PCGCleaner: Development and implementation of an R package for heart sound signal preprocessing

by

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Abstract

BACKGROUND: Heart disease has become a major health problem over the world. Valvular heart disease is one of the most common and serious forms of heart disease and can be diagnosed with cardiac auscultation. However, auscultation can be subject to inter-listener variability, subjectivity, environment, and training. Recent development of digital stethoscopes and machine learning tools enable computer-aided auscultation in clinical settings, among which the analysis of phonocardiogram (PCG) signals is one of the most popular and developed ones. In our present study, we focused on developing an R package, PCGCleaner, for the preprocessing of PCG signals. We replicated parts of a well-established algorithm for heart sound analysis in MATLAB code and translated them into R. We also implemented this tool on a heart sounds database established by the University of Michigan.

METHODS: In the package PCGCleaner, we mainly incorporated two parts of functions for heart sound signal preprocessing, including denoising and homomorphic envelope detection. The raw heart sound recordings are recommended to be firstly pre-processed with band pass filters and remove noisy spikes to reduce the background noise during the denoising step. After denoising, homomorphic envelope detection can be performed for further single cardiac cycle identification. In order to examine the use of our package, we also implemented it on larger heart sounds samples which were collected from the University of Michigan Health System between 2017 and 2020.

RESULTS AND DISCUSSION: Among the study sample, our package PCGCleaner performs well in preprocessing of the raw heart sound signals. Our works enable researchers to preprocess

their raw heart sound signals in simple steps, which are fundamental but essential work before any further experiments of segmentation, feature extraction, or classification. Our future work will incorporate more functions for preprocessing and options for segmentation. The ultimate goal is to develop an R package to accomplish the feature extraction of heart sounds with multiple simple steps and provide a set of clean, adequate features for further sound classifications with various machine learning models.

Background

1. Heart disease in the US population

Heart disease, as the leading cause of death in the United States, has become a major health problem over the years. About 647,000 Americans die from heart disease each year, which accounts for one out of every four deaths.[1] Heart disease costs, including health care services, medicines, and lost productivity due to death, were about $555 billion in 2016, and will skyrocket to $1.1 trillion by 2035.[2] According to the Center for Disease Control and Prevention (CDC), 12.1% of adults in the US were with diagnosed heart disease in 2019.[1] Given this large prevalence and mortality, identifying individuals with early vascular or cardiac disease in need of intervention is extremely important. Studies have shown that early detection and treatment of heart disease could delay or prevent the onset of symptoms and thereby reduce the incidence of cardiovascular events in susceptible individuals.[3,4]

Heart valve disease is one of the most common and serious forms of heart disease. More than five million Americans are diagnosed with heart valve disease each year.[5] There are four

valves in the heart, including aortic, mitral, tricuspid and pulmonary valves. These valves open and close as the blood flows into and away from the heart. Valvular heart disease is when any valve has damage or is diseased. These problems may include regurgitation and stenosis. Regurgitation refers to the condition that the valve flaps don't close properly, causing blood to leak backward in the heart. In valve stenosis, the valve flaps become thick or stiff, and they may fuse together, resulting in a narrowed valve opening and reduced blood flow through the valve. A moderate or severe valve disease can lead to heart failure, stroke, blood clots, and other complications if it is not discovered and treated in a timely fashion. Heart valve disease treatment depends on severity of the condition, heart valve surgery may eventually be needed to repair or replace the diseased heart valve. Some valve repair procedures require an open surgical approach whereas others can be done through an endovascular approach.[6]

An echocardiogram is the gold standard to confirm the diagnosis of a heart valve disease and to evaluate its effects on a patient's heart. As an essential tool for the accurate diagnosis of various heart conditions in the field of cardiology, an echocardiogram is an imaging procedure that uses high-frequency sound waves to create pictures of a heart's chambers, valves, walls, and blood vessels.[7] A standard echocardiogram has the advantage of being painless, safe, and without exposure to radiation. However, it can cost $2,000 or more for people who do not have health insurance in the United States, and up to half the cost for those with an insurance due to a co-pay.[8] Performing and interpreting an echocardiogram requires special expertise in cardiac imaging. This expertise is particularly limited in some developing countries, which limits the global availability of echocardiograms.

2. Heart sounds and auscultation

Heart valve diseases are also associated with and reflected by the sounds that the heart produces. The heart sounds in healthy adults are described as the first heart sound (S1) caused by the closure of atrioventricular valves, and the second heart sound (S2) caused by the closure of semilunar valves. The interval between the beginning of S1 to the beginning of the following S1 is called a cardiac cycle. *Systole* refers to the interval between the end of S1 to the beginning of the same cycle's S2. *Diastole* refers to the interval between the end of S2 to the beginning of the next cycle's S1.[9] On the other hand, cardiac cycles of abnormal heart sounds include elements other than S1 and S2.

Heart murmurs are sounds made by turbulent blood in or near the heart during the heartbeat cycle. The blood turbulence is mainly caused by the opening and closing of heart valves, as well as fast accelerations and retardations of blood flow in the heart chambers.[10] There are two types of heart murmurs in general: physiologic and pathologic murmurs. A physiologic murmur is usually harmless, but a pathologic one, on the other hand, could be an indicator of a vital heart problem such as valve calcification, rupture, or endocarditis.[11] Therefore, it is essential to identify an abnormal heart murmur at an initial stage of its onset to avoid deterioration or fatality.

Cardiac auscultation is one of the key clinical skills used by physicians to screen for cardiac pathologies, especially in the diagnosis and assessment of valvular heart disease.[12] It has been playing an essential role in the clinical workflow over a century, not only because it is cheap, quick, instantly and universally available, but also by using the stethoscope, practitioners are able to interact with the patient in a personal, tangible way that exemplifies they care about

the patient as a unique, valued individual.[13] However, interpreting auscultated heart sounds is affected by many factors, including inter-listener variability, subjectivity, environment, and training.[14] The training for auscultation takes time and focus, and the accuracy varies by the listener's skill and experience. According to a study conducted by Favret et al, the internal medicine and family medicine residents heard 40% of the extra heart sounds and made a correct diagnosis in only 24% of cases, and even experienced physicians missed 31% of murmurs.[15] Clinicians' low accuracy in auscultating heart sounds may be lead to delays in diagnosis and treatment. On the other hand, a computer assisted system may help the general physician in coming up to a more accurate and reliable diagnosis at early stages and also can reduce unnecessary referrals of patients to expert cardiologists at a distance.

3. Machine learning in abnormal heart sounds detection

Machine learning approaches have been proved to be useful for modeling complex biomedical data by offering better performance in various tasks such as image processing, identifying abnormalities, clinical decision making and so on.[16] A substantial amount of work has been done towards the identification and classification of heart sounds using machine learning tools. Beyond that, the recent development of digital stethoscopes has enabled digital recording and opened the door to a number of unique possibilities using computer-aided auscultation in clinical settings. Sounds collected by digital stethoscopes are converted to electrical signals which can then be amplified for optimal listening and be processed for signal analyses.[17] The analysis of those electrical signals, i.e., phonocardiogram (PCG) signals, is one of the most popular and developed ones, which has been proved to be useful for objective interpretation of the heart sounds and early detection of heart diseases.

Signal processing refers to the procedures applied on measured data or sampled data to reveal the information contained in the measurements.[18] Digital signal processing of the PCG enables the characterization of heart sounds into a quantified way, in other words, different heart sounds and murmurs can be distinguished by characteristics including timing (i.e., systolic or diastolic), duration, pitch (i.e., frequency), and intensity. Researchers have tried to extract various features in different domains using fast Fourier transforms (FFT), wavelet transforms, etc and have classified the PCG signals into various classes with different machine learning models.[19]

PCG signal processing usually involves three steps, pre-processing, feature extraction, and classification. The pre-processing step usually includes denoising, and sometimes segmentation. The second step, feature extraction, is to calculate the identifying parameters from segmented data. Finally, the classification of PCG signals, mostly into two classes (normal and abnormal), is based on those extracted features and generally performed by utilizing machine learning tools.[20] A conceptual diagram of heart sound signal processing module is depicted in **Figure 1**.

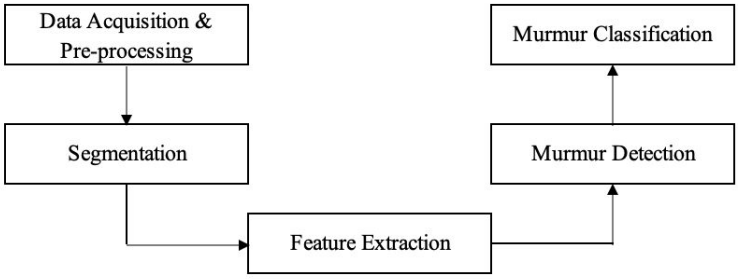


Figure 1. Conceptual diagram of heart sound signal processing module

Researchers have proposed several algorithms with fairly high accuracies for PCG signal processing and heart sound classification, where the majority of works were based on Artificial

Neural Networks (ANN) and Support Vector Machines (SVM).[21] Turkoglu et al. developed an ANN-based system in 2002 that achieved an accuracy of 94% for normal and 95.9% for pathological heart sounds.[22] Another approach developed by Wu et al. using SVM as the main classifier gave 95% of accuracy to distinguish normal heart sounds from abnormal ones.[23]

4. Objectives of the study

In our present study, we focused on developing a software package in R for the preprocessing of PCG signals. We replicated parts of a well-established algorithm for heart sound analysis introduced by Schmidt et al.[24] in MATLAB code and translated them into R. We also implemented this tool on a heart sounds database established by the University of Michigan. Given a lack of current resources in PCG signal processing in R, this work provides researchers opportunities to conduct data preprocessing, which is a foundation of any further works of PCG signal processing. Though this tool is built for PCG signal processing specifically, some functions in this package may also be introduced to other kinds of sound analysis and become an open resource for a broader audience.

Related Work

1. Preprocessing of heart sound signals

Preprocessing of heart sound signals is not a new topic, however, it is still in a developing stage as far as its embedded applications are concerned. Two general steps, denoising and segmentation, are commonly used in PCG signal processing. Denoising is generally achieved by suitable filters and wavelet transforms. Segmentation is a process in which to determine the boundaries of cardiac cycles from contiguous heart sound signals.

Because the heart sound signal is a kind of weak signal of the human body, it is highly susceptible to external noise interference during the process of signal collection. When heart sound signals are collected, it is inevitable to receive the noise around, such as electromagnetic interference, power frequency interference, electrical interference with the human body, breath sounds and lung sounds interference and so on. Those noises can sometimes contaminate the effective information and may cause great influence on the further steps of segmentation and classification in signal processing works. As a result, a certain filtering technology to further denoise the signals is crucial to lay a good foundation for the feature extraction and identification of heart sounds. Typical frequencies of heart sounds and murmurs are within the range from 20 to 500 cycles per second (Hz), which are at the lower end of sound frequencies the human ear can hear (20 to 20,000 Hz).[25] Higher or lower frequencies are not of clinical significance for analysis and diagnosis. Previous works have shown the advantage of applying high-pass and low-pass filters in PCG signals including the separation of heart sounds (S1 and S2), heart murmurs and clicks. According to Cherif et al, two types of filters, “Butterworth” and “Bessel”, are the most suitable for filtering PCG signals.[26]

After denoising, the PCG signals are ready for segmentation. As one of the most difficult steps in heart sound analysis, segmentation has been the subject of many studies. In most cases, the activities in the PCG signal relating to a given disease are contained in a single interval of cardiac cycle. Thus, detecting a single cardiac cycle is necessary and essential for future implementation of automatic analysis such as extracting features from the single cycle and then classifying the signal. Several popular approaches mentioned in the former literature include homomorphic filtering, average normalized Shannon energy, complexity signatures, energy of

wavelet coefficients and so on. All these studies fall under the envelope analysis approach and are based on analysis of the envelope signals, only different by detection methods.[27]

Among all approaches of envelope analysis, homomorphic filtering was proved to be useful to indicate a single detected cycle. Homomorphic filtering technique resulted in a smooth envelope enabling easy peak detection. Then parameters of the peaks like peak start point, end point, peak width, and distance between peaks can be found and labeled as S1 or S2. And by clustering of these parameters of the peaks, the occurrence of single cardiac cycles can be identified for further feature extraction.[28] This segmentation algorithm has shown a success rate of 90.29%.[28] Detailed mechanisms of homomorphic envelope and steps to implement are described in the **Method Section 1.2**.

On the other hand, peak detection and the segmentation of S1 and S2 can become tedious and sometimes inaccurate due to several reasons: 1) the results can depend highly on where and how hard the stethoscope is placed on the chest. Thus a threshold could be too high to miss the normal S1 or S2 or too low to detect more extra peaks; 2) the assumption that systole is shorter than diastole is not always true. Above a certain heart rate, the length of diastole could be roughly the same length as systole; 3) in cases with severe murmur, one normal heart sound may become very large and the other may disappear from the envelope signal altogether. Some cardiac cycles may be incorrectly segmented and there is no way to automatically distinguish correctly segmented cycles from incorrectly segmented ones. And allowing incorrectly segmented cycles to enter feature extraction results in bad training vectors for the classifier.[27]

In our study, we only incorporate the first step of homomorphic filtering in our R tool, that is, the homomorphic envelope detection for single cardiac cycle identification. The further

segmentation into different parts of the cardiac cycle (S1 and S2) is not supported in the current version.

2. Signal processing work in R

After the first release in 1995, R has quickly taken an important role in statistical and graphical computing. According to the 2017 Burtch Works Survey, 40% of all surveyed data scientists prefer R, compared to 34% prefer SAS and 26% Python.[29] R and its libraries are able to handle a variety of analyzing techniques, including classical statistical tests, linear and nonlinear modeling, time-series analysis, clustering, classification, and others. It has been widely used in bioinformatics, genetic research, epidemiology, and for analyzing clinical data nowadays.[30]

Most of the current heart sound signal processing work was conducted in MATLAB, which is not open source to the general public. Unlike MATLAB, R is a free programming language and software environment for statistical computing. There are some existing R packages developed by researchers for different kinds of signal processing. The *signal* package developed by Ligges et al. is one of the basic signal processing tools that contains a set of functions originally written for MATLAB and Octave, including filtering, filtering generation, resampling, interpolation, and visualization of filter models.[31] In addition to the basics, R contains some good implementations of signal processing algorithms that also can be applied to statistical analysis and machine learning. For example, *wavelets* and *fftw* are two packages that specialized in wavelet and FFT analysis respectively.[32] For machine learning tasks, R has extensive library sets to explore data, select features, validation schemes and many more, which makes machine learning easy and approachable.

R is also highly cost effective for a project of any size. Because it is an open source, developments in R happen at a rapid scale and the community of developers is huge. Along with a tremendous amount of learning resources makes R programming a perfect choice for beginners. All of these makes R an ideal choice for our tool development of PCG signal processing.

Methods

1. Development of the R package: PCGCleaner

In the package PCGCleaner, we mainly incorporated two parts of functions for heart sound signal preprocessing, including denoising and homomorphic envelope detection. In order to avoid repetition of work, the signal package is embedded in our package. The raw heart sound recordings are recommended to be firstly pre-processed with band pass filters and remove noisy spikes to reduce the background noise during the denoising step. After denoising, homomorphic envelope detection can be performed for further single cardiac cycle identification. As we mentioned before, we only included the homomorphic envelope detection, which is the first step of homomorphic filtering in our R tool.

1.1 Denoising

Common noise sources in the heart sound recordings include endogenous or ambient speech, motion artifacts, and physiological sounds, such as intestinal and breathing sounds. In order to reduce the influence of low and high frequency noise, the raw signal should be filtered with one or more band pass filters with appropriate cut-off frequencies. Two functions, `butterworth_low_pass_filter()` and `butterworth_high_pass_filter()` were

created to filter a given signal using a forward-backward, zero-phase butterworth low-pass/high-pass filter. Both filters will first filter the raw signal in the forward direction, and the filtered sequence is then reversed and run back through the filter to obtain zero phase distortion. Taking the low pass filter as an example, the inputs and outputs of the functions are as follow:

`butterworth_low_pass_filter(original_signal,order,cutoff,sampling_frequency):`

Inputs:

- original_signal: the 1D signal to be filtered
- order: the order of the filter (1,2,3,4 etc). NOTE: This order is effectively doubled as this function uses a forward-backward filter that ensures zero phase distortion
- cutoff: the frequency cutoff for the low-pass filter (in Hz)
- sampling_frequency: the sampling frequency of the signal being filtered (in Hz).

Outputs:

- low_pass_filtered_signal: the low-pass filtered signal

We also identified and removed the potential friction spikes with exceptionally high amplitudes using a function `schmidt_spike_removal()` based on methods introduced by Schmidt et al,[24] which follows the steps below:

1) The recording was divided into windows of 500 ms.
2) The maximum absolute amplitude (MAA) in each window was identified.
3) The following steps would be carried out if at least one MAA exceeds three times the median value of the MAA's, or else continues to step 4.
    a) The window with the highest MAA was chosen.
    b) The location of the MAA point was identified as the top of the noise spike.
    c) The beginning of the noise spike was defined as the last zero-crossing point before the MAA point.
    d) The end of the spike was defined as the first zero-crossing point after the maximum point.
    e) The defined noise spike was replaced by zeros.

f) Resume at step 2.

4) Procedure completed.

The inputs and outputs of the function `schmidt_spike_removal()` are as follow:

```
schmidt_spike_removal(original_signal,fs):
```

Inputs:

- original_signal: the original (1D) audio signal array
- fs: the sampling frequency (Hz)

Outputs:

- despiked_signal: the audio signal with any spikes removed

1.2 Homomorphic envelogram

The homomorphic envelogram has been shown to be effective in extracting amplitude envelopes of phonocardiograms.[33] The homomorphic envelogram can be extracted with a homomorphic filter. This approach was based on the similarity in structure of heart sounds to modulated components, assuming that the heart rate is uniform for the entire sequence of PCG signal recording. Since normal heart sound signals (S1, S2) and heart murmurs are similar to amplitude and frequency modulated waveforms, homomorphic filtering, which has been used to extract voiced components of the speech,[34] can be applied to heart sounds to find the envelope. By applying logarithmic transformation, it converts a non-linear combination of signals (multiplied in time domain) into a linear combination. And thus, the resulting spectrum can be viewed as a combination of slowly varying and fast varying parts wherein the high frequency content would be removed using a low-pass filter. Details can be explained as follow:

Since the signal is viewed as a product of a slowly varying component controlling the signal amplitude and a fast varying component representing the oscillating part of the signal:

$$x(t) = a(t) \cdot o(t) \quad a(t) > 0$$

where *a(t)* is the amplitude component and *o(t)* is the oscillating component. The log transformed signal is the addition of the amplitude and oscillating components:

$$ln|x(t)| = ln|a(t)| + ln|o(t)|$$

Thereby the multiplication is replaced by addition and it is possible to reject the high frequency component with a linear low pass filter:

$$L(ln|x(t)|) = L(ln|a(t)|) + L(ln|o(t)|) \approx L(ln|a(t)|)$$

where *L* is a low pass filter. The homomorphic envelogram is created by a reverse transformation:

$$HEnv(t) = exp(L(ln|x(t)|)) \approx a(t)$$

Given the envelope of the signal detected by homomorphic filtering, we can further do peak detection, which is important to find the locations of S1 and S2.

In **PCGCleaner**, we created a function `homomorphic_envelope_with_hilbert()` to fulfill the homomorphic envelope detection. This function finds the homomorphic envelope of a signal with the Hilbert transformation as suggested by Schmidt et al.[24] A zero-phase low-pass Butterworth filter is used to extract the envelope. The inputs and outputs of the function `homomorphic_envelope_with_hilbert()` are as follow:

`homomorphic_envelope_with_hilbert(input_signal,sampling_frequency,lpf_frequency=8):`

Inputs:

- input_signal: the original signal (1D) signal
- sampling_frequency: the signal's sampling frequency (Hz)
- lpf_frequency: the frequency cut-off of the low-pass filter to be used in the envelope extraction (Default = 8 Hz as in Schmidt's publication).

Outputs:

- homomorphic_envelope: the homomorphic envelope of the original signal (not normalized)

1.3 Normalization

Furthermore, we also included a function `normalize_signal()` to allow the envelope signals to be normalized by subtraction of the mean value and dividing with the value of the standard deviation. The purpose of the normalization is to reduce the amplitude difference from subject to subject and be prepared for machine learning applications. The signal is thereby a one-dimensional observation sequence describing the normalized signal amplitude. The inputs and outputs of the function `normalize_signal()` are as follow:

`normalize_signal(signal):`

Inputs:

- signal: the original signal

Outputs:

- normalized_signal: the original signal, minus the mean and divided by the standard deviation

2. Application of the R package to Pre-Process Sounds in the 1000 Heart Sounds database

Most of the existing studies of PCG analysis have relied on a limited number of sound samples, potentially resulting in over-fitting for a particular dataset. Some of the heart sounds were artificially created, which were not ideal for a real scenario because of the need for human interaction. In addition, the modeling buildings and predictions were mostly based on purely clinical diagnosis. It is unclear if the echocardiographic findings were taken into account during the diagnoses in those studies. Furthermore, previous studies have not considered other clinical factors, such as demographic factors, comorbidities, and laboratory results, which could also show significant impacts on the diagnosis of heart diseases.

In order to examine the use of our package, we implemented it on larger heart sounds samples which were collected in a real clinical setting.

2.1 Heart sound collection

Patients were recruited from the University of Michigan Health System between 2017 and 2020. Eligible patients were aged 18 years and older with outpatient or inpatient encounters, with a scheduled or planned transthoracic echocardiograph within 72 hours of collection. Heart sounds were recorded at four auscultatory sites (aortic area, pulmonic area, tricuspid area, mitral area), using 3M Littmann Electronic Stethoscope devices. Patients were informed with potential risks and benefits of participating in the study and their willingness to contribute to the study were taken in the form of written consent. A total of 377 patients with various pathologies were analyzed in our current study. Heart sounds were recorded in a quiet room with assistance from the patients. The recordings for analysis were saved in a *.wav format on cloud after de-identified.

2.2 Echocardiogram, basic demographic and medical comorbidities

Patients' transthoracic echocardiograph findings and their basic health information were retrieved from the Electronic Health Records (EHRs) system and de-identified under the Health Insurance Portability and Accountability Act of 1996 (HIPAA) regulation. Transthoracic echocardiograph findings were interpreted by one experienced research assistant as different categories of heart diseases, including aortic stenosis, mitral stenosis, pulmonic stenosis, tricuspid stenosis, aortic regurgitation, mitral regurgitation, pulmonic regurgitation, and tricuspid regurgitation. The severity of the disease was recorded accordingly, including mild, mild to

moderate, moderate, moderate to severe, and severe. In addition, patients' prosthetic valve information was also collected.

Basic demographic information such as age and sex and their cardiovascular related medical comobidities such as hypertension and stroke status were also collected for future analysis. By incorporating comorbidities, which alongside the development of digital stethoscopes creates an opportunity to build a diagnostic algorithm to change the paradigm on how cardiac auscultation is performed and taught to trainees.

Results

1. Summary of the package

The **PCGCleaner** package is developed for basic preprocessing for PCG signals. Two main steps are involved in this package, denoising and homomorphic envelope detection. Denoising work consists of the implementation of one or more low/high-pass filters and spike removals to reduce potential noises in the heart sound recordings such as frictions, intestinal and breathing sounds. Homomorphic envelope detection is the process of using a homomorphic filter to detect a single cardiac cycle, which can be useful for the segmentations of S1 and S2 (not supported by our package for now). Our package enables the preprocess of the raw heart sound signals in several simple steps, and offers fundamental data for segmentation, feature extraction, and classification in the PCG signal analyses. **Table 1** below summarizes the functions included in the package and the description and purpose for each function.

Table 1. Summary of functions in PCGCleaner

Function	Description
`butterworth_low_pass_filter()`	A function that low/high-pass filters a given signal using a forward-backward, zero-phase butterworth low/high-pass filter. It inputs the 1D signal to be filtered, and outputs the low/high-pass filtered signal.
`butterworth_high_pass_filter()`	
`schmidt_spike_removal()`	A function to remove potential spikes in the signals. In a window of 500 ms, if the maximum absolute amplitude (MAA) is larger than three times the median value of MAA, a noise spike will be flagged at the MAA and replaced by zero. It inputs the 1D audio signal array and outputs the signal with any spikes removed.
`homomorphic_envelope_with_hilbert()`	A function that finds the homomorphic envelope of a signal, and extracts the envelope with a zero-phase low-pass butterworth filter. It inputs the 1D signal array and outputs the homomorphic envelope of the original signal.
`normalize_signal()`	A function to normalize a 1D signal by subtracting the mean and divided by the standard deviation. It inputs the 1D signal array and outputs the normalized signal.

2. Examples

Here we use several examples to illustrate the usage of the **PCGCleaner** package. Sample heart sounds were collected from recordings in the 1000 Heart Sound database. In our examples, we intentionally chose patients with diseases at one or more of the four heart valves to explain features for different valvular diseases and observe the effects of interactions. Different severities were also selected to make comparison between signals. Pseudo patient ID, the auscultatory site of the recording, and patient's echocardiogram diagnosis are described in **Table 2**. We followed the workflow below to conduct heart sound data cleaning for each patient: 1) a

fourth order Butterworth band pass filters with frequency range cut-offs at 25 Hz and 400 Hz; 2) remove noisy spikes; 3) homomorphic envelope detection. Results along with the codes to generate are displayed side by side for comparison.

Table 2. Patient auscultation information and echocardiogram diagnosis

Patient ID	Auscultatory Site	Echocardiogram Diagnosis
1	pulmonic area	normal
2	pulmonic area	mild pulmonic stenosis and mild pulmonic stenosis, aortic prosthetic valve
3	mitral area	moderate mitral regurgitation
4	tricuspid area	moderate to severe tricuspid regurgitation, mild mitral regurgitation, mild pulmonic regurgitation
5	aortic area	severe aortic stenosis, mild aortic, mitral, pulmonic and tricuspid regurgitation
6	aortic area	severe aortic regurgitation and mild mitral regurgitation

2.1 Preprocessing of a normal heart sound signal

Figure 2 shows the preprocessing of a 30-second PCG signal from a patient with normal heart echocardiogram diagnosis. The raw signals (**2A**) show fluctuations around amplitude of zero, indicating the existence of noises in the heart sound recordings such as intestinal and breathing sounds. **2B** shows the filtered signals for the same patients after denoising with a fourth order Butterworth band pass filter with cut-off frequencies at 25 Hz and 400 Hz using `butterworth_low_pass_filter()` and `butterworth_high_pass_filter()` functions in the package. Compared to the raw sound signals, the filtered ones are more aligned to a straight line, which is less subject to the noise sources we mentioned before and peaks can be

easily detected in these normal heart sound signals. *Example codes to implement band pass filters (**2B**):*

```
# Set up the time array for plotting (30 seconds)
timeArray <- c(1:30000)

# 25 - 400Hz 4th order Butterworth band pass
ex_sound_low <- butterworth_low_pass_filter(s1,2,400,audio_Fs=4000)
ex_sound_high <- butterworth_high_pass_filter(s1,2,25,audio_Fs=4000)
plot(timeArray,ex_sound_high,type='l',col='black',xlab='Time(ms)',ylab='Ampl
itude')
```

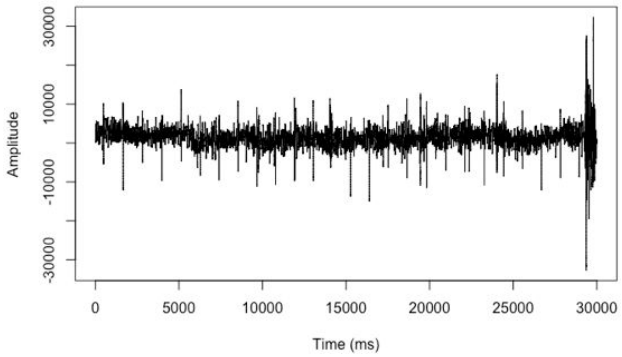
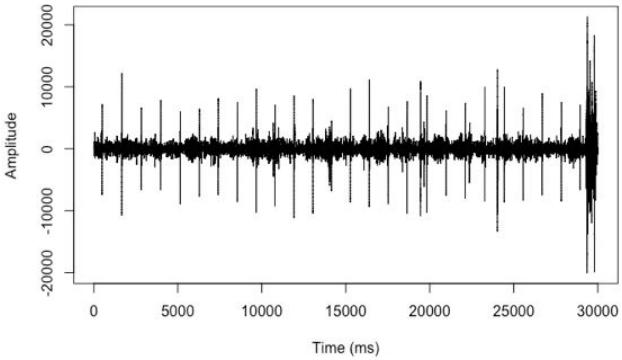
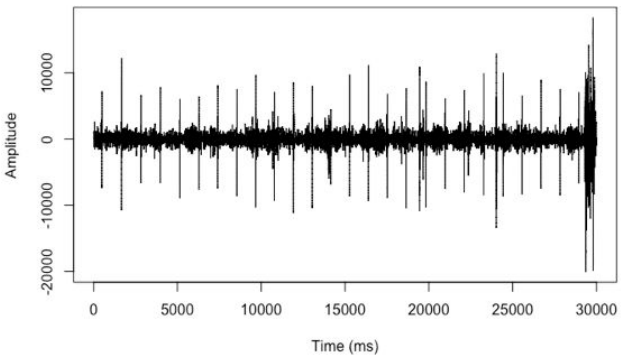
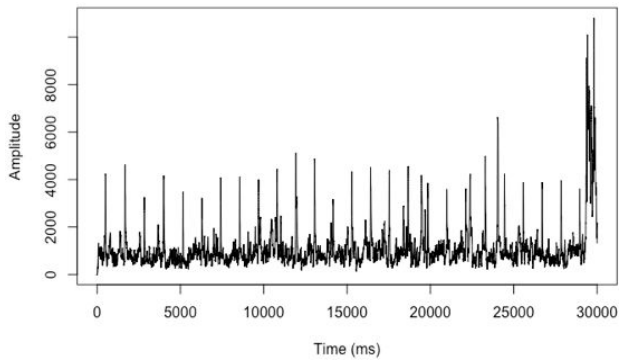
2C shows the filtered signals for the same patient after removing the potential friction spikes with exceptionally high amplitudes using the function `schmidt_spike_removal()` in the **PCGCleaner** package. *Example codes to implement spike removals (**2C**):*

```
# Spike removal for the cleaned signals:
ex_sound_spike_remove <- schmidt_spike_removal(ex_sound_high,audio_Fs=4000)
plot(timeArray,ex_sound_spike_remove,type='l',col='black',xlab='Time(ms)',yl
ab='Amplitude')
```

2D shows the homomorphic envelograms which were extracted by the function of `homomorphic_envelope_with_hilbert()` for the same patient. In our example here, a first-order Butterworth filter with an empirical decided cut-off frequency at 8 Hz was used. As we mentioned in the **Related Work** section, these smooth envelopes enable easy peak detection and thereby useful for segmentation of S1 and S2 if needed. Then a single cardiac cycle can be identified for further steps of feature extraction and classification. *Example codes to implement homomorphic envelope detection (**2D**):*

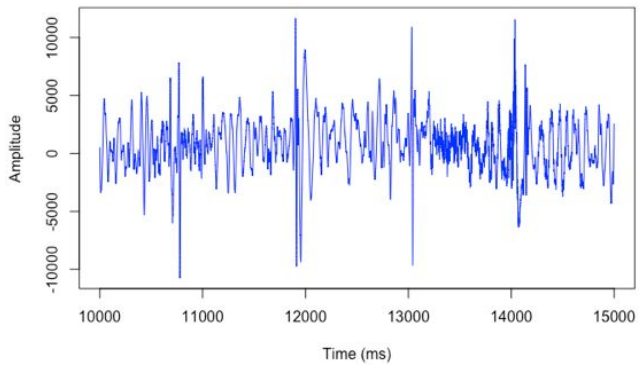
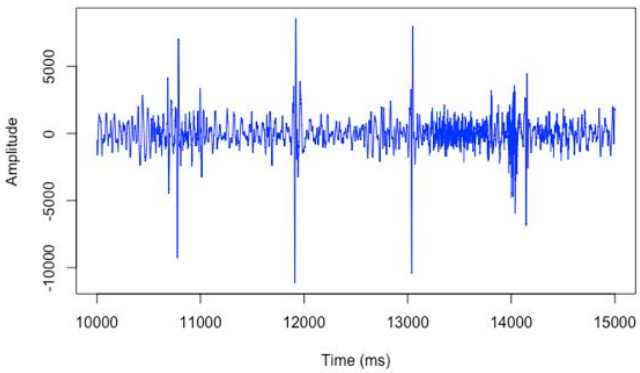
```
# Find the homomorphic envelope
homomorphic_envelope <-
homomorphic_envelope_with_hilbert(ex_sound_spike_remove,audio_Fs=4000)
plot(timeArray[1:length(timeArray)-1],homomorphic_envelope,type='l',col='bla
ck',xlab='Time(ms)',ylab='Amplitude')
```

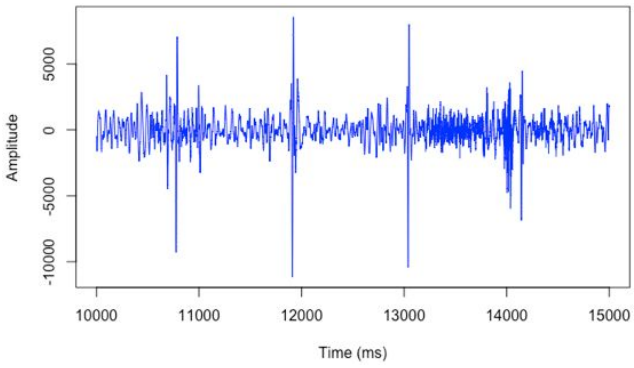
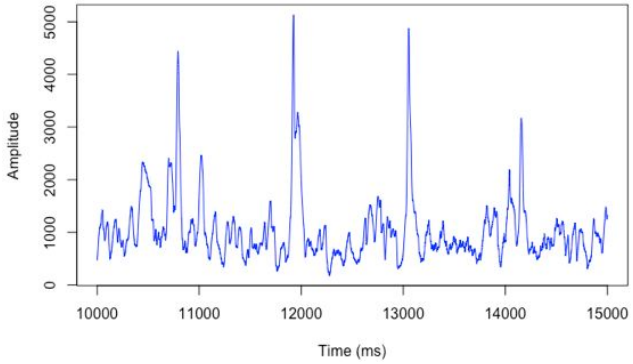
Figure 2. Preprocessing of a normal PCG signal with the PCGCleaner package

Figure 2	Step Name	PCG results
A	Raw signal	
B	25 - 400Hz 4th order Butterworth band pass	
C	Spike removal	
D	Homomorphic envelope detection	

To better observe effects of each function on the PCG signal, shorter periods (5 seconds) of the sound signals are also displayed for further exploration (**Figure 3**). Compared to **3A**, **3B** and **3C** show the signals aligned in a straighter line, indicating the removal of potential noises. Peaks are clear and easy to detect in those cleaned signals. **3D** describes the homomorphic envelograms from 10 seconds to 15 seconds of the recordings. Peaks on the homomorphic envelograms are aligned with the peaks on original signals, which indicates good performances of the current homomorphic envelope detection.

Figure 3. Preprocessing of a normal PCG signal with the PCGCleaner package (5-second signals)

Figure 3	Step Name	PCG results (5 seconds)
A	Raw signal	
B	25 - 400Hz 4th order Butterworth band pass	

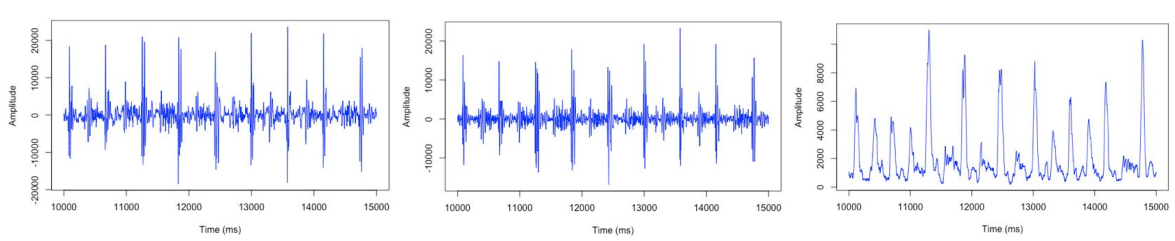
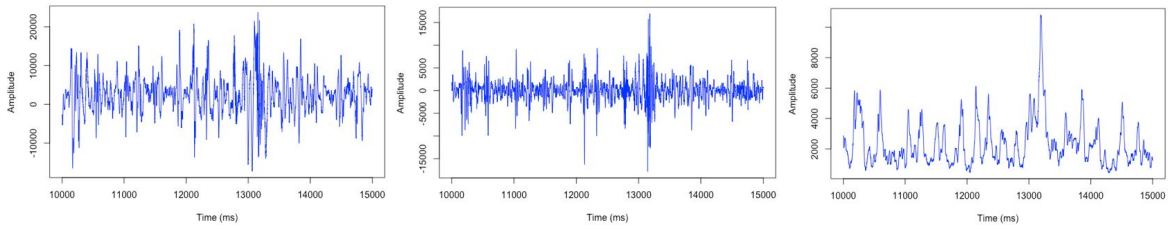
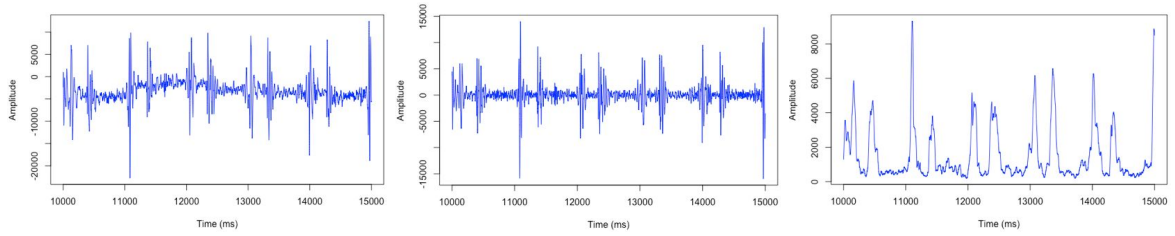
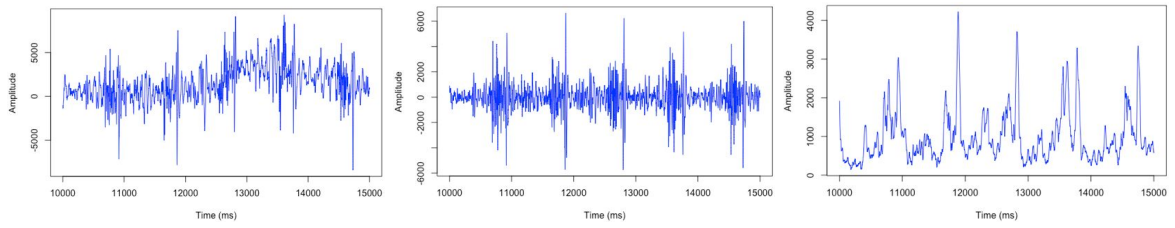
C	Spike removal	
D	Homomorphic envelope detection	

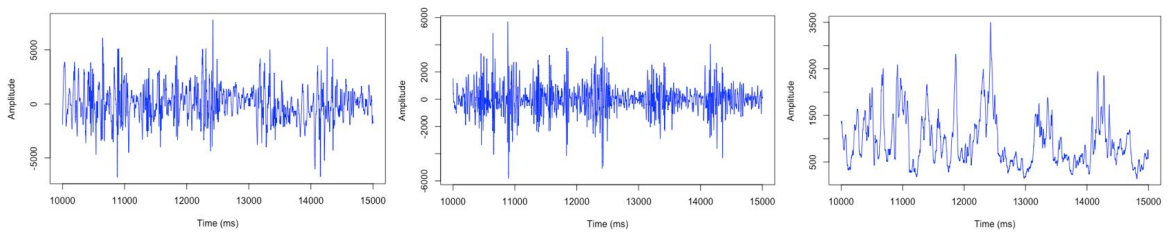
2.2 Preprocessing of abnormal heart sound signals

Abnormal heart sounds contain components that are not one of the fundamental heart sounds (S1 and S2), so it increases the difficulty of locating peaks and the detection of a cardiac cycle. This can cause problems for heart sound analysis in the segmentation state because most segmentation algorithms are based on determining the locations and types of S1 and S2. In the following examples, we listed different types of heart valve diseases of various severities. **Figure 4** shows PCG signals for each patient in the order of raw signals, denoised signals (after band-pass filtering and spike removal), and homomorphic envelogram of the signals, along with their echocardiogram diagnosis. Steps and parameters were identical to what we used in **1.2.1** for the preprocessing of the normal heart sound signal.

It can be seen that cardiac cycles still exist in mild to moderate abnormal heart sounds (Patient ID 2, 3 and 4) and we could determine the cycle by analyzing peaks from the homomorphic envelope as we did the normal heart sounds analysis. However, peaks are not typical in severe abnormal heart sounds (Patient ID 5 and 6). And it could be even harder to label the type of each peak, which may lead to the false identification of a number of peaks in the envelope signal and ultimately wrong segmentation and classification results.

Figure 4. Preprocessing of abnormal PCG signals with the PCGCleaner package (5-second signals)

ID	Diagnosis	PCG Signals (5 seconds): raw signal, denoised signal, homomorphic envelogram
2	mild pulmonic stenosis and mild pulmonic stenosis, aortic prosthetic valve	
3	moderate mitral regurgitation	
4	moderate to severe tricuspid regurgitation, mild mitral and pulmonic regurgitation	
5	severe aortic stenosis, mild aortic, mitral, pulmonic and tricuspid regurgitation	

6	severe aortic regurgitation and mild mitral regurgitation	

2.3 Normalizing the signals

We also included a function `normalize_signal()` for the normalization of the PCG signal, which allows the signals to be normalized by subtraction of the mean value and dividing with the value of the standard deviation. It limits the signal dynamic range from -1 to 1. The advantage of the normalization is to reduce the variance across subjects and could be useful for further machine learning models. **Figure 5** shows a comparison of the same person's PCG signals before and after normalization (5 seconds). *Example codes to implement normalization:*

```
# Normalize a signal
normalized_ex_sound_high <- normalize_signal(ex_sound_high)
```

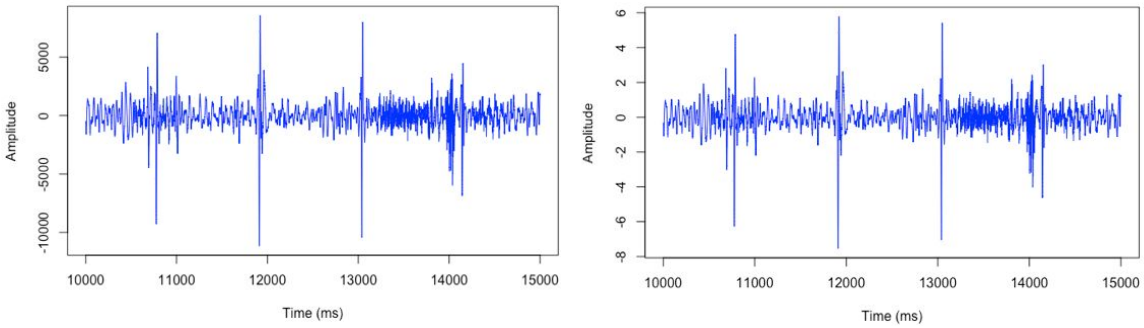


Figure 5. Normalization of a PCG signal: before (left) and after (right) normalization

Discussion and Future Work

Our present study developed an R software package for the preprocessing of PCG signals based on a study conducted by Schmidt et al,[24] and we also implemented the tool on a larger sample of heart sounds collected in the real-world setting at Michigan Medicine to evaluate its use. Based on some functions from the *signal* R package, we built the functions of denoising and homomorphic envelope detection for PCG signal processing. Recommended workflows of heart sound data cleaning are as follow: 1) use one or more band pass filters with appropriate frequency range cut-offs to reduce the background noises on the raw heart sound recordings (function `butterworth_low_pass_filter()` and `butterworth_high_pass_filter()` in the package); 2) remove noisy spikes to decrease potential frictions with exceptionally high amplitudes (function `schmidt_spike_removal()` in the package); 3) homomorphic envelope detection to identify a single cardiac cycle and further segmentation of S1 and S2 if needed (function `homomorphic_envelope_with_hilbert()` in the package).

Although many studies have been done on heart sounds analysis so far, our works have some innovations and potential impacts on the analysis of signal pre-processing. Firstly, we reimplemented some well-established works from MATLAB to R, which is more cost-effective and has a broader community of users and developers. The current stage of signal processing in R, PCG signal processing especially, is quite limited. Our works enable researchers to preprocess their raw heart sound signals in simple steps, which are fundamental but essential work before any further experiments of segmentation, feature extraction, or classification. Secondly, the heart sound library we mentioned in this study also serves as a valuable resource for future studies on

heart sounds analyses. Not only because it has a larger study population, but it collected the patients' transthoracic echocardiograph records along with other demographic and medical information, which can be extremely helpful for algorithm development and model evaluation. Furthermore, though this tool is built for PCG signal processing at the beginning, it is possible to introduce it to general sound and signal analysis in the future.

Our future work will incorporate more functions for preprocessing and options for segmentation. The ultimate goal is to develop an R package to accomplish the feature extraction of heart sounds with multiple simple steps and provide a set of clean, adequate features for further sound classifications with various machine learning models. From the long run, this tool will be beneficial to the development of smarter cardiac auscultation devices and clinical support tools of cardiovascular diseases for both researchers and health care providers throughout the world, enabling more efficient and effective clinic visits. In addition to the clinic setting, there are significant implications in a growing home health market. A digital stethoscope capable of diagnosing valvular disease could be used by care providers of any skill level to assess patients and identify need for referral. Finally, with the growth of telemedicine, a device such as the one proposed could enable cardiac screening without the physical presence of a skilled care provider in rural areas.

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