Keywords: Adventitious lung sounds, Respiratory cycles, Crackles, Wheezes, Diagnosis, Respiratory diseases, COPD, Asthma, Cystic fibrosis, Pneumonia.

Abstract: Significant research efforts have been dedicated to the automatic detection of adventitious lung sounds, using, for this purpose, different algorithms. The validation of these algorithms is based on the comparison of their results with reference annotations and therefore requires the development of user-friendly annotation software. This paper presents an application, developed in Matlab®, for the annotation of respiratory sounds. The user can identify respiratory cycles and adventitious sounds – crackles and wheezes – directly on the waveforms displayed on the screen, which may be simultaneously played back. The audio playback speed is user-adjustable and synchronised with the cursor display. Specific annotation file storage formats were defined. Preliminary usability tests performed by three health professionals using twenty respiratory sound files from six patients (with pneumonia and cystic fibrosis) indicate that the software is user-friendly and effective, allowing simple and quick annotations.

1 INTRODUCTION

It is estimated that chronic obstructive pulmonary disease (COPD) and asthma affect between 10% to 25% of the adult European population (Sovijärvi et al., 2000b). In the USA, these diseases affect more than 50 million people (Bloom et al., 2009); (Pleis et al., 2009). As a result of this high prevalence, the research effort dedicated to improving diagnosis, monitoring and treatment methods for respiratory diseases has significantly increased during the last decade.

Auscultation has been the main tool used by health professionals to diagnose and monitor cardio-respiratory diseases, as it is non-invasive, quick, effective and easy to use. The goals of auscultation are to detect adventitious lung sounds (ALSs), i.e., artefacts superimposed on the normal respiratory sounds and considered symptoms of respiratory system pathologies (Sovijärvi et al., 2000a), and to observe their characteristics (intensity, duration, etc.) in different chest locations. This is crucial in diagnosing disease severity and location.

ALSs are normally grouped into two main classes: crackles and wheezes. They can be generally characterised as follow:

- Wheezes are pitch-based sounds sustained for longer than 100 ms with frequencies above 100 Hz (Sovijärvi et al., 2000a). Wheezes can be monophonic (single frequency) or polyphonic (multiple frequencies) and are mainly associated with COPD and asthma (Waris et al., 1998). They occur mostly during expiration, but can also be observed during inspiration in more severe cases. There is a direct relationship between the wheeze occupation rate in a respiratory cycle and the severity of the pathology (Shim and Williams, 1983).

- Crackles are explosive, discontinuous sounds which can occur in both respiratory phases, being more frequent during inspiration. Crackles can be classified as fine (short duration) or coarse (long duration) according to their duration, waveform, and time of occurrence within a respiratory cycle. The number of crackles in a respiratory cycle is also an important indicator of the severity of pulmonary pathologies (Piirila and Sovijärvi, 1995).

It is difficult to objectively detect and classify ALSs, because standard auscultation is a subjective process: it depends on the experience and skill of its users (Sovijärvi et al., 2000b), their ability to memorise different sound patterns (Marques et al., 2006) and it is also influenced by stethoscope
technology. This has experienced constant evolution, through the use of not only better sensors and acoustic coupling techniques, but also electronic methods of signal transduction, conditioning, amplification and noise reduction. The advent of digital stethoscopy, allowing the application of advanced digital signal processing techniques, was pioneer in the development of algorithms for automatic detection and classification of ALSs. Numerous algorithms have been proposed for both wheezes (e.g. (Qiu et al., 2005); (Taplidou and Hadjileontiadis, 2007)) and crackles (e.g. (Vannuccini et al., 1998); (Lu and Bahoura, 2008)) automatic detection. There is also interest in automating the detection of respiratory phases (e.g. (Yildirim et al., 2008)), due to its clinical relevance.

Therefore, algorithm validation is a key aspect in this area of research and has been insufficiently addressed in the literature. Classifier performance (Fawcett, 2004) is typically based on four well-known parameters, namely the true positive (TP), true negative (TN), false positive (FP) and false negative (FN) counts (Table 1).

<table>
<thead>
<tr>
<th>Gold Standard</th>
<th>Test</th>
<th>Positive</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>True Positive</td>
<td>False Positive</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>False Negative</td>
<td>True Negative</td>
<td></td>
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</tbody>
</table>

This matrix is the basis of many common classification metrics, for example sensitivity, also known as true positive rate (TPR) and precision, also known as positive predictive value (PPV), both usually expressed as percentages. These metrics (and the parameters in which they are based) imply a comparison between the automatic detection results and a reference, or gold standard, necessarily based on the subjective judgment of human annotators. The reference should be obtained through statistical agreement among a number, as high as possible, of annotations performed by qualified professionals. It is therefore essential to have a complete and reliable computational tool for respiratory sound annotation.

The work presented in this paper is part of a broader effort aiming at establishing appropriate, clearly-defined and as widely accepted as possible validation tools and procedures.

2 STATE OF THE ART

The literature was carefully reviewed for software tools that might be useful for respiratory sound annotation. The most relevant are briefly discussed in the following paragraph.

Praat (Boersma and Weenink, 2011) is used for sound analysis, synthesis and manipulation. It was deemed insufficiently user-friendly for the intended purpose; it requires a level of programming skills which health professionals may not be assumed to possess. Windows Tool for Speech Analysis (WASP) (Huckvale, 2010) is used to record, analyse and display speech. Its main features are the ability to play and annotate the recorded sound and compute its spectrogram. However, it lacks user-friendliness and presents some drawbacks, mainly on the sound playback functions (e.g. during playback, there is no information about the current sample of the sound being played). PhiSAS (Brown et al., 2002), was developed to study the respiratory function. It allows sound recording and is equipped with a wide range of processing and analysis tools but has no annotation functions. Finally, the R.A.L.E. Repository (PixSoft), one of the most cited, is mainly a didactic application. It includes a respiratory sound database with examples of several lung sounds. However, these are not annotated by health professionals. Also, unlike all previous ones, it is not open-source software.

This led to the conclusion that while there are valuable tools for audio annotation and/or analysis, none of them are appropriate for respiratory sound annotation by health professionals. The Respiratory Sound Annotation Software (RSAS) presented in this paper fulfils this need.

3 USER INTERFACE

The annotation process is time-consuming and demands concentration and rigor, as there can be hundreds of ALSs in a file of few seconds long. It should also be noted that this tool is intended to be used mainly by health professionals, who tend to have overloaded agendas and no programming skills. For these reasons, the main requirement of the software is user-friendliness: the annotation must be simple, quick and intuitive.

The application was developed in Matlab® (Mathworks, 1994-2011) because of its rapid prototyping characteristics and because it should simplify the integration of automatic detection algorithms in the future. The software comprises two main sections:

- Wheeze and crackle annotation (Figure 1);
- Respiratory phase annotation.
It is also possible to annotate a respiratory sound simultaneously for wheezes, crackles and respiratory phases. Different formats of information storage are applied in each case. The user can check if there was a previous annotation of the respiratory sound under analysis, and if so, it can be loaded and edited. To avoid bias, users can only access their own data.

Regarding sound selection, the zoom and pan functions stand out. The zoom function allows time expanded wave analysis (TEWA) even larger than 800 mm/sec, as suggested by Murphy et al. (1977). This is particularly beneficial for crackle annotation. The pan tool makes it possible to go forward or backward on the sound graph by simply dragging the mouse, making the selection of new portions quick and intuitive. The playback tools include two buttons whose function is self-explanatory:

- Play/Pause;
- Stop.

One of the most important features of this application is the possibility of modifying the respiratory sound playback speed. There are four speeds available: normal (×1), half (×1/2), one fourth (×1/4) and one tenth of normal speed (×1/10). By using a phase vocoder (Ellis, 2002), the audio file is temporally extended with no significant change in pitch. This is especially relevant for the wheeze annotation.

The annotation tools are designed for quick and simple operation. For example, it is possible to remove annotated ALSs from the list (individually or collectively) and to modify them by changing their starting or ending times. It is also possible to change wheeze type and select signal portions previously annotated as ALS (useful for playback). When adding a new ALS, the starting and ending time can be specified in any order.

In respiratory cycle annotation, the user only needs to mark the phase transition instants and identify the first phase. The remaining phases are automatically labelled according to the respiratory phase sequence: inspiration, expiration and pause. If the user selects a point between two previously selected, the list is rearranged to maintain the correct respiratory phase sequence. All samples must belong to a respiratory phase; therefore, the start of a given phase necessarily coincides with the end of the previous one. In both sections – adventitious lung sounds (Figure 1) and respiratory phases – two plots are always present:

- Main Plot;
- Guide Plot.

On the Main Plot, it is possible to select signal portions using the selection tools (zoom and pan). The playback tools take effect on the selected signal portion. For example, if the sound is selected from 4s to 6s, this is the time interval that will be played

![Image](image.png)

Figure 1: Screenshot of the wheeze and crackle annotation section.
when the Play button is pressed. Every time a sound is being played, a red vertical line slides along the Main Plot to indicate that the current sample is being played.

The Guide Plot keeps the user informed about the location of the annotations previously made, and about the signal portion currently selected. Both plots take advantage of colour-coding ALS and respiratory phase types: crackles are marked in red while wheezes are marked in gold; inspirations, expirations and respiratory pauses are marked in yellow, green and brown, respectively.

4 DATA STORAGE

Annotation data are stored in folders identified by the name of the corresponding annotator. Two file formats are used:

- \texttt{type\_sound\_file\_name.mat},
- \texttt{type\_sound\_file\_name.csv}.

The field \texttt{type} assumes the value \texttt{wh}, \texttt{cr} or \texttt{rp}, depending on whether the file is a wheeze, a crackle or a respiratory phase annotation, respectively.

The way the data are stored depends on the type of annotation. Wheeze annotation data are stored as an \(nx3\) matrix, where \(n\) is the number of annotated wheezes. The first and second columns are, respectively, the starting and ending times of the wheeze. The third column stores the type of wheeze by means of a numeric code – 1 (monophonic), 2 (polyphonic) or 3 (unknown). Crackles annotation data are stored in an analogous way. Since this version of the software does not consider crackle classification, an \(nx2\) matrix is enough, \(n\) being the number of crackles in the respiratory sound. The annotation of respiratory phases is stored slightly differently. Because the ending time of a respiratory phase coincides with the starting time of the following respiratory phase and the phases follow a repetitive sequence, only one of them needs to be stored; starting time was the chosen one. Data are stored in an \(nx3\) matrix, where \(n\) is the number of respiratory cycles. The first, second and third columns are the starting times of inspiratory phase, expiratory phase and respiratory pause, respectively.

The software automatically assumes that the phase with the latest starting time ends on the final sound sample. If a respiratory cycle is incomplete the value \texttt{NaN} is assigned to the column cells corresponding to non-existing phases.

5 SOFTWARE TESTING

It is important to test the usability of the system, i.e., its acceptability for a particular class of users carrying out specific tasks in a specific environment (Holzinger, 2005).

Throughout the development, the software was continuously tested by a multidisciplinary team of technicians and researchers of the project. The feedback given contributed decisively to the development of user-friendly tools.

Once the development of the package reached its current version (1.1), a more formal assessment of performance was carried out, through a pilot test involving twenty 10-second respiratory sound files recorded from six patients. These files were annotated by three health professionals with experience in cardio-respiratory diseases. The file selection criteria was to have half of the files predominantly occupied by crackles and the other half predominantly occupied by wheezes (Table 2).

Table 2: Characteristics of the twenty files selected for software usability tests.

<table>
<thead>
<tr>
<th></th>
<th>Wheeze Files</th>
<th>Crackle Files</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cystic Fibrosis</td>
<td>9</td>
<td>5</td>
<td>14</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>1</td>
<td>5</td>
<td>6</td>
</tr>
</tbody>
</table>

The respiratory sounds from the patients diagnosed with pneumonia belong to a repository being built in a University of Aveiro research project (PTDC/SAU–BEB/101943/2008) and the remaining were collected during a PhD at University of Southampton (Marques, 2008).

5.1 Results

The tests allowed the estimation of annotation time per ALS (\(T_{\text{ALS}}\)), a parameter useful to evaluate the ease with which the user adapts to the software. The data shown in Figure 2 was taken from a log report generated for one of the annotators. The file sequence on the horizontal axes corresponds to the chronological order of annotation.

On average, the annotation time was 10.7±2.1 seconds per crackle and 67±15 seconds per wheeze. The use of sound playback tools during crackle annotation was 0.18±0.13 times per added crackle. On wheeze annotation, sound playback was used 7.73±3.65 per added wheeze. Only in the annotation of this type of ALS, the playback speed was changed by the user (twice).
An aspect that deserves to be emphasised is the divergence between the number of crackles identified by different annotators in every crackle file of the pilot study (Figure 3). The same is observed in wheeze files, where, although the agreement was very good (Altman, 1991), Cohen’s Kappa coefficient (Cohen, 1960) was never greater than $k=0.93$.

These results reinforce the importance of creating agreement metrics robust enough to extract reference annotations (Gold Standards).

5.2 Discussion

The first discussion topic, and perhaps the most important, is the rapid user adaptation to the software tools provided. As shown in Figure 3, $T_{CR}$ is significantly reduced especially from $Cr_2$ to $Cr_3$, remaining almost constant afterwards. The adaptation time can be estimated through the total annotation time of these two respiratory sounds: approximately 20 minutes. The annotation of the wheeze files was performed two weeks after the annotation of the crackle files. The $T_{WZ}$ decreased after the annotation of $Wz_1$, remaining almost constant until the end, suggesting that the adaptation was very quick and easy, approximately 3 minutes.

On the use of playback tools, it was observed that the number of playbacks per ALS in wheeze annotation was considerably higher than in crackle annotation. A complementary statistical analysis was conducted using SPSS® 17.0, to study the correlation between variables (Pearson’s correlation). As mentioned earlier, there was a statistically significant correlation ($p<0.05$) between the number of file playbacks and the number of wheezes added during the annotation. On the crackle annotation this correlation was not observed. These results strongly suggest that crackle annotation is mainly based on graphical analysis of the signal, while wheeze annotation is much more auditory, possibly due to the tonal character of wheezes.

Analysing the log report, it was possible to notice that the Selection Change Button was never used. This feature must be rethought or even removed in future versions of the software. In spite of using Matlab®, the application was very responsive and no significant delays were noticeable.

Despite the differences between crackles and wheezes, the typical annotation procedure adopted by the user was similar in both cases. After selecting the respiratory sound to be annotated, the user listens to the whole sound at normal speed at least once, then selects an initial portion using the zoom tool and gradually advances on the sound using the pan tool. The annotators always proceeded from the beginning to the end of the file.

6 CONCLUSIONS AND FUTURE WORK

A tool for annotating crackles, wheezes and phases on respiratory sounds was developed. Usability tests suggest that the software is user-friendly and reliable on crackle and wheeze annotation. Selection and playback tools contribute decisively to accurate annotations. More usability tests will be conducted to evaluate respiratory phase annotation performance.

A major objective of this research project is to integrate this application on a web-based platform open to the scientific community. This is intended to feature:
- A dynamic repository of respiratory sounds carefully recorded and documented for selection (e.g. by disease, age, gender);
• Gold standard annotations for each of the repository files, obtained through statistical agreement criteria in selected annotator panels;
• Performance evaluation of automatic ALS detection algorithms (or training of health professionals) comparing with gold-standards.

ACKNOWLEDGEMENTS

The authors gratefully acknowledge the funding provided to this project, “Sounds4Health”, by Quadro de Referência Estratégico Nacional (QREN), on a partnership between University of Aveiro and ISA (Intelligence Sensing Anywhere).

The authors would also like to thank to Doctors Ilka Rosa and Daniela Oliveira for their kind contribution during the software usability tests.

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