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A Computing Tool for Diagnosis Pulmonary TB Based on Cough

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Abstract:
In this work, we have described data collection and initial algorithm development in support of a cough analysis system for tracking the recovery of pulmonary tuberculosis patients. The final goal is a low-cost monitoring system that could be used in areas where laboratory facilities are not accessible, and could alert physicians to patients who may have drug-resistant tuberculosis. We have developed an initial cough detection algorithm, and have on-going work to fully validate and improve algorithm performance. Preliminary results show a decrease in cough count over time for drug-susceptible patients, suggesting that cough count may provide a useful marker of patient recovery.

Keywords: Pulmonary T B, Cough, Computing tool,

I. INTRODUCTION

In regions of the world where tuberculosis (TB) poses the greatest disease burden, the lack of access to skilled laboratories is a significant problem. A lab-free method for assessing patient recovery during treatment would be of great benefit, particularly for identifying patients who may have drug-resistant tuberculosis. We hypothesize that cough analysis may provide such a test. In this work, we describe algorithm development in support of a pilot study of TB patient coughing. We describe several approaches to event detection and classification, and show preliminary data which suggest that cough count decreases after the start of treatment in drug-responsive patients. Our eventual goal is development of a low-cost ambulatory cough analysis system that will help identify patients with drug-resistant tuberculosis. Although effective therapies have been available for many decades, tuberculosis(TB) remains among the world's most deadly infectious diseases. The emergence of multi-drug resistant (MDR) and extremely drug-resistant (XDR) TB is a major cause for concern. MDRTB accounts for roughly 3.6% of all TB cases, but accounts for as much as 28% in some regions *[WHO-11]*. In much of the developing world, diagnosis of pulmonary TB is made exclusively by sputum smear due to lack of access to skilled laboratories and culture-based methods. Patients are generally put on first-line therapy, and treatment failure (whether due to the presence of MDRTB or other reasons) is only discovered 4-6 months later. Patients who fail treatment continue to be infectious, spreading disease to other sand running increased risks of morbidity and mortality. Alab-free method to identify patients who are failing treatment would be of great benefit to clinicians without access to laboratory culture. Previous studies have indicated that cough rates (counts/hour) drop by roughly 50% in the first two weeks of treatment for patients who are responding to treatment *[LS-69]*, thus providing a potential means for detecting treatment failure. The physical infrastructure for an automated cough monitoring system is relatively simple (low-cost recording units and access to computing power, either locally or via telecommunications).
This work builds on recent progress in developing low-cost ambulatory systems that can record for extended time periods *[SW-08, Smi-07]*. We also build on past work in automated cough counting *[BDM et.al.,-06, MBP et.al.,-06, MBP et.al.,-07]*. Fully automated analysis, while key for protecting patient privacy, is challenging as patient recording soften include a large amount of environmental noise. This is particularly true in our data set, where patients are recorded going about their daily activities, and extraneous noise (speech, traffic, bangs, etc.) is common. In this work we presented on a pilot data collection and development of a cough detection algorithm. For this phase of the work, our goal is to develop an algorithm that is sufficiently accurate to evaluate the clinical utility of TB patient cough analysis. In the long term, we seek to develop a fully automated cough analysis system. Similar to previous work*[BDM et.al.,-06, MBP et.al.,-06, MBP et.al.,-07]*,our algorithm consists of event detection followed by cough classification based on time-frequency analysis features commonly used in speech processing. We discuss several event detection approaches, including an oval shape-based detector, and present results from several candidate classifiers. While a full algorithm validation is ongoing, initial results are presented.

II. METHODOLOGY:

The data collection was conducted as Subjects were provided transportation to the hospital and nutritional supplementation throughout the study. The data set consists of a series of 24-hour acoustic recordings, made using a Marant z PMD 620 hand held recorder and an Audio-Technic AT899 sub-mini micro phone attached at the patient's lapel. A24-hour recording was made before start of treatment (day0) to establish a cough base line, and 24-hour recordings were made at each sub sequent visit (days 21 ,30 and 60 after start). Additionally, extended recordings during the first 14 days are available for many patients.

Implementation Process of Algorithm

Step 1: Recorded Signals
Step 2: Event Detection
Step 3: Calculate Feature Vector

Step 4: Classify Cough to Normal / Abnormal   add by Weights
Step 5: Overall Process Computation indicates to step 6a or Step 6b
Step 6-a: Cough Data Set or Step 6-b: Non-Cough Data Set
Step 7: Create Feature Vector by MFCC
Step 8: Classify Similar Vectors
Step 9: Sequential Minimal Optimization Algorithm

The study includes drug-susceptible TB patients, MDR TB patients, and HIV/TB patients (HIV is a

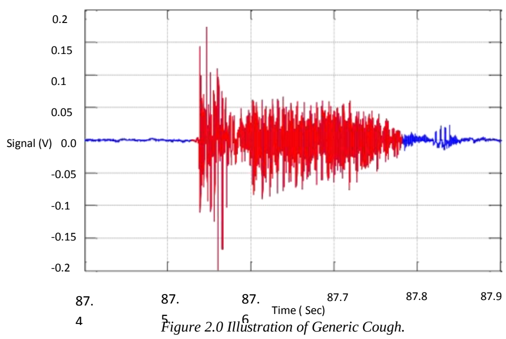

Figure 2.0 Illustration of Generic Cough.

Figure.1. Illustration of Generic Cough

complicating factor in treatment of TB). 62 patients have completed the study. Of those, 54 patients are HIV- (5 MDRTB, 49 drug-susceptible) and 8 are HIV+(5 susceptible, 1 negative, 1 pending). Extensive clinical information is linked to this data set, such as patient weight, temperature, sputum smear microscopy results, MODS culture results, CD4 count (for HIV+ subjects) and a description of symptoms at each visit. A generic recorded cough, plotted using our analysis software, is presented in *figure 2.0,* Coughs typically exhibit an initial explosive phase with a very sharp increase in energy during as air is released. A second phase follows in which voicing (vocal cord vibration) may occur

III. ALGORITHM DESCRIPTION

Figure 3.0, shows our overall algorithm flow, which is generally similar to *[BDM et.al.,-06, MBP et.al.,-06, MBP et.al.,-07]*. In analyzing a recorded signal, the first step is event detection. We describe two approaches to event detection below. Once an event is detected, it is broken up into 50% overlapped, 32ms long frames. And acoustic features for each frame are calculated. We calculated the Mel frequency cepstral coefficients (MFCC) as the primary features for acoustic analysis.

IV. EVENT DETECTION:

In our first implementation, similar acoustic events within each file were detected based on signal energy. A signal envelope was estimated by squaring the input signal and smoothing it with a running average filter (a box car filter of length 0.05s). The detector then identified events as regions of time where the signal exceeds a fixed threshold. If two events were separated by a very small gap in time (0.1 s), we merged them together into one event. While reasonably effective, this approach suffers from several short comings, as seen in *Figure 3 . 0* . In some cases (left panel) the energy threshold is not triggered until part way through the event. This is undesirable as the initial portion of the event is important for cough classification. Another common occurrence, seen in the right panel, is that the energy detector triggers on speech signals. These signals can have significant energy, but generally exhibit a much more gradual increase in signal energy than is the case for cough. In the large majority of cases, speech signals are correctly classified as non-cough, but detecting speech events does create a small number of false positives.

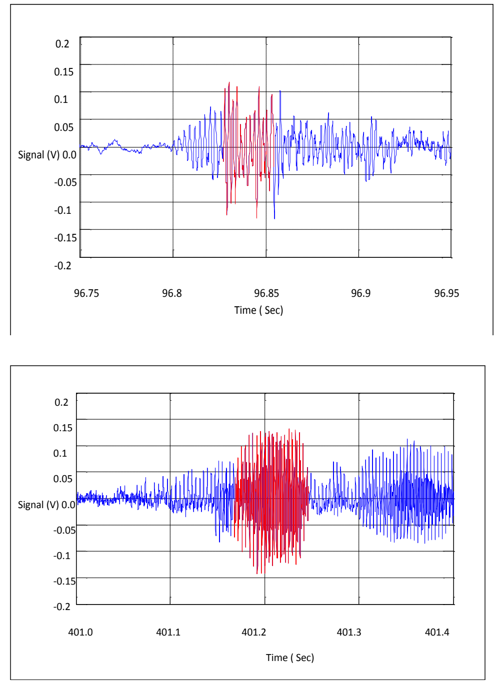

Figure.2. Acoustic event crossed during Speech

We therefore developed an improved detection scheme in which we search for a rapid increase in signal energy above a time-varying estimate of the ambient noise. The time-varying noise estimate is helpful as our dataset was collected in a wide range of acoustic environments; looking for a rapid rise in energy is helpful in screening out speech events. The smoothed signal energy is first calculated as presented in previous section, A back ground noise estimate is found by calculating the 10th percentile of energy in a sliding 20 sec time window. A fixed multiplier is added to approximate the median noise during quiet regions. To reduce computation, percentiles were calculated for a sub set of windows with 75% over lap and then interpolated to each time sample. Parameters for the noise estimation were determined empirically. An initial set of events is then found by finding all times when the signal energy exceeds the noise floor by a fixed threshold (9dB). The start and end samples for each event are found, as well as the peak energy in the event. For loud events (peak>9dB above noise) this underestimates the event duration. Therefore, the event start is adjusted earlier until the signal energy either stops decreasing or reaches the noise floor. A similar adjustment is made for the end point. If two events become overlapped as a result of these adjustments, the events are combined. The onset is next validated by calculating the median energies for 1/8sec before and after the event on set. If the energy increase after on set is >6 dB, the detected on set is considered to be valid.

D.1: OFF-LINE CLASSIFIER SELECTION AND TRAINING:

A subset of the recorded data was used as training data. Because of data availability at the time training was done, the training data is mainly taken from two male subjects. During training, an event detector was used to identify events, which were manually reviewed classified as cough, not cough, or unclear. To build a wide library of cough and non-cough events, the simple energy threshold detector described above was used, with a low threshold to allow sensitive detection of events. The training data contained 418 cough events, 1980 not cough events, and 75unclear events. The unclear events were generally combinations of coughs and other sounds (groans, speech, etc.) such that they were felt to be unsuitable for training purposes Once each event was classified, the MFCC features were calculated as described above. The *cough or non-cough* label from the overall event was then applied to all frames extracted from the event. In total, 13,429 cough frames and 43,925 non-cough frames were available for training after this step. As atone, this approach does introduce some possibility for misclassification; for example, an overall event might be classified as "cough" but an individual frame within that event may contain mainly non-cough sounds. The large number of frames used for training was felt to mitigate the effects of any individual misclassified frames. The large number of frames in the training set increases the computational load for machine learning algorithms. To address this, we used a previously developed *divide and conquer* clustering method suitable for large datasets *[TLT-06]*.In this clustering approach a subset of the MFCC vectors is first analyzed. Vectors with high correlation, defined as a Pearson correlation coefficient of 0.95 or better, are clustered together. A second subset of vector sis extracted, and any of the new vectors that have high correlation with the previously identified clusters are assigned to them. Additional clusters are formed using the remaining feature vectors. This process is repeated until the full dataset is clustered. After clustering, a single vector (the cluster centre) is used to represent each cluster. For our training data, this yielded 2074 vectors, representing half cough events and half non-cough (because there were more non-cough clusters, small non-cough clusters were discarded). Classifier training was done using the Weka 3.6 software package, which implements different machine learning algorithms. We compared performance of neural networks (multi layer perceptrons, or MLP), support vector machines (SVM), and sequential minimal optimization (SMO),a variant of the SVM approach. Performance results obtained using 10-fold cross-validation, while the multi layer perceptron gave slightly better results, the performance differences were not large and the SMO approach was chosen for ease of implementation.

D2: ON-LINE EVENT CLASSIFICATION:

During on-line processing, detected events are split into frames and acoustic features are calculated as discussed above. These features and the SMO-generated feature weights are used to classify each frame as cough or not-cough. A final processing step is required to combine the frame-by-frame results in order to classify the overall event. A previously used approach *[BDM et.al.,-06]* is to average all frames within an event; if most of the frames are found to be cough, the overall event is labelled as cough. We found better performance by first identifying the 1/3 of contiguous frames that have the most *cough-like* scores, then averaging the classifier outputs for those frames. This was found to help in cases where the detected event contains a mix of cough and other vocalizations.

V. DISCUSSION:

We have developed a cough analysis system that builds on previous approaches *[BDM et.al.,-06, MBP et.al.,-06, MBP et.al.,-07]* and have applied it to acohort of drug-sensitive TB patients. In a preliminary review, the algorithm shows 81% sensitivity and an average of 3.3 false alarms/hours; a more complete validation is ongoing. Figure 8.3 shows both the promise of cough-based TB monitoring and the need for further development. A decrease in cough count is clear, but before the algorithm can be clinically applied it is important to improve performance so we are confident that fluctuations in cough count are real. This will require improvements in algorithm performance, though metrics that quantify when are cording is too noisy for reliable analysis would also be valuable. Several concepts introduced above may prove useful for other cough analysis approaches. Previous methods require some degree of manual review. Our event detection approach is useful in the context of manual review, as it reduces the number of speech events that are detected as cough candidates. The *divide-and-conquer* clustering algorithm described here may prove useful for applications where the classifier is updated as new data become available, as it only requires storing a single representative of each previously identified cluster. Several possibilities exist for improving algorithm performance. In the work to date, our event detection n logic accounts for the expected cough shape (rapid energy increase at onset) but the classifier does not (although some information about neighbouring time periods is encoded in the MFCC time derivatives).A natural approach is to investing ate use of the Hidden Markov Model (HMM), as in [MBP et.al.,-07],which can track the time evolution of the cough sound. The HMM or other approaches that analyze the entire event may have performance advantages, especially for isolated cough events. On the other hand, it is possible that the frame-by-frame analysis used here may have advantages when the detected events contain over lapped coughs and other sounds. Improvements might also be possible by assigning different categories of non-cough noises to different classes, rather than lumping them into a single "non-cough" class as is done here. Finally, we are investigating new sensors that may be more robust to noise.

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