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Algorithm for Premature Ventricular Contraction Detection from a
Subcutaneous Electrocardiogram Signal

by

Iris Lynn Shelly

A thesis submitted in partial fulfillment of the
requirements for the degree of

Master of Science
in
Electrical and Computer Engineering

Thesis Committee:
James McNames, Chair
Fu Li
Richard Tymerski

Portland State University
2016

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Abstract

Cardiac arrhythmias occur when the normal pattern of electrical signals in the heart breaks down. A premature ventricular contraction (PVC) is a common type of arrhythmia that occurs when a heartbeat originates from an ectopic focus within the ventricles rather than from the sinus node in the right atrium. This and other arrhythmias are often diagnosed with the help of an electrocardiogram, or ECG, which records the electrical activity of the heart using electrodes placed on the skin. In an ECG signal, a PVC is characterized by both timing and morphological differences from a normal sinus beat.

An implantable cardiac monitor (ICM) is a device used to help physicians diagnose and monitor infrequent cardiac arrhythmias that may not be observed during an ECG recording performed during a normal clinic visit. These devices are implanted under the skin of the chest and simply monitor and record the electrical activity of the heart. The recorded signal is referred to as a subcutaneous electrocardiogram, or SECG.

This thesis proposes and tests a novel algorithm that uses an SECG signal to perform PVC detection and is suitable for implementation within an implantable cardiac monitoring device. The proposed algorithm uses a combination of morphological and timing criteria to identify PVCs in near real time. Current commercially-available ICMs do not provide a PVC detection feature, so the proposed algorithm could help provide physicians with valuable additional diagnostic information about a clinically-significant arrhythmia.

Dedication

This thesis is dedicated to my parents, who have supported and encouraged me during every phase of my education.

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List of Abbreviations

Abbreviation	Definition
AF	Atrial Fibrillation
AT	Atrial Tachycardia
AV node	Atrioventricular node
DFT	Discrete Fourier Transform
ECG	Electrocardiogram
FFBNN	Feed-Forward Backpropagation Neural Network
GRA	Grey Relational Analysis
Hz	Hertz
ICD	Implantable Cardioverter Defibrillator
ICM	Implantable Cardiac Monitor
MLP	Multilayer Perceptron (neural network)
MLP-BP	Multilayer Perceptron – Backpropagation (neural network)
ms	Milliseconds
PAC	Premature Atrial Contraction
PNN	Probabilistic Neural Network
PPV	Positive Predictive Value
PVC	Premature Ventricular Contraction
SA node	Sinoatrial node
SECG	Subcutaneous Electrocardiogram
SOM	Self-Organizing Maps (neural network)
V sense or Vs	Ventricular sense

1 Introduction

A cardiac arrhythmia is a disturbance in the normal rhythm of the heart. This broad term describes a wide range of specific disorders, ranging from those with abnormally slow heart rate (bradycardia) to those with abnormally fast heart rate (tachycardia) and also including a variety of arrhythmias characterized by irregular rhythms [1]. When diagnosing and treating a cardiac patient, cardiologists frequently must identify the type of heart rhythm disorder that is occurring. One of the many tools available to provide diagnostic information is an implantable cardiac monitoring device. The implantable cardiac monitor (ICM) can record the electrical activity of the heart and automatically identify rhythms of interest to a clinician [2]. Premature ventricular contractions (PVCs) are one type of arrhythmia that a cardiologist may want to have identified and that the ICM may need to classify to accurately identify other rhythms of interest. This thesis describes a novel method by which an implantable cardiac monitor may identify PVCs. To provide a basis for understanding the data and principles used in this thesis, a background in healthy cardiac physiology, the electrocardiogram, cardiac arrhythmias, and implantable cardiac monitors is provided.

1.1 Healthy Cardiac Physiology

The heart is a mechanical pump controlled by electrical signals. In a normal, healthy heart, the sinoatrial (SA) node in the right atrium (see Figure 1 below) serves as the natural pacemaker of the heart, periodically initiating an electrical impulse that propagates throughout the heart and triggers mechanical activation of the heart. This electrical signal from the SA node first propagates through the atria, the upper chambers of the heart [3].

Figure 1. Electrical pathways of the heart.

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The electrical depolarization of the atrial heart muscle, or myocardium, causes the atria to contract and push blood into the ventricles. The electrical signal then travels through the atrioventricular (AV) node into the ventricles (see Figure 1). As in the atria, this causes the ventricles to contract. As shown in Figure 2, contraction of the right ventricle pumps deoxygenated blood to the lungs to pick up oxygen, while contraction of the left ventricle pumps oxygenated blood through the aorta to the rest of the body [1].

Figure 2. Basic cardiac anatomy with blood flow patterns indicated. “Heart labelled large” by Eric Pierce is licensed under the Creative Commons Attribution-Share Alike 3.0 Unported license. See the Appendix for more licensing information.

While the mechanical function of the heart is critical to life and can experience its own set of failures, the focus of this thesis is on the electrical activity of the heart, so no further understanding of the mechanics of the heart is required.

1.2 Electrocardiograms

The electrical activity of the heart is typically studied using an electrocardiogram (ECG). The ECG uses electrodes placed on the subject’s body to record electrical depolarization of the heart. During a standard diagnostic ECG recording, several electrodes are used, with recordings made for multiple pairs of electrodes. For each electrode pair, one electrode is positive and the other is negative. When a depolarization wavefront travels

towards the positive electrode and away from the negative electrode, a positive deflection appears in the ECG. A negative deflection results from a depolarization wavefront traveling towards the negative electrode and away from the positive electrode. A repolarization wavefront traveling towards the positive electrode also produces a negative deflection, while a repolarization wavefront traveling away from the positive electrode produces a positive deflection in the ECG [4].

A single normal heartbeat has several distinct components that are visible in an ECG. First, atrial depolarization is visible as an initial small deflection, called the P wave. After a short pause, the much larger QRS complex represents ventricular depolarization. Finally, a smaller T wave represents ventricular repolarization at the end of the heartbeat [1].

Figure 3. Typical ECG pattern for a single cardiac cycle.

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While a standard ECG signal is displayed above, the actual ECG signal varies based on the patient and the position of the recording electrodes. Additionally, the ECG signal shape and timing change as a result of various arrhythmias and other heart abnormalities.

1.3 Cardiac Arrhythmias

A cardiac arrhythmia occurs when the normal pattern of electrical signals in the heart breaks down. This can occur when the electrical conduction system fails to initiate or conduct electrical signals, typically resulting in a slower than normal heart rate, called bradycardia. Cardiac arrhythmias can also occur when the electrical signals are generated too rapidly; this type of failure causes tachycardia, or a faster than normal heart rate. Finally, a variety of irregular rhythms and escape or premature beats can occur when electrical signals are generated from abnormal locations throughout the heart [1].

Ectopic beats are beats initiated by an electrical signal that does not originate at the sinus node but instead originates at an ectopic focus. If the patient has an otherwise normal rhythm, an ectopic beat must come earlier than the normal sinus beat would have occurred. Therefore these ectopic beats are often referred to as premature atrial contractions (PACs) or premature ventricular contractions (PVCs), depending on their initiating chamber [5]. While an occasional ectopic beat is considered normal and not a cause for any clinical concern, frequent ectopic beats can be a warning of more dangerous future conditions. For example, PVCs can indicate increased susceptibility to ventricular tachycardia or ventricular fibrillation [6]. Ventricular fibrillation occurs when ectopic foci rapidly activate throughout the ventricles, causing constant, random electrical activity that fails to cause a coordinated activation and contraction of the ventricular myocardium. Without this contraction, blood is not pumped throughout the body, resulting in death when fibrillation is not quickly treated

and stopped [1]. For this reason, information about the occurrence of PVCs can be of clinical significance. While PACs can also be of clinical significance, they would be a possible precursor to other atrial arrhythmias like atrial fibrillation (AF) [7]. These atrial arrhythmias, while significant, do not present the same immediate risk as ventricular fibrillation. For this reason, this thesis focuses on the detection of the more clinically relevant PVCs.

As the name indicates, a PVC occurs earlier than the next conducted sinus beat would have occurred. This is evidenced by a short interval from the previous beat to the PVC. Additionally, the interval from a PVC to the next beat is typically longer than the normal sinus interval. When a PVC occurs, only the ventricles depolarize, resulting in the SA node not being reset. This causes the SA node to start the next atrial contraction at the normal sinus interval after the previous sinus beat. Typically, this depolarization conducts through the AV node before the ventricles have repolarized from the PVC, so the beat is not conducted to the ventricles. The time to the next ventricular depolarization and QRS complex therefore consists of the short interval from the PVC to the next atrial depolarization plus the normal sinus interval. This long interval following the PVC is referred to as a compensatory pause [1].

Figure 4. ECG strip showing two normal QRS complexes followed by a PVC, indicated by an arrow, and a final normal QRS complex.

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In rare cases, the ventricles have repolarized in time to be depolarized by the atrial depolarization immediately following the PVC. In these cases, the PVC is just inserted between two normal sinus beats without otherwise affecting the heart rhythm. These PVCs are referred to as interpolated PVCs, and instead of a longer compensatory pause after the PVC, they exhibit a shorter than normal interval from the PVC to the subsequent QRS complex [1].

Figure 5. ECG strip showing two interpolated PVCs.

“PVC interpolated” by the Eccles Health Sciences Library is licensed under the Creative Commons Attribution-NoDerivs-NonCommercial 1.0 Generic license. See the Appendix for more licensing information.

A PVC is evident in an ECG recording not only from its timing but also from its shape or morphology, as is visible in Figure 4 and Figure 5. The difference in morphology for a PVC QRS complex compared to a normal QRS complex results from the difference in the depolarization pattern for the different types of beats. When the ventricular depolarization is the result of a conducted atrial depolarization through the AV node, ventricular depolarization starts in the specialized conduction system of the Purkinje fibers, which rapidly conducts the depolarization throughout the ventricles. First, the depolarization travels down the left and right bundle branches through the septum. Unlike the right bundle branch, the left bundle branch has tiny terminal filaments that activate the septal myocardium, resulting in an early left-to-right depolarization of the ventricular septum, visible as the Q wave in the QRS complex. Next, depolarization travels along the Purkinje

fiber system throughout the rest of the ventricular myocardium. This rapidly carries the depolarization wave throughout the ventricles, rather than just relying on the slower propagation of the wave from myocyte to myocyte [1]. This specialized conduction system results in a narrow QRS complex of less than 120 ms in width when normal, healthy conduction occurs [8].

When a PVC occurs, the depolarization wave originates from an ectopic focus somewhere in the ventricular myocardium rather than beginning in the atrium and being conducted through the AV node. This means that ventricular depolarization must rely more on the slower propagation through ventricular myocytes rather than utilizing the bundle branches and Purkinje fibers to rapidly conduct the depolarization throughout both ventricles [1]. This slower propagation is reflected in a wide QRS complex, typically more than 120 ms in width [5]. Not only will the QRS complex be wider, but it will also have other morphology changes compared to a normal QRS complex due to the change in the direction of the depolarization wave propagation. Area of the QRS complex resulting from a PVC is typically larger than that of a normal QRS complex because less signal cancellation occurs. For example, when depolarization is moving to the right and the left at the same time, the resulting potential recorded by the ECG electrodes is the difference between the two depolarization waves. When an ectopic beat originates from a less central location within the heart, rather than beginning propagation at the AV node, less signal cancellation occurs, resulting in larger QRS amplitudes [1]. QRS cancellation for a normal beat compared to an ectopic beat with the largest possible area is an average of approximately 62 percent [9]. Actual change in the amount of cancellation for a PVC will depend on where the PVC originates and how the signal propagates through the ventricles.

1.4 ECG Monitoring

Detection of arrhythmias is often critical to cardiac patient care. For intermittent or paroxysmal arrhythmias, it is unlikely that the arrhythmia can be observed during a clinical visit as arrhythmia onset cannot be guaranteed during the brief appointment duration. Holter monitors are commonly used in these cases to facilitate a diagnosis. A Holter monitor is a portable, external device that continuously records the ECG signal of a patient while they are wearing it. The monitor connects to electrodes that are attached to the patient's skin [10]. While these monitors can be useful for an arrhythmia that occurs fairly regularly, at least once per day, they may fail to find less frequent arrhythmias [11]. Due to their bulky and intrusive nature, Holter monitors are normally worn for only a few days at a time. To address this problem, implantable cardiac monitoring devices have been developed. These are implanted under the skin on the chest like a pacemaker or implantable cardioverter defibrillator (ICD) would be, but instead of delivering pacing or shock pulses to the heart, the implantable cardiac monitor (ICM) simply monitors and records the electrical activity of the heart. The images below show the placement and approximate size relative to the human chest of BIOTRONIK's BioMonitor 1 and 2 ICMs.

Figure 6. BIOTRONIK BioMonitor 1 ICM size and recommended placement. “Implanted BioMonitor” by BIOTRONIK, Inc. is used with permission. See the Appendix for documentation of permission to use this image.

Figure 7. BIOTRONIK BioMonitor 2 ICM size and three possible recommended placements (A, B, and C). Note that any given patient would have only one ICM implanted at one of the three locations shown in this image.

Untitled image from BioMonitor 2 Quick Reference Guide by BIOTRONIK, Inc. is used with permission. See the Appendix for documentation of permission to use this image.

When the ICM detects a cardiac arrhythmia, it can save a snapshot of the electrical signal for a short period of time before and after the detected arrhythmia. This recorded snapshot can then be sent to the physician remotely or interrogated during the patient’s next follow-up appointment for physician analysis [12]. Because an ICM is often implanted to detect infrequently-occurring events, it becomes critical that its arrhythmia detection

algorithms have a low rate of false positives when saving SECG snapshots; otherwise, false positives could easily inundate the physician with false snapshots that outnumber the snapshots that are truly of clinical interest.

Unlike a pacemaker or ICD, an ICM does not have leads attached directly to the heart. Instead, it must rely on a subcutaneous electrocardiogram (SECG). This signal is similar to a standard ECG obtained using external electrodes on a patient's body, except that the electrodes are located under the skin. While this has the obvious benefit of allowing the device to monitor the patient's ECG with no bulky external equipment, the SECG signal is particularly susceptible to interference from noise. The short signal vector and the permanence of electrode locations mean that noise is often an unavoidable aspect of the SECG. The ICM is vulnerable to measuring electrical artifacts caused by patient movement and muscle activity [13]. Typically, ICMs attempt to identify these artifacts and classify them as noise so that they are not used in arrhythmia detection algorithms. For example, BIOTRONIK BioMonitor devices assign a noise marker to SECG events that the device identifies as noise. Not only are these noise markers not used in the device's other algorithms, but the neighboring QRS complexes are also excluded from consideration in those algorithms because timing intervals and signal morphology just before and after a noise event cannot be reliably determined. Additionally, the device provides statistical information to physicians regarding the amount of noise sensed by the device each day [14]. This information can help physicians determine the reliability of the SECG signal and arrhythmia detection for their patients.

Like other implantable medical devices, the ICM is also limited in battery life and processing power. For example, the battery in a BIOTRONIK BioMonitor 1 device is

expected to last for approximately 4 years [14]. While an external Holter monitor can be recharged, the only currently available option for a low battery in an ICM is to remove the original implanted device and implant a new device [12]. Clearly it is beneficial to the patient to make this need for device replacement as infrequent as possible. As a result, each computation performed by the device must be considered and optimized to reduce battery consumption as much as is practical.

1.5 PVC Detection Problem

Undetected PVCs present two distinct problems. The first and most direct problem is simply one of diagnostic information. When a physician has chosen to implant an ICM to monitor the patient's heart activity, they typically want as much information about clinically significant arrhythmias as possible; as previously discussed, frequent PVCs can be a warning of more serious problems that will begin occurring later. PVCs are often asymptomatic, so without ECG evidence of PVCs, a patient and physician may never be aware that they are occurring [6].

Additionally, PVCs can complicate detection of other arrhythmias by the ICM. Due to the presence of noise that typically obscures electrical signals from the atria (P waves) in the SECG, ICM arrhythmia detection algorithms usually rely entirely on the much larger ventricular signals (QRS complexes). While this greatly improves robustness to noise, this can complicate detection of arrhythmias that are fundamentally based in the atria, such as AF. However, even atrial arrhythmias can be determined by looking only at ventricular signals since they typically result in a characteristic interbeat interval profile. The interbeat, or RR, interval is determined as the time from the R wave of one QRS complex to the R wave of the next QRS complex. AF results in irregular interbeat intervals because the fast atrial

activity is sometimes conducted to the ventricles and sometimes not conducted. Therefore, an ICM can look for irregular interbeat intervals as an indicator of AF [15]. A variable interbeat interval is indicative of AF if the ventricular events are the result of intermittently conducted rapid atrial activation. This may not always be the case, though, as PVCs also result in a variable interbeat interval, but this variability should not be classified as an AF event. A conducted PAC can result in a variable interbeat interval as well, but again, this is not indicative of AF [16].

1.6 Objectives

A method of identifying PVCs from an SECG signal and flagging them for exclusion from other arrhythmia detection algorithms is desired. Significant research has already been conducted into PVC detection in Holter recordings and other ECG signals [17], [18], [19], [20], [21], [22], but these have rarely been examined in the context of an ICM. The ICM provides additional difficulties due to computational, memory, and power consumption limitations that are not typically present in larger, external recording and analysis systems. The algorithm must run on the device rather than simply logging and transmitting the SECG for separate analysis because ICMs do not typically contain sufficient memory to store continuous SECG for longer than approximately one hour. For example, the BIOTRONIK BioMonitor 1 device only has space to store up to 35.8 minutes of SECG data [14]. As a result, it is critical to store only portions of the SECG that are of clinical interest.

Additionally, the SECG signal can be highly susceptible to signal artifacts and other noise. A suitable PVC detection algorithm must be computationally simple enough to be feasible for implementation in an implantable device and robust enough to function with typical SECG signal quality conditions and to recover from periods of noise. Finally, the PVC detection algorithm must not require initial manual selection of PVC or normal QRS complexes or other similar manual initialization.

1.7 Contributions of this Thesis

This thesis proposes and tests a novel algorithm that uses an SECG signal to perform PVC detection and is suitable for implementation within an implantable device. The contributed algorithm provides the benefits of reducing the computational complexity of PVC detection compared to algorithms used in current practice. In this way, it provides the possibility of real-time PVC detection in an ICM, a feature which is not currently available in commercial ICMs. An additional benefit of the proposed algorithm is improvement in accuracy of other ICM algorithms, particularly AF detection algorithms, which use interbeat intervals to detect arrhythmias.

The proposed algorithm has been developed and tested using clinical SECG data from BIOTRONIK's BioMonitor line of ICM devices. This thesis will provide details of the algorithm along with its validation, performance results, overall conclusions, and areas for future exploration.

2 Literature Summary

Several primary methods have been used to identify PVC events in ECG recordings. These include analysis using signal morphology, signal timing, frequency spectra, wavelet transforms, and neural networks. Each of these methods will be described in this chapter. This chapter will additionally discuss the shortcomings of the current practice and the contributions of this thesis in the area of PVC detection.

2.1 Literature Summary and Current Practice

2.1.1 PVC Detection using Signal Morphology

As discussed previously, PVCs are typically characterized by a greater than normal width and amplitude compared to a normal QRS complex in the ECG. This occurs because the PVC originates in an irritable ectopic focus within the ventricle and then follows an abnormal conduction pathway through the ventricles. As a result, the depolarization takes longer to progress through both ventricles, widening the QRS complex. Additionally, the normal pathway results in a large amount of cancellation due to depolarization travelling in different directions at the same time, thus decreasing the QRS amplitude. When this cancellation is reduced during the conduction of a PVC, the QRS complex has a significantly larger amplitude [1].

Because of these characteristic morphology changes, PVCs are commonly detected using signal morphology metrics. Martinez et al. [17], [23] developed a set of 5 different signal morphology metrics computed for each QRS complex in an ECG signal to classify beats as PVC or normal. All metrics were related to quantifying the greater than normal width and amplitude of QRS complexes. They computed the area of each QRS complex, the number of samples between 30 percent of peak amplitude prior to the positive QRS peak

and 30 percent of peak amplitude after the peak, the number of samples between 30 percent of the negative peak amplitude prior to the negative QRS peak and 30 percent of peak amplitude following the peak, the amplitude of the QRS peak, and the absolute value of the local minimum following the peak. Classification was based on comparing each of these metrics to its threshold value. Thresholds were dynamically determined based on the average of the most recent five normal beats. This method required manual selection of five normal beats by the physician or researcher prior to running the classification algorithm. If any one of the five metrics exceeded this threshold, the beat was classified as a PVC. This method was validated using 20 ten-hour segments of Holter data with AF and a high density of PVCs. The ECG was first filtered to remove baseline wander, high frequency noise, and power line interference. The authors reported sensitivity and positive predictivity of the algorithm as 98.62 percent and 97.86 percent, respectively.

Moraes et al. [18] also used a QRS complex morphology approach to detect PVCs. Similarly to Martinez et al., they used area and width metrics. Additionally, they created a metric to examine the sample variations within the QRS complex. This measure summed the absolute value of the difference between each point and the previous point on the QRS complex, essentially quantifying the total steepness of the QRS complex, with each summed difference being an instantaneous slope. Finally, they used a measure of the total amplitude of the QRS complex, measured as the difference between the positive and negative peaks of the QRS complex. They then used these metrics in a four dimensional space and assigned each QRS complex to a class based on minimum distance criteria. They used the Mahalanobis distance in this classification. The Mahalanobis distance is the distance from a point (in this case, a specific QRS complex) to a distribution (all of the QRS complexes in a

given class). If the centroid of the distribution is the same as the individual point, then the distance is zero. Otherwise, the distance is a Euclidian distance to the centroid of the distribution except that it is scaled so that each dimension of the distribution has a variance of one [24]. In these calculations, if the distance from a QRS complex to all of the existing classes is too large, then that QRS complex is used to define a new class. Otherwise, the QRS complex is assigned to the class that minimizes the Mahalanobis distance. This method results in groups of similar QRS complexes, but it does not actually label these classes. The method can potentially result in a large number of classes that must be identified manually by a physician to distinguish which are PVCs. In the initial study conducted by Moraes et al., this algorithm resulted in 18 different classes that required manual identification. While this is potentially inconvenient, a benefit of this method is that the threshold is one dimensional, regardless of how many or which features are being examined. In all cases, the threshold is simply a distance [18].

2.1.2 PVC Detection using Signal Timing

As explained earlier, PVCs cause changes in QRS complex timing. A PVC does not impact the sinus node, so atrial depolarization will still occur at the normal sinus rhythm. However, this depolarization typically occurs while the ventricles are still in the refractory period after the PVC, so it is not conducted to the ventricles. This results in a compensatory pause before the next QRS complex because it has to wait for the following atrial depolarization to be conducted to the ventricles [1]. This is visible as a characteristic short-long interval sequence where the PVC comes early, resulting in a short interbeat interval, and then is followed by a longer interbeat interval due to the compensatory pause. The sum of these two intervals is approximately twice the normal sinus interval.

Mateo and Laguna [25] developed a method to identify and correct for ectopic beats during heart rate variability analysis. In this context, heart rate variability measurements strive to examine only heart rate changes caused by the sinus node. This means that ectopic beats originating from other atrial foci or ventricular foci cause interbeat interval variability that should not be included in heart rate variability analysis. Mateo and Laguna used a method of calculating the first derivative of the instantaneous heart rate and imposing a threshold on that derivative to classify a beat as normal or ectopic for the purposes of heart rate variability analysis. Central to their method is the theory that the variation of instantaneous heart rate due to normal sinus beats is band limited, allowing a threshold to be chosen that will separate normal beats from ectopic beats.

Mateo and Laguna used an estimate of the derivative of the instantaneous heart rate that used the time of the current (k^{th}) beat and the time of the two adjacent beats ($k-1$ and $k+1$). When this derivative estimate exceeded a threshold, then at least one of the three beats being used in the calculation was not a normal beat. Since this calculation was performed for every set of three beats, if the oldest beat ($k-1$) in this calculation were the anomaly, it would have already been flagged when it was included in one of the previous two calculations. Therefore, only beats k and $k+1$ were candidates for anomalies. These anomalies could include a false QRS detection, a missed QRS detection, or an ectopic beat. To determine which type of anomaly is present, the authors recomputed the estimate of the derivative of the instantaneous heart rate under various conditions. First, they removed the current beat and then the subsequent beat. If either of these removals resulted in the derivative meeting the threshold, then the removed beat was classified as a false QRS detection. If this was unsuccessful, they inserted an intermediate beat between the current and the subsequent

beat. If this resulted in the derivative meeting the threshold, it indicated a missed QRS detection. Finally, they moved beat k to an intermediate position between $k-1$ and $k+1$ and then moved beat $k+1$ to an intermediate position between k and $k+2$. If the threshold criterion was met in either of these cases, then the moved beat was classified as an ectopic beat. If none of these changes resulted in meeting the threshold criterion, the same process was used, but this time assuming multiple consecutive removals, insertions, or movements until the condition was satisfied. Following identification of the anomalies, they were corrected prior to computing heart rate variability information. While this method was effective in its goal, it was designed to distinguish ectopic beats from normal sinus rhythm, not to distinguish ectopic beats from AF episodes or other arrhythmias. Additionally, it did not distinguish between PVCs and PACs.

Krasteva et al. [26] examined interbeat intervals to identify PVCs and PACs that were conducted to the ventricles. Unlike PVCs, PACs are not characterized by a full compensatory pause following the ectopic beat, but instead by a shorter incomplete compensatory pause. This occurs because, while the SA node is reset by the PAC, the sinus rate for the subsequent beat decreases slightly due to a transient parasympathetic effect of the PAC [1]. For PAC identification, Krasteva et al. looked for this characteristic incomplete compensatory pause. They used a metric for the inter-beat RR interval difference, calculated as the difference between the current RR interval and the previous RR interval, expressed as a percentage of the mean of the five preceding RR intervals. Thus, each calculation included a total of seven RR intervals. If this RR difference metric exceeded 15 percent, the interval pair was flagged for further testing. If the previous RR interval was less than 90 percent of the mean of the preceding five RR intervals, or the current interval was more than 110

percent of the mean of the same preceding five RR intervals, or the ratio of the current RR interval to the previous RR interval was greater than 1.2, the beat was flagged as a single premature heartbeat. It was further identified as a PAC if the beat's QRS width or the vectorcardiogram angle of the QRS peak were not significantly different than reference values. If these conditions were not met, then the QRS was labeled as a PVC. A PVC could also be identified just based on these morphological characteristics, even if the RR interval test did not indicate a premature heartbeat. This allowed for correct identification of the relatively rare interpolated PVCs. Krasteva et al. reported sensitivity and specificity of 92.2 percent and 96 percent for PAC detection [26]. Sensitivity and specificity for PVC detection were not reported as the authors' primary goal was PAC detection.

Raeder [27] proposed a method for identifying ectopic beats by detecting the "signature short-long sequence" in the RR intervals surrounding an ectopic beat. This short-long sequence is caused by the shorter RR interval from the preceding normal beat to the ectopic beat, followed by the compensatory pause to the next normal beat. The short-long sequence was identified using the ratio of the current RR interval to the previous RR interval. For normal sinus rhythm, this ratio is approximately equal to 1, with only slight fluctuations. For an ectopic beat, these ratios will go from significantly below 1 to significantly above 1 to somewhat below 1 as there is a sequence of short-long-normal. Raeder suggested possible thresholds as the first ratio being less than the first percentile of RR ratios, the second ratio being above the 99th percentile of RR ratios, and the third ratio being below the 25th percentile of RR ratios. When these criteria identified an ectopic beat, the ectopic coupling interval and the compensatory pause were excluded from subsequent RR interval analysis for detection of AF.

Dyjach and Carlson [28] proposed a method for identifying ectopic beats by comparing the current interval to previous non-ectopic intervals. The method was designed for use in heart rate variability calculations, so it was aimed at identifying and eliminating all non-sinus inter-beat intervals. The design included a first-in-first-out buffer to store non-ectopic inter-beat intervals; this buffer could hold any number of intervals, but the preferred number for the design was three. Each incoming interval was first compared to a lower and upper bound, such as 300 ms and 2000 ms. If the interval was outside of this range, it was classified as an ectopic and was not used in heart rate variability analysis. The oldest interval in the buffer was removed, and ectopic analysis moved on to the next interval. If instead the interval passed the first range test, it moved on to a second test. If the buffer was not full at this stage, the second test could not be conducted, so the interval was added to the buffer for ectopic detection but was labeled as indeterminate and not used for heart rate variability analysis. If the buffer was full, the median of the buffer intervals was computed. The incoming interval was compared to this median, and if it differed by more than a specified threshold value or percentage from the median, the interval was classified as an ectopic and excluded from further analysis. The oldest interval in the buffer was also removed. If the interval passed both tests, it was classified as normal and added to the buffer, removing the oldest interval in the buffer to maintain the buffer size. Only intervals that were classified as normal, not ectopic or indeterminate, were used in subsequent heart rate variability analysis. This method did not distinguish between PVCs and PACs.

2.1.3 PVC Detection using a Combination of Signal Morphology and Timing

Signal morphology and timing criteria are frequently used together in PVC detection as this encompasses the easily observable time domain changes in the ECG signal for a PVC

compared to a normal sinus beat. While other methods are also combined, those combinations are not as prevalent and will be discussed in the individual category which most closely matches the authors' main focus.

Palaniappan et al. [19] utilized several morphology features, interbeat interval timing, and blood pressure to classify beats as normal, PVC, or PAC. Their morphology analysis included the R peak amplitude, mobility, and a complexity factor. Mobility was computed by taking the square root of the ratio of the variance of the first derivative of the ECG signal to the variance of the ECG signal. The ECG signal from the Q peak to the S peak was used for this computation. This mobility metric provided an approximate ratio of the energy of higher frequency components of the signal over the energy of the signal. Both PVC and PAC QRS complexes have longer QS segments than normal beats, so they have less high frequency energy; thus, the authors expected lower mobility for ectopic beats. The complexity factor was calculated as the square root of the ratio of the mobility of the second derivative of the ECG signal to the mobility of the first derivative of the ECG signal. Again, the ECG signal from Q peak to S peak was used for this calculation. PVC beats were expected to exhibit the highest complexity.

Additionally, Palaniappan et al. computed RR interval ratios. They used the ratio of the previous to the current RR interval and the ratio of the next to the current RR interval as classification features. Finally, they used several blood pressure metrics, including systolic and diastolic pressure, mean arterial pressure, and pulse pressure. In total, they used 13 features for classification. These features were used as inputs to a Multilayer Perceptron (MLP) neural network. The MLP had 13 inputs nodes and 3 output nodes. The MLP was trained using the backpropagation algorithm to classify beats as normal, PVC, or PAC. The

authors tried networks with 10, 20, 30, 40, and 50 hidden units. Best performance was observed with 50 hidden units, achieving 96.47 percent classification accuracy [19].

García et al. [8] also used temporal and morphological features to distinguish between PVCs, PACs, and normal beats. They used eight temporal features that included intervals and interval ratios. These were the RR interval from the current to the previous beat (RR1), the interval from the current to the subsequent beat (RR2), and the interval from the previous beat to its predecessor (RR0). From these three intervals, they also calculated the ratio of RR1 to RR2 (Ratio1) and the ratio of RR1 to RR0 (Ratio2). Using the mean RR interval (RRM) from the entire ECG record, they calculated Ratio3 as the ratio of RR1 to RRM. The mean ratio, MRATIO, was the mean of Ratio1, Ratio2, and Ratio3. Finally, they calculated the robust median (MRR) by finding the median of a window of 10 RR intervals.

To complement the temporal features, García et al. also considered four morphological features. They examined a window of 210 ms around each QRS complex, using the previous 70 ms and following 140 ms after the R peak. This included the QRS wave but excluded the P and T waves. Each QRS complex was normalized to have an amplitude range from 0 to 1. Using these normalized QRS complexes, they calculated the maximum cross-correlation between the current beat and the next beat as well as between the current beat and the previous beat. They also calculated the maximum cross-correlation between a normal beat template and the current beat. Finally, they measured the QRS duration as the width of the QRS complex above normalized amplitude 0.5.

These four morphological and eight temporal features were used in a discriminant analysis method that included two linear discriminant functions to allow classification into the three beat categories. Sensitivity and specificity for PVC detection were 97.67 and 98.16

percent, respectively. For PAC detection, sensitivity and specificity were 92.78 and 97.67 percent. Positive predictivity was 97.98 for PVCs and 96.15 percent for PACs [8].

Krasteva and Jekova [29] used morphological template comparisons and temporal features to discriminate between PVCs and normal or paced beats. Their morphological comparisons required expert selection of three normal QRS complex templates. After the templates were chosen, they were saved permanently but also saved as temporary, replaceable copies. These copies were updated throughout analysis by QRS complexes that were sufficiently similar to the template copy. This allowed preservation of the originally chosen template while also permitting adaptation of the template to gradual QRS morphology changes. After the algorithm was initialized with the template QRS complexes, all future QRS complexes were compared to the templates using several metrics. The first metric was area difference between the current beat and each template, expressed as a percentage of the template area. Area was computed over the range from 100 ms before to 450 ms after the QRS complex detection. The second comparison metric was frequency spectrum difference. The frequency spectrum of the QRS complex being identified and the template were both normalized to have a maximum amplitude of 1. The difference was then computed by summing the magnitude of the amplitude difference at each integer frequency from 2 to 25 Hz, inclusive. Finally, the third comparison metric was the maximal cross-correlation coefficient. The authors used a normalized cross-correlation and found the maximum value across all possible lags. These three metrics were compared to a threshold to determine if the sample waveform was sufficiently similar to any of the template waveforms. If all three metrics qualified for a template copy, meaning that the area difference and frequency spectrum difference were less than the threshold and the maximum cross-

correlation coefficient was larger than the threshold, that copy was replaced with the current beat. If the three metrics did not qualify for a template copy, but they did qualify for one of the original templates, that template's copy was still replaced by the current beat. In all cases, the closest match was determined so that those values could be used in the actual beat classification rules.

In addition to their template comparisons, Krasteva and Jekova also used inter-beat intervals to classify PVCs. They used the RR interval from the previous beat to the one before it (RR1), the RR interval from the current beat to the previous beat (RR2), and the RR interval from the current beat to the next beat (RR3). If the current beat was a PVC, this would cause RR1 to typically be a normal interval, RR2 to be a shortened interval, and RR3 to be a prolonged, compensatory interval. They examined these intervals as ratios, with $RR21 = RR2/RR1$ and $RR23 = RR2/RR3$. Since RR2 would be the ectopic coupling interval if the current beat was a PVC, both ratios would be expected to be less than one for a PVC.

Based on the template comparison and RR interval ratio metrics, Krasteva and Jekova developed three rules for PVC classification. Rule 1 was based on the probability that a given beat was a PVC according to the area difference, frequency spectrum difference, and maximum correlation template comparison metrics. For each of these metrics, they determined ranges with approximate probabilities that a value in that range corresponded to a PVC. If any one of the three probabilities was one (100 percent chance of being a PVC), the overall probability was one. Similarly, if any one of the three probabilities was zero, the overall probability was zero. Otherwise, the overall probability was a simple average of the three individual probabilities. If the overall probability was greater than or equal to 0.7, the

beat was classified as a PVC. The second rule used a combination of the RR interval ratios and the maximum correlation metric. If either ratio was less than 0.95 and the maximum correlation was less than 0.88, the beat was classified as a PVC. Finally, the third rule used the area difference and frequency spectrum difference metrics. If both of these values were greater than a threshold (40 for the area difference and 2.5 for the frequency difference), the beat was classified as a PVC. Meeting any one of these three rules resulted in classification as a PVC, regardless of the outcome based on the other two rules. Classification of PVCs achieved a sensitivity of 98.4 percent and a specificity of 98.86 percent [29].

Ittatur et al. [30] used the RR interval, QRS width, and a classification they called QRS pattern to detect PVCs. Unlike many other methods described previously, their algorithm was designed to be implementable in embedded applications. QRS pattern for each beat was determined by classifying the QRS complex as one of four types. This classification used the first derivative of the ECG signal to determine if the pattern was Type I (dominant R wave without significant Q or S waves), Type II (no significant R wave), Type III (dominant R wave with smaller S wave), or Type IV (small R wave with dominant S wave) for each QRS complex [30]. Note that in a QRS complex, the Q wave is an initial negative deflection, the R wave is the positive deflection, and the S wave is a negative deflection following the R wave [1]. See the figure below for examples of each of the QRS pattern types.

Figure 8. QRS pattern examples provided by Ittaturut et al. [30].
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Classification as one of the four QRS pattern types used the amplitudes of the positive peak to the left of the main negative peak and the positive peak to the right of the negative peak in the ECG derivative signal. Decision rules compared these two positive peaks to each other and to a threshold value. QRS width was then calculated using threshold crossings of the ECG derivative to determine when the QRS complex started and stopped. The algorithm determined which threshold crossings to use for width measurements based on the type of the previously-determined QRS pattern. The two morphology metrics were then used in combination with the interval to the preceding beat to classify a beat as a PVC or non-PVC. If the RR interval was shorter than a set threshold percentage of the average RR interval over the last 8 non-PVC beats and the QRS width was greater than a set threshold percentage of the average width over the last 8 non-PVC beats, then the beat was classified as a PVC. Additionally, if the RR interval criterion was met and the QRS patterns of the previous 8 non-PVC beats were all the same while the QRS pattern of the current beat did not match that pattern, then the beat was classified as a PVC. Ittaturut et al. reported a sensitivity of 91.05 percent and a specificity of 99.55 percent using this method [30].

2.1.4 PVC Detection using Frequency Spectrum Analysis

Due to their different morphologies, the frequency spectra of PVCs differ from the spectra of normal QRS complexes. PVCs exhibit a wider morphology than a normal QRS complex, and as a result, the high-frequency components of a PVC QRS complex are attenuated compared to a normal QRS [20].

Talbi et al. [21] compared the power spectra of normal QRS complexes and PVC beat QRS complexes and found that the most significant discrepancies occurred at 4, 8, 16, and 20 Hz. They captured these differences by computing the slope of the line of best fit on two regions of the log-log spectra plot of each QRS complex: the region from 3 to 8 Hz and the region from 15 to 19 Hz. Using these two slopes, each beat could be classified as normal or PVC. Using a classification scheme developed by training a Self-Organizing Maps neural network on 100 normal beats and 100 PVC beats, additional PVC beats were classified with a sensitivity and specificity of 92.67 and 99.13 percent, respectively.

Lin [20] examined the frequency spectra of QRS complexes, focusing on the components between 1 and 12 Hz, to classify various arrhythmias and beat types including PVCs. Analysis used only the QRS complex, so Lin first removed the P and T waves and examined on a window of 280 ms centered on the QRS peak. Analysis of a training data set showed that the PVC QRS spectra had their peak amplitudes between 1 and 3 Hz while normal beat QRS spectra were more uniform across the range being examined. All amplitudes were normalized by dividing by the maximum amplitude of the discrete Fourier transform (DFT) to allow comparison. The frequency spectra of normal beats were predominately of smaller amplitude than that of PVCs on the range from 1 to 3 Hz and of larger amplitude on the range from 4 to 12 Hz. Lin used the frequency spectra amplitude

data along with a classifier based on grey relational analysis (GRA) to classify each QRS complex. The classifier used Euclidean distances between the test data and the comparative or template data. This method was tested on patient records containing normal beats, PVCs, bundle branch block beats, fusion beats, and “unknown” beats. Unknown beats were a combination of paced beats and unclassified beats. Accuracy for each patient record ranged from 85 percent to 98 percent [20].

2.1.5 PVC Detection using Wavelet Analysis

Wavelet transforms allow analysis in both the time and frequency domains. Unlike the Fourier transform, which provides the frequency composition of the signal over all time, the wavelet transform provides the frequency spectra at individual time windows. This allows examination of changes to the frequency components of a signal over time. While several methods provide similar functionality, including the short time Fourier transform, the wavelet transform has a variable time window width which allows more precise time localization of high frequency signal components [31]. This can be particularly useful in ECG signals where the frequency components change rapidly throughout a single cardiac cycle. A wavelet transform decomposes the signal into elementary functions that are localized in both time and frequency [32]. For comparison, the Fourier transform can be viewed as a special case of the wavelet transform in which the elementary functions (sinusoids) are localized only in the frequency domain.

Yu and Chen [33] used ECG discrete wavelet transformation to classify beats as one of six types: normal, left and right bundle branch block, PVC, PAC, and paced. They performed a two-level discrete wavelet decomposition for each QRS segment. After decomposition, Yu and Chen used several features of the resulting signals. The

decomposition produced signals in three different subbands, each of which could be examined. Their first feature was the signal variance in each subband, which represented the averaged AC power in that band. They also computed the autocorrelation of the signal in each subband. The variance of this autocorrelation function was the averaged AC power of the autocorrelation function and therefore measured the coherence of the signal; this was their second feature for analysis. Their third feature was the relative amplitude of the signal in each subband, calculated as the minimum value in that subband over the maximum value. The authors also used two additional features that were not from the wavelet transformation of the ECG: the AC power of the original QRS signal and the instantaneous RR interval. The AC power was computed as the variance of the original QRS signal, and the instantaneous RR interval was computed as the time from the current to the previous R peak. All features were normalized using the hyperbolic tangent sigmoid transfer function so that they had a mean of zero and a standard deviation of one. The authors used a probabilistic neural network that classified each QRS complex as one of six types based on probability density functions. For the largest training data size, 11,600 QRS complexes, all classification categories achieved a sensitivity and specificity of at least 99 percent. For the smallest training data size, 362 QRS complexes, PVC sensitivity was 96.17 percent, with all other sensitivities at least 98 percent. Specificity was still over 99 percent [33].

Uchaipichat et al. [22] more narrowly used wavelet power spectrum analysis to distinguish between PVCs and normal QRS complexes. They examined each beat from 200 ms before the R wave to 550 ms seconds after the R wave. For each beat, they performed a wavelet transform to get the wavelet power spectrum density. From this, they extracted the median frequency, variance, skewness, and kurtosis of the wavelet spectrum density. The

power spectrum density of PVCs tended to be more concentrated in the 0 to 2 Hz frequency range, while normal sinus beats had a more evenly distributed power spectrum. Therefore, median frequency and variance tended to be lower for PVCs than for normal beats, while skewness and kurtosis were higher for PVCs than for normal beats. The authors used the Mahalanobis distance to classify beats based on these four parameters. They achieved a sensitivity and specificity of approximately 82 percent and 90 percent, respectively [22].

Kadbi et al. [34] used wavelet transformation analysis of QRS complexes along with RR interval and form factor information about the ECG signal. They examined a segment of the ECG from 100 ms before the R wave peak to 150 ms after the peak. They used a four level decomposition for the discrete wavelet transform, resulting in 64 wavelet coefficients. Principal Component Analysis was used to reduce redundancy in the frequency dimension and obtain only 12 coefficients to be examined. Additionally, the authors incorporated the current and next RR intervals, measured as the time from the previous RR peak to the current peak and the time from the current peak to the next peak, respectively. Finally, they used a parameter called the Form Factor or complexity, computed as the mobility of the first derivative of the ECG signal divided by mobility of the ECG signal itself. Mobility was calculated as the standard deviation of the first derivative of the signal divided by the standard deviation of the signal. Combined with the 12 wavelet transform coefficients and the two RR intervals, this yielded a total of 15 features to examine for each QRS complex. These features were used to train an artificial neural network. The authors used two separate classifiers: a first round to distinguish normal beats from abnormal beats and a second round to classify the abnormal beats based on the type of arrhythmia. The authors trained and tested the classification networks on two separate data sets, each containing various beat

types: normal, left and right bundle branch block, PVC, fusion of normal and ventricular beats, PAC, paced, ventricular flutter, fusion of paced and normal beats, and aberrant conduction of PACs. Average performance, calculated as the percentage of correctly classified beats, was over 90 percent on the testing data set. PVC performance was 98 percent, while PAC performance was 86 percent [34].

2.1.6 PVC Detection using Neural Networks

Most ectopic detection methods contain two primary focuses: determining metrics or features to use and then actually classifying beats using these metrics. Several previously-discussed methods have used neural networks for the job of classifying beats using predetermined metrics. The neural network aspect of those methods will be discussed in more detail in this section, while largely ignoring the development of the metrics as this has already been discussed in previous sections.

Palaniappan et al. [19] used a Multilayer Perceptron – Backpropagation (MLP-BP) neural network for PVC and PAC detection. The input to the neural network was their 13 beat classification metrics. The output layer had three nodes, one for each possible beat class: normal, PVC, and PAC. The target output during training was 1 for the node corresponding to the input beat type and 0 for the other two nodes. During training, the MLP-BP neural network changed connection weights to minimize output error. The authors used networks with 10, 20, 30, 40, and 50 hidden nodes to compare performance. Highest classification accuracy was achieved with 50 nodes, resulting in a 96.47 percent classification rate. Twenty nodes provided the worst performance with a 95.87 percent classification rate [19].

Talbi et al. [21] utilized a Self-Organizing Maps (SOM) neural network, a popular unsupervised learning neural network, for PVC discrimination. The SOM received a vector of two inputs, their two QRS classification metrics. The beats were then categorized into one of two beat types: normal or PVC. The SOM had a structure of 5 by 5 nodes. The map was initialized randomly and trained with 100 normal beats and 100 PVC beats. Following training, the SOM was tested on an additional 27877 normal beats and 3689 PVC beats. Overall sensitivity and specificity were 92.67 and 99.13 percent, respectively [21].

Yu and Chen [33] used a probabilistic neural network (PNN) to classify beats as one of six categories, including normal, PVC, and PAC. They used 11 features of each ECG beat as inputs to the PNN. They examined the effect of the smoothing factor of the Gaussian kernel function on the accuracy of the classifier. Increasing the smoothing factor decreased the classification accuracy, but smoothing factors from 0.1 to 0.5 all resulted in specificity and sensitivities for all five abnormal beat categories of greater than 90 percent. Decreasing the training data size from 11600 to 362 decreased specificity by 0.5 percent from 99.97 to 99.47 percent and decreased sensitivities of the individual abnormal beat categories by a maximum of 2.87 percent, from 99.04 to 96.17 percent. This maximum sensitivity drop occurred for PVC beats. The relatively low sensitivity of the PNN to the Gaussian smoothing factor and the training data size indicated a robust classification system. The authors also tried using a feed-forward backpropagation neural network (FFBNN), but this achieved lower accuracy than their original PNN [33].

Kadbi et al. [34] used two neural networks to classify beats into ten different categories, including normal, PVC, and PAC beat types. The first neural network was a Multilayer Perceptron (MLP) neural network that distinguished between normal and

abnormal beats without classifying the type of the abnormal beats. The second neural network only received the beats that were already classified as abnormal. This neural network was also a MLP neural network, and it classified the abnormal beats into individual categories such as PVC or PAC. Both neural networks were three-layer feedforward backpropagation MLPs, with 15 input features for each beat, 15 hidden nodes, and one output node. The system correctly classified over 90 percent of beats during testing [34].

Tarassenko et al. [35] used an auto-associative Multilayer Perceptron (MLP) neural network and trained it to only detect normal beats. By comparing detections from a standard QRS complex detector to the beats detected by this MLP, abnormal beats could be identified as those beats not detected by the MLP. This method did not identify the type of abnormal beat that occurred. An auto-associative neural network reproduces the input data as its output. For an auto-associative MLP, the hidden layer compresses the data, reducing the dimensionality of the data in this hidden layer. The authors used one layer of linear hidden units and trained the MLP using gradient descent to minimize the mean squared error at the output. The MLP was trained using only normal beats, so PVCs and other abnormal beat types were excluded, as were ECG segments with movement artifacts or noise. For each beat, they used a one second ECG segment centered on the R peak. With a sampling rate of 64 Hz, this provided 64 samples as inputs to the MLP. The hidden layer had 16 units, achieving a 4:1 compression ratio. The output layer again had 64 nodes, like the input layer. Since the MLP was trained to reproduce the input data at the output using only normal beats, the mean squared error for a test normal beat was expected to be very small, as the MLP was trained for this type of beat. If the input was an abnormal beat, however, the mean squared error would be much larger since the MLP was not trained on this type of

beat. The authors used a cutoff threshold for the reciprocal mean squared error to determine if a normal beat was detected. If the reciprocal mean squared error was below this threshold, the beat was not detected and was therefore classified as an abnormal beat. Using PVCs as the abnormal beats for testing resulted in correct identification of 2055 out of 2067 normal beats and 28 out of 28 PVCs when the MLP was trained with 1000 normal beats.

2.1.7 PVC Exclusion through an Alternate AF Detection Method

As an alternative to explicitly identifying and excluding PVCs from subsequent RR interval variability analysis for AF detection, the AF detection algorithm itself may be designed to not respond to non-AF ectopy.

Sarkar et al. [15] developed an algorithm that identifies AF, Atrial Tachycardia (AT) with irregular ventricular response, and AT with a more regular ventricular response. This algorithm was designed to function in a Medtronic ICM, so emphasis was placed on computational simplicity to maintain feasibility in a device with limited processing power and battery life. While AF results in irregular conduction through the AV node and thus irregular RR intervals, AT can have regular RR intervals, irregular RR intervals, or regularly irregular RR intervals due to group beating. The authors developed one algorithm to identify the irregular RR intervals and a separate algorithm to detect AT with regular or regularly irregular RR intervals. To measure irregularity for the first algorithm, they used the δRR intervals, defined as $\delta RR(i) = RR(i) - RR(i - 1)$. These intervals were plotted in a Lorenz plot, which is a scatter plot of $\delta RR(i - 1)$ versus $\delta RR(i)$. They defined regions of the plot based on the interval sequence that would cause a point in that region. For example, a sequence of intervals of the same length would cause points near the origin. These regions were then used to identify whether an interval sequence had a distribution characteristic of

AF, AT, or normal rhythm. For example, normal rhythm was characterized by the majority of points being near the origin, meaning that all δRR intervals were near zero. AF, on the other hand, was characterized by points scattered throughout all quadrants of the plot.

To classify groups of intervals, the authors developed several metrics based on the distribution of points in their 13 defined regions of the plot, or segments. Each segment contained many smaller histogram bins. Segments were defined as shown in the figure below.

Figure 9. Two dimensional histogram segments, as defined by Sarkar et al. for their plot of $\delta RR(i-1)$ versus $\delta RR(i)$ [15].

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Their metric IrregularityEvidence measured how sparse the distribution of points was by summing the number of bins that contained at least one point in segments 1 through 12. This metric would show a high value during AF and a low value during normal sinus rhythm. DensityEvidence was defined as the sum over segments 5 through 12 of the difference between the number of points in the segment and the number of occupied bins in the segment. This provided a measure of cluster density along the vertical, horizontal, and diagonal segments of the plot. AnisotropyEvidence was defined to measure the orientation of the distribution. It was calculated by summing the absolute value of the total point count

in segments 9 and 11 minus the total point count in segments 10 and 12 with the absolute value of the total point count in segments 6 and 7 minus the total point count in segments 5 and 8. Finally, PACEvidence looked for evidence of a compensatory pause by summing the point count minus the number of occupied bins in regions 1 through 4, 5, 6, and 10 and subtracting the difference between the point count and the number of occupied bins in each of regions 7, 8, and 12.

These four metrics were combined to create three additional metrics: AFEvidence, ATEvidence, and OrgIndex. AFEvidence was defined as $\text{IrregularityEvidence} - \text{OriginCount} - 2 * \text{PACEvidence}$, where OriginCount was the number of points in segment 0. ATEvidence was defined as $\text{IrregularityEvidence} + \text{AnisotropyEvidence} + \text{DensityEvidence} + \text{RegularityEvidence} - 4 * \text{PACEvidence}$, where RegularityEvidence was computed as the number of short term RR interval medians that were no more than 10 ms different than the long term median in the previous T minute period. Short-term medians were calculated for groups of 6 or 12 beats. Finally, OrgIndex was defined as $\text{OriginCount} + \text{AnisotropyEvidence} + \text{DensityEvidence} + \text{RegularityEvidence} - 2 * \text{IrregularityEvidence}$.

The AF and AT detectors used these final three metrics to detect AF and AT. In base “AF/AT mode,” AF and AT with irregular ventricular response were detected if AFEvidence was greater than the threshold. In the “supplemental AT mode,” AF was detected if AFEvidence was greater than the threshold and ATEvidence was less than its threshold. AT was detected if ATEvidence exceeded the threshold and AFEvidence was less than its threshold or if RegularityEvidence was greater than its threshold. In the case where both AFEvidence and ATEvidence exceeded their thresholds, AF was detected if OrgIndex

was less than zero; otherwise, AT was detected. The detector was optimized choosing $T = 2$ minutes and bin size = 40 ms.

With these parameters, the episode sensitivity and positive predictive value for AF Detection were 94.7 and 95.8 percent, respectively, in the MIT-BIH AF database and 96.4 and 79.4 percent, respectively, in the AF database compiled by Sarkar et al. to contain AF episodes with their onset visible within the recordings. In the normal sinus rhythm databases, there were 238 false episode detections out of 174 patient records totaling 4078 hours. 100 episodes were 2 minutes in duration and 21 episodes were greater than 10 minutes in duration. Four patient records contributed 135 of the false detections [15]. This algorithm was designed to be robust to PACs and PVCs, but no specific analysis of performance in the presence of PVCs was provided.

2.2 Shortcomings of the Current Practice

Most of the current PVC detection algorithms are designed for use in Holter monitors or for offline analysis of previously collected ECG data. Because these applications are not limited by the constraints of an ICM, the algorithms have not been designed with compatibility with a low-power implantable device in mind. Many current methods use a brute-force approach where a large number of metrics are analyzed. Existing solutions that utilize complex morphological or frequency domain criteria are impractical to implement within a low-power ICM. Other methods use repeated correlation calculations to optimize alignment of a window, as in Krasteva and Jekova [29]. These computationally-intensive solutions are better suited for implementation on systems with fewer size, complexity, and power consumption restraints than an ICM. Existing research into these methods has not discussed feasibility of implementation in an implantable device.

Several simpler existing solutions that use only interbeat interval data ignore a large portion of the identifying features of PVCs. When only using timing data, PVCs are difficult to distinguish from other arrhythmias that cause uneven interval patterns, including PACs and Atrial Fibrillation. These timing-based methods may be effective in distinguishing PVCs from normal sinus rhythm, but performance would be much less robust in the presence of other rhythm abnormalities.

The Ittatur et al. [30] algorithm using the RR interval, QRS width, and QRS pattern classification succeeds in using both morphology and timing information in a method designed with real-time, embedded applications in mind. However, Ittatur et al. developed their QRS pattern classifications using the same data set on which they tested their final algorithm. While their chosen QRS pattern types cover the actual patterns observed in their test data set from the MIT Arrhythmia Database, the patterns may not adequately cover the range of signals that could be observed from an implanted device, where device position and orientation, and thus QRS morphology, can vary significantly based on patient body type and physician preference. Additionally, their method requires saving all ECG derivative values for the duration of the QRS complex for subsequent determination of a single negative peak and the positive peaks to both the left and right of the negative peak. Once these three peaks have been determined, the algorithm can classify the QRS pattern. Only after this QRS pattern classification has been made can the QRS width measurement be made, which again requires using ECG derivative values from the duration of the QRS complex to search for threshold crossings. A continuous rolling ECG or ECG derivative buffer may be required to ensure that the start of the QRS complex is included in the analysis buffer because the QRS complex is typically detected by the ICM a short time into

the actual QRS complex. This maintenance of a relatively long, possibly continuous, buffer of ECG values is costly in terms of ICM memory and is therefore inconsistent with the design constraints for this thesis, as will be discussed in the next chapter.

While the Sarkar et al. [15] method for AF Detection was designed for implementation on an ICM, it only provides exclusion of PVC intervals from consideration in an AF detection algorithm. It does not provide any data on the occurrence of PVCs, nor would it be easily generalizable from AF detection to other algorithms that could benefit from having PVCs flagged or excluded.

Additionally, many of these methods require manual initialization with known PVC and/or non-PVC beats. In these methods, such as the algorithm described by Krasteva and Jekova [29], a physician or other trained individual must select representative PVC and/or normal sinus rhythm beats before the algorithm can begin analyzing and classifying beats. Other methods produce groupings of beats without classifying each group, again requiring manual intervention to obtain meaningful results, as in Moraes et al. [18]. This kind of manual initialization or classification is not desirable for a commercially released implantable device.

3 Design Methodology

3.1 Design Constraints

A suitable PVC detection algorithm must be compatible with implementation on an ICM. This significantly constrains the permissible computational complexity and power consumption of the algorithm. Without actually implementing the algorithm in software on the implantable device and measuring power consumption with and without the algorithm running, it is difficult to quantify the power consumption of the algorithm. However, currently implemented algorithms for the detection of other arrhythmias or features of the SECG signal can be used to provide guidelines for keeping the algorithm within the constraints of an ICM. The power consumption of these existing algorithms is considered acceptable, so developing a new algorithm within similar constraints provides a strong likelihood that the new algorithm would also maintain a reasonable level of power consumption. The constraints in this section were developed in conjunction with research and design engineers with experience working on BIOTRONIK's BioMonitor line of ICMs.

First, the algorithm must not require continuous monitoring of the SECG signal except during a limited period after a QRS complex has been detected. ICMs have algorithms in place to monitor for the occurrence of a QRS complex, and only when the QRS detection algorithm has flagged a QRS event can the PVC detection algorithm start collecting or analyzing data. This means that the PVC detection algorithm must only analyze the segment of the SECG that occurs for a short period of time started by the QRS marker, also referred to as a ventricular or V sense marker. Analysis of the SECG signal prior to a V sense marker would require continuously maintaining a rolling buffer of SECG values so

that previous values could be used when a V sense marker occurred. This continuous burden of the PVC detection algorithm would be unacceptable.

The algorithm's use of SECG signal values should be active for no more than approximately one quarter of the time. For a typical heart rate of 60 beats per minute, that means that the PVC detection algorithm should only use SECG samples from approximately 250 ms or less following each QRS marker.

The algorithm should avoid requiring division by any number that is not a power of 2. SECG values in BIOTRONIK BioMonitor devices use a two's-complement representation, so division by a multiple of 2 can be performed easily using right-shifting [36]. However, division by a number that is not a power of 2 is not as simple, and while it is possible, the algorithm should avoid requiring this division where possible.

In addition to the constraints related to computational complexity and power consumption, several other constraints are also introduced by the nature of the implanted device. For example, the algorithm must be able to function in real time, or at least in near real time. This means that it is acceptable for analysis of a given beat to require waiting until the next beat occurs in order to determine the interval from the beat in question to the following beat. Upon receiving the indication that the next beat has occurred, the algorithm must be able to immediately complete classification of the beat in question.

The ICM already contains certain filters for the SECG data. Some of these filters are completely unavoidable in the current and planned future device designs and cannot be bypassed by the data. Other filtering could possibly be bypassed by introducing a parallel pathway for the SECG data that skips or alters some filters. However, introducing this new pathway would lead to additional design time and cost. The algorithm must be compatible

with the unavoidable SECG filtering and should strive for compatibility with all existing filtering if possible. Specific details of the SECG filtering will be described in the next chapter along with other information about the data sets used for this thesis.

Finally, the algorithm must be able to function without requiring manual initialization by a physician or other trained individual. In particular, the classification algorithm must not require selection of representative PVC or non-PVC template beats. At most, the algorithm can require physician selection of a small number of programmable parameters. For example, the algorithm should be able to be turned on and off by the physician, so at least one parameter will exist and be visible to the physician. It may be beneficial to have an additional option of different sensitivity levels, such as low, medium, and high sensitivity parameter pre-sets. Any other parameters must be understandable by a physician without in-depth knowledge of the details of the algorithm. If there are programmable parameters, a standard setting must be chosen that would be used unless the physician chooses to modify the parameters.

3.2 Algorithm Components

3.2.1 High-Level Overview

The proposed PVC detection algorithm uses a combination of a limited number of computationally-simple morphology and timing criteria to identify PVCs. For each beat, morphology and timing metrics are compared against rolling baseline averages for the corresponding metrics. The rolling baselines contain values from non-PVC beats, as identified by the algorithm.

The morphology criteria are chosen to identify the change in morphology from normal QRS complexes to PVCs. The criteria include two separate components: a width

metric and a peak amplitude range metric. Each metric is compared to a corresponding rolling baseline average of values from non-PVC beats, and if either the width or the peak amplitude range criterion is met, then the morphology criteria for a PVC are met.

In addition to the morphology criteria, timing criteria must also be met for a beat to receive classification as a PVC. The timing criteria consist of a pre-beat interval and a post-beat interval. Baseline comparisons are made to look for a short pre-beat interval (PVC coupling interval) and a long post-beat interval (compensatory pause). Alternately, the post-beat interval criteria can be met if the post-beat interval is short enough to likely be characteristic of an interpolated PVC or a run of PVCs. If both the pre- and post-beat interval criteria are met, then the timing criteria for a PVC are met.

If both the morphology criteria and the timing criteria are met, then the beat is classified as a PVC. If the beat is not classified as a PVC, meaning that the morphology and/or timing criteria were not met, the morphology and interval metrics are added to the corresponding rolling baselines, replacing the oldest value in each baseline.

Now that the basic flow of the algorithm has been described, a more detailed description of each algorithm component will be provided below. Tunable parameters such as actual threshold values will not be precisely specified in these sections and instead will be defined in the following chapter, along with a discussion of their impact on algorithm performance.

3.2.2 Initial Beat Eligibility Criteria

A beat is only eligible for classification as a PVC if neither the preceding nor the following detected event is classified as a noise event. Classification as a noise event occurs in a similar way to detection of a QRS complex, and a noise event marker is then available to

other algorithms running in the ICM just as a QRS marker would be. An event preceded or followed by a noise event has a high likelihood of a noisy SECG signal that could negatively impact the morphology metrics. Also, timing to the previous and following event would be uncertain when a noise event could have prevented accurate detection of one of those neighboring QRS complexes. For these reasons, a QRS complex with a neighboring noise event is a poor candidate for PVC detection. Exclusion of these QRS complexes is a common practice in other BIOTRONIK BioMonitor arrhythmia detection algorithms.

Additionally, the magnitude of at least the positive or negative peak of the current beat must exceed a small amplitude threshold of 0.05 mV, designed to ensure sufficient signal quality to derive useful morphological information. This amplitude is 10 percent of the maximum possible signal amplitude (0.5 mV). If a beat meets these initial eligibility requirements, then it moves on to comparison against the morphology and timing criteria for PVC classification. If these eligibility requirements are not met, the beat is not attempted to be classified as a PVC or normal beat, and its metrics are not added to the rolling baselines.

3.2.3 Morphology Criteria

The morphology criteria consist of two components: positive to negative peak amplitude range and a width analog. Both metrics are determined within a window started by the V sense marker. The window extends approximately 200 ms after the V sense marker. If the next V sense marker is less than this window length after the current marker, then the window is shortened to end at the next marker.

The peak amplitude range metric is computed by taking the maximum value within the window and subtracting the minimum value within the window, as shown in the figure

below. The shaded sections in the figure highlight the time periods in the morphology window after each QRS complex is detected by the ICM. The vertical double-sided arrow by each QRS complex shows its measured peak amplitude range.

Figure 10. BioMonitor 2 SECG sample demonstrating the peak amplitude range calculation for one PVC and two normal sinus beats. The shaded regions represent the morphology window following each detected QRS complex, and the vertical double-sided arrows show the peak amplitude range for each QRS complex.

The peak amplitude range metric is compared to its corresponding rolling baseline average for classification. If the range measurement for the current beat differs from the rolling baseline average by more than a set threshold percentage, then the morphology criteria for PVC detection are met. The comparison is two-sided, meaning that if the peak range is significantly less than or greater than the baseline average, the peak range criterion is met.

The width metric is calculated as the number of samples within the morphology window that have a magnitude greater than a relatively small threshold, as shown in the figure below. The shaded sections again highlight the time periods in the morphology window after each QRS complex is detected. The two solid horizontal lines are the amplitude thresholds. SECG samples within the morphology window that are outside of

these two thresholds are counted towards the width metric. These portions of the SECG signal are emphasized with a bolded line. In addition, the approximate measured width is indicated with arrows below each QRS complex. In the example below, the PVC clearly has a larger width than the two surrounding sinus beats. Note that the approximate width arrows ignore the narrow portions of the QRS complexes that are not counted towards width due to their proximity to baseline as the signal moves from a negative peak to a positive peak or vice-versa. These portions are included in the width arrows for ease of viewing, but they are not bolded, indicating that they are not actually part of the calculated width.

Figure 11. BioMonitor 1 SECG sample demonstrating the width calculation for one PVC and two normal sinus beats. The bolded portions of the SECG show the portions of each QRS complex that are counted towards the width measurement. The arrows below each QRS complex indicate the approximate width of that QRS complex.

The width metric is also compared to its corresponding rolling baseline average, but unlike the peak amplitude range comparison, the width comparison is one-sided. If the width of the current beat is greater than a set threshold percentage times the rolling baseline average, then the width criterion is met. Satisfying either the peak range criterion or the width criterion is sufficient to meet the morphology criteria for PVC detection.

3.2.4 Timing Criteria

Like the morphology criteria, the timing criteria also consist of two components: a pre-beat interval and a post-beat interval. The pre-beat interval is the interval from the current marker to the preceding QRS complex marker, and the post-beat interval is the interval from the current marker to the next QRS complex marker. A beat satisfies the timing criteria if the pre-beat interval is shorter than a threshold percentage times the rolling baseline average and the post-beat interval is longer than a different threshold percentage times the rolling baseline average. An example of this scenario is shown below, with the intervals marked in green representing the normal sinus interval, while the red and blue intervals are the short pre-beat and long post-beat intervals, respectively.

Figure 12. BioMonitor 2 SECG sample showing an example of a PVC with a short pre-beat interval and a long post-beat interval. Intervals marked in green are normal sinus intervals, while the red interval is the short pre-beat interval, and the blue interval is the long post-beat interval.

If the post-beat interval is instead shorter than a short absolute threshold, then the post-beat criterion is also considered met as this would be characteristic of an interpolated PVC or a run of PVCs. The SECG sample below shows an interpolated PVC with a short pre-beat interval in red and an even shorter post-beat interval in blue. The intervals marked in green show the relatively consistent sinus intervals throughout, continuing even through the PVC.

Figure 13. BioMonitor 2 SECG sample showing an example of an interpolated PVC with a short pre-beat interval (red) and an even shorter post-beat interval (blue). The green intervals are the normal sinus intervals.

Both the pre-beat interval criterion and the post-beat interval criterion must be met for the timing criteria for PVC detection to be satisfied.

3.2.5 Rolling Baselines

A beat is classified as a PVC if both the morphology criteria and the timing criteria are met. If a beat was eligible for classification but it is not classified as a PVC, then the rolling baselines are updated with the metrics for the new beat. There are three separate rolling baselines (peak amplitude range, width, and interval), each of which holds values for the eight most recent, eligible non-PVC beats. The current beat's peak amplitude range and width are added to the appropriate rolling baselines if the current beat was not classified as a PVC and if the morphology window was not shortened. The current beat's pre-beat interval is added to the interval rolling baseline if neither the current beat nor the previous beat was classified as a PVC. Additionally, if the interval is nearly double the current rolling baseline average or longer, it is not added to the rolling baseline because these long intervals are likely the result of a missing QRS complex marker. Only one interval rolling baseline is maintained; this single baseline is used for comparison for both the pre-beat and post-beat

interval metrics. When a metric’s value for the current beat is added to a rolling baseline, it replaces the oldest value in the rolling baseline.

3.2.6 Algorithm Initialization

Rolling baseline initialization when the algorithm first begins occurs automatically without any physician input. This may result in a short period of time in which classification accuracy is lower than normal, particularly if the patient is experiencing frequent PVCs during the initialization period. This may be mitigated by not saving PVC-related statistics during the initialization period. At a minimum, the initialization period must be long enough to collect the required number of beats to fill the rolling baselines. A longer initialization period may be beneficial to allow time to refill the baselines once PVC classification has started to improve the contents of the baselines and reduce the number of PVC beats falsely included in the baseline. For a long-term monitoring device, this comparatively short initialization period does not significantly impact overall performance of the algorithm.

For this thesis, the available SECG data is in the form of short “snapshots” with durations of approximately one to three minutes. In these short timeframes, the initialization period could significantly impact overall performance. In order to not further limit the data available for algorithm development and validation, overall performance is analyzed by initializing the rolling baselines with known non-PVC beats, as determined by manual annotation. However, a separate analysis of the proposed automatic initialization method will also be provided to demonstrate that the algorithm can recover from this condition.

3.2.7 Tunable Parameters

The design of this PVC detection algorithm leaves the possibility for many parameters to be tuned to strengthen different aspects of performance. The width, peak

amplitude range, pre-beat interval, and post-beat interval thresholds are all designed as percentages of the corresponding rolling baseline average, where the multiplicative threshold percentage can easily be modified over a range of reasonable values. Both width and post-beat interval are expected to be larger for a PVC, so any threshold multiplier greater than 1 will capture this expected behavior. The pre-beat interval is expected to be shorter for a PVC than for a normal beat, represented by a threshold multiplier less than 1. Finally, the peak amplitude range threshold is double sided, so a pair of thresholds is required to identify values that are significantly different from baseline in either direction. One threshold must be less than 1, while the other is greater than 1.

Window length is also a potentially tunable parameter. However, the rest of this thesis uses a constant value for this parameter due to its strong basis in the clinically-determined features of QRS complexes. To reduce the susceptibility of the morphology window to noise and limit the computational demand of the algorithm, window length is chosen to be as short as possible while still capturing widened QRS complexes. A normal QRS complex is expected to have a width of less than 120 ms [8]. There is not a definitive maximum width of a PVC QRS complex, but studies have found that widths can range up to approximately 200 ms [37]. The point at which a QRS complex is detected from the SECG signal will vary, but detection obviously cannot occur before the start of a QRS complex. Therefore, 200 ms after the QRS marker should be sufficient to capture the entire QRS complex for the vast majority of normal and PVC QRS complexes. Further, even if a PVC were wider than 200 ms, the measured width within the 200 ms window should still be sufficient for classification as a PVC since a normal beat should be significantly narrower than this. Since the proposed algorithm's width calculation looks for the number of samples

over a threshold rather than looking for the end of the QRS complex, a QRS complex that does not fit entirely within the window would still have a large measured width. For these reasons, a morphology window of approximately 200 ms is used in the proposed algorithm. The actual window used throughout this thesis is 195.3125 ms due to the sampling rate of the available SECG data. This window length corresponds to 25 samples at a 128 Hz sampling rate.

Similarly, while the short post-beat interval threshold could be a tunable parameter, its value is instead chosen as a fixed value based on physiological characteristics rather than being empirically determined. The average maximum heart rate for adults starts at approximately 200 beats per minute at age 20 and decreases to 150 beats per minute by age 70 [38]. This is expected to be the maximum achievable sinus rate for adults. As will be discussed in more detail in the following section along with other design tradeoffs, the post-beat interval criterion serves an important role in preventing runs of false PVC detections. As a result, limiting the possibility that this short post-beat interval criterion could consistently be met during normal sinus rhythm was of chief importance when choosing this threshold value. As a result, the threshold of 300 ms was chosen; a consistent 300 ms interbeat interval would correspond to a heart rate of 200 bpm, the average maximum heart rate for a 20-year-old. This maximum heart rate would not typically be reached during normal or even strenuous exercise, particularly for an older individual, so the risk of consistently meeting the short post-beat interval criteria outside of the scenarios of interpolated PVCs or a run of PVCs is very small.

Rolling baseline length is another potentially tunable parameter. However, in order to compute an average baseline value for a metric, the length should be a power of 2, as

discussed in the Design Constraints section. Taking this restriction into account, possible reasonable values include 4, 8, and 16 beats in each rolling baseline. Eight beats is used throughout this thesis as the rolling baseline length as it allows relatively quick adaptation to a change in heart rate or to a change in overall SECG signal morphology caused by a change in patient activity or position. It also requires fewer values to be stored in device memory for each baseline than the 16-beat baseline would require. At the same time, the 8-beat baseline is large enough that one incorrect or abnormal value in the baseline will not have a huge impact on the baseline average. Finally, an analysis of different buffer sizes found consistently better performance for an 8-beat baseline than for the 4- or 16-beat options.

3.3 Design Tradeoffs

Each of the tunable parameters discussed in the previous section comes with a tradeoff. The width and post-beat interval threshold multipliers are both larger than 1 because these metrics are expected to be larger for a PVC than for a non-PVC beat. Larger threshold multipliers for these metrics will result in stricter PVC detection criteria that are more difficult to meet, thus tending to reduce false positives (normal beats classified as PVCs) while also increasing false negatives (PVCs classified as normal beats). The pre-beat interval threshold multiplier is less than 1, with a smaller multiplier making the pre-beat interval criterion more difficult to meet, again decreasing false positives and increasing false negatives. Finally, as the two threshold multipliers for the double-sided peak amplitude range comparison move away from 1, that criterion becomes more difficult to meet. A quantitative discussion of these and other tradeoffs will be included in the following two chapters along with performance results on the development data set, so only this qualitative discussion is provided here.

The threshold tradeoffs are strictly algorithm performance tradeoffs, exhibiting the typical behavior that improving sensitivity will generally decrease specificity and vice-versa. Other tradeoffs in terms of computational complexity and implementation cost versus algorithm performance are also important in the design of this algorithm. For example, using the current beat's peak amplitude to determine the width amplitude threshold used during width calculations might provide improved performance, but it would require an additional buffer to be maintained for a portion of the morphology window so that SECG values could be compared to the peak after that peak is found. This tradeoff will be analyzed quantitatively in the following two chapters.

Similarly, using a portion of the SECG signal from just before a QRS complex marker tends to provide more complete morphological information because QRS detection is slightly delayed from the actual onset of the QRS complex. However, this additional information comes at the cost of continuously maintaining a rolling buffer of SECG values. The outcome to this tradeoff was already determined when developing the design constraints, which do not allow continuously maintaining an SECG value buffer. In this case, it was determined that the computational cost of the feature was not worth the improvement in performance it could offer, regardless of the size of this performance improvement.

Another tradeoff involves the benefits of real-time versus near real-time (one beat delayed) PVC classification. Use of the post-beat interval in the PVC detection algorithm means that classification of a beat cannot be completed until the next beat occurs. This means that any sort of real-time display of the SECG and its event markers cannot display PVC markers without requiring a delay. This behavior is considered acceptable and is

consistent with other arrhythmia detection algorithms in the BIOTRONIK BioMonitor family of devices, which are suspended during active communications when a real-time SECG signal would be available to physicians. Additionally, using the post-beat interval is an important safeguard against runs of false PVC detections due to a change in patient activity or position causing a sudden morphology change, for example. In this case, the morphology criteria could conceivably consistently be met for each new beat compared to the baseline data from before the morphology change. Furthermore, if heart rate increased even slightly, the pre-beat interval criterion could also be met consistently. Since only beats not detected as PVCs are added to the rolling baselines, the baselines in this hypothetical case without a post-beat interval criterion would never be updated with values reflecting the new morphology and heart rate. This could produce a large number of false PVC detections, with no way for the rolling baselines to be updated to adapt to the changed SECG signal. When using a post-beat interval criterion, two consecutive beats typically cannot be classified as PVCs, unless the short post-beat interval criterion is met. This short post-beat interval threshold is quite short and expected to only be met by interpolated PVCs or runs of PVCs, so it has a low risk of contributing to the run of false PVCs scenario described previously. In all other cases, a given interval is the post-beat interval from one beat and then is the pre-beat interval for the next beat. It can either meet the long post-beat interval or the short pre-beat interval criterion, but not both. Thus, even in the case of a sudden morphology change, after approximately 16 beats or less, the rolling baseline values will be replaced with values representing the new morphology because at most 8 of the 16 beats can be classified as PVCs. This is an important safeguard against runs of false PVC detections, and as such outweighs the tradeoff requiring a one-beat delay in PVC classification.

4 Algorithm Refinement

4.1 Development Data Set

The development data set for this thesis came from two BIOTRONIK BioMonitor family device types: BioMonitor 1 and BioMonitor 2. Both devices are ICMs that use a similar SECG signal, although the hardware and sensing vectors are different for the two devices. BioMonitor 1 devices use three sensing electrodes to measure the SECG signal over three different vectors, as labelled in the figure below [14].

Figure 14. BioMonitor 1 device with its three sensing vectors labeled as A, B, and C.

The measured signal from these three vectors is combined into one SECG signal that is used for QRS complex detection, arrhythmia detection algorithms, and display to physicians [14]. The relative weights of these three vectors can change from one beat to the next when combining the individual signals into the composite signal, resulting in a sudden change to signal morphology even when the three individual signals have not changed significantly. This presents an additional challenge to the morphology components of the PVC detection algorithm proposed in this thesis. In practice, the data set used for algorithm development did not frequently exhibit this behavior. Additionally, the algorithm is targeted for implementation in a future BioMonitor family device, not the original BioMonitor 1 device. Future devices do not use this three vector method, so this scenario would never be

encountered on the targeted device platform. For this reason, the remainder of this thesis will ignore this aspect of the BioMonitor 1 SECG signal.

Unfortunately, the full resolution, continuous SECG signal is not stored by the device and therefore is not available for algorithm development purposes. The only saved SECG signal that is available comes from short snapshots that are recorded when an arrhythmia is detected by the device or when the patient triggers a snapshot manually because they feel symptomatic. These snapshots are each at least 40 seconds long, with most of them being approximately one to two minutes long for the BioMonitor 1 device. These snapshots contain SECG data that are down-sampled from the device's internal sampling rate of 512 Hz to 128 Hz, while preserving peak values. The down-sampled data are then compressed into 8-bit numbers. The first 3 bits represent the time interval from the current sample to the previous sample, while the remaining 5 bits represent the amplitude of the current sample. The amplitude was originally an 8-bit value that is then compressed into this 5-bit code. This amplitude is encoded logarithmically, allowing higher linear resolution at values closer to zero. While effort is made to maintain the most important information about the signal, this is still a lossy compression. Additionally, an algorithm is used to reduce the number of snapshot data points that must be preserved. Essentially, a new data point is written if a data point has changed significantly from the previously recorded value and the same slope is not maintained to the following data point, or if the number of samples at 128 Hz since the last recorded value is 7, since this is the largest value that can be written in the 3-bit time field [39]. The output of this algorithm and the accompanying down-sampling and compression was used for the development of the PVC detection algorithm in this thesis.

In addition to the BioMonitor 1 snapshot data described previously, BioMonitor 2 snapshots were also used for PVC detection algorithm development. The BioMonitor 2 device performs a similar function to the BioMonitor 1 device, but the newer device's hardware and its sensing vector are different than those of its predecessor. Unlike BioMonitor 1, BioMonitor 2 has only a single sensing vector. This vector is longer than any of the three BioMonitor 1 vectors, and extends from the rounded right-hand side to the left-hand tip in the figure below. This vector is approximately 9 centimeters, compared to vectors of approximately 2.5, 4, and 4 centimeters for the three vectors on the BioMonitor 1 device.

Figure 15. BioMonitor 2 device.

The BioMonitor 2 snapshots contain the same 128 Hz, compressed data as the BioMonitor 1 snapshots described previously. The only significant difference is that the BioMonitor 2 snapshots all tend to be longer. While they still have the same 40 second minimum length, most snapshots are actually around two to three minutes in length.

The BioMonitor 1 data set contained 304 total snapshots from 129 different patients, while the BioMonitor 2 development data set contained 350 snapshots from only 5 patients. The use of BioMonitor 2 data is preferable as the future BioMonitor family products will more closely resemble BioMonitor 2 than the older BioMonitor 1 devices. However, the BioMonitor 2 device was still in its First-in-Man study at the time of algorithm development and validation, with only 30 total devices implanted. The majority of this data is saved for validation, so it is not available for algorithm development. For this reason, BioMonitor 1

data is used to supplement the development data set and provide a larger number of patients and therefore a larger range of normal and PVC QRS complex morphologies and timings. Altogether, the development data set includes approximately 90,000 sensed QRS complexes, with approximately 4,500 of those being PVCs.

All snapshots consist of continuous SECG data along with the event markers detected by the device. These markers include both QRS complex markers and noise event markers. The SECG data for all snapshots have been passed through a low-pass filter with a cut-off frequency of 40 Hz. This filtering is highly unlikely to change or be able to be circumvented in future products. Additionally, the BioMonitor 1 data have been passed through a 4.5 Hz high-pass filter, while the BioMonitor 2 data have been passed through a 0.5 Hz high-pass filter. All filters are first-order Butterworth filters. In order to standardize the data, the BioMonitor 2 snapshots were passed through a 4.5 Hz high-pass filter before performing any other analysis. This filtering was also recommended by BIOTRONIK engineers designing the next-generation BioMonitor device as being similar to the filtering of what will likely be the most readily available SECG data within the next BioMonitor device.

4.2 Standard of Comparison

All snapshots were manually annotated by the author of this thesis to identify which QRS complexes were PVC beats. The author was instructed by a Clinical Research Specialist at BIOTRONIK who formerly worked as a cardiac nurse. This Clinical Research Specialist provided initial guidance in PVC identification as well as spot-checking for snapshots that had already been annotated to confirm that the author was appropriately annotating PVCs in various snapshots. Manual annotations were used as the expected, correct classification against which PVC detection algorithm classifications were compared.

4.3 Performance Metrics

Each sensed QRS complex in the BioMonitor data was manually annotated as a PVC or non-PVC (normal) beat. Each sensed QRS complex was then also identified by the PVC detection algorithm as a PVC or non-PVC beat. Therefore, each beat could have one of four classification outcomes:

- True positive: PVC correctly identified by the algorithm as a PVC (true PVC)
- False positive: Non-PVC incorrectly identified by the algorithm as a PVC (false PVC)
- True negative: Non-PVC correctly identified by the algorithm as a non-PVC (true non-PVC)
- False negative: PVC incorrectly identified by the algorithm as a non-PVC (missed PVC)

The total number of beats in each category was accumulated over all snapshots or a relevant subset of snapshots and then further analyzed as sensitivity, specificity, and positive predictive value (PPV). These metrics are frequently used to analyze performance of classification algorithms and were used in many of the studies included in the literature summary of this thesis [8], [17], [23], [26], [29], [30].

Sensitivity, also referred to as the true positive rate, is the proportion of real positives that are correctly classified as positives. In other words, sensitivity is the true positive count divided by the number of true positives plus false negatives [40]. For this application, sensitivity is the number of PVCs correctly identified by the algorithm divided by the total count of manually-identified PVCs.

Specificity, also referred to as the true negative rate, is the proportion of real negatives that are correctly classified as negatives. This is calculated as the true negative count divided by the number of true negatives plus false positives [40]. For the PVC

detection algorithm, this is the number of non-PVC beats correctly identified as non-PVCs divided by the total number of manually-identified non-PVCs.

PPV is the proportion of algorithm positives that are true positives; it is calculated as the true positive count divided by the number of true positives plus false positives [40]. This number represents the probability that a beat identified by the algorithm as a PVC is actually a PVC.

In most of the available snapshots, and in most clinical patients, PVCs represent a relatively small minority of total heartbeats. This can cause some difficulties in obtaining appropriate metrics for performance analysis. For example, a snapshot with very few true PVCs could have a very high sensitivity and specificity but a very low PPV. In this case, it can also be useful to consider a breakdown of the number of false PVCs per a unit of time. For this reason, an additional metric of the number of false PVCs per hour is also used throughout this thesis. In the clinical setting, the occurrence of six or more PVCs per minute is typically considered pathological [1], so false PVCs must occur at a significantly lower rate than 6 PVCs per minute, or 360 PVCs per hour, in order to avoid falsely creating the appearance of a clinically significant arrhythmia.

4.4 Rejected Morphology Metrics

During algorithm development, several additional morphology metrics were investigated and ultimately rejected as inferior to the width and peak amplitude range metrics. Two of these rejected metrics will be discussed below.

4.4.1 Area

Use of an area metric in PVC detection is intuitively logical as PVCs are typically wider and of larger amplitude than normal QRS complexes [1], [5]. Larger width combined

with larger amplitude results in a larger area for a PVC than for a normal QRS complex. However, the filtering employed in processing SECG data can complicate this seemingly simple characteristic. Because PVCs contain more low frequency components than a normal QRS complex, the 4.5 Hz high-pass filter applied to the SECG data disproportionately affects PVCs. Lin et al. found that the frequency spectra of normal beats were predominately of smaller amplitude than that of PVCs on the range from 1 to 3 Hz and of larger amplitude on the range from 4 to 12 Hz [20]. Thus, the filtering at 4.5 Hz typically causes a more significant amplitude and area reduction for PVCs than for non-PVC beats. In practice, the unfiltered area increase of a PVC QRS complex compared to a normal QRS complex is approximately cancelled out by the area reduction caused by filtering. For this reason, area was rejected as an unsuitable metric given the filtering likely to be in place within the targeted ICM platform. Width was chosen as a more suitable metric that was significantly less affected by the high-pass filtering.

4.4.2 Slope

A measure of QRS slope was also examined as a possible morphology metric for QRS detection. Due to the design constraints discussed previously, a suitable slope metric could not require saving a large number of SECG samples before determining which points to measure the slope between. Slope from the SECG point when the QRS complex was detected to the QRS peak was chosen as easy to calculate and potentially meaningful. In practice, this slope did not exhibit a consistent change for PVCs compared to normal QRS complexes. One possible reason for this behavior is that the QRS complex marker often occurs slightly later in a PVC QRS than in a normal QRS due to a dynamic threshold used in QRS marker detection. This threshold gradually steps down from a high threshold shortly

after the previous QRS complex to lower thresholds as more time passes. Since PVCs occur earlier than a normal beat, this threshold is often at a higher level when a PVC occurs. Given that there is typically only a short delay from the marker to the QRS peak, this slightly later marker declaration significantly impacted the duration over which the slope was computed, at times hiding the actual slope change in a PVC. Additionally, these dynamic thresholds vary based on the amplitude of the previous QRS complex, resulting in changes in the detection time of even normal QRS complexes based on characteristics of the previous QRS complex. Since use of SECG points from before the QRS marker is not compatible with the design constraints for this algorithm, no easily available workaround existed to obtain the actual start of the QRS complex.

Further, a slope calculation requires division by a number that will, in general, not be a power of two. As discussed in the design constraints, division by a number that is not a power of two should be avoided when possible. While this issue could have been circumvented or possibly tolerated in the algorithm, this difficulty in combination with the metric's poor performance led to discarding this metric early in algorithm development.

4.5 Performance Tradeoffs

As discussed previously, many tradeoffs must be considered in designing a PVC detection algorithm, including both tradeoffs between false PVCs (false positives) and missed PVCs (false negatives) and tradeoffs between algorithm performance and computational complexity and device memory requirements. This section provides more detailed analysis for several of the critical tradeoffs considered when developing this algorithm. Algorithm performance on the development data set is provided separately in the following chapter to correspond with the tradeoffs discussed below.

4.5.1 Multiplicative Threshold Values

Each of the morphology and timing metrics has a threshold value that can be chosen to optimize performance, quantified by a particular cost function, on the training data set. Determination of this cost function is subjective and depends on clinical factors that can vary from physician to physician and patient to patient. A simple and obvious way to optimize performance is to minimize the total number of classification errors. However, this assumes that a false positive has the same cost as a false negative, which may or may not be true. Typically, in a clinical setting, a false arrhythmia detection is an inconvenience while a missed arrhythmia detection can be dangerous to the patient. As discussed earlier, a single PVC is not typically considered pathological and as a result is not of clinical significance by itself. Therefore, these standards can be slightly relaxed for PVCs since the more important issue is getting an overall sense of whether PVCs are occurring frequently or not, rather than needing a precise count. Further, detected PVCs would be excluded from other arrhythmia detection algorithms like AF detection. False detection of many PVCs during an actual AF episode could cause the device to fail to detect the AF episode. As a result, the PVC false positives would cause an AF false negative.

These complexities cannot easily be generalized across all patients. In many cases, the physician's knowledge of the patient's history and symptoms will impact their preferences for the sensitivity of PVC detection. As a result, this thesis will propose three sets of thresholds, designed to provide low, medium, and high PVC detection sensitivity. The physician could choose to program the ICM to any one of these three levels, and all PVC detection threshold parameters would be set accordingly. This style of customization is consistent with other BIOTRONIK BioMonitor detection parameters. For example, the AF

detection feature provides an AF Sensitivity parameter with options of Low, Medium, and High [14]. This provides the physician with a chance to customize device behavior to their preferences without needing to understand the impact of the individual low-level parameters used in the device's algorithms.

Parameters for each of these settings were determined by using the cyclic coordinate descent algorithm to minimize three different error functions. These error functions were chosen to represent low, medium, and high PVC detection sensitivity. The cyclic coordinate descent algorithm minimizes an objective or error function across multiple variables by cycling through each of the variables individually. The first variable is chosen to minimize the error function while holding the rest of the variables constant. Then, using this value for the first variable, the next variable is chosen to minimize the error function. This continues through all variables and then loops back to the first variable, which is now chosen to minimize the error function given all of the other variable values that have been chosen to minimize the error function. This process continues cycling through all variables repeatedly until each variable is at the optimal value given the other optimal values. This means that the final iteration through each variable will not be able to achieve an improvement in performance by changing any of the variables' values. This method is often used when, as in this application, it is not feasible to use the gradient of the error function to find the direction of steepest descent [41].

Algorithm performance, as determined by the chosen error functions, was optimized using the development data set described previously. The output of this optimization using cyclic coordinate descent was a value for each of the following thresholds: peak amplitude range threshold, width threshold, width measurement amplitude threshold, pre-beat interval

threshold, and post-beat interval threshold. The width measurement amplitude threshold was optimized with a resolution of 0.01mV, while all other threshold parameters were optimized with a resolution of 0.05. Given the non-trivial morphology and timing variations between patients, optimization with a higher resolution was not expected to significantly improve performance in the validation data set. Additionally, if these parameters were to be visible and programmable by physicians, this is the highest resolution that would likely be presented to them.

4.5.1.1 Low PVC Detection Sensitivity

For low PVC detection sensitivity, the chosen error function weighted false positives (false PVCs) and false negatives (missed PVCs) equally. In other words, it minimized the total number of errors (false positives plus false negatives). Due to the much larger number of non-PVCs than PVCs in the development data set, weighting these errors equally resulted in a relatively high specificity and low sensitivity. The chosen threshold values and the resulting PVC detection criteria are as follows:

- Peak amplitude range threshold = 0.3
PVC detection criterion: $\text{range} \leq 0.7 * \text{baseline_average}$ or $\text{range} \geq 1.3 * \text{baseline_average}$
- Width threshold = 1.35
PVC detection criterion: $\text{width} \geq 1.35 * \text{baseline_average}$
- Width measurement amplitude threshold = 0.08 mV
Width measurement criterion: SECG sample counts towards width measurement if the absolute value of its amplitude is at least 0.08 mV
- Pre-beat interval threshold = 0.9
PVC detection criterion: $\text{pre-beat interval} \leq 0.9 * \text{baseline_average}$
- Post-beat interval threshold = 1.05
PVC detection criterion: $\text{post-beat interval} \geq 1.05 * \text{baseline_average}$

It is interesting to note that the width measurement amplitude threshold of 0.08 mV is larger than the beat eligibility amplitude threshold of 0.05 mV. This means that for some

beats that are eligible for classification, no width measurement will be made. At these low signal amplitudes, it can be expected that noise may play too large of a role in the perceived width, as it would be measured by the proposed algorithm, for that information to be useful in PVC detection. Only at larger overall signal amplitudes, where noise is more easily distinguishable from the actual QRS complex, does width become a useful measurement. At the small signal amplitudes of just larger than 0.05 mV, the peak amplitude range criterion is the only morphology criteria in effect.

4.5.1.2 Medium PVC Detection Sensitivity

For medium PVC detection sensitivity, the chosen error function weighted false negatives twice as heavily as false positives. Therefore, the error function was the sum of the false positive count and twice the false negative count. The resulting threshold values are as follows:

- Peak amplitude range threshold = 0.25
PVC detection criterion: $\text{range} \leq 0.75 * \text{baseline_average}$ or $\text{range} \geq 1.25 * \text{baseline_average}$
- Width threshold = 1.35
PVC detection criterion: $\text{width} \geq 1.35 * \text{baseline_average}$
- Width measurement amplitude threshold = 0.08 mV
Width measurement criterion: SECG sample counts towards width measurement if the absolute value of its amplitude is at least 0.08 mV
- Pre-beat interval threshold = 0.95
PVC detection criterion: $\text{pre-beat interval} \leq 0.95 * \text{baseline_average}$
- Post-beat interval threshold = 1.05
PVC detection criterion: $\text{post-beat interval} \geq 1.05 * \text{baseline_average}$

This parameter set for medium PVC detection sensitivity would be used in the default case where a physician did not choose to modify the PVC detection sensitivity parameter value.

4.5.1.3 High PVC Detection Sensitivity

Finally, for high PVC detection sensitivity, the chosen error function weighted false negatives three times as heavily as false positives. In other words, optimization minimized the sum of the false positive count and three times the false negative count. The resulting threshold values were as follows:

- Peak amplitude range threshold = 0.2
PVC detection criterion: $\text{range} \leq 0.8 * \text{baseline_average}$ or $\text{range} \geq 1.2 * \text{baseline_average}$
- Width threshold = 1.3
PVC detection criterion: $\text{width} \geq 1.3 * \text{baseline_average}$
- Width measurement amplitude threshold = 0.08 mV
Width measurement criterion: SECG sample counts towards width measurement if the absolute value of its amplitude is at least 0.08 mV
- Pre-beat interval threshold = 0.95
PVC detection criterion: $\text{pre-beat interval} \leq 0.95 * \text{baseline_average}$
- Post-beat interval threshold = 1.05
PVC detection criterion: $\text{post-beat interval} \geq 1.05 * \text{baseline_average}$

Algorithm performance results for this parameter set, along with the low and medium sensitivity parameter sets described previously, will be provided in the following chapter.

4.5.2 Use of Current Beat Peak for Width

During development, the use of the current beat's peak amplitude for width calculations was investigated based on the idea that this method of calculating width might be more robust to morphology changes across patients and beat types. For this method, the peak was determined over a shortened window of the first approximately 50 ms of the morphology window; this reduced the length of the buffer that would need to be maintained to store amplitude values for later analysis after the peak was determined. If the positive peak within this window was larger than the negative peak, the width was calculated as the

number of samples that had an amplitude greater than a fixed threshold percentage of the peak amplitude. If the negative peak magnitude within this shortened window was larger than the positive peak amplitude, the width was instead calculated as the number of samples within the full window that had an amplitude less than the same percentage of the negative peak amplitude. Hysteresis was used to prevent switching back and forth between using the positive and negative peaks if the peaks were approximately the same magnitude: if the previous beat used the positive peak, then the negative peak magnitude must be at least a 5 percent larger than the positive peak to switch to the negative peak. Similarly, if the previous beat used the negative peak, the positive peak must be at least 5 percent larger than the negative peak magnitude to switch to the positive peak.

This method is more computationally demanding than the previously-described width calculation method because, during the short peak determination window, the width measurement amplitude threshold would not yet be known. As a result, the SECG values during that window would need to be saved for later comparison to the threshold, which would only be available at the end of the shortened window. At the BioMonitor's sampling rate of 512 Hz, the approximately 50 ms window would correspond to 26 SECG values that would need to be stored for later analysis. While not infeasible, this additional memory requirement would need to be justified by a significant performance improvement. Ultimately, this improvement was not seen and thus the simpler width method is used in the proposed algorithm. The results leading to this conclusion will be provided in the following chapter.

4.5.3 Baseline Initialization

As discussed earlier, rolling baseline initialization must occur automatically without any physician input. Due to the short SECG snapshot duration for the data used for algorithm development and testing, the baseline was initialized with known non-PVC beats before beginning classification for each snapshot during most of the algorithm development process. This essentially simulates the algorithm's state after it has been running for a sufficient period of time to achieve a baseline correctly and automatically filled with non-PVC beats.

In most cases of baseline initialization, a patient would likely have no PVCs for the first eight beats during which the algorithm is running, so the baselines would be correctly initialized with no special mechanism for excluding PVCs. Even in the case of a patient experiencing one PVC during this time, the average metrics would likely still be close enough to the correct values for an entirely non-PVC baseline that subsequent beats would be classified correctly, and within the next eight non-PVC beats, the PVC metrics in the baselines would be flushed out. In the worst case scenarios, however, a patient could be in a bigeminy episode or experiencing a run of PVCs. In these two cases, the baseline would not be appropriately initialized and PVCs would probably not be correctly detected until the episode completed. In the case of a run of PVCs, there is no good way to overcome the incorrect initialization; during the episode, there are no non-PVC beats with which the baseline could possibly be initialized. This scenario is highly unlikely, however, and as a result, this shortcoming is acceptable in the final design. Additionally, this episode would likely be recorded by a BioMonitor device as an episode with a high ventricular rate, so the physician would still be aware of the episode.

In the case of a bigeminy episode, on the other hand, it should be possible to correctly initialize the baseline, or at least to set it up to recover quickly and begin accurate classifications, since only every second beat is a PVC. In an effort to correctly respond to this scenario, a custom initialization method is proposed. In this method, metrics for the first eight eligible beats are saved as the temporary baseline values. Before using these baselines for PVC detection, however, values are chosen to maximize the chances that the values used in the baselines reflect non-PVC beats. For morphology baselines, the metric values from the four beats with the longest pre-beat intervals are used. Each of these values is repeated so that the four beats fill the eight-beat buffer. The interval baseline is initialized using the average of the eight pre-beat intervals as the value for all entries. This is expected to provide a rate that would be approximately equal to the normal sinus rate, given that the short pre-beat interval and long post-beat interval surrounding a PVC should approximately average out to two normal sinus intervals. The next chapter includes a comparison of performance using this initialization method to performance when initializing the baselines with known non-PVC beats.

5 Development Performance

This chapter provides algorithm performance results on the development data set described in the previous chapter.

5.1 Performance for Proposed Sensitivity Levels

The results in this section show algorithm performance using the low, medium, and high PVC detection sensitivity threshold values found in the previous chapter. These results use the simple width calculation method that does not require use of the current beat peak. Additionally, the rolling baseline was initialized with known non-PVC beats.

5.1.1 Low PVC Detection Sensitivity

Performance on the development data set using the low PVC detection thresholds is as follows. Note that performance is shown for two categories: all V sense (Vs) events and only V sense events above the amplitude threshold. The second category only includes V sense events that meet the 0.05 mV amplitude threshold described earlier. The result is a decrease in the number of missed PVCs because any PVCs that were missed because they failed to meet the initial eligibility criteria have been removed. Additionally, the total number of V sense events also decreases.

Table 1. PVC detection performance with low sensitivity thresholds.

	Total Vs	True PVCs	False PVCs	Missed PVCs	Sensitivity	Specificity	PPV	False PVCs per hour
All Vs	89,483	3,092	1,090	1,400	68.8%	98.7%	73.9%	48
Vs over amplitude threshold	78,704	3,092	1,090	1,256	71.1%	98.5%	73.9%	55

5.1.2 Medium PVC Detection Sensitivity

Algorithm performance on the development data set using the medium PVC detection sensitivity threshold values is as shown below. This is the algorithm performance under the proposed default parameter settings.

Table 2. PVC detection performance with medium sensitivity thresholds.

	Total Vs	True PVCs	False PVCs	Missed PVCs	Sensitivity	Specificity	PPV	False PVCs per hour
All Vs	89,483	3,415	1,488	1,077	76.0%	98.2%	69.7%	64
Vs over amplitude threshold	78,704	3,415	1,488	933	78.5%	98.0%	69.7%	74

5.1.3 High PVC Detection Sensitivity

Algorithm performance on the development data set using the high PVC detection sensitivity threshold values is as shown below.

Table 3. PVC detection performance with high sensitivity thresholds.

	Total Vs	True PVCs	False PVCs	Missed PVCs	Sensitivity	Specificity	PPV	False PVCs per hour
All Vs	89,483	3,646	2,007	846	81.2%	97.6%	64.5%	88
Vs over amplitude threshold	78,704	3,646	2,007	702	83.9%	97.3%	64.5%	101

5.2 Performance Using Current Beat Peak for Width Calculation

In this section, algorithm performance using the constant width amplitude threshold is compared to performance using the peak-based amplitude threshold. As discussed

previously, due to the increased memory requirement of the peak-based amplitude threshold method, this method would need to provide a substantial performance improvement to be considered for the final algorithm. Actual performance on the development data set did not show any significant improvement, however, as shown below. The values for the constant width amplitude threshold are taken directly from the results in the previous section, specifically the results for only V sense events above the amplitude threshold for PVC detection eligibility. The peak-based width amplitude threshold performance values are the result of using the same cyclic coordinate descent optimizations as shown in the previous chapter with the modified peak-based amplitude threshold for width calculations.

Table 4. Comparison of algorithm performance for a constant amplitude threshold and a peak-based amplitude threshold for width measurements. All values are calculated using only the V sense events that meet the signal amplitude requirement for PVC detection eligibility.

PVC Detection Sensitivity	Width Measurement Amplitude Threshold	Sensitivity	Specificity	PPV
Low	Constant threshold	71.1%	98.5%	73.9%
	Peak-based threshold	73.0%	98.4%	73.0%
Medium	Constant threshold	78.5%	98.0%	69.7%
	Peak-based threshold	78.5%	98.0%	69.3%
High	Constant threshold	83.9%	97.3%	64.5%
	Peak-based threshold	84.3%	97.2%	64.1%

While performance varies slightly between the two threshold types, there is no clear trend of one threshold type consistently providing significantly better results. As a result, the simpler method using a constant threshold is preferred. Performance results for this method are the results that were presented in the previous section.

5.3 Performance for Automatic Baseline Initialization

Results for the automatic baseline initialization method described in the previous chapter are provided below for comparison to initialization with known non-PVC beats. The

values for baseline initialization with known non-PVC beats are taken directly from the results in the previous section, specifically the results for only V sense events above the amplitude threshold for PVC detection eligibility. The automatic initialization results use the same threshold values previously chosen for low, medium, and high sensitivity, and again use only V sense events above the amplitude threshold.

Table 5. Comparison of algorithm performance for automatic baseline initialization and initialization with known non-PVC beats. All values are calculated using only the V sense events that meet the signal amplitude requirement for PVC detection eligibility.

PVC Detection Sensitivity	Baseline Initialization	Sensitivity	Specificity	PPV
Low	Known non-PVC beats	71.1%	98.5%	73.9%
	Automatic initialization	69.7%	98.6%	73.2%
Medium	Known non-PVC beats	78.5%	98.0%	69.7%
	Automatic initialization	77.4%	98.1%	69.3%
High	Known non-PVC beats	83.9%	97.3%	64.5%
	Automatic initialization	83.2%	97.4%	64.0%

These results show that, while automatic initialization does tend to slightly reduce sensitivity, the performance decrease is small. These results are for snapshots of approximately one to three minutes in length, so the initialization period has a much more significant impact on overall algorithm performance than it would in an actual implanted device, where the same initialization period would lead to months or years of running the PVC detection algorithm, rather than just a few minutes. Particularly with a short initialization period of running the algorithm before beginning to save the results towards statistics, the impact of automatic initialization should be negligible.

6 Validation Methodology and Performance

6.1 Validation Data Set

BioMonitor 2 snapshots were used for the validation data set for this thesis. These snapshots were from twelve patients, with no overlap with the five BioMonitor 2 patients used in the development data set. The use of entirely new snapshots and patients for validation minimized the possibility of bias in the validation data set. Even if new snapshots were used, it was important to avoid validating the algorithm using the same patients that were used for development because signal morphology and timing tend to be fairly similar for the same patient over time. Thus, simply taking a new set of snapshots from the same patients would still introduce significant bias into the validation process.

As with the previous set of BioMonitor 2 snapshots, all validation snapshots contain 128 Hz compressed data. Again, these snapshots have a minimum length of 40 seconds, with most snapshots around two to three minutes in length. The validation data set consisted of 540 of these snapshots from twelve different patients. Altogether, these snapshots contained approximately 102,000 sensed QRS complexes, with approximately 1,340 of those being PVCs.

All snapshots consist of continuous SECG data along with the event markers, including QRS complex markers and noise event markers, detected by the device. The SECG data for all snapshots have been passed through a low-pass filter with a cut-off frequency of 40 Hz and a high-pass filter with a cut-off frequency of 0.5 Hz. As with the BioMonitor 2 development data, the SECG data have also been passed through a 4.5 Hz high-pass filter before performing any other analysis.

Like the development data set, all snapshots were manually annotated by the author of this thesis to identify which QRS complexes were PVC beats. Manual annotations were compared to snapshot observations by members of the BIOTRONIK Clinical Research group to provide a second opinion on any beats that were difficult to classify. The annotation process introduces a possible source of bias in the validation data set because annotation of the validation snapshots occurred during the final stages of algorithm tuning on the development data set. While all major design decisions had already been made at this point, familiarity with the validation data set could have subtly influenced final design decisions.

6.2 Algorithm Parameters

The parameter values determined in the Algorithm Refinement chapter using cyclic coordinate descent on the development data set were used without change for validation. As explained earlier, three sets of parameters were chosen to provide options for low, medium, and high PVC detection sensitivity. These parameter values are reproduced below for convenience; this information is unchanged from the Algorithm Refinement chapter.

Low PVC detection sensitivity:

- Peak amplitude range threshold = 0.3
PVC detection criterion: $\text{range} \leq 0.7 * \text{baseline_average}$ or $\text{range} \geq 1.3 * \text{baseline_average}$
- Width threshold = 1.35
PVC detection criterion: $\text{width} \geq 1.35 * \text{baseline_average}$
- Width measurement amplitude threshold = 0.08 mV
Width measurement criterion: SECG sample counts towards width measurement if the absolute value of its amplitude is at least 0.08 mV
- Pre-beat interval threshold = 0.9
PVC detection criterion: $\text{pre-beat interval} \leq 0.9 * \text{baseline_average}$
- Post-beat interval threshold = 1.05
PVC detection criterion: $\text{post-beat interval} \geq 1.05 * \text{baseline_average}$

Medium PVC detection sensitivity:

- Peak amplitude range threshold = 0.25
PVC detection criterion: $\text{range} \leq 0.75 * \text{baseline_average}$ or $\text{range} \geq 1.25 * \text{baseline_average}$
- Width threshold = 1.35
PVC detection criterion: $\text{width} \geq 1.35 * \text{baseline_average}$
- Width measurement amplitude threshold = 0.08 mV
Width measurement criterion: SECG sample counts towards width measurement if the absolute value of its amplitude is at least 0.08 mV
- Pre-beat interval threshold = 0.95
PVC detection criterion: $\text{pre-beat interval} \leq 0.95 * \text{baseline_average}$
- Post-beat interval threshold = 1.05
PVC detection criterion: $\text{post-beat interval} \geq 1.05 * \text{baseline_average}$

High PVC detection sensitivity:

- Peak amplitude range threshold = 0.2
PVC detection criterion: $\text{range} \leq 0.8 * \text{baseline_average}$ or $\text{range} \geq 1.2 * \text{baseline_average}$
- Width threshold = 1.3
PVC detection criterion: $\text{width} \geq 1.3 * \text{baseline_average}$
- Width measurement amplitude threshold = 0.08 mV
Width measurement criterion: SECG sample counts towards width measurement if the absolute value of its amplitude is at least 0.08 mV
- Pre-beat interval threshold = 0.95
PVC detection criterion: $\text{pre-beat interval} \leq 0.95 * \text{baseline_average}$
- Post-beat interval threshold = 1.05
PVC detection criterion: $\text{post-beat interval} \geq 1.05 * \text{baseline_average}$

6.3 Validation Performance

Algorithm performance on the validation set is as follows for each sensitivity level. A discussion of these results will be provided in the following chapter.

Table 6. PVC detection performance on the validation data set.

PVC Detection Sensitivity	Used Vs	Total Vs	True PVCs	False PVCs	Missed PVCs	Sensitivity	Specificity	PPV	False PVCs per hour
Low	All	102,093	567	598	770	42.4%	99.4%	48.7%	24
	Over amplitude threshold	90,989	567	598	382	59.7%	99.3%	48.7%	27
Medium	All	102,093	642	821	695	48.0%	99.2%	43.9%	34
	Over amplitude threshold	90,989	642	821	307	67.7%	99.1%	43.9%	38
High	All	102,093	736	1,012	601	55.0%	99.0%	42.1%	41
	Over amplitude threshold	90,989	736	1,012	213	77.6%	98.9%	42.1%	46

7 Discussion

7.1 Validation versus Development Performance

Some decrease in performance from the development data set to the validation data set is expected given that the algorithm was optimized only on the development data set. For the proposed algorithm, sensitivity and PPV are lower while specificity is higher on the validation data set compared to the development data set for the corresponding sensitivity level of low, medium, or high. Additionally, fewer false PVCs occur per hour on the validation data set.

It is important to note that, although the validation data set contains a large number of snapshots, it only contains data from twelve patients. With very few BioMonitor 2 devices implanted when the data sets used for this thesis were created, the available BioMonitor 2 snapshots were very limited. Unlike the development data set, these snapshots were not supplemented with BioMonitor 1 snapshots due to the desire to validate the algorithm on SECG data from as similar of a device as possible to the targeted future hardware platform. As a result of the small sample size, these twelve patients may not be representative of the target patient population. As will be discussed in the final chapter, additional testing of the algorithm as more BioMonitor 2 devices are implanted is recommended to ensure that a representative sample of patients is obtained.

Interestingly, sensitivity and specificity are both higher and false PVCs per hour are lower on the validation data set for the high PVC detection sensitivity thresholds than they are on the development data set for the low sensitivity thresholds. This suggests that the fundamental algorithm structure still performs well on the validation data set but that repeating the cyclic coordinate descent optimization to obtain new multiplicative threshold

values could result in a significant performance improvement on the validation data set. A likely reason for this finding is that the development data set contains both BioMonitor 1 and BioMonitor 2 snapshots, while the validation data set contains only BioMonitor 2 snapshots. In general, signal quality is greatly improved in BioMonitor 2 compared to BioMonitor 1, with visibly less interference due to muscle artifacts and other similar non-cardiac electrical activity. As a result, the morphology criteria could likely be made easier to meet, meaning that the multiplicative threshold values could move closer to 1, while still maintaining a high PVC detection specificity. On the BioMonitor 1 snapshots, the morphology criteria needed to be more stringent because signal noise could otherwise frequently cause the criteria to be met incorrectly. On BioMonitor 2 snapshots, the same criteria are overly cautious, as evidenced by the low sensitivity values and extremely high specificities of approximately 99 percent or above.

PPV is significantly lower on the validation data set than the development data set for all sensitivity levels. However, this is expected given that approximately 5.5 percent of eligible QRS complexes in the development data set are PVCs, while only approximately 1.0 percent of eligible QRS complexes in the validation data set are PVCs. Note that these calculations only include QRS complexes that meet the initial beat eligibility amplitude criteria. This difference in the PVC burden between the two data sets can be primarily attributed to the presence of BioMonitor 1 snapshots in the development data set. Because BioMonitor 1 was released in 2012, many more patients and snapshots were available to create a data set that contained a balance of PVC and non-PVC beats. The much more limited BioMonitor 2 patient population at the time of this algorithm's validation resulted in a validation data set with a PVC burden dictated mostly by chance. Unfortunately, the twelve

patients available for use in the validation data set have a low PVC burden compared to the development data set.

This difference in the relative PVC burden between the two data sets makes comparison of the PPV between these data sets less meaningful than expected. If the purpose of this algorithm was to provide physicians with a notification or SECG snapshot for every PVC that occurs, the low PPV on the validation data set would be highly troubling because it would result in a significant amount of wasted time for physicians investigating the false notifications. However, since the primary intended purpose of the algorithm is to exclude PVCs from other arrhythmia detection algorithms, sensitivity and specificity are the most important performance metrics. For the secondary purpose of providing an overall count of PVCs or, more likely, the percent of PVCs out of total beats or the number of PVCs per unit of time, sensitivity, specificity, and false PVCs per hour are the more relevant performance metrics. These findings suggest that, going forward, PPV should not be used in the performance criteria given its lack of robustness to changes in the PVC burden between different data sets and its more limited applicability to the intended purposes of the algorithm.

7.2 Algorithm Weaknesses

To more fully understand the proposed algorithm's performance, it is valuable to investigate common causes of misclassification. Some of these weaknesses are also problematic in manual expert annotation of an ECG signal and, as such, are less an algorithm failing and more a general difficulty of diagnosis using an ECG signal. This section will discuss several prominent causes of misclassification, including causes of both missed and false PVCs.

7.2.1 Frequently Missed Morphologies

One of the most common causes of missed PVC detections in the development and validation data sets is small signal amplitude. Smaller signal amplitude results in a poorer effective resolution within the amplitude range of the QRS complex and thus makes PVCs more difficult to identify both manually and by the proposed algorithm. At smaller signal amplitudes, even relatively minor noise can obscure important aspects of the actual SECG signal, further limiting the algorithm's effectiveness. This can lead to both missed and false PVC detections. Also, as discussed previously, the width criterion is not used when the signal amplitude is at the lowest levels that meet the beat eligibility criteria, so only the peak amplitude range metric can be used to meet the morphology criteria in these cases. This makes it more difficult for a beat to receive classification as a PVC and therefore causes more missed PVCs at small signal amplitudes. The SECG sample below shows an example of small signal amplitude where the small amplitude results in relatively late detection of the PVC QRS complex, which minimizes the difference between the normal and PVC QRS complexes in the morphology window started by the V sense markers, indicated as vertical lines.

Figure 16. SECG sample with low signal amplitude of approximately 0.05 mV, corresponding to only 10 percent of the maximum possible amplitude.

Another important cause of missed PVC detections is not captured in the performance statistics used in this thesis due to the fundamental design of the algorithm. In order to limit the power consumption of the algorithm and avoid reproducing the functionality of other algorithms already running within the BioMonitor devices, the proposed algorithm only classifies QRS complexes that have been detected by the device's QRS detection algorithm. As previously mentioned, this algorithm uses a dynamic threshold for QRS detection that gradually steps down from a relatively high level just after the previous QRS complex until it reaches its lowest level at approximately the time when the next sinus beat would be expected to occur. Since a PVC occurs earlier than the next sinus beat would occur, the threshold is typically higher for a PVC than for a normal sinus beat, making it more difficult for a PVC to be detected as a QRS complex. Additionally, the QRS detection algorithm passes the SECG signal through an additional high-pass filter with a programmable cut-off frequency of 10, 18, or 24 Hz. Even with the default 10 Hz high-pass filter, PVCs are disproportionately impacted by the high-pass filtering due to typically having

more dominant low-frequency components than a normal QRS complex. Together, these factors result in PVCs being missed by the QRS detection algorithm much more frequently than normal QRS complexes are missed. These missed PVC QRS complexes, such as the one in the example below, do not meet the most fundamental eligibility requirement for PVC detection because they are not detected as V sense events, and therefore they cannot be detected by the proposed algorithm as PVCs. Solving this problem is outside of the scope of the PVC detection algorithm and this thesis and instead would need to be handled by the QRS detection algorithm.

Figure 17. SECG sample showing a PVC that is not detected as a QRS complex, indicated by the lack of a vertical V sense marker on the PVC.

Finally, some PVCs are not detected because their morphology changes compared to normal beats are minimized by the high-pass filtering of the SECG signal. This is particularly noticeable on BioMonitor 2 snapshots, where the raw snapshot data had only gone through a 0.5 Hz high-pass filter. Manual annotation was performed on this raw snapshot data before passing the data through the 4.5 Hz high-pass filter. Later examination of PVCs that were missed by the proposed algorithm showed that, in some cases, these PVCs were much more

difficult to visually identify as PVCs from the high-pass filtered SECG signal used by the algorithm than they had been during initial manual annotation. These PVCs had been easily identifiable in the raw snapshot data, but the additional high-pass filtering made both visual and algorithmic identification more difficult. The sample below depicts the raw SECG data and the 4.5 Hz high-pass filtered data over the same time period to illustrate the significant signal change often caused by filtering.

Figure 18. SECG sample showing the unfiltered (top) and filtered (bottom) signal for the same time period. The morphology of the filtered PVC is much more similar to that of non-PVC beats than is the unfiltered PVC.

7.2.2 Frequently Missed Timings

Most PVCs in the development and validation data sets that fail to meet the timing criteria are interpolated PVCs. This is unsurprising as the proposed algorithm was

purposefully designed to make the short post-beat interval criterion difficult to meet. As was discussed earlier, the post-beat interval criterion is an important safeguard against runs of false PVC detections. In order to minimize the chance that the short post-beat interval criterion could be consistently met by normal sinus beats or another arrhythmia such as atrial fibrillation, the short post-beat interval limit was set at 300 ms. At a slow to normal heart rate, an interpolated PVC could easily occur with a post-PVC interval of longer than 300 ms, as in the example below. In this case, the algorithm would fail to identify the interpolated PVC. This weakness of the algorithm is known and accepted because, given the relative rareness of interpolated PVCs, the few missed interpolated PVC detections is preferable to the alternative of increasing the likelihood of a run of false PVC detections.

Figure 19. SECG sample showing an interpolated PVC with a post-beat interval of approximately 500 ms.

7.2.3 False Detection Morphologies

One morphological cause of false PVC detections affects both algorithmic and visual identification of PVCs: sinus beats with bundle branch block can have a widened QRS

complex that can be mistaken for a PVC, as illustrated in the example below. In particular, some patients have a rate-dependent bundle branch block, meaning that the block only manifests at faster heart rates [1]. A premature atrial contraction, for example, might cause bundle branch block only on the premature beat. This premature beat with a wider QRS complex can look very similar to a PVC, and as such, is vulnerable to misclassification both manually and by the proposed algorithm. The examples below show the potential similarity between a QRS complex with bundle branch block and the QRS complex of a PVC. Typically, other factors such as the presence of P-waves would be used to distinguish between these beats, but as P-waves cannot be reliably seen in the SECG signal, differentiation remains difficult when using only ICM data.

Figure 20. SECG sample (A) showing a PVC with similar morphology to a QRS complex exhibiting left bundle branch block (B).

Sub-image B: “Left and right bundle branch block” by Nicholas Patchett is licensed under the Creative Commons Attribution-Share Alike 4.0 International license. See the Appendix for more licensing information.

Additionally, signal noise can significantly affect the morphology metrics. While most of the noise encountered by an ICM is either flagged as noise or is relatively small in amplitude and does not impact the peak amplitude range and width measurements, certain

muscle noise can look similar to a QRS complex. In some cases in the SECG snapshots used for this thesis, like the example shown below, a short period of regular muscle-related noise was detected as a series of rapid QRS complexes that was then falsely detected as a run of PVCs due to its drastically different morphology from the patient's actual QRS complexes. This myopotential noise was in some cases mistakable as a run of PVCs even with visual inspection, so the failure of the algorithm to exclude these false QRS detections is unsurprising.

Figure 21. SECG sample showing a period of noise being falsely detected as QRS complexes and as PVCs. Arrows indicate actual QRS complexes during the period of noise, occurring at a steady rate of approximately 100 beats per minute. The dotted vertical lines are noise markers while solid lines are the incorrect V sense markers, with red indicating a false PVC detection.

7.2.4 False Detection Timings

The occurrence of PACs is somewhat problematic to the proposed PVC detection algorithm because the timing of a PAC nearly always meets the PVC detection timing criteria. This is expected, and it is an important reason why morphology criteria are used in the proposed algorithm. However, PACs effectively make the algorithm depend entirely on the morphology criteria to avoid false PVC classifications, thus weakening the algorithm's

specificity. In a frequent-PAC scenario such as the one shown below, signal noise or a change in signal morphology can result in false PVC detections because the timing criteria no longer provide a second gating mechanism to prevent the false detections.

Figure 22. SECG sample showing atrial bigeminy with a false PVC detection on one PAC with a slightly larger peak amplitude range.

Another cause of false PVC detections stems from the behavior of the QRS detection algorithm. As previously described, this algorithm uses a variable threshold based on the measured peak amplitude of the preceding QRS complex and the time since the previous QRS. For some beats, this detection occurs earlier in the QRS complex than it had been occurring for other visually similar beats. For example, an initial small downward deflection in the QRS complex might normally fail to meet the threshold, with the detection occurring instead on the subsequent larger upward deflection. However, for one beat, the detection might instead occur on the small downward deflection due to a minor morphology change or a slight difference in the previous beat's peak amplitude. Thus, despite the actual timing being steady throughout all beats, a single beat would appear to have a shorter pre-beat interval and a longer post-beat interval. This timing behavior coupled with the reliance

of the morphology window on the QRS detection time can lead to false classification of these beats as PVCs, as in the example below.

Figure 23. SECG sample showing a single beat with earlier QRS detection than the other beats, resulting in a false PVC detection.

7.3 Generalization to Future Hardware Platforms

The proposed algorithm was developed and optimized over a combination of BioMonitor 1 and BioMonitor 2 SECG data; the same algorithm parameters were reasonably successful across both data sets. The sensing vector and overall hardware platform change was quite significant from BioMonitor 1 to BioMonitor 2, including the transition from three sensing vectors to just one sensing vector. The planned BioMonitor 3 platform is expected to be more similar to BioMonitor 2 than BioMonitor 2 was to its predecessor. Therefore, the successful performance of the algorithm on both current platforms suggests that the algorithm will continue to perform similarly on future hardware platforms.

8 Conclusions

8.1 Contributions of this Thesis

This thesis has proposed and tested a novel algorithm that uses an SECG signal to perform PVC detection and is suitable for implementation on an implantable device. The contributed algorithm reduces the computational complexity of PVC detection compared to algorithms used in current practice, thus providing the possibility of near real-time PVC detection in an ICM, a feature which is not currently available in commercial ICMs. The proposed algorithm has been developed and tested using clinical SECG data from BIOTRONIK's BioMonitor line of ICM devices, but it has not yet been implemented on an actual implanted device. The following future research directions are recommended before pursuing release of this feature on commercially-available devices.

8.2 Further Research

Further development and analysis of this algorithm is required before it is ready for release on an ICM. Recommended research directions are as follows:

1. Algorithm parameter optimization should be repeated when more BioMonitor 2 devices have been implanted. Emphasis should be placed on obtaining SECG snapshots from a large number of patients, rather than obtaining many SECG snapshots from fewer patients. Optimization on this expanded data set can be performed using the cyclic coordinate descent method as described previously in this thesis.
2. The algorithm, with any parameter changes from item 1, should be validated using a new set of BioMonitor 2 patients and snapshots.

3. After the BioMonitor 3 platform has been developed and initial SECG data are available, the algorithm should be tested on these snapshots to ensure that it is compatible with the new platform. Algorithm updates and additional validation should be performed as needed.
4. Pre-clinical and clinical studies should be performed with the algorithm running in real-time on the implanted device and using the full resolution SECG signal. These studies will be required for eventual approval of the feature for commercial release.

8.3 Concluding Remarks

The proposed algorithm and the performance results presented in this thesis demonstrate that an implantable cardiac monitoring device can use an SECG signal to detect PVCs in near real time. While further research is required before this algorithm is ready for release on a commercially-available device, this thesis provides significant support for the feasibility of detecting PVCs using a computationally-simple algorithm capable of running without physician initialization or intervention. This PVC detection algorithm can provide valuable data to physicians and facilitate early identification of potentially dangerous cardiac arrhythmias.

References

- [1] D. Dubin, Rapid Interpretation of EKG's, Fort Meyers: COVER Publishing Company, 2000.
- [2] G. Hindricks, E. Pokushalov, L. Urban, M. Taborsky, K.-H. Kuck, D. Lebedev, G. Rieger and H. Purerfellner, "Performance of a New Leadless Implantable Cardiac Monitor in Detecting and Quantifying Atrial Fibrillation Results of the XPECT Trial," *Circulation: Arrhythmia and Electrophysiology*, vol. 3, pp. 141-147, 2010.
- [3] D. H. Bennett, Bennett's Cardiac Arrhythmias: Practical Notes on Interpretation and Treatment, West Sussex: John Wiley & Sons, Ltd., 2013.
- [4] R. A. Rhoades and D. R. Bell, Medical Physiology: Principles for Clinical Medicine, Baltimore: Lippincott Williams & Wilkins, 2013.
- [5] T. B. Garcia and G. T. Miller, Arrhythmia Recognition: The Art of Interpretation, Sudbury: Jones and Bartlett Publishers, 2004.
- [6] G. A. Ng, "Treating Patients with Ventricular Ectopic Beats," *Heart*, vol. 92, pp. 1707-1712, 2006.
- [7] E. Hoffman, N. Sulke, N. Edvardsson, J. Ruiter, T. Lewalter, A. Capucci, A. Schuchert, S. Janko and J. Camm, "New Insights Into the Initiation of Atrial Fibrillation: A Detailed Intraindividual and Interindividual Analysis of the Spontaneous Onset of Atrial Fibrillation Using New Diagnostic Pacemaker Features," *Circulation*, vol. 113, pp. 1993-1941, 2006.
- [8] A. García, H. Romano, E. Laciár and R. Correa, "Development of an algorithm for heartbeats detection and classification in Holter records based on temporal and morphological features," in *Journal of Physics: Conference Series*, Mar del Plata, Argentina, 2011.
- [9] J. A. Abildskov and R. M. Klein, "Cancellation of Electrocardiographic Effects During Ventricular Excitation," *Circulation Research*, vol. 11, pp. 247-251, 1962.
- [10] M. Garrels and C. S. Oatis, Laboratory and Diagnostic Testing in Ambulatory Care: A Guide for Health Care Professionals, St. Louis: Elsevier, 2015.
- [11] T. Hanke, E. I. Charitos, U. Stierle, A. Karluss, E. Kraatz, B. Graf, A. Hagemann, M. Misfeld and H. H. Sievers, "Twenty-Four-Hour Holter Monitor Follow-Up Does Not Provide Accurate Heart Rhythm Status After Surgical Atrial Fibrillation Ablation Therapy," *Circulation*, vol. 120, pp. S177-184, 2009.
- [12] BIOTRONIK SE & Co. KG, *BioMonitor: Patient information*, Berlin, 2012.
- [13] J. Cao, L. B. Brian, M. R. Kane and S. R. Hurd, "Methods and apparatus for cardiac R-wave sensing in a subcutaneous ECG waveform". United States of America Patent US 7027858 B2, 11 April 2006.
- [14] BIOTRONIK, Inc., "BioMonitor: Technical Manual," Lake Oswego, 2015.

- [15] S. Sarkar, D. Ritscher and R. Mehra, "A Detector for a Chronic Implantable Atrial Tachyarrhythmia Monitor," *IEEE Transactions on Biomedical Engineering*, vol. 55, no. 3, pp. 1219-1224, 2008.
- [16] D. Ritscher and S. Sarkar, "Algorithms for detecting atrial arrhythmias from discriminatory signatures of ventricular cycle lengths". United States of America Patent US 20040092836 A1, 13 May 2004.
- [17] A. Martínez, R. Alcaraz and J. J. Rieta, "Detection and Removal of Ventricular Ectopic Beats in Atrial Fibrillation Recordings Via Principal Component Analysis," in *33rd Annual International Conference of the IEEE EMBS*, Boston, 2011.
- [18] J. Moraes, M. Seixas, F. Vilani and E. Costa, "A Real Time QRS Complex Classification Method using Mahalanobis Distance," in *Computers in Cardiology*, Memphis, 2002.
- [19] R. Palaniappan, C. N. Gupta, C. K. Luk and S. M. Krishnan, "Multi-Parameter Detection of Ectopic Heart Beats," in *IEEE International Workshop on Biomedical Circuits and Systems*, Singapore, 2004.
- [20] C.-H. Lin, "Frequency-domain features for ECG beat discrimination using grey relational analysis-based classifier," *Computers and Mathematics with Applications*, vol. 55, no. 4, pp. 680-690, 2008.
- [21] M. L. Talbi, A. Charef and P. Ravier, "Arrhythmias Classification Using the Fractal Behavior of the Power Spectrum Density and the QRS Complex and ANN," in *2010 International Conference on High Performance Computing and Simulation (HPCS)*, Caen, France, 2010.
- [22] N. Uchaipichat, C. Thanawattano and A. Buakhamsri, "Wavelet Power Spectrum Analysis for PVC Discrimination," in *Proceedings of the World Congress on Engineering*, London, 2013.
- [23] A. Martínez, R. Alcaraz and J. J. Rieta, "Ventricular activity morphological characterization: Ectopic beats removal in long term atrial fibrillation recordings," *Computer Methods and Programs in Biomedicine*, vol. 109, no. 3, pp. 283-292, 2013.
- [24] C. Aggarwal, *Outlier Analysis*, New York: Springer, 2013.
- [25] J. Mateo and P. Laguna, "Analysis of Heart Rate Variability in the Presence of Ectopic Beats Using the Heart Timing Signal," *IEEE Transactions on Biomedical Engineering*, vol. 50, no. 3, pp. 334 - 343, 2003.
- [26] V. T. Krasteva, I. I. Jekova and I. I. Christov, "Automatic detection of premature atrial contractions in the electrocardiogram," *Електротехника и Електроника E+E*, vol. 9, no. 10, pp. 49-55, 2006.
- [27] E. Raeder, "Interbeat interval monitoring and ectopic beat removal". United States of America Patent US 20130218037 A1, 22 August 2013.
- [28] J. A. Dyjach and G. M. Carlson, "Method for Exclusion of Ectopic Events from Heart Rate Variability Metrics". United States of America Patent 8,280,510 B2, 2 October 2012.
- [29] V. Krasteva and I. Jekova, "QRS Template Matching for Recognition of Ventricular Ectopic Beats," *Annals of Biomedical Engineering*, vol. 35, no. 12, pp. 2065-2076, 2007.

- [30] S. Ittaturut, A. Lek-uthai and A. Teeramongkonrasmee, "Detection of Premature Ventricular Contraction for Real-Time Applications," in *2013 10th International Conference on Electrical Engineering/Electronics, Computer, Telecommunications and Information Technology*, Krabi, 2013.
- [31] P. S. Addison, "Wavelet transforms and the ECG: a review," *Physiological Measurement*, vol. 26, pp. R155-R199, 2005.
- [32] J. Sahambi, S. Tandon and R. Bhatt, "Using Wavelet Transforms for ECG Characterization: An On-line Digital Signal Processing System," *Engineering in Medicine and Biology*, vol. 16, no. 1, pp. 77-83, 1997.
- [33] S.-N. Yu and Y.-H. Chen, "Electrocardiogram beat classification based on wavelet transformation and probabilistic neural network," *Pattern Recognition Letters*, vol. 28, no. 10, pp. 1142-1150, 2007.
- [34] M. Kadbi, J. Hashemi, H. Mohseni and A. Maghsoudi, "Classification of ECG Arrhythmias based on Statistical and Time-Frequency Features," in *Advanced in Medical, Signal and Information Processing*, Glasgow, 2006.
- [35] L. Tarassenko, G. Clifford and N. Townsend, "Detection of Ectopic Beats in the Electrocardiogram Using an Auto-Associative Neural Network," *Neural Processing Letters*, vol. 14, no. 1, pp. 15-25, 2001.
- [36] J. Arndt, *Matters Computational: Ideas, Algorithms, Source Code*, Heidelberg: Springer Science & Business Media, 2011.
- [37] J. B. Kostis, K. McCrone, A. E. Moreyra, S. Gotzoyannis, N. M. Aglitz, N. Natarajan and P. Kuo, "Premature Ventricular Complexes in the Absence of Identifiable Heart Disease," *Circulation*, vol. 63, no. 6, pp. 1351-1356, 1981.
- [38] American Heart Association, "Target Heart Rates," January 2015. [Online]. Available: <http://www.heart.org/>. [Accessed 15 September 2015].
- [39] I. B. Nigam, "Implantable medical device for improved storage of intracardiac electrograms". United States of America Patent US7657305 B2, 2 February 2010.
- [40] I. N. Sarkar, Ed., *Methods in Biomedical Informatics: A Pragmatic Approach*, London: Academic Press, 2014.
- [41] D. G. Luenberger and Y. Ye, *Linear and Nonlinear Programming*, New York: Springer, 2015.

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Figure 7. BIOTRONIK BioMonitor 2 ICM size and three possible recommended placements (A, B, and C). Note that any given patient would have only one ICM implanted at one of the three locations shown in this image.

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