

A Commercial Nocturnal Asthma Monitor

Preliminary Report

Group number: Group 26

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Background

Asthma, defined as “a chronic lung disorder that is marked by recurring episodes of airway obstruction...manifested by labored breathing accompanied especially by wheezing and coughing...” is a troublingly common disease worldwide¹. One 2006 estimate proposed that the number of asthmatics in the world is on the order of 300 million, and that “[asthma’s] prevalence increases by 50% every decade”². According to the Centers for Disease Control and Prevention, in 2010 a total of 18.7 million—or 8.0%—of America’s adult population and 6.8 million—9.3%—of children were asthmatic. This leads to 14.2 million doctor’s office visits and 1.8 million emergency room visits each year in the U.S. alone³. The visits allude to a large total cost of asthma in society, incurred both directly—from hospitalization and treatment—and indirectly (due to absenteeism from work, etc.). Numerous studies have estimated the total cost per year of asthma in the United States in the billions, specifically in a range from 2.3-7.2 billion USD. Summing across the entire globe, asthma incurs greater total costs than HIV/AIDS and tuberculosis combined⁴.

Daytime symptoms are not, however, the whole story; many asthmatics experience a marked exacerbation of symptoms such as cough and wheeze at night, causing significant reductions in quantity and quality of sleep. This phenomenon, dubbed Nocturnal Asthma (NA), is thought to affect between 47-75% of asthmatics worldwide⁵, though its prevalence is difficult to quantify. This is partially due to the lack of an objective means of detecting NA symptoms. Currently, the most popular way to monitor NA is through self-reported questionnaires. However, those who complete such surveys often underreport; many of those suffering from NA often do not wake up during symptoms or fail to remember if they do⁶. Disturbingly, a study of 13,493 asthmatics “found that only 48% had agreement between their actual NA situation and what was recorded by their general practitioner [through questionnaires]. Moreover, 42% of patients who declared they had no nocturnal symptoms had NA according to objective tests,”⁵.

This problem applies specifically to children as well, with multiple studies finding that children are underdiagnosed by surveys whether they were completed by the children themselves or by their parents^{7,8}. In fact, one such investigation discovered that “less than 40% of parents with a child who is asthmatic report their child’s NA symptoms appropriately”⁵.

Another tool for gauging asthma symptoms at home are peak flow spirometers. Though these provide a more objective measure of nocturnal asthma than questionnaires, they have generally been ineffective. Spirometry, long considered a firm standard by which to diagnose asthma, proves unreliable when left to the patient at home. Indeed, diurnal spirometric data obtained by the asthmatic child or parent has been shown to be “not clinically useful,”⁵. Recently, other methods of quantifying asthma symptoms have been researched, which incorporate EMG, piezoelectric sensors, accelerometers, and microphones. The great majority of these clinical monitors focus on patient coughs. In addition to being the “dominant feature of asthma exacerbations,” cough frequency is also a useful metric for COPD, emphysema, and other conditions⁹. Further, it has been found to be independent of age, so a cough monitoring device could treat a range of potential patients. Cough frequency is, however, strongly correlated with airway inflammation and has even been proposed to be a more sensitive measure of inflammation than simple spirometry¹⁰. Cough frequency has also been found to increase significantly at the onset of an asthma exacerbation¹¹. Interestingly, the cough frequencies of non-asthmatics, stable asthmatics without nocturnal asthma symptoms, and chronic coughers all decrease drastically between 2-5 AM¹². There is a distressing contrast between these findings and the disproportionate number of asthma deaths and respiratory arrests that happen at night⁵. This indicates a distinction between NA and most manifestations of asthma, and that the presence of NA likely reflects improperly treated asthma.

Need

Unfortunately, most of the newly proposed monitors are designed to perform a clinical and/or diagnostic function and are not suitable for home monitoring, simply because they require clinicians to operate and interpret results¹³. The remaining, fully automated solutions are also not ideal for long-term nighttime monitoring because they involve wires running from sensors that may constrain the person and disrupt his/her sleep¹⁴. These shortcomings stem from the goal of most of these devices, which is ambulatory asthma monitoring.

The lack of a suitable means for objective nocturnal asthma monitoring is especially disconcerting when one considers the observed consequences of the disorder in children. Those suffering from NA are more likely to awaken during the night than their non-asthmatic peers and experience lower-quality sleep in general, which causes increased daytime sleepiness¹⁵. Furthermore, NA is significantly correlated with other symptoms resulting from sleep disturbance such as depression, anxiety, and poor memory¹⁶, as well as “developmental, emotional, and behavioral problems,”^{5, 17}. Sleep disturbances due to NA are also linked to higher numbers of school absences compared to non-asthmatic peers, compounding the educational problems naturally caused by the aforementioned effects¹⁸. Fortunately, restoration of sleep has been found to correct many of these problems¹⁷. Additionally, minimum lung function typically occurs near 4:00 am. As a consequence, nighttime exacerbations are particularly dangerous, with 80% of respiratory arrests and 70% of deaths caused by asthma occurring at night^{19,20}. Thus, there is a clear need for a device that can alert a caregiver in the case of nocturnal asthma exacerbations so that the child may receive proper treatment.

Scope

Nocturnal asthma is a widespread and costly disorder that is currently very difficult to accurately and conveniently monitor. Given the particular prevalence and negative effects of NA in children, we propose to design a commercial, home-based device capable of monitoring

symptoms and alerting parents or caregivers if intervention may be required (i.e., during an asthma attack). The product will not be diagnostic for asthma, and is intended for children who have already been diagnosed with asthma and may suffer from NA. Our device will also not disrupt the child as she/he sleeps, and will be easy to configure and use since its target audience is not medically trained. Given the desire for a low-cost, home-based, autonomous device, we plan to use audio signals, at least in part, to monitor an asthmatic child's nocturnal coughs. Preliminary analysis of audio signals, which include coughs, is shown in the calculations section.

Design Specifications

- Cost: must cost less than \$100
- Size: Must have width and depth less than 12 inches by 12 inches. Must have a height less than 24 inches.
- Weight: Less than 8 pounds
- Accuracy: Must recognize at least 70% coughs. Can falsely recognize up to 2 coughs per hour²¹.
- Recording time: 12 hour minimum
- Sampling rate: Appropriate for chosen modality such as;
 - Audio spectra: At least 48 kHz
 - EMG: At least 2 kHz²²
 - EEG: At least 4 kHz²³
- Minimum audio alert volume: 0 dB
- Maximum audio alert volume: 80 dB
- Transmitter range: An open field range of at least 1,500 feet
- Operating noise: Must be less than or equal to 30 dB

Other considerations:

- Intended for children of ages 5-18
- The device is not diagnostic
- Must not harm the child being monitored and must not disturb the child's sleep
- Must recognize coughs in real-time or near real-time
- Must not constrain the child
- Must have a minimal, easy setup comparable to a baby monitor.

Justification for specifications:

The upper cost limit of \$100 is the average price of several higher-end baby monitors, which share this project's goal of child monitoring. The size was determined based on the average size of a nightstand, which is about 18" wide by 18" deep. Because our device must be able to fit on this surface, it must, conservatively, have a footprint less than 12" by 12". The device's height should be less than an average desk lamp's (around 24") to be aesthetically pleasing. The 8 pound weight limit is equivalent to a gallon of milk. Because our device is not ambulatory, it does not need to be moved frequently, though it should still be relatively easy to position in the child's room. Because the device must monitor a child for the duration of sleep, it must be able to record continuously for at least 12 hours. The device should also not disrupt the child's sleep, and so its operating noise must be less than or equal to 30 dB; according to the world health organization, noises below this intensity have no significant biological impacts on sleep²⁴. The sensitivity and specificity limits are based on those reported by the ADAM system mentioned in the current solutions section²⁵.

The sampling rate required by our device will depend on our selected sensing modality, though at this point we believe our device will likely use audio signals, at least in part, to detect coughs and/or wheezes. Based on the spectrograms presented in the calculations section, our device must be able to recognize frequencies of up to 24 kHz, which translates to a minimum

sampling rate of $24 \times 2 = 48$ kHz. Once the monitor determines the presence of nocturnal asthma symptoms, it must alert parents who are likely not in the same room. Based on current baby monitors, our transmitter should have an open field range of at least 1,500 feet, which translates to a conservative indoor range of about 100 feet through 6 walls²⁶. The receiver must sound an audio alarm, which has maximum and minimum volumes that were determined from current baby monitor alarms.

Exploration of current solutions

The current solutions may be divided into clinical and commercial asthma monitors. Clinical monitors are an area of active research, though they are yet to be incorporated in hospitals¹³. As mentioned earlier, the overwhelming majority of these devices monitor coughs. A table of current instruments, their descriptions, and their associated studies is shown in Table 1 for convenience. Of these devices, only the LCM, LR102, and LifeShirt provide fully automated monitoring as the rest of these solutions require a clinician to analyze at least a portion of the recorded information^{13, 14}.

Automated wheeze detection has also been studied. The system, called acoustic respiratory monitoring (ARM), involves five piezoelectric sensors that are placed on the chest and allow for the frequencies of lung sounds to be analyzed in real time. However, the process requires a technician to constantly watch over the patient and to physically correct any potential false-positive wheezes¹⁷.

Table 1: Clinical cough monitors^{14, 27, 28, 29}

Device Name	Sensors	Description	Recording conditions	Author, year
Hull Automatic Cough Counter	Microphone	Analyses sound spectrum to recognize coughs. Requires manual review. It has a sensitivity of 80% and does not recognize coughs in real-time.	Overnight in laboratory setting	Barry, 2006
LifeShirt	Plethysmography ECG EMG	A vest with a number of sensors. It is no longer available due to relatively low sensitivity (less than %80).	Continuous recording over 24 hours	Coyle, 2005
Leicester Cough Monitor (LCM)	Microphone	A microphone that is worn as a necklace. Recognition method is similar to voice recognition, where time series data is analyzed. Median sensitivity of 86% with median false positive rate of 0.8 events/hour	6 hour ambulatory recording	Matos, 2006 Birring, 2008
Logan Research 100 series (LR 100-102)	Microphone EMG	Three EMG sensors and a sound sensor are attached to the chest. Provides a slightly overestimated cough frequency.	Ambulatory or in bed in clinic	Hamutcu, 2002 Corrigan 2003 Leconte, 2011
Self-contained monitor	Accelerometer	An accelerometer placed on the skin at the suprasternal notch. Study found a .998 concordance correlation coefficient for audio counts, which compares to a .997 coefficient for video counts.	15-60 minute ambulatory recordings	Paul, 2006

Few commercial monitors exist and none target nocturnal asthma in children. By far, the most common are peak flow meters. While inexpensive (less than \$40) these typically measure peak expiratory flow alone. While a digital solution called the Microlife can provide an additional measure of FEV1 (the volume of air forcibly exhaled in one second), it still cannot provide continuous monitoring or be used by a sleeping person³⁰. A commercial wheeze monitor called AirSonea was recently developed, though it is not yet available in the United States. It is a handheld sensor that determines if a user is wheezing once it is held to his/her neck for thirty

seconds. While this could technically be used on a sleeping child, the parent would need to be awake already. The device also costs \$150 dollars and must be paired with a smartphone to function³¹. There are two ambulatory continuous monitoring solutions that are currently under development. The first is called VitaloJAK and is worn on the hip like a Holter monitor. It promises to detect coughs over periods of 24 hours with 98% sensitivity through a single sensor placed on the user's chest. Due to its design, however, the product is intended for elderly patients who require continuous at-home respiratory monitoring due to COPD or severe asthma³². The second solution is a smartphone application called the Automated Device for Asthma Monitoring (ADAM) that aims to measure coughs and wheezes using the phone's microphone and accelerometers. During clinical trials, it recognized 7/10 coughs and incorrectly labeled 2 coughs/hour. It could not accurately monitor wheezes^{25,1}.

Patent search

This is not a complete list of all patents associated with cough monitoring. However, it includes a broad range of monitoring and detection methods that will help us shape our product design. These patents, in general, are very specific because frequency analysis of signals is not patentable. Therefore, they will not necessarily limit us, but will instead serve as a source for ideas and guidance. Identifiers and relevant information from each patent are listed in the following table.

Table 2:

Identifying information	Description
Title: Cough monitor Publication number: CN202235373 U Publication date: 5/30/2012	A clinical device for long-term cough monitoring that consists of a vibration sensor that is placed on the patient's chest. The sensor provides information on a patient's cough frequency and cough intensity. ³³

<p>Title: Diagnostic cough-monitoring techniques Publication number: US 3593703 A Publication date: 7/7/1969</p>	<p>A clinical ambulatory device that consists of a microphone placed on the patient's throat and a small transmitter that could be placed in the patient's pocket. The transmitter sends information to a receiver nearby (within 300 feet), which distinguishes coughs from speech sounds.³⁴</p>
<p>Title: Systems and methods for monitoring cough Publication number: US 7207948 B2 Publication date: 6/24/2005</p>	<p>A computerized system that monitors cough through measuring lung tidal volume and by processing sound events with one or more microphones and one or more accelerometers. Tidal volume is determined by measuring changes in a patient's rib cage and abdomen. The system also uses EEG and EOG to determine sleep arousals. A physician can then interpret this data to tailor a medication plan that will reduce sleep arousals.³⁵</p>
<p>Title: Cough detecting methods and devices for detection coughs Publication number: WO 2013040485 A2 Publication date: 3/21/2013</p>	<p>A cough monitoring system that performs principal component analysis (PCA) on an audio recording to identify coughs. It promises to improve patient privacy because the stored recording information (basis vectors) cannot be used to reproduce the original audio signal.³⁶</p>
<p>Title: Cough detector Publication number: US 8241223 B2 Publication date: 8/14/2012</p>	<p>An ambulatory sensor worn as a necklace that contains an ultrasound generator and receiver, which determines if a cough is present based on Doppler frequency shift. The signal power in a number of frequency bands and the duration of this signal is used to recognize coughs in real-time.³⁷</p>
<p>Title: Portable monitoring system for recognizing wheeze in lung sounds Publication number: US 20060077063 A1 Publication date: 4/13/2006</p>	<p>A portable monitoring system composed of an acoustic sensor that is attached to an asthmatic person's windpipe. The sensor is connected to a transmission module that wirelessly sends information to a receiver that analyses the signal. If wheezes is recognized, the system sounds an alarm to alert a caretaker or the asthmatic person. This occurs if the largest frequency component is greater than 350 Hz and if this component has a duration greater than 250 ms.³⁸</p>
<p>Title: Lightweight wheeze detection methods and systems Publication number: CN 102781318 A Publication date: 11/14/2012</p>	<p>A portable respiratory health monitor that uses a "lightweight algorithm" to generate short-time Fourier transforms (STFT). The algorithm stops the calculation once a wheeze criterion is unmet, and also tracks breathing rate.³⁹</p>
<p>Title: Techniques for prediction and monitoring of coughing-manifested clinical episodes Publication number: US 8517953 B2 Publication date: 8/27/2013</p>	<p>A patent for predicting an onset of a clinical episode with a breathing sensor. They propose to compare the sensed breathing pattern to a baseline pattern and predict the onset based on the comparison. They aim to monitor the following diseases: asthma, chronic obstructive pulmonary disease (COPD), congestive heart failure (CHF), cystic fibrosis (CF), and epilepsy with both an acoustic and mechanical vibration sensor. It is a noncontact device that finds a</p>

	correlation between the timing of the subject's breathing cycle and timing of the breathing-related sound, which can be either coughing or wheezing. ⁴⁰
Title: Prediction and monitoring of clinical episodes Publication number: US 8403865 B2 Publication date: 3/26/2013	A technique for predicting the onset of an asthma attack using at least one sensed parameter without touching or viewing the patient in a clinical. The parameters include at least one that is breathing related and another that comprises a pressure gauge under a reclining surface. The sensor should be able to operate while the sleeps and operate without human compliance. This technique could work for other clinical episodes, including: COPD, CHF, periodic limb movements in sleep (PLMS), and stroke. ⁴¹
Title: Respiratory disease monitoring system Publication number: US 8758262 B2 Publication date: 6/24/2014	An automated, medically diagnostic device for monitoring respiratory disease in outpatients. The inventors use a microphone to conduct time and frequency domain analyses to discriminate symptoms of interest from background sounds, and an accelerometer to determine activity level. The recorded sonic events' (coughs and wheezes) peak frequencies, power spectral densities, time durations, and amplitudes are compared to predetermined values in the system. The computational part is handled by one of the following: cell phone, personal digital assistant (PDA), handheld computer, pager, and portable media player. ⁴²
Title: Portable asthma detection device and stand-alone portable asthma detection device Publication number: US 20120116241 A1 Publication date: 5/10/2012	A portable asthma detector with a gas detection module, airflow sensor, and turbine that interfaces with a smartphone or stand-alone microprocessor. For determining the chemical components and physical properties of the breath, the authors propose to use at least one from the following: electronic nose, temperature sensor, gas detector. Additionally, they offer optical, electromagnetic, or power-generating type gas sensors as solutions, as well as a potential drug delivery module to the device. ⁴³

Calculations

While wheezes, muscle activity, chest movement, and breathing patterns have all been researched as possible parameters for asthma monitoring, these measurements require special sensors. Computer microphones are readily available, however, and so we have examined how cough sounds compare with speech sounds and other noises. In our analysis, we first examined both the time-series (sound intensity) and the spectrograms (frequencies) of sounds. To begin

examining frequencies, we first determined how frequencies attenuate with distances. Knowing how these values change with distance may be useful in developing a more robust symptom recognition software, as the monitor distance may affect recognition. A sample calculation and the attenuation of different frequencies at 2, 5, and 10 feet are shown in Figure 1.

Figure 1⁴⁴:

Sample calculation:

At 1kHz tone at a distance of 5ft:

$\text{dB/km} = 4.7$ attenuation per length (retrieved from chart)

$\text{dB} = (4.7\text{dB/km}) * (1\text{km}/1000\text{m}) * (1\text{m}/3.28\text{ft}) * (5\text{ft})$

$\text{dB} = 0.0072$ attenuation

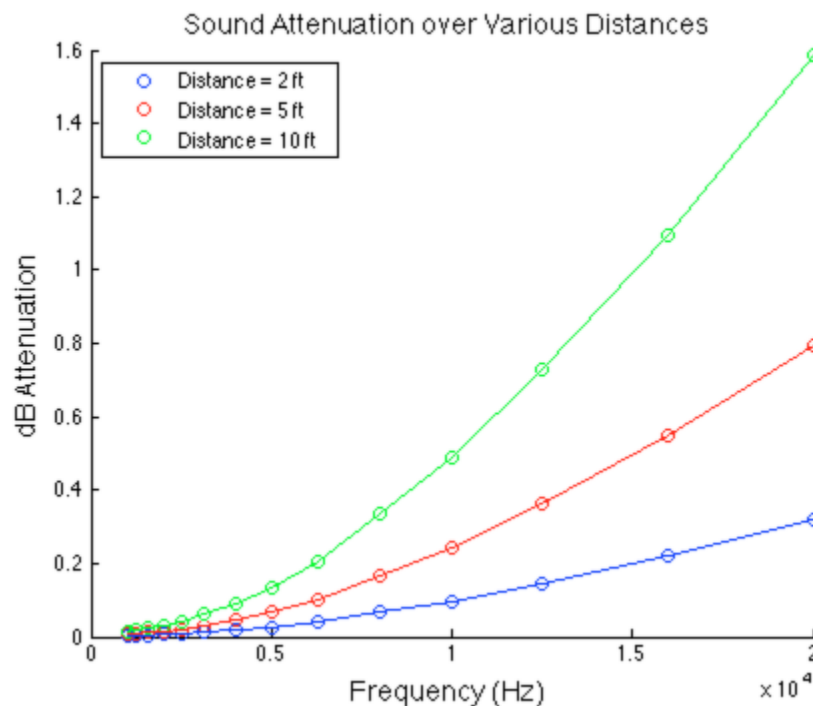


Figure 1: Higher frequency signals are attenuated more than the lower frequencies. Higher frequencies are attenuated more with increasing distance than lower frequencies. These values were measured at 50% relative humidity.

The time-series and short-time Fourier Transforms (STFT) spectrograms of a sample recorded cough, the word “hello”, the word “cheek”, and a clap were then taken and are shown in Figure 2. The word “hello” was chosen because its consonants are a soft and unvoiced (H) and a voiced approximant (L), which have little in common with the sharp, raspy sound of a

cough. On the other hand, the word “cheek” was chosen because of its affricate (CH) and a voiceless stop (K) that may resemble cough sounds. The clap was chosen because it shares a rapid onset and a lack of harmonics with coughs.

Figure 2:

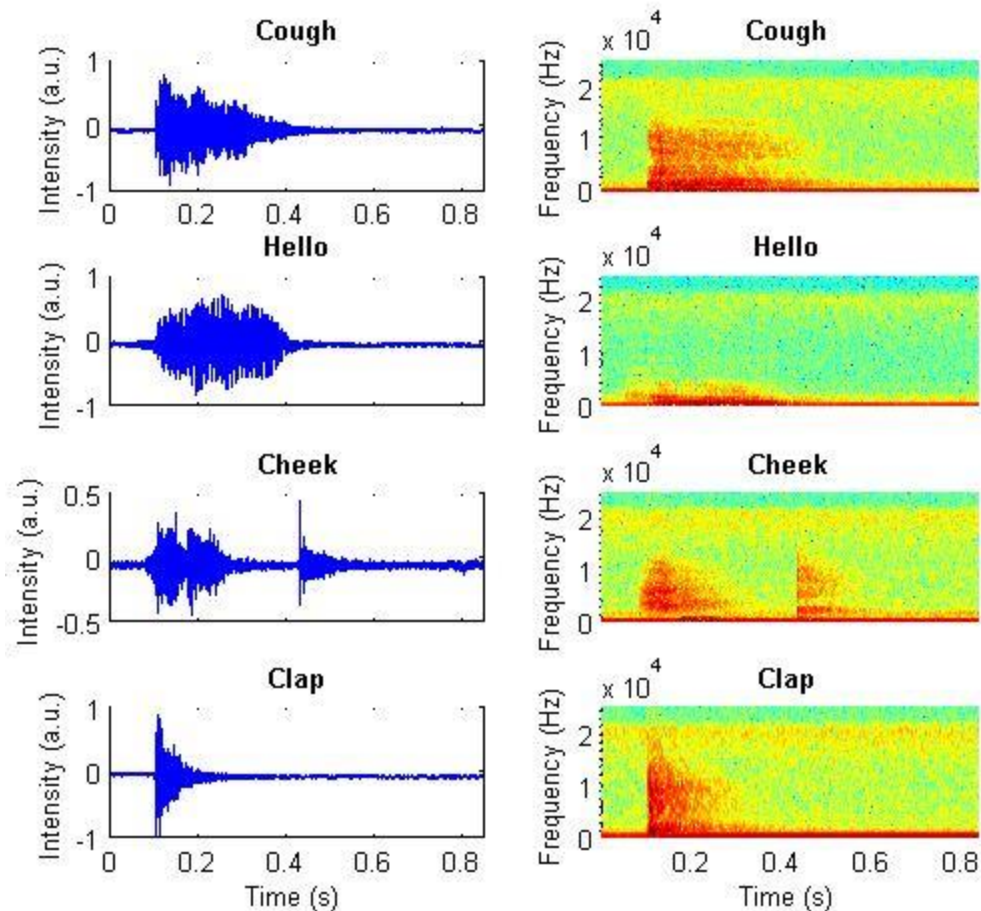


Figure 2: On the left column, four time-series plots of a cough: the word “hello”, the word “cheek”, and a clap are aligned by their starting points (first large deflection from baseline). To capture the maximum frequency possible frequency range in Matlab, the sampling rate was set to 96,000 samples/sec. On the right column: the sound spectrograms computed using the STFTs of the signals are shown. For each spectrogram, the window size is 256, nfft is 256, and the overlap is 128.

There are a few noticeable differences in the time-series signals. As expected, the cough has a very different onset and duration from the word “hello”. It is also noticeably different from the first part of the word “cheek” (CH-EE). The cough onset is not noticeably

difference from the last part of “cheek” (K) and the clap, however. The cough does have a longer duration than these two sounds, and this could potentially be used to set it apart. The spectrograms appear to diverge more than the time-series signals. The clap has significantly higher power in the 15-20 kHz band than the cough or the “K” sound. The cough has more sustained power its highest frequency bands than the clap and “K” sounds. These features may allow for robust recognition of coughs.

Next, the effects of cough loudness were examined. Three coughs of varying loudness were produced 5 feet away from a microphone with the person facing away from it. Five feet was chosen because this is the width of a twin-size bed. Another person listening next to the microphone could barely recognize the quietest cough and could clearly recognize the loudest cough. The time-series and spectrogram for this recording is shown in Figure 3. Note the spectrograms for each cough are very similar, even though their time-series intensities vary.

Figure 3:

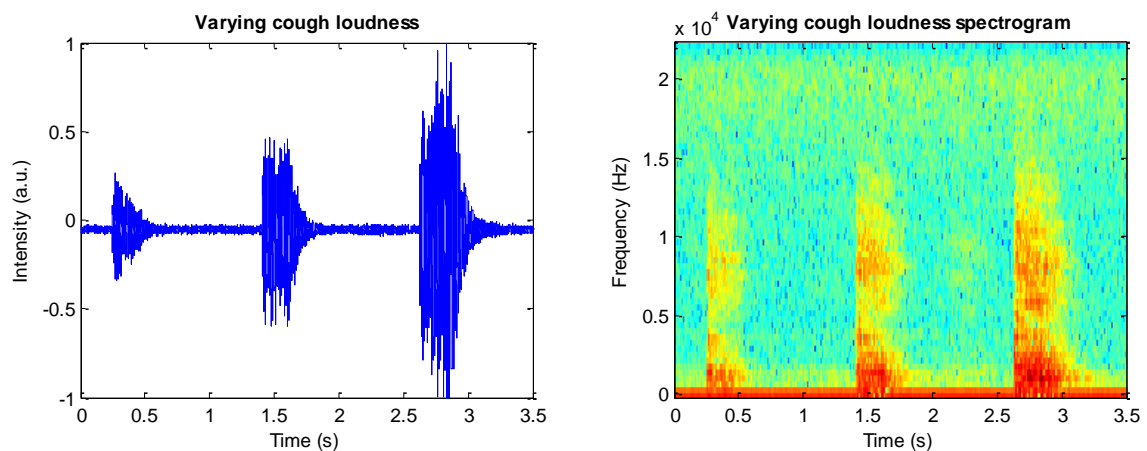


Figure 3. On left, the time-series of three coughs with increasing relative loudness as determined by a listener next to the microphone. On right, the spectrogram of this recording. Note the similarity of coughs when viewed on the right plot and the differences in the signals on the left plot.

The effects of background noise were also tested and the results are shown in Figure 4. A loud room fan was placed next to the cougher, who was 5 feet away from the microphone. Note the

baseline in the time-series plot is relatively noisy. There is also higher power in lower frequency bands in the spectrogram than the other figures, but the cough is still clearly recognizable.

Figure 4:

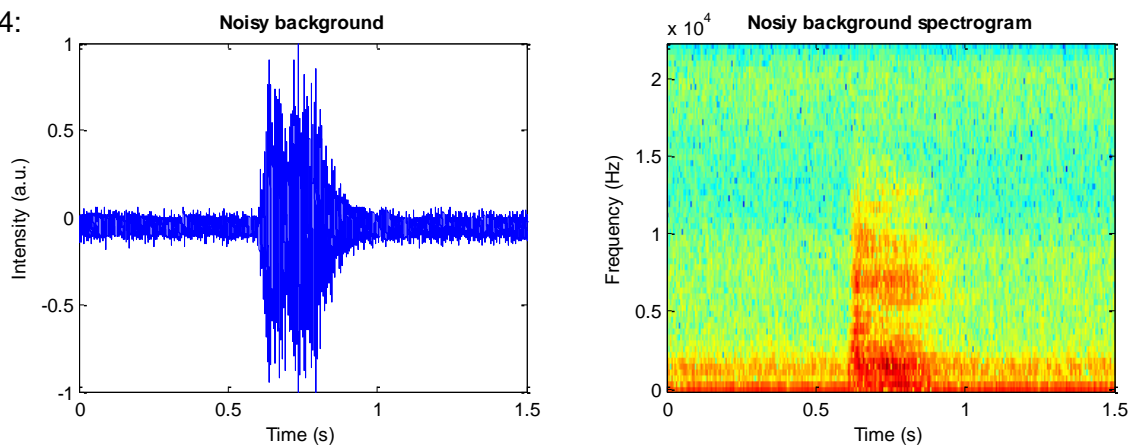
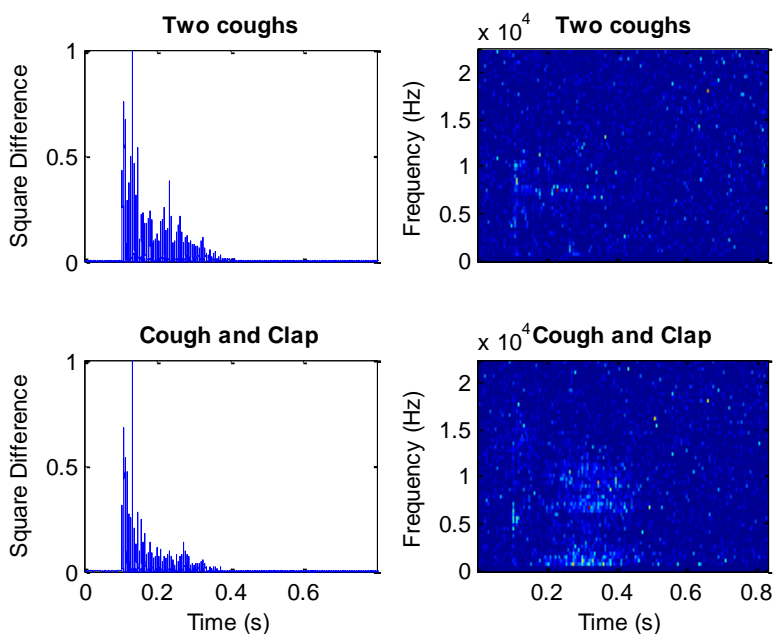


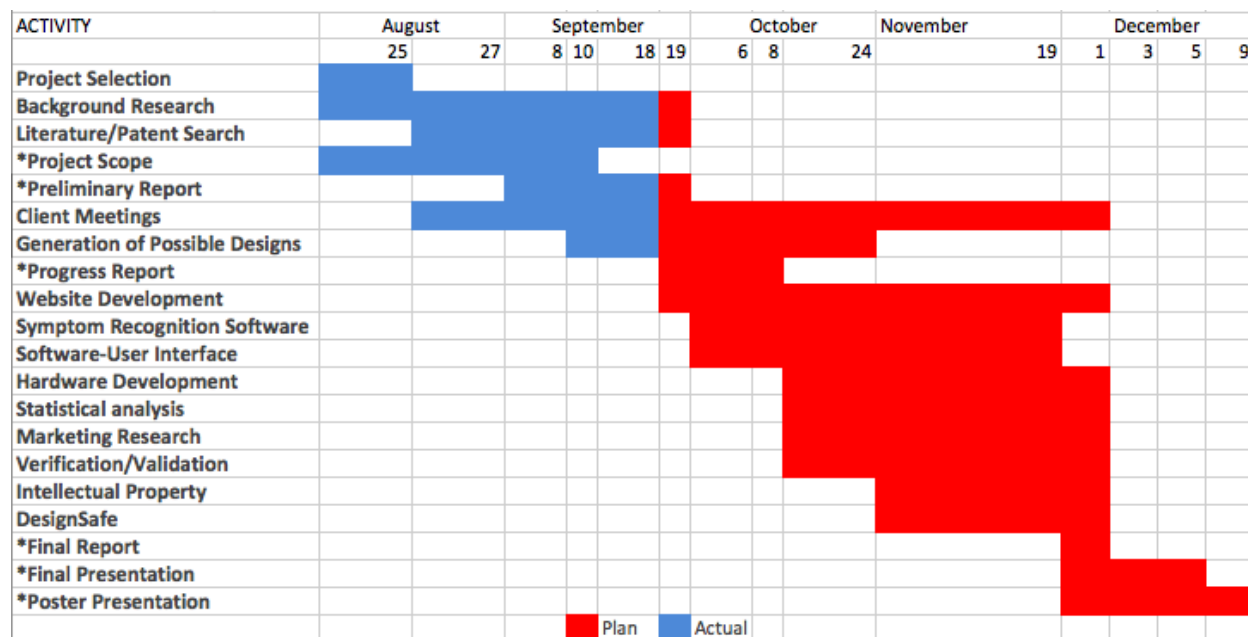
Figure 4. On left, the time-series of a cough over a noisy background. On right, the spectrogram of this recording. Though there is more significant power in lower frequency bands than in recordings without the background fan, the spectrogram of the cough is relatively unchanged.

Last, the repeatability of signals was examined briefly. The differences between two cough recordings and between a cough and a clap are shown in Figure 5. There appears to be significant variation between the two cough time-series that is comparable to the difference between a cough and a clap. However, there is much less variation between the two cough spectrograms than between the cough and clap spectrograms.

Figure 5: In each plot, the normalized square difference of two traces was taken. Top left, the time-series of two coughs. Bottom left, the time series of a cough and a clap. Top right, the spectrograms of two coughs. Bottom right, the spectrograms of a cough and a clap.



Preliminary Design Schedule



Organization of team Responsibilities

Task	Chris Beyer	David Kim	William Padovano
Background research	Actual		
Literature/patent search	Actual		
Marketing research	Actual		
Project scope	Actual		
Project selection	Actual		
Symptom recognition software			Actual
Software user interface		Actual	
Hardware (including sensors)	Actual		
Statistical analysis		Actual	
Website	Actual	Actual	Actual
Intellectual property			Actual
Preliminary report	Actual		
Progress report		Actual	
Final report			Actual

Bibliography

- ¹ Asthma. 2014. In Merriam-Webster.com. Retrieved May 8, 2014, from <http://www.merriam-webster.com/dictionary/asthma>
- ² Braman, S. S. (2006). The global burden of asthma. *Chest Journal*, 130(1_suppl), 4S-12S.
- ³ FastStats - Asthma. Centers for Disease Control (2014, July 14). Retrieved September 15, 2014.
- ⁴ Bahadori, K., Doyle-Waters, M. M., Marra, C., Lynd, L., Alasaly, K., Swiston, J., & FitzGerald, J. M. (2009). Economic burden of asthma: a systematic review. *BMC pulmonary medicine*, 9(1), 24.
- ⁵ Ginsberg, D. (2009). An Unidentified Monster in the Bed—Assessing Nocturnal Asthma in Children. *McGill Journal of Medicine: MJM*, 12(1), 31.
- ⁶ Mallol, J., & Castro-Rodríguez, J. A. (2006). Differences in prevalence of asthma, rhinitis, and eczema between parental and self-completed questionnaires in adolescents. *Pediatric pulmonology*, 41(5), 482-487.
- ⁷ Steenhuis, T. J., Landstra, A. M., Verberne, A. A., & van Aalderen, W. M. (1999). When Asthma Interrupts Sleep in Children. *BioDrugs*, 12(6), 431-438.
- ⁸ Levy, M. L., Godfrey, S., Irving, C. S., Sheikh, A., Hanekom, W., Bush, A., & Lachman, P. (2004). Wheeze detection: recordings vs. assessment of physician and parent. *Journal of asthma*, 41(8), 845-853.
- ⁹ Li, A. M., Tsang, T. W., Chan, D. F., Lam, H. S., So, H. K., Sung, R. Y., & Fok, T. F. (2006). Cough frequency in children with mild asthma correlates with sputum neutrophil count. *Thorax*, 61(9), 747-750.
- ¹⁰ Li A., Lex C., et al. Cough frequency in children with stable asthma: correlation with lung function, exhaled nitric oxide, and sputum eosinophil count. *Thorax* 2003; 58: 974-78.
- ¹¹ Chang, A. B., Harrhy, V. A., Simpson, J., Masters, I. B., & Gibson, P. G. (2002). Cough, airway inflammation, and mild asthma exacerbation. *Archives of disease in childhood*, 86(4), 270-275.
- ¹² Hsu J.Y., Stone R.A., et al. Coughing frequency in patients with persistent cough: assessment using a 24 hour ambulatory recorder. *European Respiratory Journal* 1994; 7: 1246-53.
- ¹³ Leconte S., Ferrant D., et al. Validated methods of cough assessment: a systematic review of the literature. *Respiration* 2011; 81(2):161-74.
- ¹⁴ McCrory DC, Coeytaux RR., et al. Assessment and Management of Chronic Cough. Agency for Healthcare Research and Quality 2013; Report No. 13-EHCO32-EF.
- ¹⁵ Chugh IM, Khanna P, Shah A. Nocturnal symptoms and sleep disturbances in clinically stable asthmatic children. *Asian Pacific journal of allergy and immunology / launched by the Allergy and Immunology Society of Thailand*. 2006 Jun-Sep;24:2-3. 135-42.
- ¹⁶ Stores G, Ellis AJ, Wiggs L, et al. Sleep and psychological disturbance in nocturnal asthma. *Archives of disease in childhood*. 1998 May;78(5):413-9.

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- ¹⁷ Bentur L., Beck, R., et al. Wheeze monitoring in children for assessment of nocturnal asthma and response to therapy. *European Respiratory Journal* 2003; 21: 621-26.
- ¹⁸ Diette GB, Markson L, Skinner EA, et al. Nocturnal asthma in children affects school attendance, school performance, and parents' work attendance. *Archives of pediatrics & adolescent medicine*. 2000 Sep;154(9):923–8.
- ¹⁹ Hetzel MR, Clark TJ, Branthwaite MA. Asthma: analysis of sudden deaths and ventilatory arrests in hospital. *British medical journal*. 1977 Mar 26;1(6064):808–11.
- ²⁰ Calhoun WJ. Nocturnal asthma. *Chest*. 2003 Mar;123(3 Suppl):399S–405S.
- ²¹ Rhee, Hyekyun, et al. "The development of an automated device for asthma monitoring for adolescents: Methodologic approach and user acceptability." *JMIR mHealth and uHealth* 2.2 (2014).
- ²² De Luca, G. (2003, March 1). Fundamental Concepts in EMG Signal Acquisition. Retrieved September 16, 2014, from http://www.delsys.com/Attachments_pdf/WP_Sampling1-4.pdf
- ²³ Hämäläinen, M, et al. (1993). Magnetoencephalography—theory, instrumentation, and applications to noninvasive studies of the working human brain. *Reviews of Modern Physics*, 65(2), 413-497
- ²⁴ Night Noise Guidelines for Europe. (2009). World Health Organizations, (ISBN 978 92 890 4173 7), 17.
- ²⁵ Rhee H., Miner S., et al. The development of an automated devices for asthma monitoring for adolescents: methodological approach and user acceptability. *JMIR mHealth and uHealth* 2014; 2(2):e27.
- ²⁶ Spurrier, R. (2012, May 28). The Best Baby Monitor. *BabyGearLab*. Retrieved September 18, 2014.
- ²⁷ Schmit KM, Coeytaux RR., et al. Evaluating cough assessment tools: a systematic review. *Chest* 2013; 144(6):1819-26.
- ²⁸ Leconte S., Listro G., et al. The objective assessment of cough frequency: accuracy of the LR102 device. *Cough* 2011; 7(11). Published online.
- ²⁹ Paul I., Wai K., et al. Evaluation of a new self-contained, ambulatory, objective cough monitor. *Cough* 2006., 2(7). Published online.
- ³⁰ Welcome to Microlife. (n.d.). Retrieved September 18, 2014, from <http://www.microlife.com/home/>
- ³¹ The AiroSonea Opportunity. (n.d.). Retrieved September 18, 2014, from <http://airsonea.com.au/>
- ³² McGuinness K., Holt K., et al. P159 validation of the VitaloJAK 24 hour ambulatory cough monitor. *Thorax* 2012; 67:A131.
- ³³ 李, 云飞, and 卉 张. Cough Monitor. 苏州大学, assignee. Patent CN202235373 U. 30 May 2012. Print.

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- ³⁴ Burn, Donald A., and Leonard C. Gunn. Diagnostic Cough-monitoring Techniques. Abbot Lab, assignee. Patent US 3593703 A. 20 July 1971. Print.
- ³⁵ Coyle, Michael. Systems and Methods for Monitoring Cough. Vivometrics, Inc., assignee. Patent US 7207948 B2. 24 Apr. 2007. Print.
- ³⁶ Patel, Shwetak N., Eric C. Larson, Shih-Yen Liu, and Tien-Jui Lee. Cough Detecting Methods and Devices for Detecting Coughs. University Of Washington Through Its Center For Commercialization, assignee. Patent WO 2013040485 A2. 21 Mar. 2013. Print.
- ³⁷ Gavriely, Oren, and Noam Gavriely. Cough Detector. Isona Limited, assignee. Patent US 8241223 B2. 14 Apr. 2012. Print.
- ³⁸ Cheng, Yi P., and Chin J. Ku. Portable Monitoring System for Recognizing Wheeze in Lung Sounds. Cheng Yi P, Ku Chin J, assignee. Patent US 20060077063 A1. 13 Apr. 2006. Print.
- ³⁹ 付, 永吉. Lightweight Wheeze Detection Methods and Systems. 夏普株式会社, assignee. Patent CN102781318A. 14 Nov. 2012. Print.
- ⁴⁰ Lange, Daniel H., Yosef Gross, and Avner Halperin. Techniques for Prediction and Monitoring of Coughing-manifested Clinical Episodes. Earlysense Ltd, assignee. Patent US8517953B2. 27 Aug. 2013. Print.
- ⁴¹ Halperin, Avner, Daniel H. Lange, Yosef Gross, and Itzhak Pinhas. Prediction and Monitoring of Clinical Episodes. Earlysense Ltd, assignee. Patent US8403865B2. 26 Mar. 2013. Print.
- ⁴² Rhee, Hyekyun, and Mark Bocko. Respiratory Disease Monitoring System. University of Rochester, assignee. Patent US8758262B2. 24 June 2014. Print.
- ⁴³ Shieh, Dar-Bin, and Chyi-Her Lin. Portable Asthma Detection Device and Stand-alone Portable Asthma Detection Device. National Cheng Kung University, assignee. Patent US20120116241A1. 10 May 2012. Print.
- ⁴⁴ The speed and attenuation of sound 2.4.1. (n.d.). Retrieved September 17, 2014, from http://www.kayelaby.npl.co.uk/general_physics/2_4/2_4_1.html