A FRAMEWORK FOR ACOUSTIC CARDIAC SIGNAL ANALYSIS

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Abstract: Cardiac auscultation is a traditional, yet highly sensitive and specific diagnosis technique for cardiovascular diseases. We present a Matlab framework for cardiac signals processing and analysis, which includes a new toolbox specifically designed for the main processing tasks related to heart sound analysis. Existing frameworks for acoustic cardiac signal analysis usually limit themselves to noise contamination detection, S1 and S2 segmentation and murmur diagnosis. Besides these operations, the proposed framework includes algorithms developed for segmentation of the main heart sound components capable of handling situations with high-grade murmur, S3 detection and identification, S2 split identification as well as systolic time intervals (STI) measurement using heart sound. Methods for cardiac function parameter extraction based on STI are also included. Most of the algorithms outlined in the paper have been extensively evaluated using data collected from patients with several types of cardiovascular diseases under real-life conditions. The achieved results suggest that the algorithms developed for the framework exhibit performances that are comparable and, in most cases, surpass existing state of the art methods.

1 INTRODUCTION

Cardiovascular diseases (CVD) are the leading cause of death worldwide. According to the European cardiovascular disease statistics report (Allender, *et al.* 2008), 44% of all deaths in men in Europe are due to CVD, whereas the disease accounts for 54% of all deaths in women. CVD is not solely a problem of developed countries, quite the contrary. In fact, as is mentioned in the WHO report on chronic diseases (WHO, 2005), 80% of all deaths worldwide due to chronic diseases occur in middle and low-income countries, being CVD by far the most prevalent chronic disease. Recent studies have shown that premature CVD and its consequences can be largely prevented and controlled by fostering healthy lifestyles and by timely detection/control of progression of the disease. For the population that already exhibits the disease, the later is of paramount importance since timely diagnosis usually leads to more successful and cost effective therapies. Due to the unprecedented aging of the world population (Rechel et al., 2009), timely action has decisive impact on health provision systems' sustainability.

The first line of defense against CVD is the regular follow-up by primary care physicians. Given the medical, social and economical implications of CVD, a significant research trend is observed in science and technologies to deploy personal health (pHealth) systems for CVD management (e.g. Habetha, 2006). The goal of these systems is to support physicians and patients in detecting trends and in collecting data for clinical decision support.

In order to implement cost effective CVD prevention strategies, pHealth systems as well as physicians require affordable, comfortable and highly discriminative information sources for diagnosis. Traditionally, the electrocardiogram (ECG) and heart sound (HS) auscultation are among the most used signals for CVD diagnosis. These information sources provide complementary information: the ECG enables to assess the electrical activity of the heart, while heart sounds provide information on the mechanical activity of the heart (Tavel, 1967). Other signals, such as the impedance cardiogram (ICG) as well as the photoplethysmogram (PPG), are less common in daily practice or are still used mainly in research scenarios.

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In this paper we introduce a Matlab framework for the acquisition and processing of cardiac signals. The framework (see fig. 1) includes a general real-time signal acquisition toolbox to interface medical

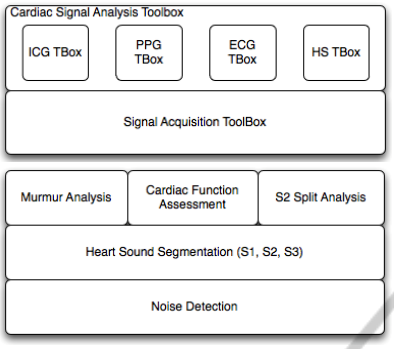

Figure 1: (top) Layer architecture of the proposed framework. (bottom) Detailed layer architecture of the heart sound processing toolbox.

sensor networks and a collection of signal analysis toolboxes for the most pertinent signals to deploy portable and non-invasive devices for CVD diagnosis. Regarding the signal processing layer of the framework, the focus of this paper will be to present the algorithms developed by the team for the HS toolbox. These include methods for noise detection, heart sound segmentation into its main components (S1, S2 and S3) as well as higher level operations such as S2 split detection (important to assess pulmonary artery pressure), regurgitation and stenosis murmur detection and classification, and left ventricle cardiac function assessment (systolic time intervals, contractility and stroke volume). The remaining toolboxes are presented elsewhere: a description of the ECG toolbox can be found in (Henriques *et al.,* 2008); the ICG algorithms implemented in the ICG toolbox are described in (Carvalho *et al.*, 2011), whereas the PPG toolbox is based on the segmentation method introduced in (Chan *et al.*, 2007).

Heart sound is a consequence of turbulent blood flow and vibrating cardiovascular structures, which propagate to the chest. These vibrations typically result from myocardial and valvular events that are affected by the function, the hemodynamics and electrical activity of the cardiac muscle. The later have a direct impact on the morphological, spectral and the timing characteristics of the main heart sounds (S1, S2 and S3), which have been found to be highly sensitive and specific for several important diagnosis tasks ranging from heart valve dysfunction (Durand & Pibarot 1995), (Abbas&Bassam, 2009) to systolic cardiac function (Paiva *et al.* 2009; Tavel 1967).

Unfortunately, cardiac auscultation - the interpretation of heart sounds - requires highly proficient physicians. Several studies (e.g. Lam *et al.*, 2005) have shown that the ability of physicians to perform cardiac auscultation is reduced and significantly impaired as time progresses. It is estimated that this might lead to a number of missed diagnosis and to a high rate of unnecessary referrals to cardiologists with a consequence of waste of scarce resources (Pease, 2001). Hence, the existence of signal analysis algorithms for HS to deploy decision support systems, both for the physicians in their clinical practice as well as to deploy pHealth systems, are one possible solution to fully explore this highly informative, low cost and non-invasive information source on cardiac state.

There are few known integrated frameworks for heart sound acquisition and processing. Most of the existing literature is concentrated on algorithms for elementary processing functions (most of the efforts focus on HS segmentation and murmur classification). An extensive review on algorithms for heart sound analysis as well as CVD diagnosis algorithms based on HS can be found in (Abbas&Bassam, 2009; Durand&Pibarot, 1995; Tavel, 1967). Rajan *et al.* (1998) introduce an integrated framework for HS processing based on Morlet wavelet bank of correlators. Their framework tackles the problems of noise detection, S1 and S2 segmentation and murmur/click/snap classification. Javed *et al.* (2006), describe a signal processing module that includes a signal acquisition functionality. Time-frequency processing is wavelet-based and is limited to HS segmentation and murmur detection. More recently, Syed *et al.* (2007) introduced a framework with similar functionalities as the one described in (Rajan *et al.*, 1998). Kudriavtsev *et al*. (2007) introduce a framework for HS analysis based on time-frequency signatures assessed using the Wigner-Ville distribution. This framework enables HS segmentation, including S3 and S4 detection, as well as murmur detection. It is observed that none of the sited frameworks include modules for systolic time interval measurement, i.e. the pre-ejection period (PEP) and the left ventricle ejection time (LVET), which is related directly to the left ventricle function. Some of these frameworks include facilities to assess the so-called electromechanical time interval, RS2, defined by the ECG's R-peak and the S2 sound; it should be noted that RS2≈PEP+LVET. However, as was mentioned

by Oh and Tajik (2003), reduced systolic left ventricle function will have opposite effects on PEP and LVET, possibly cancelling each other out.
The paper is organized as follows: Section 2 outlines the algorithms that have been developed by the team and are integrated into the heart sound processing toolbox. In section 3 we present and discuss results of the main modules that comprise the toolbox. Finally, in section 4 some main conclusions are drawn and the main directions for future work are outlined.

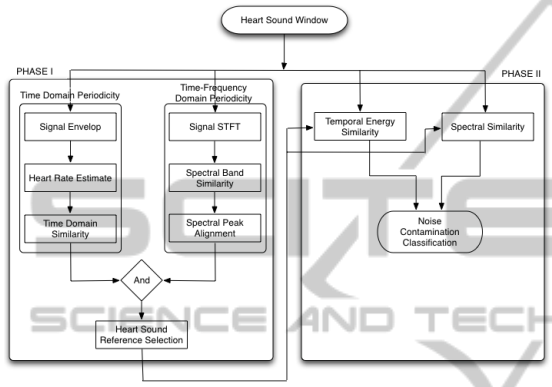

Figure 2: Noise detection algorithm.

2 HEART SOUND ANALYSIS TOOLBOX

2.1 Noise Detection

The first step in developing a clinical application based on HS is to exclude signal portions with noise contaminations. Noise interference in HS might come from internal (e.g. physiological noises) as well as external (e.g. noises by bystander) sources and interfere in highly complex and unpredictable ways. These noise sources exhibit a very broad range of spectral bands, loudness and durations. Noise detection is tackled in the toolbox by observing that HS are quasi-periodic signals. This characteristic manifests itself both in the time domain as well as in the time-frequency domain for different frequency bands. The proposed strategy is depicted in the flowchart in fig. 2: in phase I a non-contaminated HS clip of one complete heart cycle is selected. This HS will serve as a reference template for further processing; since this selection operation is always performed at the start of the signal acquisition process, it ensures that the method exhibits resilience towards auscultation site, posture changes and changing physiological characteristics. In order to grant that this reference template does not exhibit noise contamination, the template is selected from candidates that exhibit the aforementioned quasi-periodicity characteristics. In the second phase this template is applied to each signal window using temporal energy and spectral similarity criteria to check for noise contamination.

Regarding phase I, first each individual heart beat is identified in the HS signal. If an ECG is available, this can be obtained using the R-peaks. Otherwise, the heart cycle limits can be estimated from the prominent peaks (which correspond to S1 and S2) of the signal's envelop and the heart rate assessed from the singular value decomposition (SVD) of the envelop of the signal. Let $y(t)$ be the envelop of the HS obtained using the Hilbert transform. Let $k(wT) = [y(wT), \ldots, y((w+1)T)]$ and $S(T) = [k^T(T), \ldots, k^T(nT)]^T$, nT is limited by the available duration of $y(t)$. The cardiac beat period T can be obtained from $T = argmax_{\gamma \in \Omega}(\alpha_2/\alpha_1)^2$, where α_1 and α_2 are the singular values of $S(\gamma)$ and the search interval Ω is defined using physiological limits of admissible heart rates. Once each heart cycle section of the signal's envelop has been identified, time domain similarity is checked using the inner product. Only those cycles which exhibit a similarity towards its neighbor greater than 0.8 are retained for further processing. The second test performed during this phase is performed in the time-frequency bands. First the spectrogram (0-600Hz) is split into 15 contiguous, non-overlapping frequency bands. Since the main energy sources in HS are due to the S1 and S2 components, it is observed that the envelops in each time-frequency band tend to exhibit linear dependent auto-correlation functions (with decreasing linear dependency for natural and bioprosthetic valves and with increasing linear dependency for mechanical valves) with aligned peaks (see fig. 3). The linear dependency is assessed using the SVD of the matrix Λ, whose rows are the autocorrelation functions of the time-frequency bands. Namely, it is observed that it has to verify $\rho_1 \geq \rho_2 \geq \rho_3$ or $\rho_1 \leq \rho_2 \leq \rho_3$, where $\rho_k = (\alpha_{k+1}/\alpha_k)^2$ and α_k represents the kth singular value of Λ. The heart cycle with the highest average similarity (radial distance) with respect to all available heart cycle template candidates is selected as the template.

Once the reference heart sound has been defined, phase II is initiated where a template matching approach is applied to each HS signal window using the following spectral and temporal features: first the

correlation between spectral power of the template and the signal under analysis is assessed. If it is greater than 0.98, then the signal is subject to a temporal energy test (required to capture very short duration contaminations). In this test, the energy of each 50ms signal window is checked against the energy of the template. The complementary contributions of these two features in the noise contamination problem are shown in fig.4.

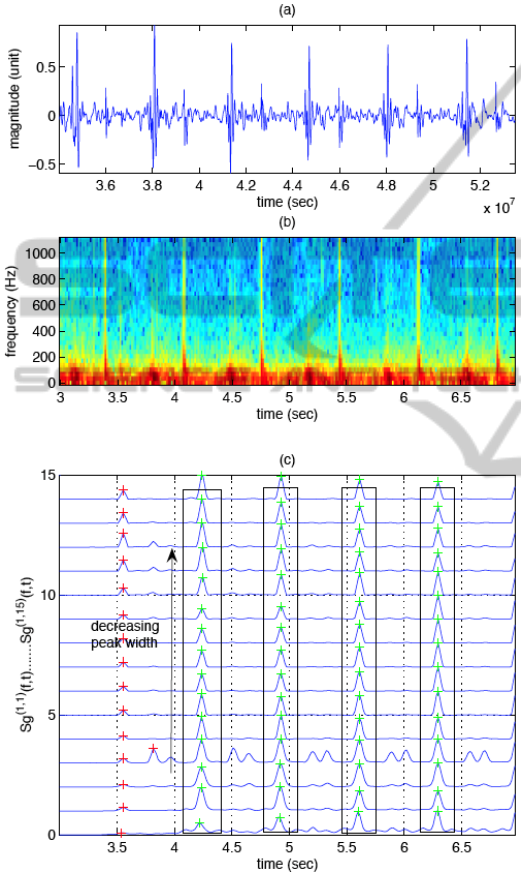

Figure 3: a) Heart sound from mechanical valve. b) Spectrogram. c) Auto-correlation functions of the time-frequency bands.

2.2 Segmentation

HS segmentation into its main constituent parts is approached using two distinct methods: one is based on the signal's envelogram, the other is based on a wavelet-simplicity filter. The former algorithm is very efficient computationally. However, its performance degrades rapidly for HS with murmur. This type of HS are segmented using a method developed by the team based on the wavelet-simplicity filter, which is computationally more demanding. To automatically select between both methods, a selection stage has been incorporated into the segmentation module (see fig. 5).

Heart sounds, particularly those with murmur, contain nonlinear and non-Gaussian information that is not tackled by the widely known Fourier or time-frequency based analysis techniques. Nonlinear

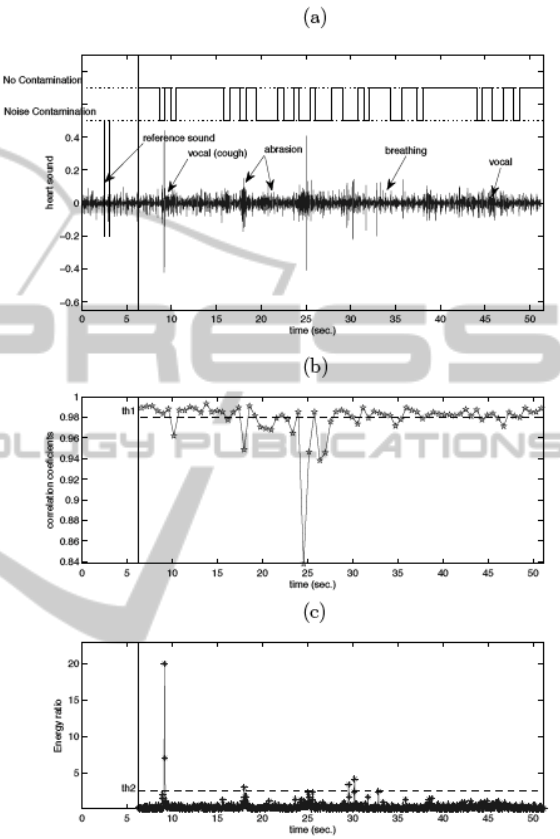

Figure 4: (a) Noise contamination detection results. (b) Spectral correlation feature. (c) Temporal energy feature.

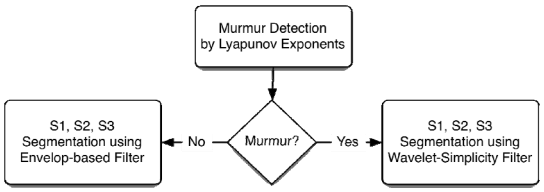

Figure 5: HS segmentation method.

dynamic techniques not only enable to deal with the nonlinearity and the non-Gaussianity of a signal, but also project its dynamic behavior, such as chaos and complexity, in the state space or the phase space that is constructed using embedding theory. Based upon the constructed phase space, the features of a heart sound signal can be computed. In the proposed

method, the degree of chaos is measured via the Lyapunov exponents estimation.

Suppose the heart is considered as a nonlinear dynamical system $X(t + 1) = F[X(t)]$ that generates the heart sound time series $x(t)$, $t = 1....N$. Signal $x(t)$ can be treated as a one dimensional projection of the unknown multidimensional dynamic variable $X(t)$. Phase space transformation of the one dimensional observation $x(t)$ is performed using the embedding theorem, attributed to Taken's theorem, which states that, using some suitable assumptions, a phase space can be formed that is topologically equivalent to an original system (Abarbanel, 1996). The method of delay is applied to reconstruct the attractor in the multidimensional space or embedding space P, i.e. $y_i(t) = [x(t), x(t - \tau), ..., x(t - (m - 1)\tau))] \in IR^m$, where $i = 1, 2, 3...P$ and $y_i(t)$ are row vectors of the embedding matrix $Y(t)$. To determine the exponents from the embedded matrix $Y(t)$, the nearest neighbor points are located to measure their distance from the initial points as given in equation.

$$\lambda = \frac{1}{t_M - t_0} \sum_{k=1}^{M} \log_2 \frac{L'(t_k)}{L'(t_{k-1})}$$

where M is the number of repetitions the trajectory takes in traversing the entire data and denotes the Lyapunov exponents. For a chaotic dynamical system it is observed that the Lyapunov exponents are positive (Abarbanel, 1996). Fig. 6 depicts the average of 150 exponents obtained from 35 HS clips (20 clips without murmur and 15 clips with murmur). As can be observed, HS without murmur are significantly less chaotic. The decision stage in fig. 5 is implemented using a simple threshold decision rule.

The segmentation method based on the signal's envelop is basically formed by two simple steps (Kumar *et al.*, 2006a): (i) first the S1 and S2 candidates are identified using the zero-crossings of the envelop of the approximation coefficients of the 5th level wavelet decomposition. The envelop is computed with a running average of the Shannon energy. The identification of the S1 and S2 components is based on the observation that pressure gradients are higher across the aortic valve compared to the mitral valve. Hence, the S2 heart sound should exhibit more pronounced high frequency components compared to S1 or S3. In order to capture this, a new high frequency feature was introduced. This new feature is composed by the Shannon energy of the detail coefficients of the wavelet transform. As can be seen in fig. 6 (top), this signature coupled to some simple physiological motivated rules enable the discrimination between the different components of the heart sound.

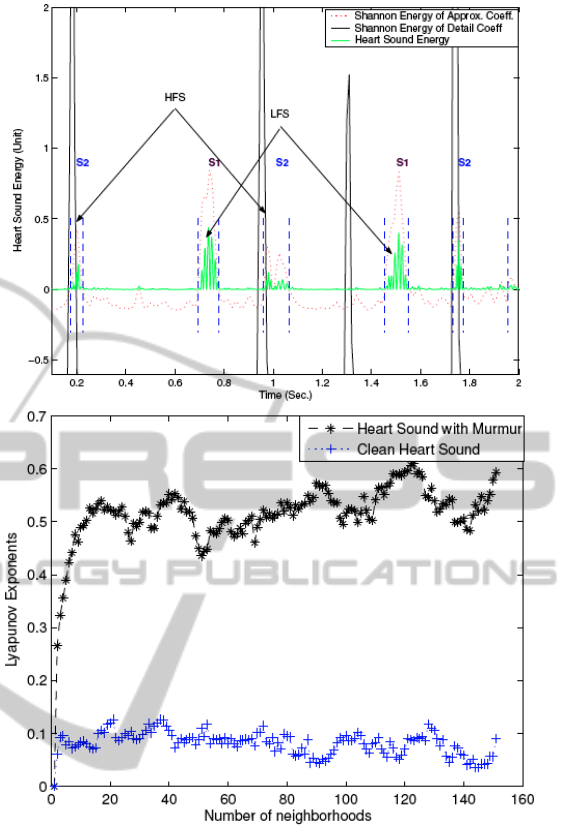

Figure 6: (top) High frequency signature applied to detect the S2 sounds; HFS and LFS stand for high and low frequency segment, respectively.. (bottom) Lyapunov exponents for sound heart sounds with and without murmur.

Regarding the wavelet-simplicity filter algorithm, it follows the same steps of the algorithm we developed using the Wavelet-Simplicity transform (Kumar *et al.*, 2006). Therefore, only fundamental changes in the steps of the basic algorithm are described herein. Murmurs occur between S1 and S2 or S2 and S1 sounds. Therefore, the first task consists of the identification of the boundaries of the S1 and S2 sounds. The main steps for achieving S1, S2 and murmur separation using the strength and simplicity features are (see fig.7):

Step 1: Heart sound is decomposed using the wavelet *db6*. The approximation coefficients are used in further processing.

Step 2: Simplicity (S^l) and global strength (GS^l), where l is the depth of wavelet decomposition, of the decomposed signal is computed.

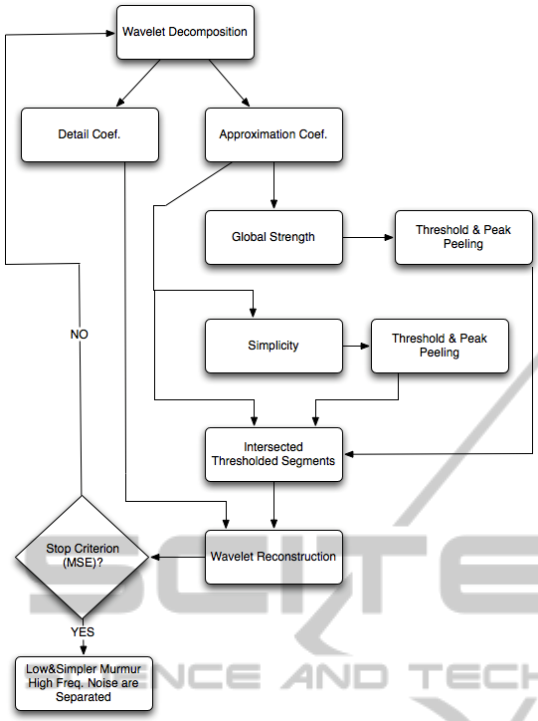

Figure 7: Wavelet-Simplicity Filter segmentation algorithm.

Step 3: The S1 and S2 components of a heart sound exhibit high strength and simplicity, hence clear peaks can be seen in these curves (see fig. 8). In severe heart murmurs, murmurs overlap S1 or S2 sounds. Other unknown sounds may occur due to physiological events (e.g. S3) that exhibit similar characteristics of S1 and S2 components. Usually, S1 and S2 sounds exhibit relatively high simplicity as well as strength, whereas other artifacts exhibit high simplicity but on the contrary low strength. Therefore, the width (or duration) of S1 and S2 sounds are separately segmented using both feature curves. For this task, the peak peeling algorithm (PPA) (Hadjileontiadis and Rekanos, 2003) based upon an iterative thresholding process is applied. PPA is applied first to the *GS* curve and then to the *S* curve successively. Subsequently, start and stop times of S1 and S2 sounds are achieved and can be gated. The segmented time gates using both feature curves are shown in fig. 8.

Step 4: It is observed from fig. 8 that correct start and stop times of S1 and S2 sounds can be achieved by common segmented time gates in both thresholded feature curves.

Step 5: The suitable decomposition depth is found by applying the mean square error criterion on gated decomposed heart sound signal.

To segment occurrences of the S3 sound, two additional steps are carried out using physiological motivated criteria:

1 - Availability of S3 check: two criteria have been considered to check for the availability of S3 sounds in a heart sound sample: (i) if the duration of more than 75% of S2 sounds exceed 250ms. This occurs when the segmentation algorithm was not able to separate the S2 and S3 boundaries. (ii) If more than 75% small low complexity segments exhibiting low duration (50ms-70ms) are detected in the diastolic phase.

2 – Recognition of S3: S3 are characterized by low loudness, small duration, low frequency range (typically between 25-70Hz) and their diastolic nature, i.e. S3 tend to originate around 150ms after the onset of the A2 (aortic component of the S2). Using these properties the following validation criteria are considered:

- Loudness: $(loudness)_{S3}<1/3(loudness)_{\{S1,S2\}}$
- Simplicity: due to their lower spectral content, S3's simplicity tends to be higher compared to simplicity of S1 and S2, i.e. $S_{S3}>S_{\{S1,S2\}}$.
- The time interval between the onset of S3 and the onset of the preceding S2 is between 120-180ms.
- The duration of S3 is between 40-70ms).

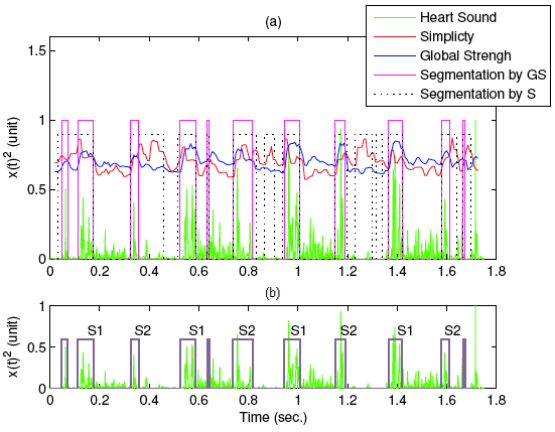

Figure 8: Segmentation results in severe (grade V) mitral regurgitation murmur.

2.3 Murmur Characterization

This module of the toolbox performs murmur classification using features extracted from the systolic, i.e. S1-S2, or the diastolic intervals, i.e. S2-S1. The approach followed is a classical pattern

recognition approach composed by two layers: feature extraction and classifier (a SVM with cubic polynomial kernel function, trained using the one-against-one binary classification). The classifier considers seven distinct classes of mrmur: 1) Aortic Regurgitation (AR), 2) Aortic Stenosis (AS), 3) Mitral Regurgitation (MR), 4) Pulmonary Regurgitation (PR), 5) Pulmonary Stenosis (PS), 6) Subaortic Stenosis+Ventricular Septal Defect (SAS+VSD), 7) Systolic Ejection (SE). It should be noted that murmur presence detection is based on Lyapunov exponents described earlier.

Murmur classification is a challenging task, whose success is mainly conditioned by the quality of the features. The features implemented in this toolbox have been obtained using a feature selection approach from a pool of 256 features. These features have been collected using a two-fold approach: features have been collected from two well-known methods described in literature and a set of new features has been introduced (Kumar *et al.*, 2010). Regarding the feature sets taken from the literature, the sets introduced by Alhstrom *et al.* (2006) and by Olmez and Dokur (2003) have been considered. The most discriminative features have been selected using Pudil's sequential floating point forward selection method. The module allows for two alternative sets of features: the first set is composed by 17 features that have been selected from the aforementioned 256 feature pool, and the second one is composed by 10 features selected among a much smaller pool of features defined by the team. By default we favor the less complex solution, although (as will be discussed later) it exhibits a slightly smaller sensitivity and specificity compared to the first set. The implemented features in the second feature set are those listed in table 1. The transition rate is defined by *transition rate* = T_{asc}/T_{desc}, where T_{asc} is the transition time taken from the first minimum of the energy curve to the maximum energy, and T_{dsc} is the time interval from the energy maximum to the last subsequent minimum energy. The remaining features are well-known in signal processing.

Table 1: feature set for murmur classification.

Loudness	*Zero crossing rate*
Transition Ratio	*Skewness (time domain)*
Fundamental frequency	*Spectral Shape*
Spectral power (100-200Hz)	*Spectral Flux*
Spectral power (200-300Hz)	*Max. Lyapunov Exponent*

2.4 Cardiac Function Assessment

The assessment of the left ventricle cardiac function is based on the extraction of the left ventricle systolic time intervals (STI), i.e. the pre-ejection period (PEP) and the left ventricule ejection time (LVET). These are of major diagnostic importance, since it is this ventricle's function to insure the blood flow in the systemic circulation. STI are defined by the events of the aortic valve. Namely, PEP is defined by the time interval between R-peak of the ECG and the opening of the aortic valve, while LVET corresponds to time span between the closing and the opening events of this valve. We have shown (Carvalho *et al.*, 2009) that S1 and S2 can be applied to extract the aortic valve events from S1 and S2 using synchronized echocardiography and HS under resting conditions. It should be mentioned that, the framework has other methods to extract STI that can be applied. For instance, when no ECG is available, the PPG and the HS can be combined to extract the STI. These might also be estimated using the ICG signal, if available. A comparative analysis of some of these methods and principles in STI estimation can be found in (Carvalho *et al.*, 2010).

The details regarding the algorithm for the detection of the aortic events using HS were presented in (Paiva *et al.*, 2009). The method is based on a Bayesian approach using instantaneous amplitude. Once the beat-by-beat STI have been extracted, the toolbox enables the calculation of the following cardiac function measures:

Corrected STI with Respect to Heart Rate and Classification: The implemented correction algorithms are those described in (Weissler *et al.*, 1968) and (Warrington *et al.*, 1988). For STI correction under exercise, the correction steps described by Mertens *et al.* (1981) have been considered in the toolbox. The toolbox presents diagnosis information regarding if the STI are pathological or not.

Contractility Index and Classification: The contractility index PEP/LVET is computed average runs of 5 beats. Heart Failure diagnosis is automatically provided based on clinically validated threshold.

Stroke Volume and Cardiac Output: The beat-to-beat as well as the average stroke volume and the cardiac output are calculated using the model described in (Rietzschel *et al.*, 2001). It should be mentioned that these parameters are also extracted in the ICG toolbox of the framework, where the Bernstein and Kubicek models have been

implemented (see e.g. Wang *et al.*, 1995).

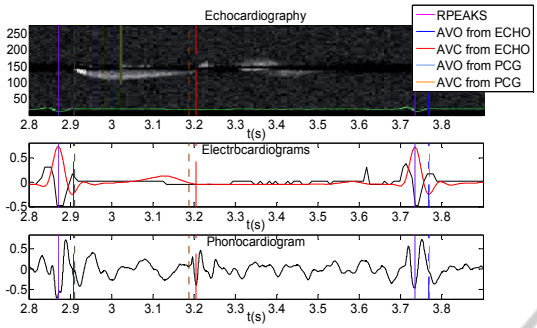

Figure 9: Synchronized echocardiography and heart sound.

2.5 S2 Split Detection

Pulmonary hypertension (PH) is a serious heart condition that is difficult to diagnose. Heart sounds is one of the most relevant diagnosis signal. Usually, PH leads to wide S2 split between the aortic component (A2) and the pulmonary component (P2). Loud P2 is another usual consequence of PH. The toolbox implements a simple algorithm to assess S2 splitting. The following steps compose the method:

Step 1: S2 frequency range is typically limited to 240Hz. The first step is low-pass filtering using a Butterworth filter with 240Hz cut-off frequency.

Step 2: The signal's envelop is extracted using the Hilbert transform.

Step 3: The two most prominent are extracted. If their amplitude ratio is greater than a predefined threshold, then a split is assumed.

Step 4: The split duration is estimated as the time interval between the two peaks of the signal's envelop (see fig. 10).

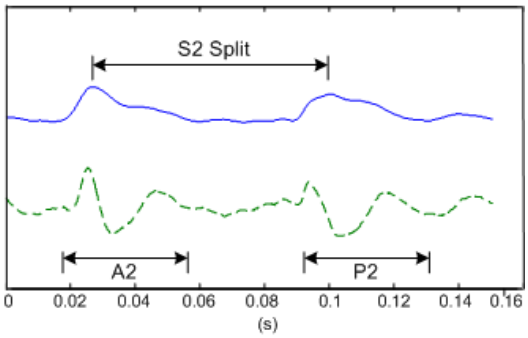

Figure 10: S2 Split. Upper curve represents the signal's envelop. The lower dashed curve is the S2 heart sound. Time split interval as well as A2 and P2 components are shown.

3 RESULTS AND DISCUSSION

Table 2 presents the sensitivity and specificity results of the algorithms implemented in the heart sound toolbox of the framework. The STI estimation entries, i.e. PEP, LVET and RS2 entries, refer to the absolute estimation error with respect to echocardiography (the clinical gold standard). These results were obtained using heart sounds acquired at several hospitals from typical target populations, i.e. patients suffering from several types of cardio-vascular diseases such as atrial fibrillation, tachycardia, premature ventricular contractions, several types of valve problems with regurgitation and stenosis, patients with artificial valve implants, as well as several degrees of heart failure. One exception to this is the data acquisition protocol followed to assess the STI measurement algorithms. In this case, only healthy subjects have been used so far. The data acquisition study with patients suffering from heart failure is currently being carried out. It should also be mentioned that the data collection study with CVD patients for S2 split assessment is also ongoing. Regarding the data acquisition for noise detection, the protocol followed included contaminations by several distinct internal and external noise sources at different intensity levels. All databases have been collected and annotated under medical supervision. Table 3 summarizes the population characteristics and the amount of data collected for each validation database.

Table 2: Summary of results.

Function	*SE/Abs. Error*	*SP/Corr.*
Noise detection	95.88%	97.56%
Segmentation (without murmur)	97.95%	98.20%
Segmentation (grade I-IV murmur)	91.09%	95.25%
S2 Split*	-	-
S3 Identification	90.35%	92.35%
Murmur classification (set of 10 features)	95.74%	95.01%
Murmur classification (set of 17 features)	96.15%	96.16%
PEP	7.57±6.17*ms*	0.52
LVET	11.21±9.27*ms*	0.88
RS2	9.88±8.65*ms*	0.92

As can be observed from the results in table 2 and 3, most of the algorithms developed by team and integrated into the toolbox have been evaluated thoroughly. Furthermore, these methods exhibit very high sensitivity and specificity values. Regarding the results achieved for STI, the achieved results so far, suggest that HS enables much better results

compared to other competing measurement principles for portable and non-invasive devices (a detailed analysis can be found in (Carvalho *et al.*, 2010)). As already mentioned, these results have still to be confirmed for CVD patients. Regarding the evaluation of the S3 identification module, it should be mentioned that currently the algorithm has been evaluated on sound clips collected from 5 patients. Hence, the provided results should be considered as preliminary. As for the S2 split algorithm, evaluation as been performed only on healthy subjects so far.

Table 3: Validation conditions.

Function	*N*	*BMI*	*Age*
Noise detection	71	25.1±7.8kg/m^2	35.3±12.0y
Segmentation (without mur.)	55	24.4±1.5kg/m^2	32.6±9.7y
Segmentation (grade I-IV mur.)	21	24.9±2.3kg/m^2	54.73±6.0y
Murmur classif.	51	25.4±2.2kg/m^2	64.65±8.6y
S2 Split*	-	-	-
S3 Identification	5	NA	15.7±8.7y
STI	33	24.5±2.4kg/m^2	29.7±8.5y

Given the achieved maturity level of the toolbox, it is being used to deploy clinical applications. Currently, the team is developing three distinct applications using the framework: the first application is called the intelligent stethoscope that enables the automatic annotation of HS to support the decision of the physician (for details, the reader may refer to (Ramos *et al.*, 2011)); the second application build on top of the first one and is intended to auscultation training; finally the third and last application targets prosthetic heart valve implant dysfunction detection. Applications related to heart failure management are planned, once the STI measurement module tests have been concluded.

4 CONCLUSIONS AND FUTURE WORK

Heart sound is a valuable biosignal to build diagnosis systems for cardiovascular diseases for the daily acute clinical practice as well as for systems dedicated to long-term follow-up of chronic CVD patients. In this paper we introduce a Matlab toolbox for acoustic cardiac signal processing. This toolbox is integrated into a framework for cardiac signal processing that includes a general real-time signal acquisition toolbox to interface medical sensor networks and a collection of signal analysis toolboxes for the most pertinent signals to deploy portable and non-invasive devices for CVD diagnosis. The main algorithms developed specifically for the heart sound toolbox are outlined. These include solutions for the main challenges that are encountered in real life applications based on heart sounds. In comparison to other existing heart sound processing frameworks, the proposed toolbox includes methods for the processing functionalities that are commonly handled, i.e. noise contamination detection, heart sound segmentation (including S3 identification) and murmur classification, but also tackles problems that most known frameworks do not contemplate. More specifically, methods to detect S2 splitting and cardiac function assessment are part of the proposed toolbox. To the best of the authors' knowledge, the proposed toolbox is the first one that enables STI measurement using heart sounds. This opens new application areas to heart sounds such as heart failure management.

The proposed framework exhibits a significant maturity level. Most of the integrated algorithms have been tested using heart sound clips obtained under medical supervision and using typical CVD populations under real-life conditions. The achieved results are comparable and in most cases exceed the state of the art in competing methods. It should be mentioned that the proposed algorithms for STI measurement and S3 identification have still to be fully evaluated using a significant database of data collected from real CVD patients. This is an ongoing task that will be finished in the near future. It is also foreseen to continue the research of a more evolved version of the S2 split detection module. More specifically, currently the team is researching a solution to accurately identify the onset of both S2 components, i.e. A2 and P2. This might enable to correlate the time split to pulmonary artery pressure measurement as was previously suggested by (Popov *et al*., 2004).

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