LVAD Occlusion Condition Monitoring Using State Augmented Acoustic Spectral Images

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LVAD Occlusion Condition Monitoring Using State Augmented Acoustic Spectral Images

by

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Thesis submitted to the Department of Mechanical Engineering in partial fulfillment of the requirements for the degree of

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Abstract

Each year, thousands of people die from heart disease and related illnesses due to the lack of available donor organs. Left ventricular assist devices (LVADs) aim to mitigate that occurrence, serving as a bridge-to-surgery option. While short term survival rates of LVAD patients near that of orthotopic surgery they are not viable long term options due to varied reasons. This work examines one cause, outlet graft thrombosis, and develops an algorithm for increasingly robust classification of device condition as it pertains to thrombosis or more generally occlusion. In order to do so an in vitro heart simulator is developed so that varying degrees of signal non-stationarity can be simulated and tested over a wide range of physiological blood pressure and heart rate conditions. Using a seeded-fault methodology, acoustics are acquired at the LVAD outlet graft location and subsequent spectral images of the sounds are developed. Statistical parameters from the images are used as features for classification using a support vector machine (SVM) which yields promising results. Given a comprehensive training space classification can be performed to fair accuracies (roughly 80%) using only the spectral image parameters. However, when the training space is limited augmenting the image features with patient state parameters elicits more robust identification. The algorithm developed in this work offers non-invasive diagnostic potential for LVAD conditions otherwise requiring invasive means.

Thesis Supervisor: Dr. Jason Kolodziej
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Chapter 1

Introduction

Left ventricular assist devices (LVADs) are commonly used as a bridge to surgery treatment option for patients with advanced heart conditions. This is mainly due to the large disparity between transplant candidates and compatible/available donors. In the United States, roughly 15% of eligible candidates receive a donor heart [18]. In less developed countries there is a much more significant gap, nearing an estimated transplant rate of less than 1% of possible cardiac transplants met [18]. When first introduced, LVAD recipients roughly had a 50% [6] one year survival rate, however this has changed in recent years with subsequent generations of the devices. Current LVAD models have shown to have one year survival rates of 80%, which is nearly that of orthotopic heart transplant, 86% [6], the historically optimal treatment. There is a desire for LVADs to become terminal treatments rather than bridge to surgery treatments, however in order to do so select short-term issues must be mitigated or resolved.

1.1  Background

1.1.1  Circulatory/Thoracic System

The human circulatory system is the primary organ system responsible for the circulation of blood throughout the body along with varied nutrients, organic elements,
etc. In its essential role, oxygenated blood is transported from the heart to significant tissues and bones, while the subsequent deoxygenated blood is returned to the heart for re-oxygenation. To accomplish this process the circulatory system is comprised of several key components, each with unique physiological characteristics and subprocesses. For purposes of this work, the lymphatic subsystem of the circulatory system is not considered. In accomplishing its primary functions, as it pertains to this research, the system’s integral components are the heart, the circulatory vessels (veins and arteries), and blood.

Of particular interest for this work is the architecture and cyclical function of the heart, as it is the organ responsible for the pulsatile flow of the circulatory system. The human heart is comprised of four chambers, two atria and two ventricle, along with four major valves. All components function in a joint process producing the cardiac cycle, or the pseudo-periodic process of the heart. The three most significant phases of which are atrial systole, ventricular systole, and cardiac diastole (atrial and ventricular diastole lumped together). Systole and diastole can be considered inverse processes of each other. When in systole the heart contracts, ejecting blood from the respective chambers. Alternatively, when in diastole the heart tissues relax allowing blood to re-enter the heart. In terms of progression diastole is the first stage, followed by atrial systole, and finally ventricular systole, however ventricular systole and atrial diastole overlap to where they can be assumed to occur concurrently or continuously.

In order to prevent a continuous process (lack of distinct phase) the four heart valves function in accordance with the phase to control blood flow (Note Figure 1-1 for architecture). When in diastole both the aortic and pulmonary valves close, preventing ejection, while the tricuspid and mitral valves open intaking blood. During atrial systole the tricuspid and mitral valves open, sending blood from the atria to the ventricles. Finally, during ventricular systole the tricuspid and mitral valves close, while the pulmonary and aortic valves open circulating blood from the right and left ventricle to the pulmonary artery and aorta respectively.

The systolic and diastolic phases of the heart cycle are of significant importance as they are directly related to heart sounds. Heart sounds are those sounds produced
as a result of the fluid (blood) turbulence generated from the opening and closing of the heart valves. In most healthy individuals only the first two heart sounds are prevalent, the S1 and S2 sounds. However, in other individuals the remaining two sounds, the S3 and/or S4 sounds may manifest, with the potential for other sounds such as murmurs.

Both the S1 and S2 originate from closing valves, and specifically align with the cardiac phase. The S1 is caused by the initial systolic contraction, or the closing of the tricuspid and mitral valves. The S2 is the result of the end of systole, or rather the closing of the aortic and pulmonary valves caused by cardiac tissue relaxation. The S1 and S2 are more so referred to as the "normal" heart sounds as both the S3 and S4 are indicative of health issues such as congestive heart failure and systemic hypertension respectively. It should also be noted that the presence of the S3 or S4 is not the sole indicator of health/condition. Referring to Figure 1-2, many of the more commonly seen conditions (stenosis - narrowing of vessel area; regurgitation -
leakage from a valve upon relaxation) do not manifest as either the S3 or the S4. They are instead more typically characterized by completely different sounds, and often perturb and alter how the S1 and S2 occur and appear.

1.1.2 Left Ventricular Assist Devices

The S3 sound, being an indicator of congestive heart failure (CHF), is caused by ventricle overload. Left ventricle overload, or more generally systemic volume overload, is the heart condition in which the left ventricle is not strong enough to eject an adequate (55% or more) blood volume resulting in suboptimal circulation. In mild cases CHF can be treated with angiotensin converting enzyme (ACE) inhibitors and
angiotension receptor blockers (ARBs) among others, however in more severe cases the historical optimal procedure has been orthotopic surgery [20].

Since the initial REMATCH trial of 2002 [20] left ventricular assist devices (LVADs) have been used as a bridge to surgery option for patients awaiting orthotopic surgery. These devices graft from the left ventricle to the aorta (Figure 1-3) acting as a pump, i.e. increasing circulation and thus compensating for CHF and/or the related issues (coronary artery disease, etc.). While the LVAD itself is internally contained within the thoracic cavity the controlling unit and power supply are housed externally of the patient.

Assuming the optimal mean arterial pressure (MAP - systolic aortic pressure over diastolic aortic pressure) is 110/70 mmHg, a 40 mmHg blood pressure range is considered ideal. Patients who suffer from CHF or similar do not exhibit these same characteristics. They are more likely hypertensive (high blood pressure) or hypotensive (low blood pressure), deviating from the optimal MAP range. Approximately 90% of LVADs [6] are continuously driven, meaning that they operate at fixed speeds and do not pulsate. The physiological effect of this, in terms of MAP, is a reduction in range that roughly scales with speed (Figure 1-4). Upon increasing the influence of the LVAD (i.e. increasing speed) the MAP range is decreased, theoretically approach-
ing a constant pressure (no difference depending on systolic and diastolic phase). Of particular importance is the realization that the electrocardiogram (EKG) signal of an LVAD patient is unaltered by the device. The EKG can be leveraged as a high fidelity signal for identifying phase and cycle when the MAP cannot be, due to the previously mentioned LVAD dynamics.

Figure 1-4: ECG, respiration (Resp), finger blood pressure (FBP), and muscle sympathetic nerve activity (MSNA) tracings for 1 patient at baseline (top) and at 3200 rpm LVAD speed (bottom) [23].
1.2 Need for Research

Since the REMATCH trials LVADs have become increasingly common and practical. When first approved (2001) LVAD patient one year mortality rates were roughly 50% [6] while two year survival rates were just 28% [21]. As of 2016 one year survival rates have improved to 80%, just short of the orthotopic surgery survival rate (86%). The notable improvement in patient survival can be attributed to several factors such as improved designs [2] and diagnostic capability advancements concerning both VADs and related thoracic implants [13],[9] among other factors.

Regardless of short-term viability, LVAD long-term practicality remains a considerable issue for several reasons. Even thought two year survival rates of 76% have been reported [12] these numbers are heavily skewed by extraneous factors. The patients from this test sample were originally of the lowest risk. Under a more representative sample this rate would be expected to decrease. Additionally, these patients were treated post-opt (regular anticoagulation therapy and routine in-patient management), as is typical with implantees. This further complicates the reported figures as varied treatments (anticoagulation) have counterintuitive adverse effects on health, predisposing patients to increased likelihoods of issues such as bleeding. These issues are less device orientated, and so one must further make the distinction between mortality and device related mortality.

Patient mortality is attributed to a wide range of issues stemming from the instance of surgery as alluded to previously. The key categorical complications of implantation are bleeding, thromboembolic events, infection, aortic insufficiency, and right ventricular failure [5]. This work focuses solely on thrombosis based events, which also extends to device graft stenosis. In more general terminology, thrombosis and stenosis based events may be classified as occlusion events.

Thrombosis is the condition in which a blood clot locally develops in the circulatory system, in either a vein (venous thrombosis) or artery (arterial thrombosis). Arterial occlusion (blockage) can be a result of either direct thrombosis formation or arterial embolism (event in which a clot "breaks off" and travels downstream). Direct
thrombosis formulation is due to local coagulation as a result of atheroma (fatty deposit on the internal vessel wall) rupture. Arterial embolism however may be a result of cardiogenic (originating from the heart) clots. For purposes of this work arterial thrombosis will be focused on, as venous thrombosis is not localized to the immediate area of the heart.

Due to the range of LVADs approved for use, biocompatibility is not guaranteed [24] and so thrombosis has been and continues to be an issue for implantees, especially at the location of the device, particularly the outlet stators. Older LVAD models, being larger, tend to produce embolisms while newer, smaller models lead to hemolysis (red blood cell destruction), although thrombosis may still occur. Thrombosis of newer LVADs (continuous models - previously stated 90% implantee population usage) is dependent on several parameters involving the patient, clinician, and the device itself. Specifically speaking to pump thrombosis events (exclusive of graft thromboembolic events) the frequency of such events have been reported to be in the range of 1-4% of test patients with a HeartMate II (continuous flow axial model) and in the range of 2-8% for HeartWare (continuous flow centrifugal model) [19] patients. Even with anticoagulation treatments, under-anticoagulation remains an issue for patients. Protocol for such treatment is dependent on the individual clinician/institution and so a universal and robust procedure does not exist for mitigation of thromboembolic events, aside from LVAD replacement in severe cases. Clearly, widespread and complete remediation of thromboembolic events is not short-term plausible given the current state of the issue.

Current diagnostics of adverse LVAD conditions are not restricted to any singular means. Both clinician laboratory testing and diagnostic imaging methods have been shown to indicate varied conditions [24]. Specifically, with respect to thromboembolic events, transthoracic (TTE) echocardiography (TTE), transesophageal echocardiography (TEE), and computed tomography angiography (CTA) are the most important imaging diagnostic methods. Both TTE and TEE can be specifically used for thrombosis diagnoses while CTA is more so complementarily used in diagnosing outlet flow mechanical problems, when indicated based on echocardiography.
Figure 1-5: LVAD diagnostics methods for determining localized fault area [24].

Even though diagnostic methods do exist for discerning device condition and events, determining the exact localization of the issue is more difficult (Figure 1-5). Echocardiography and CTA can be used for examining both the inlet and outlet grafts, with specific caveats requiring direct examination (invasive operation) such as the extracardiac portion of the inlet graft. While imaging is appropriate for the implant graft, examining the LVAD itself cannot be done with such, requiring direct examination, which is problematic for stator thrombosis/occlusion. A combination of laboratory testing and imaging can be robustly used to identify general conditions, however it is evident that localization identification, especially concerning the areas requiring invasive procedures, is not optimal. It would instead be of great value and importance to develop a robust and more practical method for the noninvasive discernment of occlusion localization.

1.3 Proposed Methodology

To discern an LVAD patient's health a signal containing the key indicator/s of their condition must first be identified. The goal of noninvasively collecting the identifica-
tion signal limits the potential collection methods. Furthermore, the innate variation in physical and biological traits [3], as well as implanted device types does not support the practice of creating a universal baseline for condition evaluation, practically speaking. In fact a common diagnostic method using TEE [24] requires baselining the individual patient post initial surgery.

It has been widely accepted that thoracic sounds, or rather more specifically heart sounds, correlate to specific health conditions (Figure 1-2). Given this correlation, it can be extrapolated that a device modified thoracic environment will exhibit the same relationship, to some degree. Various authors have verified this theory with regards to both VAD specific devices and to general thoracic implants. Masson et al [14] showed that artificial heart acoustics can be used to determine prosthetic valve operation, and correlated the sound to physiological occurrences. Makino et al [13] proved that artificial heart acoustics are relative to lifespan, in that there is a relationship between the produced acoustics and physical condition of the artificial heart pump. Whereas Makino et al focused on variable condition, Kim at el [9] showed that the same acoustic signal could be used to discern early stage device failure. Yost et al [28] showed that LVAD specific thromboembolic events manifest in the frequency spectrum of the thoracic acoustics. Slaughter et al [20] confirmed Yost’s findings and expanded the work to include mechanical failures. Kaufmann et al [7] studied the acoustics of centrifugal VADs, and found that regardless of VAD design (axial/centrifugal) events and conditions manifest in the produced acoustics in a similar manner. Thoracic acoustics have been proved by several authors to be a viable signal in preforming diagnostics, specific regarding the cardiac system/cardiac implants.

The purpose of this work is to determine a viable and noninvasive method for diagnosing LVAD related health issues, specifically outlet graft occlusion, or thrombolic events. To do so in vitro (artificial) heart sounds are simulated (mimicked) using a one sided (left) heart chamber simulator which simulates circulatory system characteristics and behaviors. The right side is not included as the LVAD device boundary conditions only pertain to left side and terminal components (left ventricle and aorta).
Acquiring the acoustics from this setup is performed using a digital stethoscope. Various authors have previously used electronic stethoscopes for the exact purpose of acquiring thoracic acoustics [22] for post-processing and have shown that the devices are appropriate for LVAD modified cavities as well [13],[28].

In order to determine the effects of physiological state variation (blood pressure and heart rate) both the healthy and unhealthy system (manually faulted) are operated over a non-hypotensive and non-hypertensive region for all test iterations. The process frequency of the simulator (akin to heart rate) is similarly modulated for specific diagnostic determinations. Testing occurs at both constant heart rate and variable heart rate. Outlet thrombolic events are simulated through seeded-fault testing, wherein a blockage is inserted downline of the LVAD in the simulated system and the system is operated as if it were healthy, i.e. still in the non-hypo/hypertensive region. The resulting in vitro acoustics are compared against similar in vivo acoustics to confirm mimic validity.

Once collected, the audio signals are post-processed for classification, to determine diagnostic potential. Due to the non-stationarity of natural heart sounds more traditional frequency spectrum techniques such as the Fourier transform are not appropriate. Time-frequency techniques that enable the specific identification of spectra events are much more practical for use [1],[27], however a suitable resolution must be attained [15]. Alternatively, the greater the resolution of the technique the more resource intensive the technique is. There is a clear desired to manage the trade-off between resolution and computational resources especially when concerning potential embedded processor application. As such this work focuses on utilizes the continuous wavelet transform (CWT) as means of determining time-frequency representations (spectra) of both the in vitro and in vivo acoustics. The CWT is a multi-resolution technique that leverages increased processing cost to produce improved resolution over techniques such as the short time Fourier transform (STFT). The technique is modified to maintain minimal computational cost for this work.

Resolution is an important factor in the diagnostic process as one would expect that the component of the derived spectra that indicates a specific condition is not
necessarily consistent in occurrence. Rather the indicator is expected to manifest in specific regions or frames, regarding the time-frequency plane. Under this assumption it is beneficial to only examine those locations, or regions of interests (ROIs). Doing so reduces dilution of the indicators caused by spectra regions of no discernible impact or importance and increases overall processing efficiency. Similarly, should an indicator manifest in a specific phase, limiting the spectra to said phase will decrease bias and warping caused by the adjacent phase.

The resulting ROI spectra can now be examined to identify discrete metrics used in evaluating patient condition. This is done so by generating a series of identification features from derived images of the ROI spectra. These identification features range from grayscale image texture properties to binary (black and white) shape features. Rather than just operating on the raw complex spectra matrix, this process of reducing down through images allows for a more systematic control of identification feature production.

The resulting identification feature vector, a 31x1 array of discrete image parameters, therein contains the desired indicator/s. Although this is true, the most optimal combination of these values is not known a-priori, assuming some features have no significance, are redundant, etc. Additionally, this dimensional space cannot be visualized in order to discern feature weighting, making the identification process difficult. A support vector machine (SVM) is trained with the a specific set of the feature vectors to develop the classifier model. This model is then used in determining the class (condition) of an independent set of testing data. Several different training-testing iterations are performed, utilizing both the constant heart rate acoustics along with variable heart rate acoustics.

Chapter 2 details the process of generating and acquiring the audio signals of the in vitro simulator and compares them to the related in vivo trials. This includes verification of the correlation between the generated in vitro acoustics and the physiological in vivo signals. Chapter 3 provides the theory and methodology for the post-processing of the acquired data. Cycle decomposition, time-frequency spectra generation, ROI partitioning, and feature composition are covered. Chapter 4 pro-
vides classifier information and the results of the respective trials. In Chapter 5 the conclusion of this work is given along with the next steps to be taken to advance this work. A guide of the process performed in this work is given in Figure 1-6.

Figure 1-6: Flow chart of research methodology.
Chapter 2

Data Generation and Acquisition

The sounds produced by the human heart are complex acoustic signals with shown correlations and causalities to physical events (Figure 1-2). Additionally, the location and medium through which the signals, which are essentially vibrations, propagate significantly affect the observable signal [3] and the ability to accurately measure said signal. The process by which a synthetic biological component is created is called mimicking, or phantoming, with the resulting component being termed the phantom.

For purposes of this work, the in vitro simulator is an active phantom, in that it both produces the objective signal (heart analogy) and passively transmits it (soft tissue, fat, etc.). For the in vivo trials phantom components are not necessary, however it is necessary to acknowledge the innate variations between both patients and controlled trials, and how they correlate and/or deviate from each other.

2.1 In Vitro Generation and Acquisition

2.1.1 Cardiac Phantom

Artificially generating heart sounds is non-trivial due to the non-stationarity nature of the signals. Non-stationarity is the term used to define the characteristics of the acoustic signal generating process, specifically as it pertains to the cyclical nature of the heart sounds. In this context (non-mathematical, will later be defined in more
appropriate terms) non-stationary defines the variability of the sounds. If a process were stationary it would be perfectly cyclical, or rather it would be predictable. A non-stationary process would then be defined as one that is not entirely predictable, or requires more information to describe/quantify. Heart sounds are considered non-stationary events for several observable reasons (among others),

1. Valvular (S1 and S2) and non-valvular (S3 and S4) occurrences

2. Variable heart rate

3. Discrete loading perturbations produced by valvular activity (S1 and S2 variation) [27]

The non-stationarity of the physiological process is due to the nervous system’s modulation of purkinje fibers, which enable instance synchronized ventricular contraction. Fiber contraction is not modulated over intervals, rather at each individual heartbeat, thus the process is not stationary. In short and controlled intervals, heart cycles can be considered pseudo-stationary, however in general this not true, notably when the duration and timing of events (S1, S2, etc.) are not consistent.

From a biological definition, the electrocardiography (EKG) signal is the measure of the electrical signals propagating through the heart, due to cardiac muscle depolarization (loss of net charge across the muscular membrane). The four de/polarization intervals (Figure 2-1) or waves (P - atrial depolarization, QRS complex - ventricular depolarization, T - ventricular repolarization, and U - Purkinje repolarization. U wave not shown in Figure 2-1 as it is intermittently observed and often discussed as a parameter lumped with the T wave) occur concurrently with cardiac phase, rather than pulse which occurs as a post-product. The QRS complex interval of the EKG signal is of the most importance for this work. The QRS complex indicates not only ventricular depolarization, but also ventricular systole (repolarization equating to systole, while depolarization equating to diastole), meaning that the peak magnitude of the QRS relates to a process event. The QRS is the greatest magnitude component of the EKG, and so generally speaking the heart cycle process can be initially referenced relative to the interval maximum of the EKG, the R wave.
As stated EKG propagation and cardiac phase are concurrent processes. In actuality cardiac phase is the causality of EKG propagation, however this assumedly does not cause a significant time varying phase difference. As this is assumed, then it follows that the inverse holds true for phantoming, specifically a synthetic EKG may be used to modulate cardiac phase without significant phase effects. It can then be stated that the specific cardiac phases can be modulated through specific intervals/events of the synthetic EKG.

While the local maxima of the EKG relates to the timing of ventricular systole, no analogous minima - diastole relationship exists. The T wave interval of the signal identifies ventricular diastole, however identifying this component is less obvious than that of the QRS complex. In a similar sense, while generating an EKG signal indicative of the physiological signal is not difficult, practically implementing such with the phantom is difficult. This is due to the increased need in control surfaces and components. Rather, to simplify the phantom design it is assumed that atrial systole occurs concurrently with ventricular diastole and that atrial diastole occurs concurrently with ventricular systole. Doing so reduces the cardiac cycle to two generalized intervals, ventricular systole (atrial diastole) and ventricular diastole (atrial
systole). The EKG accordingly reduces down by one interval. It should also be noted here that the U wave of the EKG is a manifestation of ventricular repolarization as well, and so both the U and T waves can be practically combined. Making the above generalizations yields an EKG signal of two distinct intervals, the same as the approximated cardiac cycle.

The EKG maxima (QRS complex maxima) is preserved from the above theory, while the remaining waves are lumped into a new interval relating to ventricular diastole. The new interval can then be created in such a way to initiate diastole, with the obvious choice being to generate a specific minima to time the phase. If a phantom is chosen to modulate phase based on only the locations of the maxima and minima then any alternating signal is adequate. Thus any finite closed bounded alternating signal may be used to modulate phase, with the simplest choice being an alternating ramp signal. The slope of the ramp (+/-) denotes cardiac phase and the maxima and minima location control phase duration.

The ramp input that modulates cardiac phase for the developed phantom is generated using an Instek function generator. Doing so limits the phase duration split to 50/50 however allows for easy control of the simulated phase period, and thus the process frequency (simulated heart rate). The downside to this application method is the loss of non-stationary elements, namely heartbeat-to-heartbeat variable frequency (unless manually modulated as such) and variable event occurrences (signal variation). The generated signal is then used to modulate a compressed air controller, which ports to the ventricle phantoms.

The ventricle phantom (Figure 2-2) is comprised of a hollow flexible polymer encased in an air-tight metal-plastic shell. The polymer acts as the ventricle itself, in terms of functionality, while the shell is the component which regulates the shape of the polymer. The shell is pressurized using the external air supply ported through the back of the phantom. When the pressure of the shell is greater than that of the polymer it forces the polymer to constrict (ventricular systole). When the pressure of the polymer is greater than that of the shell, the polymer expands (ventricular diastole) (Figure 2-3).
When the polymer is filled with liquid, constriction causes the ventricle to purge the liquid, while relaxation allows liquid to re-enter the polymer. The polymer has three openings that permit fluidic movement, an inlet pathway, an outlet pathway, and a backend pathway. Without unidirectional valves, all three openings permit
multidirectional flow. The inlet and outlet paths are used to interface the phantom with the atrial and aortic pathways respectively. The backend path (at the rear) of the phantom, is used as the inlet to the VAD graft, but is otherwise sealed should there be no VAD implemented.

The pressure difference between the polymer and shell modulates the phase propagation rate (the rate at which the ventricle phantom compresses/expands) of the phantom. The compressed air controller pressurizes (Figure 2-4) the shell through the air port on the back of the shell. The controller itself receives air through a facility main (>100 psi), which is regulated down to 40 psi (so that the controller can bleed off excess pressure). The timing of the controller is modulated by the synthetic EKG. The magnitude of the pressure is controlled via analog controls on the controller front panel. Systolic pressure can be regulated from 0 mmHg to 300 mmHg, however diastolic pressure is a fixed 0 mmHg. The fixed diastolic pressure is not an issue as physiological ventricular diastolic pressure is approximately 0 mmHg. As previously stated phase is arbitrarily split 50/50, however the exact duration of

![Compressed air controller](image)

Figure 2-4: Compressed air controller used to regulate ventricular phase of the phantom.
the active compression/expansion transient is related to the pressure difference of the polymer-shell. This is the most significant shortcoming of the simulator. Due to only modulation of the phase triggering, propagation of systole and diastole are entirely dependent on the pressure gradients of the simulator. Due to the lack of control there is no guarantee that the ventricle will entirely expand/contract for a given pressure, heart rate setting, an issue that will be examined in Section 2.3.

Using the function generator, air controller, and ventricle phantom systolic and diastolic ventricular phase are mimicked. The characteristics of the generated cycle however do not yet correlate to that of the physiological cycle, specifically in terms of pressure and flow. Given that fluids across a control volume cannot travel to passively produce a positive gradient, it is assumed that if the pressure conditions for the phantom are met, then the flow conditions will be suitable met. Additionally, flow is not a direct boundary condition relating to VADs, thus not requiring further attention. Instead the ratio of uncompensated flow (No VAD) to compensated flow (with VAD) is more practical to use in examining the fidelity of the phantom although neither are of significant importance for this work.

The idealized model of the physiological cardiac cycle is the Wiggers diagram given in Figure 2-1. While used to describe the healthy (no VAD/illness) three phase cardiac cycle (lumping repolarizations), it can similarly be used to describe the approximated two phase cycle. Additionally, the Wiggers diagram only describes left chamber characteristics and functions, making it pertinent for achieving the desired phantom architecture. As previously stated, the ability to mimic phase is already achieved, leaving only the pressure states to be met.

Valvular events are known to be the source of the predominant healthy heart sounds (S1 and S2) due to the fluidic turbulence generated as a result of the events. As expected, the valves are the physiological elements that maintain circulatory unidirectional flow. The need for such elements is apparent when examining points of the cardiac cycle in which the downstream pressure is greater than that of the upstream pressure. An example of this occurrence is during diastole, when aortic pressure is greater than left ventricular pressure, or during systole when ventricular pressure is
greater than atrial pressure. When such is true the heart’s valves change orientation, preventing backflow. In order to mimic this in the phantom, a set of bileaflet valves are implanted prior to and post to the ventricle element.

Bileaflet valves are a traditional prosthetic used in cardiovascular operations that offer low resistance to flow. One valve is positioned prior to the ventricle phantom (after the atrium) and is orientated in such a way as to close should ventricular pressure exceed atrial pressure (Figure 2-5). Similarly, the other valve is positioned after the ventricle (before the aorta) and is orientated in such a way as to close should the aortic pressure exceed ventricular pressure. Bileaflet valves do have a slight delay in changing orientation, resulting in a small amount of backflow during the event transient, however is assumed to be negligible as flow will be significantly skewed to one direction over the entire cardiac cycle. Additionally, this delay is affected by the pressure difference across the valve, and so with given specific pressure differentials the valve lag may be insignificant.

The last parameter to achieve with the system phantom is aortic pressure. Due to the effects of the valves systolic aortic pressure is regulated by systolic ventricular pressure. During compression, ventricular pressure spikes causing a pressure equal-
ization across the aortic valve. The valve opens, resulting in aortic pressure tracking ventricular pressure. During late systole ventricular pressure begins to drop, at a similar rate of the previous spike. Due to this rapid change, ventricular pressure drops below aortic pressure causing the aortic valve to close, thus maintaining diastolic pressure as the valve orientation prevents equalization.

Controlling diastolic pressure requires controlling the point at which the aortic valve changes orientation. To do so the pressure difference across the valve must be changed in such a way to elicit valvular activity. The pressure at the interior (ventricle side) of the valve is approximately set by ventricular pressure leaving the exterior pressure (aortic pressure) as the sole controllable parameter. In order to alter the aortic pressure of the system a pipe clamp is used (Figure 2-6) to restrict system flow, thus increasing the induced aortic pressure, at the external side (aorta side) of the valve. The inclusion of the valve gives the ability to alter the aortic pressure of the closed loop system to varying degrees based on how restrictive the clamp orientation is (more restrictive yields greater aortic pressure).

A capacitive element is added to the backend of the clamp to allow for (Figure 2-6) control over atrial pressure. The capacitive element is a fluid retaining vessel which is open to ambient. The vessel is not pressurized for two key reasons: 1) Ambient serves as a consistent backend pressure basis for the system/clamp 2) At the other adjacent end of the vessel is the left atria component (closed system design) which cycles significantly closer to zero than ventricular pressure. By having an element near the atrium component base at zero (vent to ambient) it can be ensured that diastolic atrial pressure roughly minimums at zero while systolic atrial pressure is minimally affected by ventricular pressure (early rising ventricular pressure will result in a large pressure gradient across the mitral bileaflet valve, causing the valve to close, limiting the maximum of the atrial pressure).

In the prescribed architecture, the aortic pressure is regulated, then vented to ambient before recirculation to the atria. This design however neglects all non-heart local physiological components (blood vessels, arteries, capillaries, etc.) that otherwise affect blood flow, of particular importance concerning the left heart chambers.
Circulatory system resistance, as a generalized and lumped parameter, is inherently incorporated by way of the clamp, however biological compliance is not. Compliance is essentially the elasticity of hollow organs, particularly for this work, circulatory vessels. Compliance is the factor by which a vessel or artery will change volumetrically in response to a change in pressure. Due to the pressure changes that occur as a result of cardiac phase, circulatory compliance is an important factor as it pertains to both observable blood pressure and to regulation/control of the simulator.

Modeling circulatory system compliance, in a non-generalized model, is not practical as compliance is not localized. It is dependent on several factors such as tissue type, circulatory system location, and health, among others. It is however known that blood vessel compliance is significantly higher than arterial compliance, specifically by a factor of as much as 30. Being the case a singular phantom element suffices for
incorporating both vessel and arterial compliance factors.

A compliant phantoming element is integrated into the system, using the same fluid retaining vessel as used previously with the post-clamp venting element (Figure 2-6). The element is positioned prior to the clamp in the loop (post aortic valve), so that compliancy can be generated from fluid compressibility (Figure 2-7). Whereas compliancy is a quantification of solid elasticity based on pressure differentials, compressibility is essentially a fluid analogous parameter. An arbitrary compliant factor can be integrated by means of a compressible fluid volume within the vessel, specifically an air pocket. This air pocket compresses upon systolic phase, and respectively decompresses during diastolic phase, mimicking circulatory compliance. Exact control over the parameter is not feasible as the system is barometrically vented, and so any desired pressurization is altered by the venting boundary. Instead the relative degree of compliance is used to alter system pressure. As the ratio of air to water in the compliant element is decreased (increasing water level) greater pressure states are
achievable, with the pressure state defined as the mean arterial pressure (MAP) or systolic pressure over diastolic pressure. Conversely, as more air is added to the compliant element, the feasible MAP range decreases. Thus by controlling the relative compliance effect, a wide range of pressure states are able to be simulated.

2.1.2 Acquisition and Seeded-Fault Testing

The cardiac system phantom (Figure 2-8) is probed at several locations to acquire four core measurements, the synthetic EKG (trigger), ventricular pressure, aortic pressure, and system flow. All four are acquired using an NI USB-6212 module and are sampled at 10 kHz. The trigger function is directly split into the module from the function generator. System flow is acquired using a Transonic Emtec ultrasound flow sensor located prior to the compliance vessel (post aorta, pre-vessel). Ventricular pressure is probed at the face of the ventricle phantom, while aortic pressure is probed

Figure 2-8: Component annotated in vitro simulator without VAD implemented. Dashed red lines indicate flow direction through system.
at a tee connection (for purposes of including VAD graft line) post aortic valve, pre-compliance element. Both pressure measurements are acquired using TDH40 pressure transducers. These four parameters are used only for referencing system state and are not used in any significant post-processing algorithm, other than the trigger. Given this the resolution of the signals is not scrutinized.

Comparing the in vitro generated pressures (Figure 2-9) to the Wiggers model (Figure 2-1), the only relatively significant difference occurs during ventricular diastole, when ventricular pressure does not minimum to zero mmHg. This occurrence is a by-product of increasing system resistance to meet aortic pressure conditions and is unavoidable. It should also be noted that for the presented iteration (Figure 2-9) the system was tuned to an approximate mean arterial pressure (MAP) of 110/70 rather than the Wiggers MAP of 120/80. This is of no significance; it is simply presented to show the fidelity of the simulator, respective to the idealized model (Wiggers model).

Oscillations in pressure (Figure 2-9) are a result of both system compliance and transducer interface compliance. The transducers measure fluid pressure at the face

![Figure 2-9: In vitro simulator pressure curves at a heart rate of 57 BPM.](image)
of the device, which under stationary conditions (non-pulsating) would not require interfacing compliance. Due to both the pressure spikes caused by alternating phase and bileaflet valve delay, the fluid surface at the face of the transducers are not in constant contact with the transducer. Bileaflet valves are previously discussed to permit a small amount of backflow due to their inherent delay in changing orientation. During this delay, the pressure differential across the valve propagates to the transducer face. Specifically, during diastole the fluid at the face is pulled away during the delay interval, causing an intermittent vacuum at the transducer face. This occurrence is an unfortunate by-product of the transducer arrangement, and so the transducer interface is modified as to maintain constant contact. This is done so by slightly pressurizing the transducer line prior to filling the in vitro system, creating an air pocket at the transducer face. During systole and diastole, the system fluid will force the air pocket to compress and expand respectively, however during both phases, due to gaseous properties, the transducer face will remain in fluidic contact - preventing intermittent vacuuming. Both transducers are arranged as such for consistency, which is the reason for the non-zero diastolic ventricular pressure shown in Figure 2-9.

Acquiring phantom acoustics is less trivial due to the measurement surface and location having a significant effect on the observed signal. Given the system shown in Figure 2-8 there is no appropriate location for probing with a stethoscope diaphragm. The system lacks both a flat surface and the appropriate transmission phantom (i.e. soft tissue). Similarly, the positioning of the VAD needs to be considered in advance.

Left ventricular assist devices require two graft surfaces, the left ventricle (inlet) and aorta (outlet). The ventricle phantom includes three connection surfaces (Figure 2-2), the front two being used for inlet and outlet flow, and the backend surface which is the location of the VAD inlet graft. The VAD outlet graft connects to the tee connection where the aortic pressure is probed, completing the VAD graft loop of the system phantom (Figure 2-10). For accomplishing seeded-fault testing an additional blockage element is inserted into the loop, prior to the tee connection, simulating an outlet graft occlusion.
Figure 2-10: Component annotated in vitro simulator with VAD implemented. Dashed red lines indicate flow direction through system. Note that the purge line is used only for draining the system.

The blockage element is comprised of two individual pieces, one containing the physical blockage surface, while the other acts as both a housing for the blockage piece, and provides a flat instrumentation surface for a stethoscope diaphragm. The element is designed with several flat surfaces, however acoustics are acquired at only one surface, the top most for consistent weighting. Using this component, two different levels of occlusion are implemented, 0% and 75%.

The stethoscope used for acoustic collection is a ThinkLabs Digital One stethoscope (Figure 2-11). Unlike other piezo-electro sensor based digital stethoscopes, the Digital One utilizes a capacitive sensor, which offers comparatively improved performance capabilities [11] due to improved signal magnification/resolution. The stethoscope has several preset filter notches (depending on practical use wants) and amplifications levels. For all test iterations the stethoscope is used in wideband (20 hz - 2000 hz bandpass) filter mode at a sound amplification level of 7. The filter mode
is chosen as to not filter out any potentially pertinent signal components, while the amplification level was chosen heuristically based on acoustic properties and trends found in preliminary results. The upper filter band of 2000 hz, while not optimally chosen, is suitable as the HeartMate 2 does not operate in a regime in excess of 20000 RPM (330 Hz) nor do heart sounds significantly manifest in high frequency bands (1000 Hz).

The thoracic cavity is a very non-homogenous region of the body. In terms of cardiac auscultation, the are four predominant locations for listening to valvular sound, of which all are intercostal spaces (Figure 2-12), composed of different dermal and internal tissues, structures, etc. Additionally, listening to VAD noises may require probing non-typical auscultation sites, such as the subcostal region or anterior axillary line. Without a full cavity phantom with varying compositions, creating an physiologically inclusive tissue phantom is impossible. Instead, it is more appropriate
to develop a consistent and replicable tissue phantom [3] that can be consistently used across iterations. Yost et al [28] previously used a silicone based molding, EcoFlex 00-10, to develop a soft tissue phantom for transmitting VAD acoustics to a stethoscope. The molding material was previously documented to have properties similar to soft tissue, and thus is chosen as the soft tissue mimic for this work.

In their work Yost et al set a HeartMate 2 VAD into a block of EcoFlex, with 3 cm of material separating the VAD to the outside surface of the silicone, asserting that this thickness mimics physiological soft tissue acoustic transmission. In this work acoustics are acquired at both the obstruction site (Figure 2-11) and at the VAD surface, with the obstruction site being the primary focus. The obstruction site is chosen as it makes logical sense to directly probe at the expected fault location, as it would manifest most directly there. To facilitate transmission at the obstruction site a 1.5 cm block of EcoFlex is used as the transmission phantom. The material
thickness was reduced from Yost’s application due to the blockage structure transmission properties. The properties of the component are unknown, and so it is assumed that using a 3 cm silicone thickness results in overly attenuated signals, and so the thickness is arbitrarily cut in half. The physical parameters of the material are not as important as is consistent use of the phantom. When probing at the VAD surface, a 2.8 cm thick molding of EcoFlex is layered over the VAD, in an attempted to replicate Yost et al’s experimental setup.

Without a VAD implemented into the system systolic ventricular pressure strongly matches systolic aortic pressure (Figure 2-9), as by design. Diastolic pressures are correlated to a significantly lesser degree, however a general direct trend does exist (increasing system resistance results in increased aortic and ventricular diastolic pressures). The inclusion of a VAD into the system (Figure 2-13) does not eliminate these trends, however the degrees to which they occur are decreased as a result of the additional circulation resulting from the device. To achieve a similar ‘non-VAD’ MAP, ventricular pressure and resistance must be decreased, resulting in a diastolic ventricular pressure aligning more closely to zero. Systolic pressures now exhibit a positive offset due to the additional head resulting from the LVAD.

Using the simulator various ranges of boundary condition pressures and heart rates are simulated, with the healthy range of such is undefined by the non-hypertension and non-hypotension (systolic pressure in the range of 130-90 mmHg, diastolic pressure in the range of 80-60 mmHg) region of MAP. For all tests this region is referenced as the healthy mean arterial pressure region (HMAPR). With the LVAD incorporated into the system the boundary conditions must change such that the resulting MAP is in the HMAPR, rather than the boundary conditions. Of course this is generally speaking as it is shown by Tank et al [23] that device speed affects the resulting MAP and may induce hypo/hypertension pressures. As such the HMAPR is used as a general guide with the intent of maintaining the majority of tests into this region, however this is not a hard constraint. Tests within a +- 10 mmHg of MAP are simulated to be inclusive of the occurrence shown [23].

Tests are run in 15 second increments at the previously specified sampling rate of
10 kHz. The state of the test is defined by the average MAP over that interval along with the average heart rate of the acquisition interval. The specific MAP setting is kept constant over the test interval however heart rate is modulated to be either constant or variable. Tests are run at these specific rates for reasons detailed in following chapters as each condition requires different post-processing operations and elicits different diagnostic results. While the terminal goal is to develop a methodology that is applicable to physiological sounds (highly variable sounds), by testing several different levels of non-stationarity the feasibility of such can be more clearly identified. Table 2.1.2 provides a summary of the testing conditions for sounds acquired at the blockage surface. Sounds acquired at the VAD are collected on a much less intensive basis, as the goal of which was limited to determining the feasibility of using sounds acquired from that location and so a similar table is not provided.

Figure 2-13: In vitro simulator pressure curves with VAD integrated (HM2 at 9200 RPM) at a heart rate of 57 BPM.
The constant heart rate sets (referenced as constant BPM states) are partitioned into two equal sized groupings of unfaulted and faulted test iterations. Of each group, 100 iterations are used only for classifier training (Chapter 4), while the remaining 30 are reserved solely for classifier testing. Both training and testing iterations are modulated over the HMAPR. The training sets approximately span the HMAPR, with no specific gridding, while the testing sets are randomized across the region. The partitioning of data as such ensures independence in eventual model testing.

![Variable BPM State Distribution](image)

Table 2.1: In vitro test conditions.

<table>
<thead>
<tr>
<th>ID</th>
<th>Heart Rate [BPM]</th>
<th>Pressure State Region</th>
<th>Test Points (Total)</th>
<th>Test Points (Healthy)</th>
<th>Test Points (Faulted)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>47</td>
<td>HMAPR</td>
<td>260</td>
<td>130</td>
<td>130</td>
</tr>
<tr>
<td>2</td>
<td>57</td>
<td>HMAPR</td>
<td>260</td>
<td>130</td>
<td>130</td>
</tr>
<tr>
<td>3</td>
<td>67</td>
<td>HMAPR</td>
<td>260</td>
<td>130</td>
<td>130</td>
</tr>
<tr>
<td>4</td>
<td>78</td>
<td>HMAPR</td>
<td>260</td>
<td>130</td>
<td>130</td>
</tr>
<tr>
<td>5</td>
<td>Variable</td>
<td>HMAPR</td>
<td>60</td>
<td>30</td>
<td>30</td>
</tr>
</tbody>
</table>

Figure 2-14: State distribution of the variable BPM experimental data sets parsed by condition.

![Figure 2-14](image)
Table 2.2: Quadrantized breakdown of HMAPR in vitro training and testing state locations categorized by MAP Range.

<table>
<thead>
<tr>
<th>Heart Rate [BPM]</th>
<th>Systolic Pressure Range [mmHg]</th>
<th>Diastolic Pressure Range [mmHg]</th>
<th>Training Data Set Points</th>
<th>Test Data Set Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>47</td>
<td>&gt;130 - 111</td>
<td>&gt;80 - 71</td>
<td>40</td>
<td>18</td>
</tr>
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<td></td>
<td>&gt;130 - 111</td>
<td>70 - &lt;60</td>
<td>70</td>
<td>17</td>
</tr>
<tr>
<td></td>
<td>110 - &lt;90</td>
<td>&gt;80 - 71</td>
<td>29</td>
<td>10</td>
</tr>
<tr>
<td></td>
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<td></td>
<td>&gt;130 - 111</td>
<td>70 - &lt;61</td>
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<td>23</td>
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<td></td>
<td>110 - &lt;90</td>
<td>70 - &lt;60</td>
<td>-</td>
<td>17</td>
</tr>
</tbody>
</table>

in instances were a classifier trained at a specific BPM state must be validated at the same state. Additionally, due to the randomness of the partitioned testing set, states are not constrained by any means, other than approximately falling within the HMAPR. Testing points may lie well outside of the space defined by the training points, and so the randomized sets test for model predictive power and observable signal variation. An example of the randomized scheme used is given in Figure 2-14 in which the distribution of states in the variable BPM space is shown. The BPM state and pressure state (normalized to systolic pressure) are defined for the variable set as the average values of BPM and pressure over the acquired 15 second interval. Additionally training/testing space mappings are provided in Chapter 4 when discussing results, however the an immediate general breakdown of state locations relative to the HMAPR is given by Table 2.1.2.
2.2 In-Vivo Generation and Acquisition

LVAD patient data collection is performed by Karl Schwarz M.D. of University of Rochester Medical Center (URMC) using a 3M Litmann digital stethoscope. Both the patients heart sounds and EKG were collected, and compiled using an NI USB 6212 module. The acoustic signals were sampled at 20 kHz in wideband (no applied filter) for various auscultation locations and VAD models (Table 2.3). Data collection is performed externally and so there was no direct control over the consistency of the data sets, which is most apparent as it relates to the stethoscope positioning ('x' denotes valid data set). Stethoscope positioning (Figure 2-12) is as follows,

1. Tricuspid: Left 5th intercoastal space
2. Pulmonic: Left 2nd intercoastal space
3. Mitral: Left 5th intercoastal space in the mid clavicular line)
4. Aortic: Right 2nd intercoastal space
5. AAL: Anterior axillary line
6. Subcostal: Area of the subcostal angle

Acoustics are acquired from 18 patients, spanning four different LVAD models: HeartMate 2 (HM2), HeartMate 3 (HM3), HeartWare (HW), and HVAD. Due to cycle-to-cycle variation the time domain representation of the heart sounds do not lead to any intuitive hypothesis. The frequency spectrum however is more telling, as one can discern trends based on the general distribution of the signal components.

The fast Fourier transform is applied to each patient’s heart sounds resulting in the signal’s respective frequency spectrum. Across all patients the main frequency band ranges from 0-50 hz (Figures 2-15 - 2-17). This band contains signal components specifically relating to native heart sounds and blood flow resulting from the LVAD. Each LVAD model is run at a frequency either outside of the main frequency band, or at the extrema of, and so identifying the device frequency component is obvious.
Figure 2-15: Frequency spectrum of HeartMate 2 (9400 RPM) heart sounds acquired at the 4 valvular auscultation sites

Additional spectrum components are harmonic factors of the device primary frequency (PF) as they occur at integer multiples of the PF. The HM2 manifests only a first harmonic (Figure 2-15) at roughly 350 hz, which is most visible when probed at the mitral auscultation site, where harmonic propagation appears to be strongest.

While component magnitude may not be greatest at the mitral site, harmonic propagation (in terms of visible order) is greatest there, while minimal propagation occurs at the pulmonic site. Both the HW and HVAD (Figures 2-17,2-18) exhibit high order harmonics around 350 hz due to their comparatively low operating speeds (2650 and 2800 RPM respectively), while both only exhibit a third harmonic at the pulmonic site. The HM3 follows a similar trend.

Component magnitude does not appear to follow a consistent trend. The most obvious reason for such would be patient physicality. Patients with different body compositions attenuate signals at different rates and so one would not expect there to be a consistent trend across a multi-patient sample population. What is promising is that the site of auscultation probing does not appear to affect the shape of the
spectrum significantly. While magnitudes change depending on the site, the main frequency band remains consistent, and any additional signal components outside of this band can be identified as a harmonic of the PF. This similarly appears to be consistent across the four device models, even those where the PF is at the edge of the mainband band.

The provided in vivo data is used solely for comparison against the in vitro data, so that the fidelity of the generated signals can be quantified. Patient information is tabulated in Table 2.3, however it is not used extensively in this work aside from comparisons to the in vitro acoustics.

2.3 Data Comparison

It is shown in Figures 2-15-2-18 that the most physiologically significant frequency bands are 0-50 hz and the PF of the VAD, which may overlap with the previous band for specific device models and speeds. Given a perfect phantom the same frequency

![Figure 2-16: Frequency spectrum of HeartMate 3 (5400 RPM) heart sounds acquired at the 4 valvular auscultation sites](image-url)

Figure 2-16: Frequency spectrum of HeartMate 3 (5400 RPM) heart sounds acquired at the 4 valvular auscultation sites
Figure 2-17: Frequency spectrum of HeartWare (2650 RPM) heart sounds acquired at the 4 valvular auscultation sites

Figure 2-18: Frequency spectrum of HVAD (2800 RPM) heart sounds acquired at the 4 valvular auscultation sites
content would manifest in the acoustics of the simulator, with no restrictions on component magnitude as the content can be normalized accordingly. No additional information is given regarding patient blood pressure, demographics, etc. and so this is the limit of comparison.

The frequency content of the generated in vitro acoustics (Figures 2-19 & 2-20) consists of the same general two bands, the PF band, and the lower frequency sound band, termed the mainband. Physiologically, the mainband is resultant from thoracic and pulmonic sound, along with the process acoustics. The simulator however does not account for either extraneous thoracic or pulmonic sounds thus all content below the PF is characteristic of the process (induced flow). The generated mainband matches the shape of the related band in the patient spectrums (Figure 2-15-2-18), however the content is located at a higher frequency band, 50-150 hz, with greater dispersion at the trailing frequencies. Frequency content below roughly 20 hz does
not exist as the maximum bandwidth of the stethoscope is 20-2000 hz, and so content at this point is attenuated by the device filter. Peak content is centralized about 110 hz, and so the loss of low frequencies is not expected to be inherently problematic in discerning condition indicating components however this cannot be definitively stated. Additionally, high frequency content propagates slightly more so than as was seen in patients, however this content is not restricted by the bandwidth of the filter.

Within the in vitro mainband two distinct peaks can be identified, which is unlike the singular peak mainband identified in the in vivo acoustics. These two peaks are located at approximately 70 hz (noted as PF-A), and at 115 hz (noted as PF-B), however their exact locations and shape depend on the state. As can be seen in comparing the spectrums of same pressure states, the peaks do not manifest consistently relative to neither state nor health condition (unfaulted or fault). The inconsistent fault characteristics can be seen when comparing the states of Figure 2-19 to those of Figure 2-20, namely in the alteration to the mainband dual peaks.

When the 120/74 mmHg state data is faulted, the simulated 57 beats per minute
Figure 2-20: Frequency spectrum of HM2 (9200 RPM) heart sounds acquired at the occlusion surface of the simulator unfaulted(left) and faulted(right) consistent state. State defined as 106/62 at 57 BPM (top) and 106/62 at 78 BPM (bottom).

(BPM) signal is characterized by decreased magnitudes, with a relatively more decreased PF-B than PF-A. When the heart rate is increased to 78 BPM, the exact opposite occurs. The PF-B peak sharply increases in magnitude while the PF-A peak is attenuated. Concerning only the pressure state of 120/74 mmHg this inconsistency would allude to a dependence on state. In order to verify this, a pressure state of 102/62 mmHg is analyzed, ultimately finding a different trend. Just as the PF-B of the 120/74 mmHg, 78 BPM state signal had amplified when faulted, so too does the PF-B of the 106/62 mmHg 57 and 78 BPM states, however in this scenario so does the PF-A, contrary to what was previously seen. In a similar trend, based on the findings of Figure 2-19 one would assume both PF-A and PF-B peaks of the faulted 106/62 57 BPM state to attenuate however both arguably amplify. These inconsistencies between states indicate a strong dependence on state which is most likely nonlinear across the HMAPR. This is problematic for diagnostic purposes as this may mean that diagnostic ability is directly related to the variability that can be identified, i.e. identifying the inconsistencies, developing peace-wise models, etc.
Figure 2-21: Time history of HM2 (9200 RPM) heart sounds acquired at the occlusion surface of the simulator unfaulted(left) and faulted(right) consistent state. State defined as 120/74 at 57 BPM (top) and 120/74 at 78 BPM (bottom). Both signals sets are sync’d to the same EKG reference for consistent reference, i.e. 57 BPM sets are aligned to each other, and 78 BPM data sets are aligned to each other.

Definitive variation and nonlinearity are identified in the frequency spectrum of the generated acoustics, however the origin of such can be better visualized in the time domain. When examining the respective time series representations of the signal spectrums shown in Figures 2-19 and 2-20 uniquely occurring components (the S1 and S2) can be identified. These sounds differ in both magnitude/shape and time of occurrence. The changes in signal shape can be determined based solely on the respective comparisons shown in Figures 2-21 and 2-22 however sound event occurrence is not aggressively clear without examining a normalized time space.

When examining the constant heart rate acoustics (for consistent comparison), a defining characteristic is found. The sound produced by the system does not strictly depend on the heart rate (BPM state) modulated by the function generator, but rather is affected by the MAP state as well (Figure 2-23). As the MAP decreases (i.e. pressure becomes increasingly constant - LVAD dominant system) the S1 and S2
Figure 2-22: Time history of HM2 (9200 RPM) heart sounds acquired at the occlusion surface of the simulator unfaulted(left) and faulted(right) consistent state. State defined as 106/62 at 57 BPM (top) and 106/62 at 78 BPM (bottom). Both signals sets are sync’d to the same EKG reference for consistent reference, i.e. 57 BPM sets are aligned to each other, and 78 BPM data sets are aligned to each other.

shift inwards, becoming more closely timed to each other. This is a very particular and problematic occurrence. The non-stationarity of the signal has been decreased somewhat because of the constant heart rate modulation, however there remains a dependence on state. Going forward a constant event frame is desired for examining specific signal components, however given this system characteristic determining the exact time of sound occurrences is difficult to achieve. More will be discussed about this in Chapter 3.

The variations in timing caused by the pressure state is the most likely explanation for the inter-state inconsistencies seen previously in the in vitro frequency spectrums. The dependence itself is theorized to be the result of how phase and state are modulated. It was previously noted that due to the constraints of the function generator, the phase trigger is set to an arbitrary 50/50 timing split, while the exact rate at which each phase occurs is dependent on the pressure differentials. Because
Figure 2-23: S1 and S2 in vitro sound event occurrences varying by state. Both acoustic signals are sync’d to the same EKG reference (bottom graph). Heart rate of both acoustic signals is 57 BPM. Red boxes indicate S2 sounds, while black boxes indicate S1 sounds.

of this dependence each phase occurs at varying rates across the HMAPR. It is also noted that heart sounds (including in vitro signals) are directly resultant from events such as valvular action and flow perturbations. Thus as the state affects the timing of events of the in vitro system, the resultant timing of components such as the S1 and S2 also change.

The HMAPR of the in vitro system is characterized by state and condition non-linearities that make potential diagnostics difficult over the generalized region. Given the nonlinear timing trend, manual determinations of condition indicating components cannot be made with only time series or frequency spectrum definitions of the acoustic signal. Additionally, there appears to be innate signal set variation (variation between adjacent cycles) between acoustics at consistent states requiring a robust processing algorithm that can mitigate variation, and identify condition from state dependent effects.
Chapter 3

Digital Signal Processing and Feature Generation

In general terms, physiological heart sounds are significantly more non-stationary than the generated in vitro sounds from the heart simulator. The in vitro sounds are not characterized by any type of cyclical drift, or innate variable rate (can be modulated as such however), nor are they affected by adjacent tissues, organs, and organ system processes. While the timing of events does vary with state, this characteristic is a nonlinearity, not necessarily a non-stationarity.

For this purpose the constant heart rate in vitro acoustics may be considered a stationary signal, however this is counterintuitive for applications regarding physiological heart sound analysis and the variable heart rate in vitro sounds. There is a similar issue concerning both signals, in which the intra-cycle variations are not explicitly indicative of the underlying signal itself, further complicating the analysis, especially concerning fault scenarios. There are instances when healthy intra-cycle variations may appear as abnormalities, indicating a false positive diagnostic. There are also instances where the state dependence would indicate the same incorrect diagnostic result. Eliminating this potential, along with developing a consistent frame for examining significant signal health components are the objectives of this chapter.
3.1 Digital Preprocessing

A stationary signal is a signal whose statistical properties do not change over time for all degrees (expectations, variances, etc.). Absolute stationarity is an aggressive term, and so for purposes of this work, second order stationarity will be equated to the general term, stationary. Second order stationarity is the statistical property of having having constant mean and variance over an interval \( t \in [t_0, \tau] \) where \( \tau \) is the translation from an arbitrary origin, \( t_0 \). Neither the mean nor variance depend on \( t \), and the autocovariance between states \( (X_t, X_{t+\tau}) \) depend only on the translation, \( \tau \).

Conversely, non-stationary processes are defined as those stochastic processes which cannot be defined by only \( \tau \). As the process’s statistical properties evolve over time propagation, the interval time, \( t \), is also required to fully define the process statistical states. This is a very significant process characteristic specifically for signal transformations. Stationary signals require only the translation parameter to be statistically fully defined, and thus can be defined by \( n \) parameters, where \( n \) is the degree of the signal. Non-stationary signals however, require both the translation parameter along with the specific instance, \( t \), requiring \( 2n \) parameters for definition. This quadratic transformation characteristic will become crucial when determining spectral properties of the signal.

As to why heart sounds are non-stationary, it is quite obvious. Given two scenarios, S3/S4 occurrence and variable interval period, it becomes apparent to different degrees. If both the mean and variance of a cardiac cycle are defined for solely the S1 and S2, then the occurrence of additional sounds (S3, S4, etc.) alters the process statistical states for the given interval. Given a variable interval rate, the signal statistical properties may remain constant, or near constant, however full definition of the signal requires quadratic parameters due to the variable interval \( t_0 \). As the in vitro simulator is digitally regulated, neither of these statements hold true for constant modulated frequency, however as the generated signal is an approximation of the non-stationary signal, it is processed under the assumption that it is non-stationary.

Assuming a non-stationary heart sound, the first objective is to develop a con-
sistent objective signal to further analyze. The obvious first option is to normalize the time-series to a [0 1] scale, creating a consistent intra-cycle time scale. Doing so reduces the variation of the signals as a whole (neglecting storage of the normalization parameter) however does not alter statistical property variation, nor the signal stationarity properties - both of which are problematic moving forward.

Instead, a new objective signal is generated through ensemble averaging. Ensemble averaging (EA) is the process of creating a set of cyclical data sets (the set is called the ensemble) and then taking the point-by-point average of the ensemble to generate a new signal (Figure 3-1). Ensemble averaging reduces signal variation in the similar way that a moving average does so, reducing, if not eliminating, the need for filtering (in this instance, eliminating). The resulting statistical properties of the averaged signal are also unique, in that they are indicative of the most predominant and common properties of the ensemble, thus "filtering" out cycle variation that is not representative of the underlying signal (such as cycles with additional sounds/elements/occurrences). Ensemble averaging innately handles process non-stationarity, however leaves the issue of ensemble period variation and identification of the cycles from the whole acoustic signal. The following work considers only in

![Figure 3-1: Ensemble averaging general theory/methodology.](image)

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vivo signals in developing the algorithm as the produced in vitro acoustics are simpler and can be processed with the same techniques.

In determining the ensemble, the individual cycles of the objective signal must first be parsed using an identification routine. The two trialed methods are:

1. Sound Extrema Parsing: Parse individual cycles based on the local maximum amplitude of the acoustic signal.

2. EKG Extrema Parsing: Parse individual cycles based on the local maximum amplitude of the relating EKG signal.

Sound extrema parsing involves identifying acoustic signal maxima and accordingly parsing the signal by them. In a non-LVAD patient the maximum signal component occurs during the S1 beat and can be regularly timed (to some degree) and observed (less than so when unhealthy - Figure 1-2), however as aforementioned in Chapter 2, the time domain representation of an LVAD patient’s heart sounds are characterized by significant variation and state dependence reducing feasible application of the signal. EKG extrema parsing is the process by which the peaks of the EKG signal are identified and subsequently used to parse the acoustic signal. Since the EKG is a cleaner, and higher fidelity signal, this assumedly results in a more accurate parse, however requires the EKG signal to be collected, and synchronized with the acquired sound. This method is specifically examined do to the work performed with the URMC research group. In which a stethoscope is being developed with integrated EKG leads, enabling EKG extrema parsing.

When using sound extrema parsing (Figure 3-2) the related EKG references (not peaks as a peak in one signal does not necessitate a peak in the other) do not consistently align at the same EKG wave component. In the dual sense, using EKG extrema parsing (Figure 3-3) yields a very consistent set of EKG peaks (at the R wave peak) with no discernible pattern in the acoustic signal, implying that the non-stationarity of the acoustic process is quite significant. Statistically, parsing by the EKG consistently results in both a lower cycle period deviation (Figure 3.1) and increased identifiable cycle count as compared to parsing by the acoustic signal. As the EKG is
Figure 3-2: In vivo signal cycle identification using sound extrema parsing. Black overlay circles indicate locations of detected peaks of acoustic signal. Peak locations are overlay on EKG to show correlation.

a relatively high fidelity signal, the deviation of the EKG parsing can be attributed to the patient’s variable heart rate, i.e. over the one minute acquisition window of the in vivo signal, the patient’s heart rate did not remain constant, creating a quantifiable minimal deviation in cycle period.

Even though signal variable rate is identified by each parsing algorithm, the after effects manifest during the point-by-point averaging of each ensemble due to non-alignment (error resulting from non-equal length signal averaging). As discussed, there is a minimum quantifiable deviation of each ensemble which is be attributed to signal variable rate. Even if perfectly parsed, this deviation will cause the cycles
Figure 3-3: In vivo signal cycle identification using EKG extrema parsing. Black overlay circles indicate locations of detected peaks of EKG signal. Peak locations are overlay on acoustic signal to show correlation.

of each ensemble to become misaligned where the severity of the misalignment is proportional to the distance from the sync point (maximum sound peak or maximum EKG peak). Assumedly then, signals with the greatest ensemble deviation will yield the most misalignment resulting in the terminal average not necessarily being representative of the underlying signal. Given an inconsistent sync point such as that produced by sound extrema parsing, the misalignment error will propagate much more quickly than that resulting from EKG extrema parsing. For this reason, the EKG signal is used going forward as the universal syncing signal for parsing the ensemble.
Table 3.1: Cycle parsing statistics for both sound extrema and EKG extrema parsing algorithms.

<table>
<thead>
<tr>
<th>Auscultation Location</th>
<th>Parsing Method</th>
<th>Cycles Identified</th>
<th>Cycle Period Mean (s)</th>
<th>Cycle Period STD (s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aortic Sound</td>
<td>Sound</td>
<td>62</td>
<td>.9597</td>
<td>.2721</td>
</tr>
<tr>
<td>Aortic EKG</td>
<td>74</td>
<td>.7952</td>
<td>.0154</td>
<td></td>
</tr>
<tr>
<td>Mitral Sound</td>
<td>71</td>
<td>.8313</td>
<td>.1668</td>
<td></td>
</tr>
<tr>
<td>Mitral EKG</td>
<td>75</td>
<td>.7864</td>
<td>.0217</td>
<td></td>
</tr>
<tr>
<td>Pulmonic Sound</td>
<td>72</td>
<td>.8259</td>
<td>.1885</td>
<td></td>
</tr>
<tr>
<td>Pulmonic EKG</td>
<td>78</td>
<td>.7623</td>
<td>.0087</td>
<td></td>
</tr>
<tr>
<td>Tricuspid Sound</td>
<td>73</td>
<td>.8161</td>
<td>.1572</td>
<td></td>
</tr>
<tr>
<td>Tricuspid EKG</td>
<td>77</td>
<td>.7751</td>
<td>.0179</td>
<td></td>
</tr>
</tbody>
</table>

for both the in vivo and in vitro sounds.

With the acoustic cycles identified by their respective EKG peaks the ensemble (set of cycles) is now averaged to reduce variation and noise. Four routines are implemented to study the effects of the misalignment in averaging and potential remediation actions for such,

1. Unscaled point-by-point averaging (UA).
2. Unscaled point-by-point averaging with acceptable deviation bound (BUA).
3. Linearly scaled point-by-point averaging (SA).
4. Linearly scaled point-by-point averaging with outlier removal (BSA).

Unscaled averaging is the nominal routine, where the ensemble misalignments are not corrected for - ensembles are aligned and averaged regardless of signal length. During BUA and BSA the ensembles are reduced according to their deviation from the average cycle period prior to averaging. Based on a bound control parameter, all the cycles of the ensemble which lie outside the deviation boundary are omitted from averaging as it is assumed that they are either not indicative of the underlying signal or would result in significant misalignment error if included. This process reduces the overall size of the ensemble, the magnitude of which inversely scales with the size of the boundary, however assumedly results in an ensemble with reduced misalignment error.
The final technique, linear scaling, involves taking each cycle, and through a process of scaling and resampling, maps each to the time-series space of the ensemble’s average period. This allows for complete point-by-point alignment without reduction of the ensemble. While beneficial for the above reasons, the validity of scaling [potentially] significantly different cycles to a consistent basis is unclear, which is the reason for the fourth remediation routine, BSA. During BSA the ensemble is first reduced as with BUA, however the remaining ensemble is then scaled and averaged. Given a small deviation, it can be assumed that cycles within the boundary are approximately the same signal, and so error propagation inherently arising from scaling is minimized, if error is in fact an algorithmic product. When using BUA the control parameter is required to be adequately tight to reduce peak misalignment thus effectively reducing ensemble size. BSA on the other hand does not remove ensembles for the purpose of alignment correction, and so the control parameter used in re-parsing the ensemble is used more so as an outlier removal parameter.

In Figure 3-4 the ensemble misalignment resulting from UA can clearly be seen at the second R wave of the EKG. Whereas the first peaks of the ensemble align well, due to it serving as the sync point, the misalignment severity increases away from this point, creating the peak range seen at the second R wave of the EKG. This, to a lesser degree, can be seen by the related acoustic average. About the first R wave peak, the acoustic signal is characterized by increased oscillation, which decreases at the T wave of the EKG. This however is not the case about the second peak as the local acoustic signal here is more or less indiscernible from the preceding T wave. The second R wave peak interval itself is not important as it is just an appended cycle portion added for comparison, however the visible misalignment propagation that it indicates is an issue. It is assumed that misalignment is prevalent, to a lesser degree, during the previous T wave interval as error must propagate along the time scale. Any indicator of health contained within this interval would then be corrupted posing a problem in future classification. This is a commonality among all auscultation sites.

By reducing down the ensemble, the BUA routine is able to minimize the alignment variation seen at the second R wave peak location (Figure 3-5). There is still
Figure 3-4: UA ensemble averaging of in vivo heart sounds from the aortic auscultation site. Black overlay is the averaged signal. RMSE between peak regions is 2.26e-5.

A finite variation to the ensemble, but it has been significantly reduced from what it was. In order to do so, a 1% variation bound is placed on the ensemble - any cycle whose period differs from the mean period by more than 1% is omitted from the ensemble composition. While it produces an improved average signal, it also reduces the ensemble from 74 cycles to 26, a reduction of two-thirds. Such a reduction is not practical as it requires a three fold increase in raw data collection. Additionally, there is nothing inherently wrong with the committed data sets (assumedly) and so
the omittance of such is not necessarily justified.

The misalignment resulting from UA and BUA is a direct result of patient heart rate variability. The relative error of the alignment is thus directly related to heart rate variation. Extrapolating this to the in vitro data, given the constant heart rate modulated data sets, UA results in a near perfect point-by-point ensemble average (+- a sample due to decimation or rounding) thus not requiring a more intensive algorithm. This however is not true for the variable frequency tests, nor the in vivo

Figure 3-5: BUA ensemble averaging (>1% deviation from mean period reduction) of in vivo heart sounds from the aortic auscultation site. Black overlay is the averaged signal. RMSE between peak regions is 2.72e-6.
3.1.1 Polyphase Decomposition Scaling

As shown in Figure 3-5 BUA reduces the ensemble misalignment at the cost of significant data quantity loss (66%), the severity to which scales with the degree of the permitted misalignment. This is both extremely impractical for real-time application and allows for a permissible misalignment which propagates error along the time scale. The misalignment error propagation is a result of the process frequency non-stationarity rather than that which manifests in various signal components. The magnitude of the latter of the mentioned non-stationarities is reduced through ensemble averaging, while the frequency based non-stationarity is mitigated through control of the ensemble size in BUA.

Both SA and BSA apply a scaling transformation to the ensemble to reduce misalignment propagation along the time scale of the ensemble without inherent data reduction. The transform essentially dilates or constricts the objective ensemble cycle given its deviation from the average time scale of the ensemble. This results in a transformed signal, with a process frequency exactly matching the average of the ensemble process. This, however, does pose two issues,

1. The transformation must be compatible with point-by-point averaging.

2. The transformation must be applied in such a way to preserve as much frequency content as possible, without generation of erroneous content.

The transformation must first off be compatible with how the ensembles are averaged, point-by-point. To achieve this with no misalignment propagation, each transformed signal must be of the same size and discretization assuming the same sampling rate. This is problematic as scaling any discrete set results in a new discretization of the set, that is assumedly inconsistent with the related ensemble. Assuming this condition will be met, the transformed signal must still be indicative of the original signal to be of potential use. Clearly in terms of reducing non-stationarity charac-
teristics this is beneficial, however scaling transformations do not [exactly] preserve stationarity components.

The PF and harmonics of the VAD variably manifest in the frequency spectrum of patients (Figures 2-15-2-18) and the simulator (Figures 2-19-2-20). Considering that 90% of VADs are continuous flow devices with speed control, the frequency content related to the devices are considered stationary components that do not require scaling. Dilation of the cycle will result in all frequency content of the cycle shifting down (decreasing) while constriction results in an upwards shift (increasing) in content. A scaling transformation across the entire ensemble then shifts each cycle’s device frequency content to an assumedly different frequency band. While this is not entirely problematic, once the ensemble is averaged, due to the inconsistent bands, the PF and harmonic bands are either warped or eliminated. Potential condition indicators within this band are then also lost, however as the device process is stationary and controlled, one would not expect an indicator to manifest here and is therefore inconsequential for identification purposes. To ensure that the inconsistencies resulting from this do not affect classifications they are later further dealt with in Chapter 3.3.

In order to compensate for the re-discretization of the signal caused by scaling, the signal is first resampled in such a way that post-scaling aligns the ensemble to the desired length and original discretization. Re-discretization is performed by upsampling, smoothing, and subsequently low pass filtering and downsampling, however this procedure is non-optimal for this work. As is shown in Figure 3.1 parsing by the EKG signal significantly decreases cycle period deviation from the mean of the ensemble. This, while obviously beneficial for parsing, essentially ensures that resampling must be done with relatively high factors. To be computationally optimal both the upsampling and downsampling must be performed with factors of the least common multiple (LCM) between the mean cycle and individual cycle lengths as period scaling is the desired transformation. By achieving small period deviations, non-integer ratios between lengths result. Conversion from these ratios to rational approximations, so that resampling can be performed, results in large LCMs, meaning resampling must be performed at very high computational costs due to large filter
coefficient vectors. Additionally, in order to resample, by means of the method prescribed above, requires filtering after upsampling and prior to downsampling. The design of both filters depend on the resampling factors resulting in two fold large filter applications, an obvious inefficiency.

Algorithmic efficiency is increased by instead performing polyphase decomposition (PD) filtering to achieve the desired discretizations of the ensemble. Given that the resampling ratio (quotient of upsample factor and downsample factor) is rational, a singular FIR filter (polyphase resampler filter - PRF) can be designed for both upsample smoothing and downsample anti-aliasing. If resampling cost is defined as the product of the resampling factors, PD reduces said cost by the maximum factor, making resampling much more efficient than two step resampling.

In PD, upsampling is performed by re-discretizing based on the upsampling rate and inserting zeros at the added points. Downsampling is performed by removing points based the downsampling rate. The PRF both smooths the added zeros, while low pass filtering at the desired Nyquist frequency for anti-aliasing. The filter properties are achieved through the design of the windowing function, a kaiser window [16].

The kaiser window, a modified zero-ith order Bessel function is defined as,

$$w[n] = \begin{cases} I_0[\beta(1 - [(n - \alpha)/\alpha])^2]^{1/2}], & 0 \leq n \leq M \\ 0, & else \end{cases}$$  \hspace{1cm} (3.1)$$

where $I_0[*]$ is the Bessel function, $M$ is the filter order, $\alpha = M/2$, $\beta$ is a window shape parameter, and $n$ is the sample. Design of the window depends only the filter order, $M$, and the shaping parameter, $\beta$, but the choice of each depends on the filter characteristics, which are normalized to the sampling rate (frequency units are $\pi$ rad/sample).

Given a rational resampling rate, $R = p/q$, the following equations define the transition band of the filter (Figure 3-6),
Figure 3-6: FIR filter frequency response [26].

Passband Frequency $[\pi \text{ rad/n}]$ : $\omega_p$ \hspace{1cm} (3.2)

Stopband Frequency $[\pi \text{ rad/n}]$ : $\omega_s$ \hspace{1cm} (3.3)

Transition Band (TB) $[\pi \text{ rad/n}]$ : $\Delta \omega = \omega_s - \omega_p$ \hspace{1cm} (3.4)

TB Center Frequency $[\pi \text{ rad/n}]$ : $\omega_c = \frac{\omega_s + \omega_p}{2} = \frac{1/2}{\max(p, q)}$ \hspace{1cm} (3.5)

The transition band center of the filter, $\omega_c$, generates the Nyquist frequency of the resampled signal. In PD, a singular filter is used, requiring $\omega_c$ to be set to the more restrictive Nyquist frequency that would be used regarding separate upsample and downsample filters. This guarantees that the other Nyquist frequency condition, being less restrictive, will inherently be satisfied. If resampling to a smaller sampling rate ($p > q$) then $\omega_c$ is most restricted by equating to $0.5p^{-1}$. Conversely, if resampling to a larger rate ($p < q$) then $\omega_c$ is most restricted by equating to $0.5q^{-1}$.

The shape parameter, $\beta$, controls sidelobe attenuation, $\delta_s$ and affects mainlobe width, while the filter order, $M$, affects mainlobe width. The relation between beta
and $\delta_s$ is as follows,

\[ Sidelobe\ Attenuation\ [dB] : \ A = -20\log_{10}(\delta_s) \quad (3.6) \]

\[ Beta\ [-] : \ \beta = \begin{cases} \ .01102(A - 8.7), & A > 50 \\ .5842(A - 21)^4 + .07886(A - 21), & 21 \leq A \leq 50 \\ 0, & A < 21 \end{cases} \quad (3.7) \]

Sidelobe attenuation is only affected by $\beta$, i.e. increasing $\beta$ results in increased attenuation of the sidelobe. Increasing $\beta$ also has the effect of increasing the width of the mainlobe. As it exhibits both behaviors, the viable range of $\beta$ is quite significant as $M$ can reduce the mainlobe width while still achieving high stopband attenuation. Given the order of the filter, the mainlobe width and specific transition bands can be determined (mainlobe indirectly from transition band),

\[ Filter\ Order\ [-] : \ M = \frac{A - 7.95}{2\pi 2.285\Delta \omega} \quad (3.8) \]

\[ Filter\ Order\ Normalized\ [-] : \ n = \frac{M}{\max(p,q)} \quad (3.9) \]

\[ Window\ Length\ [samples] : \ L = M + 1 \quad (3.10) \]

where $n$ is the order of the downsampling anti-aliasing filter. Thus, given the window length and $\beta$ of the window nearly all filter characteristics can be approximated. The passband ripple, $\delta_p$ is a result of both the window type and $\beta$ and so it is not an exact design parameter, however the ripple width is inversely related to the window length, i.e. longer window gives shorter ripples. This realization is not significant unless there is significant frequency content about the passband boundary as ripple error increases with frequency.

As the design process would suggest, in order to achieve a specific set of filter characteristics based on a unique $R$ requires a unique set of $(\beta, L)$. This is impractical

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due to both the magnitude of the cycles to transform (requires a different filter per - each must be auto-generated) and for the fact that under specific permutations, achieving specific parameters may require inefficient design parameters (arbitrarily high order). Instead, knowledge of the ensemble’s frequency content can be leveraged in order to design a filter that is applicable for all cycles.

The highest frequency content seen in patients and from the in vitro simulator is roughly 500 hz (Figures 2-15-2-18,2-19-2-20) seen with the HM2, with the most significant band spanning 0-50 hz irregardless of device and 50-150 hz. Assuming these bands are indicative of the population, the maximum frequency, $\omega_{max}$ can be finitely defined. This frequency would is then defined as the absolute minimum resampled Nyquist frequency admissible in order to preserve significant signal content. There is significant higher frequency content, however the exact preservation of such is negligible as it is shown that this content is harmonic based which ensemble averaging innately warps/eliminates. Given an ideal LPF the transition band center (ideal filter implies: $\omega_c = \omega_p = \omega_s$) can be placed at $\omega_{max}$ however the PRF is non-ideal. The passband of the filter must then be placed, at minimum, at $\omega_{max}$ to ensure, assumedly, non-attenuation of the desired passband ($\omega_{p-min} = \omega_{max}$).

Placing $\omega_p = \omega_{p-min}$ is problematic as the passband ripple increases in amplitude near $\omega_p$, resulting in warping of the content. An arbitrarily high order filter can in theory mitigate this, however is computationally inefficient. The practical solution is obvious, placement of the passband arbitrarily far away from the highest frequency content will preserve the necessary content while achieving the desired resampled Nyquist frequency.

How far the Nyquist is placed away depends only on $R$ which is inherently beneficial. As explained in Chapter 2, the M3 stethoscope samples at 20 kHz, meaning the frequency band of 500-10000 hz (referenced as the ‘voidband’) carries no significant content. The resampled Nyquist frequency, the transition band center, is a scaled version of the original Nyquist, specifically by $R$ (3.5), thus to achieve the nominal resampled Nyquist, the normalized $\omega_c$ must be scaled by the upsample factor and original sampling rate. Thus given an arbitrary void band, the minimum permissible
Given \( p > q \), \( \omega_c \) is placed at the original Nyquist, thus the constraint. Given the solution, \( R^* \) to (3.11) the necessary condition for ensemble resampling is,

\[
R^* > \frac{w_{\text{max}}}{f_s}
\]  

(3.12)

The minimum frequency of the voidband, denoted \( w_{\text{max}} \), is the minimum permissible frequency that the transition band center can be placed. Placement of \( \omega_c \) at \( \omega_{\text{max}} \) however results in attenuation of passband content due to the transition band so the passband is instead bounded, \( \omega_p \geq \omega_{\text{max}} \), to ensure no loss of content. Placement of \( \omega_p = \omega_{\text{max}} \) constitutes the bandwidth requirement for a minimal order filter. Given the large void-bandwidth, the passband is significantly smaller than the transition band for the minimal order filter ("Bad filter practice"), and so an additional constrain is imposed, \( \omega_p > \Delta \omega \). With the above constraints,

*Passband Frequency \([\pi \text{ rad/} n]\): \( \omega_p = a \omega_c \)  

(3.13)*

*Stopband Frequency \([\pi \text{ rad/} n]\): \( \omega_s = b \omega_c \)  

(3.14)*

where \( \omega_{\text{max-norm}} < a < 1 \), \textit{such that} \( a \geq 2/3 \)  

(3.15)

\( 1 < b < 2 \), \textit{such that it is symmetric}  

(3.16)

\text{with a about } \omega_c

where

\[
\omega_{\text{max-norm}} = \frac{\omega_{\text{max}}}{f_s p}
\]

(3.17)
The filter frequency properties are fully defined by the given equations and constraints. The passband is placed relative to content, the Nyquist is resultant from $R$, and the stopband is arbitrarily symmetric. Given that the passband is placed such that $a = 2/3$, the modified requirement for minimum order design is now been met.

In the traditional kaiser window design process, window length and $\beta$ are inputs that define the shape and characteristics of the resulting filter, which are then used to define the transition bandwidth (3.8). By constraining the problem as in 3.13-3.16 the transition band is know, and if $a = 2/3$ the necessary condition for minimum order is met. Using (3.8) the minimum required order of the filter is found such that it achieves the desired stopband attenuation with the designed band parameters.

Analyzing the ensemble of Figures 3-4 and 3-5 the highest significant frequency content is the harmonic at 150 hz (Figure 2-15, however there is sparse content from 150-500 hz. With the ensemble characterized by $R^* = .9725$ placement of $w_p$ must be at a minimum nominal frequency of 6484 hz to satisfy $a \geq 2/3$. The attenuation, $\delta_s$ was arbitrarily set to .001. The normalized, minimal filter order of the ensemble is 6. Using SA (Figure 3-7) the error propagation is severely decreased, as is the case with BUA (Figure 3-5), however without the reduction in ensemble size. Additionally, it can be inferred from the R wave zooms (Figure 3-5 - 3-7) that SA results in a higher fidelity average due to the decrease in error propagation, which is confirmed from R wave RMSE quantification.

In taking the same approach as was done with BUA, the ensemble is likewise bounded in BSA using deviation from the mean period as criteria. Bounding the ensemble deviation by one standard deviation results in an ensemble size reduction of 36% with little obvious effect (Figure 3-8). The effect of the reduction is consistent, the difference between signals (Figure 3-9) oscillates about zero with no trend. The relative effect of bounding is most apparent between R wave peaks as signal magnitude is comparatively less in this region, which does indicate an intermittent trend. During this interval (approximately .3-.7 seconds) whichever way the BSA signal inflects is of greater magnitude than the related SA signal indicating the signals that were omitted create a bias towards zero. This could indicate that the omitted data carries some
sort of intrinsic error or more interestingly could imply that scaled signal fidelity is related to the magnitude of the scale. This remains an undetermined fact and so for the practical application of the algorithm SA is strictly used in this work.

Between the SA and BSA there is little discernible difference. Even when comparing the scaled averages to the BUA signal, the difference in error propagation isn’t as obvious a determination, as a time series. Instead, the frequency content (3-10) of the signals better characterize the effects of each routine.

The correlation between the BUA, SA, and BSA signals are comparatively high,

Figure 3-7: SA ensemble averaging of in vivo heart sounds from the aortic auscultation site. Black overlay is the averaged signal. RMSE between peak regions is 4.19e-7.
with UA being the signal of objectively lesser fidelity. The non-alignment caused by UA creates a different frequency spectrum shape, as compared to the other spectrums, where prominent components are degraded to a degree. Those most significant components, being located at 12 hz and 20 hz, are more clearly defined in BUA, SA, and BSA implying that these components are directly related to the improvement in ensemble alignment. This theory is supported by the fact that the scaling routines result in equal magnitude significant components. Being that those two magnitudes

Figure 3-8: BSA ensemble averaging (36% ensemble reduction) of in vivo heart sounds from the aortic auscultation site. Black overlay is the averaged signal. RMSE between peak regions is 4.19e-7.
are globally the greatest it can be assumed that they relate to acoustic components
timed at the R wave peaks, which are previous used to compare error propagation in
the time domain (Figures 3-4-3-8). Outside of those peaks, the trailing band (20-40
hz) is of a slightly different shape comparing between the scaling routines and BUA.
The BUA signal is attenuated slightly more and with less peaking compared to the
scaling algorithms. As theorized, the PF at 155 hz is attenuated by the scaling-
averaging combination, however the PF is not significantly present in either the UA
or BUA signals. While scaling does increase stationary component attenuation, av-
eraging appears to be of more significant impact. Finally, there is little difference
between spectrums resulting from SA and BSA, confirming the decision that SA is
to be used until more is known about the impact rejection has on the scaled signal
averages.

Figure 3-9: Comparison of averaged signal resulting from both the SA and BSA
algorithms.
3.1.2 Ensemble Averaging Nonlinear Spectrum Effects

All four averaging routines (UA, BUA, SA, and BSA) are able to effectively reduce both the noise and cycle-to-cycle variation, or non-stationarities, of the ensemble. Temporal misalignment decreases proportional to the degree of which the ensemble is bounded, or is entirely eliminated when scaling the ensemble to a consistent basis. Alternatively, the device frequency is seen to severely attenuate as a result of both averaging and scaling, which poses the question of how the frequency spectrum is altered as a result of ensemble averaging.

Figure 3-10: Comparison of the frequency content of the averaged signals resulting from UA (top), BUA (middle-top), SA (middle-bottom), BSA (bottom).
Ensemble averaging can in theory be defined through filter parameters however such assumes that the signal being averaged is statistically stable, or rather stationary. If a signal is completely stationary then its quality can be defined in terms of its signal-noise ratio. If then averaging an ensemble of this type of signal, the averaged signal’s signal-noise ratio can be defined as [25],

\[
\left(\frac{S}{N}\right)_n = \sqrt{n} \left(\frac{S}{N}\right)_i \tag{3.18}
\]

where:

\[S = \text{Signal Power}\]
\[N = \text{Signal Noise}\]
\[n = \text{Size of Ensemble}\]

The ratio of S to N is defined as the signal-noise ratio (SNR). Given that the signal is stationary, the SNR of the average scales with the square root of the ensemble size, and so by increasing the ensemble size the resultant average is increasingly filtered. This formulation however requires that the noise is zero mean and constant variance, i.e. the signal is statistically invariant. For this work the non-stationarity of the in vivo acoustics (and in vitro acoustics to a lesser degree) is generalized as a noise term. Due to this, the signal is no longer statistically invariant and so the SNR must be left in its generalized form,

\[
\left(\frac{S}{N}\right)_n = \frac{\sum_{i=1}^{n} S_i}{\sqrt{\sum_{i=1}^{n} \sigma_i^2}} \tag{3.19}
\]

From 3.19 it becomes apparent that the performance of the average as a filter depends on the individual cycles of the ensemble and their statistical characteristics. Filter performance is no longer improved by arbitrarily increasing the ensemble size. Of more consequence to this work is if the noise is not zero mean, constant variance over an individual cycle. Given the generalization that non-stationarities are considered signal noise, the resulting noise is then skewed to reflect the properties of the variation. This may be resulting from an inconsistent sound, or may result
from misalignment. Additionally, due to the inherent nonlinear phase timing of the system, it is theorized that noise is specifically dependent on phase for the in vitro acoustics.

The in vitro acoustics are the optimal test of ensemble average filter performance and/or characteristics. The constant BPM sets are not characterized by misalignment, nor is the system characterized by inconsistent events (S3,S4) as the in vivo acoustics may be. This being the case, if the system is not characterized by phase specific non-stationarities, then the performance of the algorithm is expected to follow the definition of 3.18. In examining the spectra of the in vitro UA signal (3-11), this roughly appears to be the case with some exception. The first noticeable characteristic of the spectrums is that they all share the same shape near the mainband. Additionally, as the ensemble size increases, noise, specifically within 200-500 hz, decreases with increasing ensemble size which is expected. A more problematic occurrence is the attenuation of the LVAD PF and related harmonic signals. As the ensemble is increased to a size of two, the PF immediately attenuates, and continues to do so with increasing size. This occurrence may suggest a handful of realizations. Ensemble averaging may innately filter the ‘point’ components as noise, meaning that any component that manifests consistently at very specific frequency may be attenuated. This is weakly backed-up by harmonic component attenuation, however that does not occur at a consistent manner to PF attenuation, and by the local spectrum about the PF. The content about the PF is filtered, however is not disproportionately attenuated, supporting this theory. Outside of the the device frequency content, the mainband components maintain shape, and roughly converge to the raw signal (unaveraged) spectrum magnitudes (top left plot of Figure 3-11).

These spectrum characteristics are consistent across the in vitro data. The PF and related harmonic content is diminished however the mainband content is comparatively unaltered. Additionally, when examining the area under the curve for the averaged signal spectrums the area does appear to consistently follow a decaying exponential trend, as in the area asymptotes with increasing ensemble size.

In examining the in vivo signal frequency component averages, not only can the
Figure 3-11: Frequency content of in vitro signal after varying ensemble size unscaled averages. Circles in indicate three most significant components of the individual cycles. BPM state is 78 BPM.

difference between the scaled and unscaled averages be seen, but a clear deviation from the optimal SNR filter (3.18) can be quantified. While the PF and harmonic content is similarly attenuated and the mainband magnitudes show asymptotic behavior, the mainband content is somewhat magnified, or at least inconsistently with respect to the in vitro manifestation of the mainband. While not necessarily a nonlinear filter effect, this does suggest that lower frequency content converges at a slower rate than higher frequency content. Specifically in this case, in order to approximately achieve the magnitudes of the raw signal spectrum compiled from 16 cycles, requires an ensemble size of 64 cycles. Unlike the phenomenon seen with the PF and harmonic content, the entirety of the mainband content appears to consistently magnify/attenuate. Although this is true, the ‘area under the curve’ metric as a function of ensemble size does asymptote as with the higher frequency in vitro signal averages, indicating some optimal filtering characteristics.

Although showing some linear filter characteristics, ensemble averaging is a non-
Figure 3-12: Frequency content of in vivo signal after varying ensemble size unscaled and scaled averages. Circles indicate three most significant components of the individual cycles.

Linear transformation. Asymptotic behavior of the signal spectrum shape implies that the resulting signal is stable, however the rate at which the routines converge to relatively invariant ensemble size definitions cannot be analytically quantified. Examining how the signal spectrums change as a result of algorithm and size shows that the unscaled routines exhibit more linear behavior, in the impact on the resulting averaged signal. The unscaled in vivo spectrums (Figure 3-13) achieve rough asymptotic behavior at an ensemble size of 10, whereas the scaled spectrums (Figure 3-14) require a larger size, approximately 15. Similarly, at low ensemble sizes (< 5) the scaled averages are characterized by high variation in shape exceeding that seen with the unscaled signals. These differences are believed to be resultant from resampling. Upsampling and downsampling are time-varying operations (do not commute) and so this characteristic of the operations further increases the generalized degree of nonlinearity of the averaged signal, which is most prominent at low ensemble sizes. Without prior knowledge of how the signal statistical parameters (both noise-wise and non)
change with respect to time, the full effects of ensemble averaging cannot be quantified. However, based on the empirical results, stability of the resulting signal appears to be guaranteed (assuming the PRF is correctly designed), along with the related frequency content of the signal asymptotically trending to an ensemble-size invariant shape. If the feasible ensemble size is restricted (low number of cycles), scaling is not appropriate as it has the highest chance of spectrum shape distortion at low sizes. If the ensemble size is not limited then scaling is the optimal algorithm relative to the preservation of timing and content.

Figure 3-13: Stability metrics for unscaled average of in vivo signal spectrums of Figure 3-12.
Figure 3-14: Stability metrics for scaled average of in vivo signal spectrums of Figure 3-12.

3.2 Time-Frequency Spectra Composition

From the time series definition of the SA acoustic and EKG signals, the specific cardiac cycle intervals can be inferred. Using the EKG as a reference this is elementary, however the QRS complex peak acoustic is characterized by increased magnitude oscillations, as seen in healthy heart sounds of non-VAD patients (Figure 1-2). By analyzing the effects of scaling on the EA signals, select R wave components are able to be identified in the related frequency domain definitions of said signals, however in general there is no general visual correlation that can be determined.

Specific events in the cardiac cycle are known to elicit specific resulting sounds. In the event of occlusion we expect some quantifiable event to indicate that such
has occurred, which would then manifest as an observable sound. Due to the non-stationarity of the cycle, along with the lack of time resolution in the frequency domain, or the lack of frequency resolution in the time domain, the identification of specific events is not possible. Identification of such requires a signal definition with both time and frequency resolution so that specific signal components can be discerned from the adjacent space which would otherwise create bias and redundancy. When considering only two conditions, such a resolute definition may not be required [28] however a clearly emanating bias/trend cannot be assumed for every malcondition. Similarly, compounded issues may manifest uniquely, in which case having both time and frequency resolution would be helpful in parsing condition.

A common technique historically used for time-frequency definition of signals is the short time Fourier transform (STFT). As the name would imply, the transform like the Fourier transform provides frequency information about a signal, however over a short time interval, by decomposing a signal into a trigonometric basis. Thus by compiling many iterations of the transform, a resulting time-frequency definition is determined.

\[
STFT \{x(t)\} (\tau, \omega) \equiv X(\tau, \omega) = \int_{-\infty}^{\infty} x(t)w(t - \tau)e^{-j\omega t} dt \tag{3.20}
\]

where:
\(x(t) = \text{original time series signal}\)
\(t = \text{time variable}\)
\(\omega = \text{frequency variable}\)
\(\tau = \text{translation parameter}\)
\(w = \text{window function}\)

The STFT utilizes a translated windowing function to achieve specific frequency resolution at a given time instance. The wider the window, the greater the frequency resolution, at the cost of time resolution. The narrower the window, the greater the time resolution at the cost of frequency resolution. This trade-off is the result of the
frequency discretization of the window function. Given a window of \( N \) length and sampling rate \( f_s \), the frequency discretization is defined as \( f_s/N \). Thus the only way to improve frequency resolution is to increase window length, resulting in fewer samples per unit time. Over specific intervals this trade-off may not be significant, however when concerning the entirety of a signal results in skew resolution. This is specifically important to this work as potential indicating components, of wide ranging conditions, may appear at any region of the spectra. With that being the case it is important to generate a time-frequency representation with consistent resolution across the space it defines.

The STFT utilizes a constant length window function to define a fixed frequency resolution, which was shown to limit time resolution. Given an additional transformation variable, multi-resolution analysis of the signal can be achieved as is done with the continuous wavelet transform (CWT). The CWT operates on a similar principle as the STFT, in that it decomposes a signal into a basis set, however the CWT does so without a window function, 3.21. Instead, the CWT utilizes a modulated scalable window to achieve multi-resolution across a signal,

\[
CWT \{x(t)\} (a, b) \equiv \gamma(a, b) = \frac{1}{|a|^{1/2}} \int_{-\infty}^{\infty} x(t) \tilde{\psi} \left( \frac{t - b}{a} \right) dt \tag{3.21}
\]

where:
- \( x(t) = \) original time series signal
- \( t = \) time variable
- \( a = \) scaling variable
- \( b = \) translation variable
- \( \tilde{\psi} = \) mother wavelet complex conjugate
- \( \gamma(a, b) = \) wavelet coefficients

Whereas the window function of the STFT is dependent only on the translation parameter, the mother wavelet is both translated and scaled, to produce the daughter wavelets that are convolved with the objective signal. The mother wavelet is not an
explicit function, there are several potential basis functions for such, however this then means that the coefficient matrix of the transform is uniquely dependent on the choice of basis function. To be a valid basis function the mother wavelet must satisfy,

\[ \text{Admissibility} : \quad \int \frac{|F\{\psi(t)\}|^2}{|\omega|} d\omega < \infty \quad (3.22) \]

\[ \text{Zero Frequency} : \quad |\psi(\omega = 0)|^2 = 0 \quad (3.23) \]

\[ \text{Time Domain Zero Mean} : \quad \int \psi(t) dt = 0 \quad (3.24) \]

\[ \text{Regularity}^* : \quad \gamma(a,0) \text{ decays at } a^{n+2} \quad (3.25) \]

where: \( F\{\} = \text{Fourier transform} \)

Admissibility states that the frequency normalized \( L^2 \) norm of the of the basis Fourier transform is finite. By restricting the basis as such guarantees that the signal can be reconstructed from the coefficient matrix without loss of information. While not entirely obvious the zero frequency condition implies that wavelets have a band-pass like spectrum. In order to have finite frequency content the spectrum must inflect upwards (and subsequently downwards) an arbitrary distance from \( \omega = 0 \). As the basis is a set of transformed wavelets, the transform can be thought of as an iterated filter bank (in actuality a constant-q filter bank). Time domain zero mean implies the basis function must oscillate, and thus is a wave. Whereas the previous set of conditions are straightforward, regularity is a very complex condition. Regularity is essentially the smoothness of the wavelet, and is important for both frequency resolution and convergence properties.

Expanding the CWT about \((t = 0, b = 0)\) up to order \( n \),
\[
\gamma(s, 0) = \frac{1}{\sqrt{s}} \sum_{p=0}^{n} x^p(0) \int \frac{t^p}{p!} \psi(s^{-1}t) dt + O(n + 1) \quad (3.26)
\]

where: \( x^p = p^{th} \) order derivative of \( x \)

\( O = \text{remainder of expansion} \)

The moment of the wavelet, \( M_p \), is then defined as,

\[
M_p = \int t^p \psi(t) dt \quad (3.27)
\]

Substituting 3.27 into 3.26 yields,

\[
\gamma(s, 0) = \frac{1}{\sqrt{s}} \left[ x(0)M_0s + \frac{x'(0)}{1!} M_1s^2 + \frac{x''(0)}{2!} M_2s^3 + ... + \frac{x^n(0)}{n!} M_n s^{n+1} + O(s^{n+2}) \right] \quad (3.28)
\]

From the admissibility condition 3.22, \( M_0 = 0 \). Thus if the moments up to \( M_n \) are set to zero, (3.25) results. This principle, known as vanishing moments, defines the order of the transform - i.e. if the wavelet has \( N \) vanishing moments, the approximate order of the transformation is \( N \). As the number of vanishing moments increases, so does the smoothness of the basis, resulting in decreased localization at high frequencies (fine resolution at low frequencies, more broad resolution at high frequencies).

Although the CWT offers improved resolution over the STFT [generally] there are three issues with it,

1. Redundancy
2. Shift Variance
3. Computational Resources

The transform maps a 1-D signal to a highly redundant 2-D space continuously. To limit the transform the mother wavelet is discretized such that the scale (and by
result frequency) is dyadic. The discretization of the basis function is similar to the effect of vanishing moments, in that the dyadic discretization causes fine localization at high scale (low frequency) and decreased localization at decreasing scale.

While the discretization of the basis function makes the transform practical, it also causes the transform to become shift variant, meaning that the transform output depends on when the input occurs. Although this is potentially very problematic, as the application of SA improves the overall consistency of the ensemble pool it is assumed that shift variance is minimized as a result of a consistent relative initial reference. If this were to be found erroneous, then there are alternative wavelet routines that aim to increase transform shift invariance available, however are not considered in this work.

The most problematic issue of the transform is by far the resources required to perform it. Both the STFT and CWT are defined by $n^2$ transformation variables, an interesting parallel to non-stationary signal statistical definitions. Unlike the STFT, where the window modulates, the mother wavelet both modulates and scales. The scaling function is inherently problematic as an infinite number of scales is required to analyze to a frequency of zero (dyadic scale backwards from Nyquist). If finer scale information is required, then the cost of such is increased processing. To mitigate this the scale is redefined as a function, where each scale can be expressed in terms of translated smaller scales up to scale $j$, however due to this resolution is lost at the terminally highest scale proportional to the spectrum width of the scaling function (wider bandwidth means less computation but worse resolution and vice-versa). For this work, the ensembles are averaged to reduce non-stationarities, however it also suggests that the resulting signals are of increased value, i.e. classification requires less individual training states (averages, cycles, etc.). Thus the cost associated with multi-resolution is traded-off with the inherent benefit of the ensemble averaging.

Spectral generation is performed in MATLAB, restricting the choice of CWT basis functions - without considering strictly orthogonal or biorthogonal wavelets. A Morlet basis was used based on its existing application in heart sound analysis [15]. The Morlet basis is essentially a Gaussian windowed sine wave and so it parallels to
the trigonometric basis of the STFT and related Fourier techniques.

Performance of the CWT is primarily dictated by the design of the scale, \( a \) as translation is determined respective of the sampling rate (Minimum time discretization). From the scale, the frequency discretization ultimately results and so through careful design an optimal frequency spectrum is designed. Through the zero frequency condition of the transform, the wavelet basis has a bandpass like spectrum. Now considering the scale discretization, the basis will essentially produce a bandpass filter bank given the design parameters. This filter bank must be carefully designed as to be inclusive of signal components, at a suitable resolution/discretization, without being heuristically resource intensive. Given this, three parameters must be designed for: minimum bandpass center frequency (CF), maximum bandpass CF, and the discretization of the filter bank.

The in vitro data spectrum approximately spans 20-1000 hz and so the filter bank must have this minimum bandwidth. Both the minimum and maximum CFs of the filter bank result from the energy spread of the basis function, the Morlet wavelet. The maximum CF, \( \omega_x \), is modulated by the termination, cutoff percentage, of the lowest scale wavelet at the Nyquist frequency. Increasing the cutoff moves the CF towards the Nyquist, and so by decreasing the cutoff the maximum CF can be decreased. The minimal scale, \( a_0 \) is then defined by that CF,

\[
a_0 = \frac{\omega_x}{\pi} \tag{3.29}
\]

The maximum scale, \( a_{\text{max}} \), corresponding to the minimum CF, is defined by 3.30. Whereas minimum scale depended only on wavelet propagation, the maximum scale is relative to several parameters, making the maximum scale unique to each signal analyzed. Increasing the standard deviation of the wavelet in time causes the minimum CF to increase as well, thus so long as the the minimum CF is less than the 20 hz boundary we use the maximum standard deviation to generate the maximum scale. For example, given a signal of length 9551 samples, a wavelet standard deviation of 14 places the minimum CF at 19.7 hz, satisfying the minimum frequency requirement.
The resulting filter bank is given in Figure 3-15.

\[ a_{\text{max}} = 2^{\text{floor}(NV \log_2(\frac{N}{\sigma_0^2}))} \]  

(3.30)

where:  
- NV = voices per octave  
- N = signal length (samples)  
- \( \sigma_t \) = standard deviation of the wavelet in time

The discretization of the transform is given by NV. Increasing the voices per octave likewise increases the discretization quantity resulting in higher resolution, however increased computational cost. As can be seen by Figure 3-15 the density of the filter bank increases with decreasing frequency (increasing scale) as the scale

Figure 3-15: Morlet wavelet filter bank used to generate the spectra for the in-vitro acoustics.
Figure 3-16: Morlet wavelet increased resolution filter bank used to generate the spectra for the in-vitro acoustics.

is dyadic and propagates from the minimum scale (highest frequency). By limiting the scale to the minimum bandwidth, specifically the maximum scale, the range of frequencies (octaves) to discretize over is decreased, allowing for increased voices without impractical processing cost. The filter bank given in Figure 3-15 is discretized by 10 voices per octave. Increasing the voices to 40 yields the filter bank of Figure 3-16. Resolution is crucial in identifying events for the purpose of prognostics and so a moderate 20 (feasible range is 4-48) voices are used in all spectral generations - concerning both the in vitro and in vivo acoustics.

The scale is designed similarly for the in vivo data. Since the in vivo data is characterized by different properties and spectrum elements the resulting filterbank is different from that produced when analyzing the in vitro acoustics. The in vivo data is notably characterized by lower frequency components and so the maximum
Table 3.2: Wavelet scale parameters used in spectra generation.

<table>
<thead>
<tr>
<th>Data Type</th>
<th>Parameter</th>
<th>Value</th>
<th>Affected Scale Parameter</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitro</td>
<td>Cutoff</td>
<td>1</td>
<td>Minimum Scale</td>
</tr>
<tr>
<td>Vitro</td>
<td>Standard Deviation</td>
<td>highest such that CFmin &lt; 20</td>
<td>Maximum Scale</td>
</tr>
<tr>
<td>Vitro</td>
<td>Voices per Octave</td>
<td>20</td>
<td>Scale Discretization</td>
</tr>
<tr>
<td>Vivo</td>
<td>Cutoff</td>
<td>1</td>
<td>Minimum Scale</td>
</tr>
<tr>
<td>Vivo</td>
<td>Standard Deviation</td>
<td>2</td>
<td>Maximum Scale</td>
</tr>
<tr>
<td>Vivo</td>
<td>Voices per Octave</td>
<td>20</td>
<td>Scale Discretization</td>
</tr>
</tbody>
</table>

scale of the transform must be comparatively higher than that of the in vitro specific transformation. The parameters used in generating wavelets for both types of acoustics are provided in Table 3.2.

In order to resolve localized signals the basis function is constrained such that it vanishes outside of a specified time frame, called the support of the wavelet. This is problematic near the time boundary of the signal, as no frame exists or which the wavelet to propagate and so to implement the algorithm the frame is padded with zeros. This causes discontinuities within these regions that impact the fidelity of the transformation. The degree to which this occurs increases with increasing scale, producing a region where these "edge" effects are most prominent, and thus the transformation coefficients are characterized by increased error. The boundary that separates the high error region is called the cone of influence (COI). As this work is interested in the identification of timed events, the input signal must be formed such that the events will fall inside of the COI, where there is no impact from edge effects. The COI boundary directly scales with transformation scale, making the CWT very restrictive to low frequency signals.

Derived spectras of both the faulted and unfaulted in vitro acoustics (similar boundary conditions) are given in Figures 3-17 and 3-18. The overlayed black lines of each spectra indicate the COI boundary.

 Derived spectras of both the faulted and unfaulted in vitro acoustics (similar boundary conditions) are given in Figures 3-17 and 3-18. The overlayed black lines of each spectra indicate the COI boundary.

From the spectras several things can be identified. The first of which is the lack of a defined harmonic band. Due to the constant process frequency of the simulator scaling is not applied and so the harmonic band would be expected to manifest, however this is not the case. What appears to occur is that due to the placement of the stethoscope the spectras exhibit characteristics as if they were determined from
Figure 3-17: Time-frequency spectra comparison between faulted and unfaulted in vitro acoustic signal at a state of 106/62 mmHg at 57 BPM with HM2 at 9200 RPM. Black line indicates COI boundary.

scaled physiological sounds. While not important it does lend support to the occlusion orientated position of the stethoscope in reference to the in vitro simulator.

In section 2.3 it is discussed that event timing is dependent on the state of the device (MAP). Figures 3-17 and 3-18, being of consistent states, provide a more detailed analysis of this. At this point it should be noted that the time-frequency images presented are normalized to their respective maximum intensity (magnitude). Subsequent processing of the images maintains this normalization and so consistent states are not normalized to a consistent intensity scale. This normalization occurrence is revisited in the following section.

The time scale of Figures 3-17 and 3-18 are normalized to a [0 1] scale for consistent referencing of the timing at which components occur. A normalized time of 0
Figure 3-18: Time-frequency spectra comparison between faulted and unfaulted in vitro acoustic signal at a state of 106/62 mmHg at 78 BPM with HM2 at 9200 RPM. Black line indicates COI boundary.

and 1 indicate the beginning of systole (end of diastole) while a normalized time of .5 indicates the end of systole (beginning of diastole). With the phase partitioned as such, intensity peaks in [0 .5] are attributed to systole (S1 sounds) while those occurring in [.5 1] are attributed to diastole (S2 sounds). Considering the 57 BPM state spectra (Figure 3-17) both the S1 and S2 sounds are identifiable. In the unfaulted signal the S2 is subtly present about $t_{\text{norm}} = .8$ however when faulted becomes much more prominent and occurs later. The S1 component also occurs later in systole when faulted, however is characterized by reduced energy spread about its occurrence. The faulted intensity scale is greater than that of the healthy spectra intensity scale and so faulting resulted in a definitively stronger spectral events.

The unfaulted 78 BPM spectra (Figure 3-18) correlates to the unfaulted 57 BPM
spectra in two primary ways. In comparing the S1 to S2, the S1 components are relatively more intense. The S1’s of both healthy BPM states are also characterized by more significant energy spreads (compared to their respective faulted S1’s). When faulted the 78 BPM state spectra deviates from the trends seen with the 57 BPM state spectra. Whereas faulting the 57 BPM state delayed sounds, faulting the 78 BPM state appears to hasten the S1 occurrence. Also inconsistent to the 57 BPM state, the S2 of the faulted 78 BPM state either appears to have [comparatively] disappeared or has shifted into the component assumed to be the S1. Additionally, the S1 region of the faulted 78 BPM state lies right at the boundary of the COI, meaning that if the entire S1 were desired for analysis, then the signal would have to be altered in a way that shifts the S1 inward. This can be done by partitioning the signal with cycle overlap, however this will change the energy spread of the signal since the transform is shift variant. As such the signals of the in vitro are not modified with any additional content, termed "padding".

Examining the spectra of the in vivo signal determined from SA (Figure 3-7) an immediate issue is noticed. The S1 sound (located about the $t_{norm} = .1$ region) lies on the COI boundary, which occurs for several reasons. The mainband of the in vivo data, 0-50 hz, spans lower frequencies than the in vitro generated signals. Due to this shift, the in vivo data is more prone to COI effects as the COI scales with transform scale (increases at low frequency). If the in vivo S1 were shifted up to the mainband of the in vitro signal, most of the signal would lie outside the COI, however some content would remain influenced, as was the case with the faulted 78 BPM state S1. Additionally, the S2 of the in vivo signal occurs much closer to the S1 ($t_{norm} = .4$ roughly) that was generated in vitro - indicating a deficiency of the simulator. The signal peak seen at $t_{norm} = .85$ appears to be part of the S1 that was truncated off, however exact determination of this cannot be made based on Figure 3-19 due to the COI edge effects altering the signal. In order to better examine the signal, the in vivo data is padded to such that a complete cycle lies outside of the COI boundary. This is done so by padded each end of the signal with a 40% overlap to the adjacent cycle. This data is not further evaluated, and so the overlap was chosen based purely on a
Figure 3-19: Time-frequency spectra of LVAD patient acoustics collected at the aortic site. Device is the HM2 (9400 RPM), and the ensembling method is SA. Signal period is limited to one cycle.

value that would appropriately relocate the components.

After padding the S1 is fully outside of the COI, and enough padding was added such that the next adjacent S1 lies outside the COI (Figure 3-20). The reduction in edge effects is apparent when comparing S1s, while the spectra originally outside of the COI is unchanged. What is most important from this spectra (Figure 3-20) is the comparison between S1 events. The events are identical, indicating that the SA algorithm perfectly aligned the signal with no misalignment error propagation occurring. When examining the same spectra derived from varying degrees of UA, and BUA (Figure 3-21) the benefit of SA over all unscaled algorithms is confirmed. The UA spectra shows no signs of the second S1 proving that error has significantly propagated away from the sync point (EKG reference). When restricted to 2% deviation the S2 begins to manifest however more closely resembles the UA signal. At a .5% restriction the second S1 becomes more visible, however the ensemble has been reduced so much (73 to 13 cycles) that the entire spectra is altered from the ensemble reduction. The UA algorithm maintains the most prominent PF band while both BUA routines
increasing degrade it. The UA signal is also characterized by the least noise across the spectra due to the largest ensemble being utilized for filtering. As the ensemble is parsed down to align the cycles more closely, the reduction in ensemble size also reduces the innate filter that ensemble averaging results in. The traces of which are most noticeable in the 32-512 hz band.

Because of the bandwidth of the in vitro acoustics the majority of the signal is able to avoid influence from the COI. If the in vitro acoustics were characterized by the same bandwidth as the in vivo sound additional analyses would be necessary to determine spectral padding, however at this point remains unnecessary given the shift variance of the algorithm. Using the SA routine, extremely high fidelity spectras are achievable, from which events can be easily identified, although not consistently. The lack of S2 manifestation in the faulted spectra of Figure 3-18 is concerning as it is a clear deviation from the signal components expressed in the in vivo spectra.

A potential explanation for the omission of the S2 (along with timing variation) is
Figure 3-21: Time-frequency spectra of LVAD patient acoustics collected at the aortic site. Device is the HM2 (9400 RPM), and the ensembling method is both UA (top) and BUA (middle and bottom). Signal period is extended to an additional 80% of the ensemble mean to show error propagation of the S1.

the location of the stethoscope. The occlusion element is implemented down the graft line of the VAD, meaning that there is a time delay between when water exits the
VAD and enters the blockage element. Along with the phase dependence on state, the timing delay may also depend on the state. Coupled together these two characteristics could feasibly create a very nonlinear relationship between sound timing and state, one of which could cause sound omission, relocation, and potentially generation nonlinearities and non-stationarities. Acquiring acoustics at the obstruction site followed a diagnostic reasoning - probe at the expected fault site however given this finding a more immediate location is also examined to determine if the location affects the observed event timing.

When acquired directly at the VAD, the in vitro acoustic spectra is significantly different from the obstruction based spectra. The first observation is that the PF band is one of the two most prominent components, the other being the S1 sound located about $t_{\text{norm}} = .25$. The other observation is made after comparing several same pressure state healthy-faulted data sets. Even though the sample set is statistically insignificant, there appears to be a potential indicator of condition present. Across 12 same state tests of varied condition, the S1 component occurs earlier in 10 of the 12 spectras. While a striking observation, this occurrence was not further studied due to time constraints and due to the contour of the spectra at this location. The spectra is characterized by a prominent PF band and shows no signs of an S2, both of which conflict with the in vivo spectra. To remain consistent with the in vivo acoustics, sounds are not further collected at the VAD surface, however should there be a location on the body which manifests sounds similar to this, further testing at the VAD surface would be strongly merited. This may potentially occur if sounds are acquired directly at the VAD surface of a patient, rather than at the valvular auscultation sites.

### 3.3 Feature Generation

In the time domain, the S1 and S2 of both the in vivo and in vitro acoustics can be generally identified by the two highest magnitude waves/components of the cardiac cycle. While generally holding true, it is also seen in Figure 2-21 that this varies
Figure 3-22: Time-frequency spectra of in vitro LVAD acoustic acquired at VAD surface. Signal is averaged using UA algorithm. VAD is operating at 9400 RPM at a state of 107/63 mmHg at 78 BPM.

depending on both state and health (unfaulted/faulted) for the in vitro data, for which the health relationship correlates to Figure 1-2 for physiological sounds (cannot confirm the state correlation). In the frequency domain the simulated acoustics are characterized by the dual peak components shown in Figures 2-19 and 2-20, which differs from the singular peak seen in the respective in vivo spectrums. Using the time-frequency domain representation resultant from the CWT, not only are the S1 and S2 defined by intensity peaks, the localization and energy spread of the events are shown - which can be leveraged for classification.
Due to the timing dependence on state it is impossible to identify a consistent region in the signal spectra, called the region of interest (ROI), which across the HMAPR indicates a condition change (healthy vs. faulted). Each state of the system manifests uniquely in the resulting spectra in the form of energy spreads, preventing visual discernment of indicators from state dependent components, variation components, etc. Given the inability to manually determine indicators or the ROI, the location of the indicators relative to consistently identifiable events of the signal/spectra are assumed.

When parsed by the trigger signal, no additional cycle data is partitioned onto the ensemble averaged in vitro signal in order to eliminate the potential shift variance effects of the CWT. As a result of this, not all of the resulting cycle spectra can be used due to the transform edge error propagation (defined by the COI). The choice of non-partitioning also has the effect of maintaining a relative time reference frame across the ensemble averages. When normalized to a [0 1] space, the endpoints, 0 and 1, indicate trigger peaks, or physically the end of diastole/beginning of systole. The midpoint of the scale, .5 indicates the end of systole/beginning of diastole. If each ensemble were partitioned with additional data, assuming each ensemble is not of the same length and period, the only phase change that could be consistently identified is the end of systole if the partitioning is symmetric (equal amounts at each endpoint).

The identification of phase is significant because at minimum the spectra can be analyzed in terms of systole and diastole independently rather than its entirety. If not for edge effects the normalized time frames of systole and diastole would be [0 .5] and [.5 1] respectively. To avoid edge error propagation the the frequency frame of the ROI must first be determined so that the maximum COI effect can be quantified. As discussed when generating the wavelet coefficient matrix, edge effects become more significant with increasing scale. Thus, as with the case with the in vivo spectra, as the scale increases more of the signal becomes corrupted. To maintain the widest time frame possible, the lowest frequency of the ROI must be maximized such that the COI does not impact significant content. The mainband of the in vitro data is defined by the bandwidth of 50 hz to 150 hz, and so this is used to bound the ROI. The ROI
must inclusive of this bandwidth and so the highest dyadic integer that is inclusive of
this region (32 hz) is chosen as the lower bound. The relationship between COI and
wavelet basis is complex, depending on basis support (propagation) along with the
transform variables. Analytically defining the COI boundary for a desired frequency
is difficult. This value is instead found empirically by generating the COI for multiple
BPM data sets. The COI is seen to increase (in restriction) with increasing BPM so
by analyzing the 78 BPM data the maximum boundary of the COI is determined. At
a frequency of 31.94 hz a maximum COI normalized time boundary of .0546 results,
which then is rounded down to .05 for computation.

With the COI boundary identified, the respective phase time frames are modified
as the COI restriction is symmetric about the spectra time scale midpoint (another
reason for no partitioning). The ROI minimum frequency bound is constrained to
be 32 hz in the COI analysis, leaving only the ROI maximum frequency bound to
be determined. The maximum bandwidth of the mainband is defined as 150 hz, at
which point the PF band of the HM2 occurs for the in vitro tests. As shown in
the spectrums of Figure 3-10 and the time-frequency spectras of Figures 3-17 - 3-18
ensemble averaging results in a warped PF band. The degree to which this occurs
is assumedly related to the degree of misalignment (in unscaled algorithms) or the
degree to which the data was resampled and shifted (in scaling algorithms). To avoid
introducing this inconsistency into the ROI the maximum frequency of the region is
bounded at maximum to be 150 hz.

Using the phase bounds as defined above five ROIs are defined, as given in Table
3.3. The first region, ROI 1, is the performance benchmark of the others, being
that it is only frequency bounded (time bounded only by COI restriction, not by
any empirical/theoretical significance). ROI 1 is expected to perform the worst of
any region, in determining condition as it is the largest, which makes its derived
parameters prone to influence from redundant space. Both ROI 2 and 3 (Figure
3-23) are specific to systole and diastole respectively, which eliminates parameter
biasing from the adjacent phase. These regions can further be decomposed however
requires event timing analysis, which is how ROI 4 and 5 are determined.
Table 3.3: ROI boundaries developed from phase and sound occurrence.

<table>
<thead>
<tr>
<th>ROI ID</th>
<th>Minimum Time [-]</th>
<th>Maximum Time [-]</th>
<th>Minimum Frequency [Hz]</th>
<th>Maximum Frequency [Hz]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>.05</td>
<td>.95</td>
<td>32</td>
<td>150</td>
</tr>
<tr>
<td>2</td>
<td>.05</td>
<td>.5</td>
<td>32</td>
<td>150</td>
</tr>
<tr>
<td>3</td>
<td>.5</td>
<td>.95</td>
<td>32</td>
<td>150</td>
</tr>
<tr>
<td>4</td>
<td>.1</td>
<td>.4</td>
<td>32</td>
<td>150</td>
</tr>
<tr>
<td>5</td>
<td>.7</td>
<td>.95</td>
<td>32</td>
<td>150</td>
</tr>
</tbody>
</table>

To determine the regions within ROIs 2 and 3 in which the S1 and S2 most frequently occur the timing of when the peak signal value occurs in systole and diastole are examined. Given a low simulated heart rate the data trends linearly with pressure, with both the S1 and S2 occurrence converging to the beginning of systole (Figure 3-24). There isn’t a necessarily clear differentiation between faulted and healthy sound occurrences, however faulted sounds may appear to occur earlier than healthy sounds. When the simulated heart rate is increased this trend, while it still roughly exists, is characterized by increased deviation and outliers, occurrences which span a greater

Figure 3-23: Phase ROIs (2 and 3) parsed from in vitro generated acoustic spectra of state 106/62 mmHg at 57 BPM. Note the image intensity scale normalization effects of parsing.
time range, and S2 sounds that occur at the very end of diastole (Figure 3-25). When examining the remaining two test sets (57 and 67 BPM) the S2 timing appears to roughly scale with heart rate (increasing rate yields later occurring sounds). Occurrence deviation on the other hand does not follow such a trend. The approximated boundaries of the sounds occurrences are provided in Table 3.3.

S1 sounds are generally limited to the space of [.1 .4] while the S2 most commonly occurs within [.7 1]. Even though the sounds primarily lie within these regions there are non-outlier instances of sounds occurring outside of these bounds, most typically with the 78 and 57 BPM data sets, about the COI restricted boundaries. As a result, the ability to classify the condition of those points may be affected as their occurrences cannot be leveraged, unless the region is augmented with another in which condition can be discerned, without skewing the existing classification potential of the original region.

The ROIs are 2D mappings of the objective signal, they can be converted into images from which statistical parameters can be computed, resulting in the classification features. The ROIs are each converted into a grayscale image and a binary

Figure 3-24: In vitro occurrence of S1 and S2 sounds at 47 BPM. Pressure axis in normalized by systolic pressure.
Figure 3-25: In vitro occurrence of S1 and S2 sounds at 78 BPM. Pressure axis in normalized by systolic pressure.

A (black and white) image as each has specific parameters that can be extracted. From the grayscale image 13 texture based parameters are extracted while 18 shape based parameters result from the binary image. Table 3.3 provides all image based features extracted. The compiled vector of all 31 parameters is called the feature vector, and is used as the input to the classifier. The individual parameters are computed using the "regionprops" algorithm in MATLAB in which the provided listed parameters are numerically computed for images.

When parsing the spectra into the five ROIs, each resulting matrix image is re-normalized according to the maximum element of the parsed ROI matrix. Due to this the resulting ROI image (and eventual grayscale/binary) differs in appearance from

Table 3.4: Summary of boundaries of S1 and S2 occurrences for test data set simulated heart rates. Boundaries are approximated to omit outlier points.

<table>
<thead>
<tr>
<th>Heart Rate [BPM]</th>
<th>S1 Occurrence Minimum Bound [t/tmax]</th>
<th>S1 Occurrence Maximum Bound [t/tmax]</th>
<th>S2 Occurrence Minimum Bound [t/tmax]</th>
<th>S2 Occurrence Maximum Bound [t/tmax]</th>
</tr>
</thead>
<tbody>
<tr>
<td>47</td>
<td>.1</td>
<td>.35</td>
<td>.7</td>
<td>.95</td>
</tr>
<tr>
<td>57</td>
<td>.1</td>
<td>.4</td>
<td>.7</td>
<td>1</td>
</tr>
<tr>
<td>67</td>
<td>.125</td>
<td>.35</td>
<td>.8</td>
<td>1</td>
</tr>
<tr>
<td>78</td>
<td>.1</td>
<td>.4</td>
<td>.8</td>
<td>1</td>
</tr>
</tbody>
</table>
Table 3.5: Parameters extracted from images of ROI.

<table>
<thead>
<tr>
<th>ID</th>
<th>Parameter</th>
<th>Type</th>
<th>Image</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Mean</td>
<td>Texture</td>
<td>Grayscale</td>
</tr>
<tr>
<td>2</td>
<td>Standard Deviation</td>
<td>Texture</td>
<td>Grayscale</td>
</tr>
<tr>
<td>3</td>
<td>Skewness</td>
<td>Texture</td>
<td>Grayscale</td>
</tr>
<tr>
<td>4</td>
<td>Kurtosis</td>
<td>Texture</td>
<td>Grayscale</td>
</tr>
<tr>
<td>5</td>
<td>Contrast Mean</td>
<td>Texture</td>
<td>Grayscale</td>
</tr>
<tr>
<td>6</td>
<td>Correlation Mean</td>
<td>Texture</td>
<td>Grayscale</td>
</tr>
<tr>
<td>7</td>
<td>Energy Mean</td>
<td>Texture</td>
<td>Grayscale</td>
</tr>
<tr>
<td>8</td>
<td>Homogeneity Mean</td>
<td>Texture</td>
<td>Grayscale</td>
</tr>
<tr>
<td>9</td>
<td>Contrast Range</td>
<td>Texture</td>
<td>Grayscale</td>
</tr>
<tr>
<td>10</td>
<td>Correlation Range</td>
<td>Texture</td>
<td>Grayscale</td>
</tr>
<tr>
<td>11</td>
<td>Energy Range</td>
<td>Texture</td>
<td>Grayscale</td>
</tr>
<tr>
<td>12</td>
<td>Homogeneity Range</td>
<td>Texture</td>
<td>Grayscale</td>
</tr>
<tr>
<td>13</td>
<td>Entropy</td>
<td>Texture</td>
<td>Grayscale</td>
</tr>
<tr>
<td>14</td>
<td>Area</td>
<td>Shape</td>
<td>Binary</td>
</tr>
<tr>
<td>15</td>
<td>Centroid X</td>
<td>Shape</td>
<td>Binary</td>
</tr>
<tr>
<td>16</td>
<td>Centroid Y</td>
<td>Shape</td>
<td>Binary</td>
</tr>
<tr>
<td>17</td>
<td>Bounding Box X</td>
<td>Shape</td>
<td>Binary</td>
</tr>
<tr>
<td>18</td>
<td>Bounding Box Y</td>
<td>Shape</td>
<td>Binary</td>
</tr>
<tr>
<td>19</td>
<td>Bounding Box Width</td>
<td>Shape</td>
<td>Binary</td>
</tr>
<tr>
<td>20</td>
<td>Bounding Box Height</td>
<td>Shape</td>
<td>Binary</td>
</tr>
<tr>
<td>21</td>
<td>Major Axis Length</td>
<td>Shape</td>
<td>Binary</td>
</tr>
<tr>
<td>22</td>
<td>Minor Axis Length</td>
<td>Shape</td>
<td>Binary</td>
</tr>
<tr>
<td>23</td>
<td>Eccentricity</td>
<td>Shape</td>
<td>Binary</td>
</tr>
<tr>
<td>24</td>
<td>Orientation</td>
<td>Shape</td>
<td>Binary</td>
</tr>
<tr>
<td>25</td>
<td>Convex Area</td>
<td>Shape</td>
<td>Binary</td>
</tr>
<tr>
<td>26</td>
<td>Filled Area</td>
<td>Shape</td>
<td>Binary</td>
</tr>
<tr>
<td>27</td>
<td>Extreme Right Y</td>
<td>Shape</td>
<td>Binary</td>
</tr>
<tr>
<td>28</td>
<td>Equivalent Diameter</td>
<td>Shape</td>
<td>Binary</td>
</tr>
<tr>
<td>29</td>
<td>Solidity</td>
<td>Shape</td>
<td>Binary</td>
</tr>
<tr>
<td>30</td>
<td>Extent</td>
<td>Shape</td>
<td>Binary</td>
</tr>
<tr>
<td>31</td>
<td>Perimeter</td>
<td>Shape</td>
<td>Binary</td>
</tr>
</tbody>
</table>
Figure 3-26: Sound occurrence ROIs (4 and 5) parsed from in vitro generated acoustic spectra of state 106/62 mmHg at 57 BPM. Note the image intensity scale normalization effects of parsing.

how it appears in reference to the entire spectra. Given the spectra of Figures 3-23 and 3-26 the peak intensity component is located about the S1. When parsing into the individual ROIs, those that contain the S1 (ROI 2 and 4) maintain their appearance as they are intensity normalized to the same value. However when the spectra maximum is excluded from the ROI, the resulting region image is re-normalized according to its maximum intensity. This most commonly occurs when parsing ROI 3 and 5, due to the absence of the S1. Due to this the S2, if it exists in this region, becomes pronounced. This however is not considered an algorithm deficiency as ROIs are only consistently used and compared against the same ROI, i.e. ROI 2 is only compared against ROI 2 and so image normalization based on region is appropriate.

The ROI matrix is converted to a grayscale image using a discretization of 256 levels with a floor/ceiling (max minimum value) of ± 8. Each element of the matrix represents an image pixel and so the size of the image matches the matrix dimensions. The grayscale image is then used to convert to binary by determining the average gray level of the grayscale image, and using that threshold to convert to black and
white, with any conversion artifacts (random spots) being removed from the binary image. After each image is generated they are then resized due to the discretization of the wavelet coefficients. The sampling rate of the input signal (to the CWT) matches the time discretization of the coefficients and so the time axis length scales proportionally with sampling rate. The scale (and by result frequency) discretization however is dyadic and bounded specifically by the filterbank design (Table 3.2). For example, given the bounds on the S1 region, a 3343x66 matrix is formed. When converted to an image it has a 50:1 width-height ratio, skewing it and its associated parameters. To adjust for the discretization scheme the images are resized to a square \( n \times n \) pixel frame. After empirical trials, a 400x400 frame was found to be practical as further increasing the dimension did not elicit any further classification differences. It is true that resizing does affect the parameters extracted from the images, however none of the parameters are only dependent on image size, i.e. no parameter becomes redundant or obsolete from resizing. The resized grayscale and binary versions of the ROIs of Figure 3-23 and 3-26 are given in Figures 3-27 and 3-28 respectively.
Figure 3-27: Conversion of phase ROIs (2 and 3) parsed from in vitro generated acoustic spectra of state 106/62 mmHg at 57 BPM to grayscale and binary. Note the image intensity scale normalization effects of parsing.
Figure 3-28: Conversion of sound occurrence ROIs (4 and 5) parsed from in vitro generated acoustic spectra of state 106/62 mmHg at 57 BPM to grayscale and binary. Note the image intensity scale normalization effects of parsing.
Chapter 4

Results

Classification of the healthy and unhealthy data is performed using a support vector machine (SVM), with the feature vector used as the input. The SVM is a type of supervised (generally) machine learning algorithm. The algorithm essentially creates an $n-1$ hyperplane through an $n$ dimensional space such that the space from the plane to two distinct data classes is maximized. This is also called the maximum margin hyperplane. Thus when new data is introduced, it can be binned to a class depending on where it falls with respect to the hyperplane. The vectors used to directly develop the maximum margin hyperplane are called the support vectors.

Often two data sets are not linearly separable in their given space and require a more complex classification approach. When $n$ dimensional linear classification may not be possible, higher space domains ($n+$) presumably make such classifications possible. In order to do so an SVM 'kernel trick’ transforms data to a higher order space using a kernel function to reduce computational resources. The kernel function simply allows for mapped space computations to be performed in terms of the original space variables, specifically dot product computations. There are several feasible kernel functions that can be used for higher order classification, however the appropriateness of the kernel is not guaranteed for all feasible functions. The SVM is chosen over alternative machine learning algorithms as it is assumed that the acoustic feature data would be non-linearly separable, which the SVM can efficiently handle. Additionally the feature vector is relatively small, and so more complex classifiers and
machine learning algorithms are not required.

4.1 Classifier Performance

Prior to classification three model parameters must be determined along with a pre-process of the feature vector. The features that are developed from the ROIs span a large numerical range. This being the case, there is a disparity in relative parameter values. For example convex area is roughly 1,000,000 times larger in magnitude that correlation range, which if nominally used would skewly weight convex area. The feature vectors of the SVM are normalized to a [-1 1] space to standardize each parameter to equal weighting. This is consistent across all tests.

The three model parameters that must be determined are kernel function, kernel scale, and box constraint. Both kernel parameters define the function used to transform the feature space while the box constraint alters misclassification cost. The larger the box constraint the more strictly the training space is separated, requiring increased resources to do so. The choice of model parameters varies based on the ROI and feature selection resulting in several unique combinations to be determined.

Model parameters are determined through a 10 fold cross validation optimization of each unique model. In the optimization scheme the training set is randomly partitioned into 10 subsets. An SVM model is trained on 9 randomly selected subsets, while the tenth is used to test the resulting model. This is iterated ten times resulting in an average cross validation error of the model. Both the kernel scale and box constraint are optimized against this value for a given set of iterations or until parameter convergence is met. The optimization scheme used to determine the parameters is a Bayesian scheme which assumes a Gaussian process and so the final model parameter, the kernel function, is constrained to be the Gaussian kernel. While the optimization scheme permits minimal model definition a priori it also constrains the model space to the training data based on minimal cost. Because of this the classifier is expected to perform well only in instances in which the testing feature vectors do not vary from the training feature vectors space, assuming that the classification space is tightly
bounded to the training vectors. This optimization outcome is highly impractical for physiological signal classification due to the changes a patient may undergo in between classification routines, i.e. baselined at time of implantation, then tested for thrombosis several months later when the patient’s state (MAP and heart rate) has changed. In order to compare models three metrics are compiled per model validation (test), score, positive predictive value (PPV), and negative predictive value (NPV). Score is the total percentage of correct classifications while PPV and NPV are the correct healthy (unfaulted) classifications and correct unhealthy (faulted) classifications respectively. Classifier nomenclature is as follows,

1. BPMA classifier: model trained on one constant BPM
2. BPMB classifier: model trained on two constant BPMs
3. BPMC classifier: model trained on three constant BPM
4. BPMD classifier: model trained on four (all) constant BPMs

Classifiers are evaluated absolutely by their kfold error, score, PPV, and NPV. Several metrics are developed for comparisons between models derived from different ROIs. These parameters are:

1. BPMA Common Predictive Value (BPMA-CPV): average value of BPMA model scores tested with the same BPM used in training.
2. BPMA Foreign Predictive Value (BPMA-FPV): average value of BPMA model scores tested with different BPM used in training.
3. BPMD Common Predictive Value (BPMD-CPV): average value of BPMD model scores tested with constant BPM set.
4. BPMD Variable Predictive Value (BPMD-VPV): BPMD model score tested with variable BPM set.
5. BPMC Foreign Predictive Value (BPMC-FPV): average value of BPMC model scores tested with different BPM used in training.
6. BPMC Variable Predictive Value (BPMC-VPV): average value of BPMC model scores tested with variable BPM set.

These parameters are chosen to quantify several model abilities, namely the potential to classify states of which it is trained on (Common Predictive Value), the potential to classify states that it is not trained with (Foreign Predictive Value), and finally the potential to classify states similar to physiological signals (Variable Predictive Power). BPMA and BPMD are both used as they are expected to the respective worst and best performance training spaces due to their spans. The BPMC derived models are chosen to evaluate predictive performance based on how training set deviations affect performance as compared to the expected best training space, BPMD. Performance metrics for all image feature only classification iterations are given in Table 4.1.

The performance of the baseline classifiers (Table 4.1), those derived from ROI 1 image features, are found to be very dependent on the training space, as is expected. BPMA-CPV is significantly higher than BPMA-FPV with few exceptions (1.12). Given the most comprehensive training set (1.17-1.21 - BPMD) the model scores per each testing set are higher than the related BPMACPV iterations (with the 67 BPM exception again). This is an interesting finding as it was expected that the BPMA models (1.1-1.16) would result in the global highest scores. The kfold values of the models supports this assumption, however the scores do not. This is believed to stem from either the optimization scheme or the training space modification.

Due to the HMAPR variation induced during experimental testing it is likely that a portion of the testing states are not in the near vicinity of a training point (assuming same BPM sets). When the classifier is trained by this set, due to the optimization scheme the space is constrained for optimality relative to the training set, meaning that the space is constrained as tightly as permitted to the training space. Given that the test state is not in the immediate space of the training state the model results in misclassification, due to training space over-constraining. When additional states are introduced during training two possible events may occur which explain the score-kfold inconsistency. Given that the states of the training space are relatively
Table 4.1: Classification results using ROI 1 image features. Training and testing set nomenclature refers to the simulated BPM of the set.

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similar and of the same class (health condition), the optimization routine may project the sets to the same approximate space during the kernel transform resulting in both sets being used as support vectors, thus increasing the space span. The second theory essentially states the opposite of the first, when projected the states of opposite classes align resulting in the separation boundary becoming more under-constrained.

The BPMC models classify the variable set more accurately than the foreign sets (VPV > FPV) as is expected. The foreign sets are located at BPM states of maxi-
minimum margin away from the training space, thus are the worst case test sets for the BMPC models, assuming maximum margin/deviation yield maximum misclassification. Because the training data sets are discretized by 10 BPM increments, assuming uniform distribution, the variable set will be within <5 BPM of a training state over 75% of the training space, while over the remaining space will be within <10 BPM. The foreign set is consistently at the maximum margin of 10 BPM deviation and so we expect the PV of this set to be significantly lower, which it is. In reference to the BPMD models, the BPMC models perform very similarly in terms of VPV due to the additional BPM set of the BPMD model altering only the 25% 10 BPM margin to a 5 BPM margin - a relatively small change with little results. The classifiers are

Table 4.2: Classification results using ROI 2 and 3 image features. Training and testing set nomenclature refers to the simulated BPM of the set.

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slightly skewed towards PPV rather than NPV (75.7% vs. 68.9%).

When the classifier is developed from the phase specific ROIs (ROI 2 and 3) the trends previously seen in the baseline classifier become less prominent (Table 4.1). Both BPMD model (systolic and diastolic) CPV values roughly equal the BPMA-CPV values, whereas before the they had been greater. Additionally, scores derived from both phase classifiers are comparatively lower on average to the baseline classifier indicating that both phases contribute some classification ability. The diastolic classifiers are more accurate compared to the related systolic classifiers with less score deviation. The bias towards PPV remains in both phase classifiers, however due to the comparatively lower scores, the bias becomes more significant. The diastolic classifiers also performed much more accurately that the systolic models when classifying the variable data states. This is believed to occur due to the S2 timing spread being greater than that of the S1 respective of the variable BPM set, allowing the classifier to constrain to a larger space.

The S1 and S2 classifiers (those derived from ROI 4 and 5) perform generally the same as the phase derived classifiers. Both are characterized by the same bias to PPV and the S1 outperforms the S2 on average with the exception of testing against the variable test set just as was seen in comparing the phase classifiers. The S1 score metrics correlate very strongly with that of the systolic classifier, however the S2 metrics deviate from those of the related diastolic models, most notably in reference to VPV and FPV. The S2 classifier scores lower in these two categories, which is justifiable as the S2 ROI spans roughly half the time space as the diastolic ROI, meaning that the outlier points to this region cannot be used for classification. Similarly, the S1 performing better than the S2 can also be explained by the region span difference, being that the S2 ROI is reduced by 44% of the original phase whereas the S1 ROI is reduced by 33%.

Both the phase and sound classifiers share the common traits of performing significantly worse than the baseline classifier on average and having a trade-off between VPV and CPV. The reduction in spectra space clearly impacts classification potential, while trade-off implies that the diastolic phase specifically impacts classification
Table 4.3: Classification results using ROI 4 and 5 image features. Training and testing set nomenclature refers to the simulated BPM of the set.

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Table 4.4: Classification results using combined image features (ROI 2+3 and ROI 4+5). Training and testing set nomenclature refers to the simulated BPM of the set.

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Table 4.5: Classification results using combined image features (ROI 2+3 and ROI 4+5) with a discretization, n = 2. Training and testing set nomenclature refers to the simulated BPM of the set.

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<td>53.3</td>
<td></td>
</tr>
<tr>
<td>4.7</td>
<td>78</td>
<td>Variable</td>
<td>85.0</td>
<td>90.0</td>
<td>80.0</td>
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<td>Variable</td>
<td>73.3</td>
<td>73.3</td>
<td>73.3</td>
<td></td>
</tr>
<tr>
<td>4.8</td>
<td>47 67</td>
<td>3.33</td>
<td>57</td>
<td>58.3</td>
<td>100.0</td>
<td>1.7</td>
<td>57</td>
<td>46.7</td>
<td>66.7</td>
<td>26.7</td>
<td></td>
</tr>
<tr>
<td>4.9</td>
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<td>66.7</td>
<td>83.3</td>
<td>50.0</td>
<td></td>
<td>Variable</td>
<td>68.3</td>
<td>80.0</td>
<td>56.7</td>
<td></td>
</tr>
<tr>
<td>4.10</td>
<td>47 57</td>
<td>5.00</td>
<td>67</td>
<td>58.3</td>
<td>100.0</td>
<td>16.7</td>
<td>67</td>
<td>69.0</td>
<td>84.0</td>
<td>54.0</td>
<td></td>
</tr>
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<td>Variable</td>
<td>65.0</td>
<td>96.7</td>
<td>33.3</td>
<td></td>
<td>Variable</td>
<td>75.0</td>
<td>76.7</td>
<td>73.3</td>
<td></td>
</tr>
<tr>
<td>4.12</td>
<td>47 57</td>
<td>3.33</td>
<td>78</td>
<td>76.7</td>
<td>90.0</td>
<td>63.3</td>
<td>78</td>
<td>68.3</td>
<td>93.3</td>
<td>43.3</td>
<td></td>
</tr>
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<td>4.13</td>
<td>67</td>
<td>Variable</td>
<td>68.3</td>
<td>93.3</td>
<td>43.3</td>
<td></td>
<td>Variable</td>
<td>66.7</td>
<td>93.3</td>
<td>40.0</td>
<td></td>
</tr>
</tbody>
</table>

of the variable set. Given these determinations the phase and occurrence models can be seen as complimentary (systole compliments diastole, S1 compliments S2). To elicit classifiers with characteristics of the compliment set, phases ROI features are augmented together, and sound ROI features are augmented together. The phase augmented classifier is trained on the image features of ROI 2 and 3 (the phase regions), while the sound augmented classifier is trained with the image features of ROI 4 and 5 (the sound regions), resulting in training vectors of length \( n = 62 \) for each augmented classifier.

The augmented classifiers both perform better on average as compared to the models derived from either of their individual augmented ROIs. The metrics of augmented classifiers are either greater than those of the individual ROIs, or approximately the maximum of either. This lessens the bias towards PPV, however augmented models still are characterized by PV skewness. While the models are an improvement over their components, both still underperform compared to the baseline classifier (10% mean score disparity). In order to attempt to improve performance, each augmented classifier ROI is discretized. Image features are developed for each sub-ROI and subsequently compiled into the final image feature vector. Although this is the first
Table 4.6: Classification results using image features with augmented states. Comparison is made between baseline ROI and optimal found ROI. Training and testing set nomenclature refers to the simulated BPM of the set.

<table>
<thead>
<tr>
<th>ID</th>
<th>Training Set</th>
<th>Kfold Error [%]</th>
<th>Baseline Classifier (ROI) Augmented with Full State</th>
<th>Kfold Error [%]</th>
<th>Sound Augmented Classifier (n = 2 Discretization) Augmented with Full State</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Testing Set</td>
<td>Score [%]</td>
<td>PPV [%]</td>
</tr>
<tr>
<td>6.1</td>
<td>47</td>
<td>2.38</td>
<td>47</td>
<td>93.3</td>
<td>86.7</td>
</tr>
<tr>
<td>6.2</td>
<td>57</td>
<td></td>
<td>57</td>
<td>91.7</td>
<td>86.7</td>
</tr>
<tr>
<td>6.3</td>
<td>67</td>
<td></td>
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<td>75.0</td>
<td>100.0</td>
</tr>
<tr>
<td>6.4</td>
<td>78</td>
<td></td>
<td>78</td>
<td>93.3</td>
<td>96.7</td>
</tr>
<tr>
<td>6.5</td>
<td>Variable</td>
<td></td>
<td>Variable</td>
<td>90.0</td>
<td>86.7</td>
</tr>
<tr>
<td>6.6</td>
<td>57 67</td>
<td>2.50</td>
<td>47</td>
<td>75.0</td>
<td>100.0</td>
</tr>
<tr>
<td>6.7</td>
<td>78</td>
<td></td>
<td>Variable</td>
<td>86.7</td>
<td>80.0</td>
</tr>
<tr>
<td>6.8</td>
<td>47 67</td>
<td>1.50</td>
<td>57</td>
<td>70.0</td>
<td>93.3</td>
</tr>
<tr>
<td>6.9</td>
<td>78</td>
<td></td>
<td>Variable</td>
<td>88.3</td>
<td>93.3</td>
</tr>
<tr>
<td>6.10</td>
<td>47 57</td>
<td>2.67</td>
<td>67</td>
<td>43.3</td>
<td>36.7</td>
</tr>
<tr>
<td>6.11</td>
<td>78</td>
<td></td>
<td>Variable</td>
<td>70.0</td>
<td>50.0</td>
</tr>
<tr>
<td>6.12</td>
<td>47 57</td>
<td>2.67</td>
<td>78</td>
<td>88.3</td>
<td>93.3</td>
</tr>
<tr>
<td>6.13</td>
<td>67</td>
<td></td>
<td>Variable</td>
<td>86.7</td>
<td>90.0</td>
</tr>
</tbody>
</table>

Mention of ROI discretization, the phase augmented ROI is a n = 2 discretization of the baseline ROI. Although that discretization did not result in improved performance additional discretization may. A discretization of n = 2 of the augmented classifiers yield the results provided in Table 4.1. The discretization results in significantly better scores, and lower score deviations which imply less bias towards specific metrics, a good indication.

In discussing the discretization of the classifiers, the degree of discretization will be denoted by a subscore. For example phase augmented\textsubscript{2} denotes a classifier derived from the phase augmented ROI which has been discretized into two nodes, or since the phase augmented ROI was already discretized, is equivalent to baseline\textsubscript{4}.

The phase augmented\textsubscript{2} classifiers outperform the sound augmented\textsubscript{2} classifiers in every metric, including metric deviation. Even at this discretization level the classifier does not perform as well on average as compared to the baseline. The one improvement that the phase augmented\textsubscript{2} classifiers offer is an improvement in FPV, arguably the most significant parameter as it is the worst case metric. This is an interesting finding as one would expect that CPV and VPV would roughly scale with improving FPV, however they appear to do so at an decreased rate, perhaps
Table 4.7: Summary of classifier score results.

<table>
<thead>
<tr>
<th>Classifier</th>
<th>BPMA(-)CPV [%]</th>
<th>BPMA(-)FPV [%]</th>
<th>BPMD(-)CPV [%]</th>
<th>BPMD(-)VPV [%]</th>
<th>BPMC(-)FPV [%]</th>
<th>BPMC(-)VPV [%]</th>
<th>Average Metric Score [%]</th>
<th>Average Metric Deviation [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>78.75</td>
<td>49.03</td>
<td>80.42</td>
<td>85.00</td>
<td>60.84</td>
<td>80.00</td>
<td>72.34</td>
<td>14.15</td>
</tr>
<tr>
<td>Systole</td>
<td>76.25</td>
<td>43.47</td>
<td>77.92</td>
<td>48.33</td>
<td>52.92</td>
<td>47.92</td>
<td>57.80</td>
<td>15.24</td>
</tr>
<tr>
<td>Diastole</td>
<td>68.33</td>
<td>42.78</td>
<td>68.75</td>
<td>70.00</td>
<td>48.75</td>
<td>66.25</td>
<td>60.81</td>
<td>11.87</td>
</tr>
<tr>
<td>S1 Occurrence</td>
<td>79.99</td>
<td>43.75</td>
<td>80.83</td>
<td>46.77</td>
<td>50.00</td>
<td>47.50</td>
<td>58.13</td>
<td>17.38</td>
</tr>
<tr>
<td>S2 Occurrence</td>
<td>70.42</td>
<td>44.03</td>
<td>68.75</td>
<td>60.00</td>
<td>41.67</td>
<td>58.33</td>
<td>57.20</td>
<td>12.10</td>
</tr>
<tr>
<td>Phase Augmented</td>
<td>73.75</td>
<td>43.05</td>
<td>83.75</td>
<td>65.00</td>
<td>49.58</td>
<td>62.09</td>
<td>62.87</td>
<td>15.05</td>
</tr>
<tr>
<td>Sound Augmented</td>
<td>79.58</td>
<td>44.17</td>
<td>80.84</td>
<td>58.33</td>
<td>56.67</td>
<td>57.50</td>
<td>62.85</td>
<td>14.42</td>
</tr>
<tr>
<td>Phase Augmented (n = 2)</td>
<td>74.58</td>
<td>53.89</td>
<td>80.42</td>
<td>76.67</td>
<td>65.42</td>
<td>71.25</td>
<td>70.37</td>
<td>9.54</td>
</tr>
<tr>
<td>Sound Augmented (n = 2)</td>
<td>73.32</td>
<td>50.41</td>
<td>76.25</td>
<td>76.67</td>
<td>57.25</td>
<td>70.83</td>
<td>67.46</td>
<td>10.98</td>
</tr>
<tr>
<td>Phase Augmented (n = 4)</td>
<td>77.50</td>
<td>45.27</td>
<td>78.75</td>
<td>90.00</td>
<td>48.33</td>
<td>84.59</td>
<td>70.74</td>
<td>19.10</td>
</tr>
<tr>
<td>Phase Augmented (n = 8)</td>
<td>72.08</td>
<td>47.78</td>
<td>75.83</td>
<td>88.30</td>
<td>49.58</td>
<td>85.83</td>
<td>69.90</td>
<td>17.52</td>
</tr>
<tr>
<td>Phase Augmented (n = 16)</td>
<td>72.08</td>
<td>51.66</td>
<td>75.83</td>
<td>90.00</td>
<td>48.33</td>
<td>83.34</td>
<td>70.21</td>
<td>16.86</td>
</tr>
<tr>
<td>Phase Augmented (n = 32)</td>
<td>72.50</td>
<td>55.56</td>
<td>73.75</td>
<td>83.33</td>
<td>51.25</td>
<td>80.83</td>
<td>69.54</td>
<td>13.22</td>
</tr>
</tbody>
</table>
due to the relatively higher initial magnitudes. An additional level of discretization improved both augmented classifiers performances by a considerable amount, and so additional discretization levels are applied. Discretization of the only the phase augmented region was trialed due to the phase augmented classifiers outperforming the related sound augmented models. The levels are dyadically implemented, up to 32 nodes.

Additional discretization of the ROI does not yield improved results. FPV improves while the other metrics either decrease or remain constant. FPV is theorized to improve due to the appended images deconstraining the training space. When developing the ROI image it was previously shown that the image is normalized by the maximum matrix element of the region. In higher discretizations, several different normalizations are applied to the image sets resulting in increased region to region image variation which is believed to deconstain the training space. Decreasing CPV metrics support this theory as deconstraining would reduce classification potential of common states.

The baseline metric is not exceeded by any ROI selection/discretization, leaving few options. The disparity between classifiers is projected to be the result of the variation seen between unique states in combination with the natural variation of the in vitro system acoustics. Given the timing nonlinearity of the system it is believed that similar images from different states and conditions overlap with each other making identification of each impossible. In order to elicit the potential to discern similar images apart from each other, the signal state is appended to the feature vector.

Throughout this work, the state is defined by MAP and heart rate, however the full state of the signal includes ventricular pressure as well, being that it is a boundary condition of the LVAD. The full state of the signal is then defined by the following parameters: systolic aortic pressure, diastolic aortic pressure, systolic ventricular pressure, diastolic ventricular pressure, and heart rate. The SVM feature vectors are modified by the full state, resulting in the new classifier inputs. Augmentation of the feature vector is not affected by discretization nor ROI selection.
Table 4.8: Summary of state augmented classifiers trialed.

<table>
<thead>
<tr>
<th>Classifier</th>
<th>BPMA-CPV [%]</th>
<th>BPMA-FPV [%]</th>
<th>BPMD-CPV [%]</th>
<th>BPMD-VPV [%]</th>
<th>BPMC-FPV [%]</th>
<th>BPMC-VPV [%]</th>
<th>Average Metric Score [%]</th>
<th>Average Metric Deviation [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>87.92</td>
<td>50.00</td>
<td>88.33</td>
<td>90.00</td>
<td>69.17</td>
<td>82.92</td>
<td>78.06</td>
<td>14.35</td>
</tr>
<tr>
<td>Phase Augmented (n = 2)</td>
<td>76.67</td>
<td>50.00</td>
<td>93.33</td>
<td>91.67</td>
<td>78.75</td>
<td>91.67</td>
<td>80.35</td>
<td>15.07</td>
</tr>
<tr>
<td>Phase Augmented (n = 32)</td>
<td>74.59</td>
<td>50.14</td>
<td>75.42</td>
<td>81.67</td>
<td>52.08</td>
<td>79.59</td>
<td>68.91</td>
<td>12.82</td>
</tr>
</tbody>
</table>

To analyze the effects of state augmentation the baseline, phase augmented\textsuperscript{2} and phase augmented\textsuperscript{32} classifier metrics are requantified. State augmentation results in significant score improvements for both the baseline and phase augmented\textsuperscript{2} models, while the phase augmented\textsuperscript{32} performs roughly the same. Underperformance of the phase augmented\textsuperscript{32} classifier is projected to be the result of the discretization level. The high level of discretization over-dimensionalizes the feature space (n = 1984) thus augmenting by the n = 5 state vector results in little to no improvement.

Augmentation of the feature vector results in the first instance of a classifier outperforming the baseline classifier (augmented with the state). The phase augmented\textsuperscript{2} classifier outperforms the baseline in every metric other than BPMA-CPV, with the most significant improvement being the ability to correctly identify the 67 BPM states - the most closely timed states (Table 3.3). The most significant improvement attributed to state augmentation is in the ability to identify foreign and variable sets (FPV and VPV) - the most desired ability however there is now a dependence on training state variation. State augmentation constrains the space such that it requires at minimum two unique BPM training states (Referencing BPMA-FPV). When trained on a singular BPM state the classifier is completely unable to discern foreign BPM states. The BPMA-FPV metrics are the result of the models attempting to classify all points as either healthy or unhealthy (flooring/ceiling), an obvious deficiency.

To determine the scaling of the deficiency the BPMB models are examined. Once a second BPM state is introduced into the training space the FPV score increases
for both classifiers (Table 4.1). BPMA is the assumed worst training space while BPMC would be an assumed improvement over BPMB being that the BPM state range is increased. As such it would be expected that the FPV for the BPMB models would fall in-between the FPV range of BPMA and BPMC, which was found to be true for all augmented state permutations trialed. As the image feature is augmented with more state information the classifier’s predictive ability increases. Weighting wise, ventricular pressure appears to carry more significance however it is the least feasible of the states to practically acquire. The state combination with the highest practicality and most benefit is the combination of BPM and aortic pressure, however with a caveat. It makes logical sense to augment the image vector with at minimum the BPM state however both FPV and VPV suggest otherwise. When the BPM state is augmented, baseline classifier performance either decreases or stays roughly the same. No similar consistent trend exists for the phase augmented classifier however there are instances when it does occur. Given this trend inconsistency no definitive statement can be made regarding how BPM state augmentation affects model predictive ability.
Table 4.9: Summary of optimal model foreign and variable predictive score based on various augmented state combinations.

<table>
<thead>
<tr>
<th>Classifier</th>
<th>Augmented States</th>
<th>BPMB FPV [%]</th>
<th>BPMB VPV [%]</th>
<th>BPM FPV [%]</th>
<th>BPM VPV [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>None</td>
<td>60.42</td>
<td>68.61</td>
<td>60.84</td>
<td>80.00</td>
</tr>
<tr>
<td></td>
<td>BPM</td>
<td>53.19</td>
<td>58.33</td>
<td>52.49</td>
<td>70.41</td>
</tr>
<tr>
<td></td>
<td>Aortic Pressure</td>
<td>58.75</td>
<td>63.89</td>
<td>60.84</td>
<td>73.75</td>
</tr>
<tr>
<td></td>
<td>BPM</td>
<td>53.75</td>
<td>58.06</td>
<td>53.33</td>
<td>69.50</td>
</tr>
<tr>
<td></td>
<td>Aortic Pressure</td>
<td>70.97</td>
<td>74.17</td>
<td>71.67</td>
<td>82.92</td>
</tr>
<tr>
<td></td>
<td>BPM</td>
<td>65.97</td>
<td>72.50</td>
<td>69.17</td>
<td>82.92</td>
</tr>
<tr>
<td></td>
<td>Aortic Pressure</td>
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<td>75.56</td>
<td>65.42</td>
<td>71.42</td>
</tr>
<tr>
<td></td>
<td>BPM</td>
<td>57.36</td>
<td>72.22</td>
<td>69.58</td>
<td>72.49</td>
</tr>
<tr>
<td></td>
<td>Aortic Pressure</td>
<td>65.42</td>
<td>72.50</td>
<td>68.75</td>
<td>81.94</td>
</tr>
<tr>
<td>Phase Augmented</td>
<td>None</td>
<td>56.25</td>
<td>75.56</td>
<td>65.42</td>
<td>71.42</td>
</tr>
<tr>
<td>(n = 2)</td>
<td>BPM</td>
<td>57.36</td>
<td>72.22</td>
<td>69.58</td>
<td>72.49</td>
</tr>
<tr>
<td></td>
<td>Aortic Pressure</td>
<td>58.06</td>
<td>72.50</td>
<td>65.42</td>
<td>70.42</td>
</tr>
<tr>
<td></td>
<td>BPM</td>
<td>57.36</td>
<td>72.22</td>
<td>69.58</td>
<td>72.49</td>
</tr>
<tr>
<td></td>
<td>Aortic Pressure</td>
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<td>81.95</td>
<td>80.41</td>
<td>87.50</td>
</tr>
<tr>
<td></td>
<td>BPM</td>
<td>65.42</td>
<td>81.94</td>
<td>78.75</td>
<td>91.67</td>
</tr>
</tbody>
</table>
Chapter 5

Conclusion

The phase augmented\textsubscript{2} classifiers are the most practical identifiers of conditions derived from this work. On average they perform the best without state augmentation (neglecting the baseline) and with augmentation they consistently outperform the baseline. Unfortunately the most significant states appear to be ventricular pressures which are the least practical to acquire. With that being the case, the selection of the optimal ROI is even more important in developing the most robust classifier.

Due to the nonlinear timing of the S1 and S2 finding a specific frame of the spectra image that manifests condition is difficult. Due to this the most logical choice of ROI may be one which spans the maximum time range, accounting for the COI, however all ROIs parsed in this work are derived from physiological parameters or empirical observations, and thus are justified. The alternative option is to preprocess the acquired acoustics such that the space that the states span is reduced. Doing so would reduce the variation in sound occurrences, possibly allowing for a more specific ROI to be discerned, and ultimately a more accurate classifier can be developed. Given this approach the entirety of the HMAPR can be parsed into subsections, each with a unique ROI and derived classifier model. Discretization of the HMAPR would theoretically result in greater classification potential however is less practical as it would require unique preprocessing for each patient, speaking in terms of human trials. However given this theory, in a proof of concept baseline ROI classifiers were developed for different levels of HMAPR discretization and tested against the variable
Figure 5-1: Classification scores of a discretized HMAPR using baseline ROI with and without full state augmentation.

BPM set. All four BPM states are used in developing the classifier, and the SVM parameters were optimized in the same manner as was discussed in Chapter 4.

The results are promising (Figure 5-1) in that state augmentation continues to improve score. It should be noted that the training spaces and testing spaces are not constrained to have a consistent number of states which manifests in the scores of the n = 8 subregion spanning a systolic pressure of [90,100] and diastolic pressure of
Due to the difficulty in tuning the simulator to the desired pressure states, fine, consistent, and uniform state resolution over the HMAPR is not possible - thus the approach that was taken. The next iterations of testing should further parse down the HMAPR, while still examining discretization, and more data should be collected at more BPM states. Additionally, training a classifier on variable BPM state data should be trialed, however practically doing so would require a new trigger function generation procedure. Related to hardware/physical parameters, additional stethoscope locations (Increased attention to at the VAD surface) should be examined along with more occlusion conditions and possibly extending identification to inlet blockage as well.

This work fails to quantify how training space density and state proximity affect classification results, which is a serious issue. It was shown when iterating classifiers from BPMA to BPMD that the density and spacing of the training space has a direct correlation to predictive potential. Discretizing the HMAPR produced insufficient training points in the [90,100][70,80] partition, which would presumably skew non-discretized ROI classifiers when attempting to classify within this region. Subsequent work should study this metric intensively. Projected metrics can be scored within a chosen training state radii, score vs. closest proximity, and ROI proximity score.

The spectra generated are of fairly high quality, however due to the COI, there is a loss of feasible ROI space. To account for this one of two options should be examined: 1) Use a wavelet transform variant that is less shift variant so that extraneous data can be appended to the signal such that the original signal is not affected by edge effects. 2) Append the minimum amount of data to adjust for the COI. Option 2 is the easier of the options however requires that information about the original signal (sampling rate, trigger/EKG, and BPM) are used to parse the ROI.

The classifier family, SVM, was chosen out of practicality not so much functionality. Other classifiers (deep learning algorithms) such as convolutional neural networks have been proven to perform image recognition/classification to very high degrees of accuracy however are more difficult to develop and implement. The next step in progressing the classification potential of the acoustic signal would be to develop a deep
learning classifier.

This work shows that outlet occlusion classification is feasible using only the sound produced from an LVAD along with the related EKG signal. The degree to which this is feasible scales with the states augmented to the derived image feature vectors, however information such as aortic pressure can be noninvasively acquired making it a feasible application. At minimum, the heart simulator resulting from this work appears to be a fair mimic for developing a diagnostic method. Even though control of the system is heuristic and manual, the signals derived from it share similar spectral properties with the in vivo data acquired, and are characterized by nonlinearities/nonstationarities like the physiological organ system.

The results presented herein support the feasibility of further developing the image recognition algorithm for practical use. The HMAPR space is induced with significant variation, however fair classifier performance is still feasible. This work suggests that there does exist a spatial boundary in which device condition can be evaluated against. In a more practical scenario a patient is baselined at implantation, generating the boundary (1 class classifier model). In subsequent tests, new data is acquired and tested against the boundary to determine if any of the newly acquired data is classified as an outlier, ultimately indicating a health concern.
Bibliography


