conducted, the signal length was 321 samples, which was zero extended to 512 samples, and therefore required 9 stages of iteration. The entire analysis was repeated three times, using three different filter orders, 2, 8 and 32. The highpass filters were obtained by transforming the lowpass filters using Fourier series coefficients [36] such that:

$$h(n) = (-1)^n l(n) \quad (\text{EQ 18})$$

Figures 37 through 39 show the impulse response of the low and highpass filters for the

three filter orders involved.

FIGURE 37. Impulse response for 2nd order a) lowpass and b) highpass filters used in DWT

FIGURE 38. Impulse response for 8th order a) lowpass and b) highpass filters used in DWT

FIGURE 39. Impulse response for 32nd order a) lowpass and b) highpass filters used in DWT

As an example of the results obtained from the DWT, figure 40 shows a section of recording made with zero blockage of the valve, followed by the output of the DWT. Figure 41 shows similar features but for a valve with $>25\%$, $< 50\%$ blockage.

FIGURE 40. Unobstructed valve recording and extrema of wavelet bands

FIGURE 41. Obstructed valve recording and extrema of wavelet bands

4.3.6 Results

As described previously in section 4.3.2, the evaluation of each spectral estimator was based on the amount of correlation between the amount of obstruction and the factor scores. Correlation coefficients with magnitudes greater than 0.7 were considered significant. In each case, the statistics examined for the factor scores were the first four moments of expectation, i.e. the mean, the variance, the skew and the kurtosis. Table 6 shows the number of significant correlations for each spectral estimation technique, broken down by the moments of expectation.

Table 6: Number of factors with significant correlation with amount of obstruction

Spectral Estimation Technique	Mean	Variance	Skew	Kurtosis
FFT	5	2	4	3
Pole-Zero (P=Q=14)	3	6	4	2
Pole-Zero (P=Q=20)	4	3	- 1	4
Filter Bank (2nd order)	3	3	3	1
Filter Bank (8th order)	2	5	3	1
DWT (2nd order)	0	1	2	1
DWT (8th order)	0	1	0	1
DWT (32 order)	0	2	1	2

As can be seen from the table, the variance of the factors produced greater numbers of significant correlation than the other moments. As can be seen from table 7, it also produced the highest average coefficient values, in particular, 0.94 for the variance of the FFT method and 0.91 for the variance of the 2nd order filter bank method. This shows that for instance, by using the FFT and computing a spectrogram of the power of the flow noise, it is possible to linearly combine the values at different time and frequency bins such that there is an average of 0.94 correlation between the variance of the linear combination and the amount of obstruction present around the heart-valve.

Table 7: Averaged magnitude of significant correlation coefficients

Spectral Estimation Technique	Mean	Variance	Skew	Kurtosis
FFT	.78	.94	.88	.85
Pole-Zero (P=Q=14)	.82	.86	.89	.90
Pole-Zero (P=Q=20)	.81	.83	.70	.78
Filter Bank (2nd order)	.84	.91	.88	.80
Filter Bank (8th order)	.88	.83	.90	.80
DWT (2nd order)	-	.80	.81	.90
DWT (8th order)	-	.73	-	.91
DWT (32nd order)	-	.75	.88	.74

Interestingly, increasing the filter order with the Pole-Zero method did not improve the correlation values whereas with the Filter Bank method, increasing the filter order resulted in an improvement in the correlation of the mean and skew of the factors but a decrease in the correlation of the variance of the factors. As an example of the significance of some of the correlation coefficient values, figure 42 shows the values for one of the FFT computed factors which has a correlation value of 0.98 for its variance.

FIGURE 42. Box plots of factor 3 (FFT computed) showing correlation between variance and amount of blockage

5.0 Analysis of Calf Recordings

Two series of calf recordings were made shortly after surgical implantation of an EHVAD and prosthetic valves. Two valves were used, an inflow and an outflow valve, separated by approximately 3 inches. During recording, the position of the microphones was adjusted from directly above the valves, to slightly downstream and upstream from the valves. All recordings were made on the outside of the chest wall of the animal, although the surgical incisions were still open. Figure 43 shows a sample cycle taken from the clearest recording. Comparing this to figure 23 on page 45, two main differences are evident. Firstly, there is a higher noise level than in figure 23 and secondly, as expected, the sounds from the inflow valve and pulsatile pump are much louder than the *in vitro* case.

FIGURE 43. Single cycle from calf recording, with microphone positioned above outflow valve.

Figure 44 shows the results of performing a FFT based spectrogram on the single cycle. A Hamming window length of 64 ms was used with a 75% overlap between adjacent windows. (Total number of windows was 59.) The two predominant features of the cycle, the inflow and outflow valves' closings are clearly visible as large bandwidth artifacts at the 0.2 and 0.5 seconds location, respectively.

FIGURE 44. FFT based spectrogram of a single cycle.

Another prominent feature of the spectrogram is the high power level occurring at approximately 150 Hz for the entire cycle duration (approximately 1 second). This power band is shown more clearly when an average of 42 cycles is plotted, as in figure 45. Note: the

averaging procedure was performed in the frequency domain, after the spectrogram of each of the 42 cycles had been computed.

FIGURE 45 Average spectrogram, FFT based.

By rotating the view so that one is looking directly along the time axis, an interesting observation can be made regarding the 150 Hz power band. During the interval between the outflow valve opening and closing, i.e. the time when flow is occurring, the energy shifts to a slightly higher frequency of 225 Hz. As well, a power band appears at 900 Hz and midway through the interval, at 450 Hz. See figure 46.

FIGURE 46. Average spectrogram, FFT based, looking almost directly along the time axis.

By constructing a filter bank of 98 narrow band-pass filters (8th order Butterworth with 3 dB bandwidth of 20Hz each), a filter bank “spectrogram” is attainable with a higher frequency resolution than the FFT spectrogram. Figure 47 shows 42 cycles averaged together using the filter bank method.

The location within the pump cycle most likely to contain the determining sounds of obstruction is between the opening and closing sounds of the outflow valve [40]. In figures 48 and 49 this area is isolated from the full spectrogram using the FFT method and filter bank method respectively.

FIGURE 47. Average spectrogram, filter bank based

FIGURE 48. Close up view of flow area, FFT based

FIGURE 49. Close up view of flow area, filter bank based

6.0 Conclusions

6.1 DISCUSSION OF RESULTS

Previous studies have shown that when a thrombus formation directly interferes with an artificial heart valve's occluder movement, detection is possible through the use of spectral analysis [30]. In this study, thrombus simulants were applied to artificial heart valves in positions which do not interfere with the occluders and results indicate that detection is possible using a number of different techniques.

In the time-domain, the closing and opening behaviour of the valves, when an obstruction is present upstream from the valve, demonstrates a larger variance in the duration of opening and closing times, referred to as jitter. It was also shown that valves with obstructions present produced significantly different power levels in the acoustic signal immediately following the opening click. This may be due to a greater number of occluder "bounces", which in turn may be due to flow disturbances created by the flow obstructions.

In the frequency domain, FFT analysis of the flow noise during maximum flow rate gave the highest amount of correlation (0.94) with the amount of obstruction present. In terms of the number of factors produced by each spectral analysis method which showed good correlation (> 0.70), the Pole-Zero method with 14 poles and 14 zeroes gave the best results, with 15 significant indicators of obstruction. The discrete wavelet transform method using Daubechie compact orthogonal scaling functions performed the most poorly, although some improvement was made by increasing the order of the filters involved in its implementation. Other DWT methods may be more appropriate for this

application.

6.2 CONSIDERATIONS FOR CLASSIFICATION TECHNIQUES

Classifying valve states based on features of their acoustic "signature" has both advantages and disadvantages. In one sense, it is difficult to obtain high levels of accuracy because there is a good deal of overlap of the feature vector clusters in feature space. See for example figure 19 on page 40. On the other hand, one advantage is that in contrast with many classification problems that must classify individual cases on a case by case basis, the valve classification problem can operate on a set of measurements, obtained over some arbitrary time period. This allows for the statistical features of the set of measurements to be used in the decision rule. The classification of heart valves has another advantage over traditional problems where "good" and "bad" objects are introduced at random to the classifier, e.g. a classifier for monitoring quality control at an assembly line. In the heart valve case, the valves will tend to deteriorate over time, not improve with time. This would mean that the feature clusters' position and orientation (in feature space) would tend to "travel" smoothly through the feature space and suggests that the rate of change in any of its statistical properties may also be used as an indicator of valve dysfunction.

6.3 CONTRIBUTIONS

The author has demonstrated the ability of acoustic analysis to detect levels of obstruction in prosthetic heart-valves due to thrombus simulant deposits which do not impede the valve's occluder movement, in an *in vitro* environment.

6.4 FUTURE RESEARCH

Although the FFT and Pole-Zero methods resulted in numerous variables showing a high degree of correlation with the amount of obstruction present, all comparison analysis was performed on *in vitro* recordings where the acoustic isolation of the valve from the heart was, to some extent, possible. An obvious next step in this research area would be to repeat the comparisons with *in vivo* recordings. One such recording has already been performed by the author, during an operation at the Ottawa Heart Institute, where a Holstein calf was implanted with an artificial heart and mechanical valves. The recorded sounds in this case were from unobstructed valves and due to the lack of corresponding obstructed valve recordings, were not used extensively in the present study. The least expensive method to obtain *in vivo* obstructed valve recordings (using calves) would be to obtain recordings, on a daily basis, of a long-term calf implant. Following autopsy, the state of the valves at death could be correlated with the transition of acoustic characteristics over the period of monitoring. Such a study would provide a more realistic assessment of the diagnostic capability of acoustic analysis for detection of non occluder interfering thrombosis.

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