Interrogating the Lungs Through Wearable Fabric Electronics

by

Johnny Fung

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Abstract

Lung disease such as pneumonia is one of the leading causes of mortality throughout the world. Currently, many screening techniques performed on the lungs are too expensive, cumbersome, not continuous, and not easily understood without proper medical training. Furthermore, with the pandemic of Covid-19, the demand of screening patients in a non-invasive method has skyrocketed. Stethoscopes require training to understand the abnormalities when listening to the sounds the body makes, also known as auscultation. In this thesis, we sought to develop a lightweight, flexible, wearable fabric that can perform auscultation on the lungs. These fibers were created using the thermal drawing process that allows the fibers to perform various functions depending on the materials used for the draw. The initial solution used a conductive fiber created by injecting a liquid metal into a hollow fiber. This was deemed inadequate as the fiber generated a lot of noise and was only capable of detecting respiratory rates on a body with minimal movement. With minimal movement, this destroyed the purpose of having the fiber be mobile and flexible. The second solution utilized a nanostructured piezoelectric fiber to listen to the sounds the body makes. The piezoelectric fiber was successfully able to detect the sound of a heartbeat, but the lung sounds were overwhelmed due to the loudness of the heart. These sounds were measured with the fiber placed on the chest. For future studies, the fiber will be placed in various locations on the body to determine the optimal location for auscultation of the lungs. Furthermore, the shape of the fiber network will be optimized, creating an amplifying effect in the direction of interest. This will be an attempt to minimize the noise coming from the heart and focus more on the sounds the lung makes.

Thesis Supervisor: Yoel Fink

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1. Introduction

Pneumonia is the primary diagnosis for 1.7 million people in the US each year in the emergency department. In 2017, 49,157 deaths in the US were caused by pneumonia (CDC, 2017). Many lives are affected by lung related diseases, and they continue to prevail in humans today. Pneumonia is a buildup of fluid in the lungs, which can cause difficulty breathing, and in extreme cases, death. In figure 1, the buildup of mucus in the lungs causes blockages in the bronchial tubes, which will block airways. It can be difficult to detect pneumonia due to its symptoms being similar to the common cold or flu. One of the first steps doctors use when looking for pneumonia is to listen to the patient's breathing using a stethoscope.

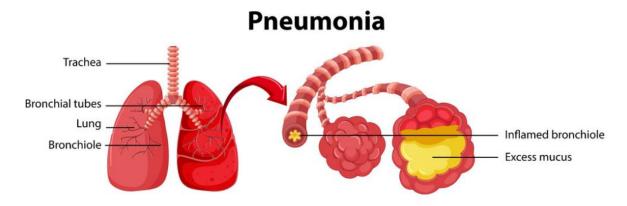


Figure 1: Lung diagram with symptoms caused by Pneumonia. Figure from Vector Stock

Another common condition that occurs in the lungs is bronchiolitis. This condition occurs more often in infants and babies due to their weakness in their immune system. It is an infection that causes inflammation and congestion in airways. The symptoms are fairly similar to the common cold, but as the condition gets worse, it can cause difficulty breathing. Typically, bronchiolitis can be treated at home with care, but there are instances where hospitalization is needed (Mayo Clinic 2020).

About 80,000 people go through spontaneous pneumothorax every year in the US (Wakai 2008). Pneumothorax is the collapse of the lung, and there are various reasons for the cause of it. Pneumothorax occurs when there is a buildup of air between the lungs and the chest cavity. In severe cases, the pressure from the air causes the lung to collapse. Once the lung collapses, the patient is at serious risk of death if not treated immediately. The most common treatment at hospitals is to release the excess air using a needle or tube, usually requiring the patient to be punctured in the chest.

2. Background

2.1 Current Methods to Interrogate the Lungs

After a doctor uses a stethoscope, if the condition is severe enough, further testing will have to be conducted. These tests range from blood tests, x-rays, sputum tests, and/or CT scans. During a physical exam, a doctor will use a stethoscope to listen to specific organs in the human body: the heart, lungs, and intestines. Auscultation, which is listening to the internal sounds of the body, is the first line of information for doctors to recognize if there is any abnormality in the human body. Aside from measuring the heart rate and blood pressure, the doctor listens to the lungs to ensure there is no blockage and breathing is normal.

Stethoscopes have been used in the medical field since its invention in the 1800s (Geddes 2005). At its invention, the stethoscope was a quire, or 24 sheets of paper turned into a roll, and it was placed onto the patient's chest while the doctor's ears were on the other end. This idea was thought of by R.T.H. Laennec as he thought of how if he put his ear onto a plank, it was much easier to hear if a pin was scratching on the other side of the plank. Over the years, with the progression of technology, the stethoscope has been improved.

The modern stethoscope consists of the chest piece which includes the diaphragm and the bell, the tubing, and the headset, as shown in figure 2. The diaphragm is the larger part of the chest piece that is flat, and it is more commonly used when screening a patient. The other side of the chest piece is the bell, and it is a smaller, more concave piece. The diaphragm creates a sealed surface between the patient's chest and the chest piece, similar to how eardrums work in the human body. This mechanism has become the method that most state-of-the-art stethoscopes use. The vibration moves air up and down, which travels through the tubing into the headset and into the ears. The pressure gets magnified due to the air needing to travel a longer distance from the diaphragm to the ear. Higher pressure makes louder sounds, allowing the doctor to perform auscultation. The diaphragm is used for higher pitched sounds; such as sounds from breathing or from the heart. The bell side is better suited for lower pitched sounds, like heart murmurs and sounds from the bowel (Kubin 2011).

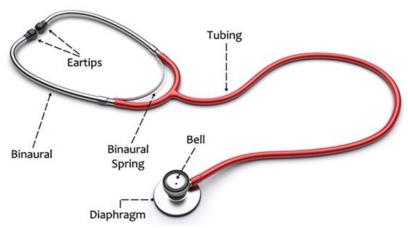


Figure 2: Layout of the modern stethoscope and the names of each part. From Nurselly (2020)

Breathing sounds are created from the air that travels through to the chest wall and lungs. Typical lung sounds have frequencies ranging from about 40 to 1000 Hz. When listening to the lungs, a healthy breath would be soft and low pitched, clearly hearing the intake and outtake of air. However, some abnormal sounds would be defined as rales, rhonchi, stridor, and wheezing. Rales is heard when someone inhales, and it makes a small clicking or rattling noise. Rhonchi makes a sound that resembles snoring, and it indicates that the air is being blocked by fluid or mucus. Its frequency is low, less than 200 Hz. Stridor indicates a harsh vibrating sound caused by a narrow airway in the upper part of the lungs. Wheezing is high pitched sounds which is caused by narrow airways in the lungs. Its frequency is higher, greater than 400 Hz. The various sounds can be seen in waveforms in figure 3. These different abnormal sounds may indicate obstruction, inflammation, infection, fluid in the lungs, and/or asthma (Kahn 2018).



Figure 3: Sound waveforms of each lung condition under auscultation. The waves were recorded from a digital stethoscope. Picture courtesy of (Easy Auscultation)

2.2 Limitations in Current Methods

Currently, many of the screening methods to determine the type of lung condition after using a stethoscope can be expensive, bulky, and inaccessible. The most common step after auscultation is to use an X-ray machine. For an x-ray, many patients would have to travel to a hospital or clinic in order to be screened. These screenings may also cost large amounts of money.

Even though x-rays are ideal in mapping out the insides of the lungs, the instruments are heavy, slow, and they can only perform non-continuous tests.

While a stethoscope can be quite portable, it requires medically trained ears to determine the type of lung condition one may have. The average human may not understand the difference in the way unhealthy lung sounds are when listening to a stethoscope. Even then, the training to use a stethoscope can vary depending on the textbook or tutor. While the diaphragm is much better for listening to lung sounds in general, some practitioners still prefer to use the bell side (Welsby et al. 2003). Furthermore, the observations using a stethoscope can differ depending on the person, and the stethoscope does not provide an objective data point for the patient. The practitioner has to decipher the noises and draw a conclusion as to whether the sound is healthy or not. The stethoscope is also a vector of infectious diseases from patient to patient. The stethoscope has to be disinfected regularly, but some health personnel do not follow these recommendations correctly (Youngster et al. 2008). If the average human can carry along with them a personal portable device that can detect various lung conditions, a lot of the preliminary screening methods can be avoided as well as reducing the rates of infections amongst people in a hospital or clinic.

3. Motivations and Aims

The purpose of this study is to reduce the number of fatalities from lung conditions. If certain lung conditions can be detected before they develop into severe instances, many trips to the hospital or emergency room will be unnecessary. There have been deaths from spontaneous pneumothorax which is the collapse of a lung. These cases can be extremely unpredictable, and people suffering from this condition have little time before their lungs fail. At failure, death is imminent. Many lives will even be saved. Current methods today require trips to the hospital or the medical expertise of a doctor. Many screening equipment are bulky and expensive.

As technology continues to advance, there have been developments to monitoring health. The most prevalent feature being sold is a wearable device that can track heart rate and the number of steps walked. The wearers of these devices use the data for multiple reasons. They can view the data as a method to improve their quality of life, make healthier decisions or use as encouragement to maintain a healthy lifestyle. A study at University of California San Francisco used Fitbit as a tool to collect objective data on subjects with multiple sclerosis. Standard disability scales do not consider how much a person walks, but with the help of Fitbit, they were able to perform daily assessments through how many steps were taken each day (Block et al. 2016). However, most wearable devices that people can purchase today only measure heart rate and steps. There has not been a device that measures the respiratory rate or listens to the lungs.

A lightweight wearable device that can detect various lung conditions will improve the everyday life of people. The human body can be unpredictable at times, and some abnormalities will occur. This device will look for these abnormalities to preemptively determine whether the wearer is in imminent danger. More specifically, this device will be worn on the chest area, and it will listen to the respiratory sounds as well as cardiac sounds. Utilizing both sounds as data points allows the device to have a strong understanding of what is normal for the user and can more easily detect abnormalities if they occur. In this thesis, our aim is to develop a wearable device to make auscultation much more feasible for the average human without having to see a doctor.

To improve the wearable devices that exist today to encompass a larger set of capabilities, there are three main aspects that need to be focused on. They are weight, flexibility, and its performance. People do not want a device that is bulky because it can impair their movement or it may feel uncomfortable. The appeal to many of these devices is to make it lightweight so that the users do not notice the device is on them. Furthermore, wearing a stiff device will make the device much more noticeable as movements will cause discomfort. Flexible devices allow for more options for integration and locations for where the user can place them. Most importantly, the performance of the device is what users care most about. They want to know what information the device can provide and what they can do with that information. In order to do so, the device needs to output accurate data for the specific measurement it is taking and be able to output the data in an interpretable fashion for the user.

The device that the study will focus on creating will follow these three criteria. The device should be lightweight and flexible, providing the least amount of discomfort for the user. As for performance, this device will have the capability to detect the respiratory rate of the user as well as performing auscultation on the lungs of the user. This device will output data into an external device and will be processed and analyzed.

4. Method & Results

The initial idea was to create a stretchable fiber. A stretchable fiber would meet all three criteria while providing the most flexibility in terms of application and implementation. These fibers would be embedded with various sorts of microelectronics to meet performance specs. This would be done by preparing preforms made of a specific polymer and placing these electronics into the polymer. These preforms were fabricated with specific dimensions to ensure that the thermal drawing would proceed without issues. The preform undergoes thermal drawing to be turned into a long fiber. These polymers are flexible and can easily be sewn into an article of clothing.

The thermal drawing process begins with making a macroscopic preform. The preform is made up of specific materials for the fiber during the drawing process as different polymers undergo different levels of stress at various temperatures. The preform is then drawn in a draw tower with a vertical furnace at a pre-set temperature. The furnace in the draw tower has three sections, the top, middle, and bottom, each of which their temperatures can be controlled. The middle typically has the hottest temperature. The purpose of heating the sections is to have the preform undergo necking, where it softens and begins to stretch from gravity. The preform stretches into a fiber, where the fiber is then fed through a capstan which pulls at a constant speed, maintaining constant thickness of the fiber. Figure 4 is a representation of the thermal drawing process. This drawing can produce fibers at hundreds of meters in length at a time.

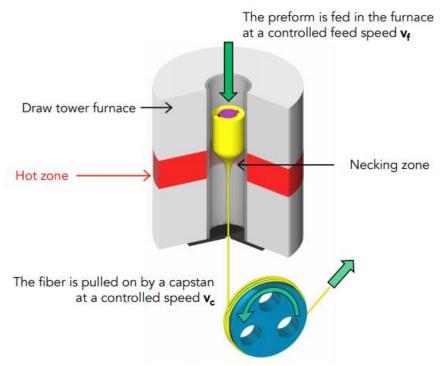


Figure 4: Schematic of the thermal drawing process. Figure courtesy of B. Grena (2017).

Device 1: Stretchable Conductive Fiber

One method is to inject liquid metal into a fiber with a channel in the center. The outer material will be made of a polymer called poly(styrene-b-(ethylene-co-butylene)-b-styrene) (SEBS) (See figure 5). For this method, we looked into 2 different liquid metals: The first is gallium with a melting point of about 303 K. The second is a eutectic Indium Gallium with a melting point of about 289 K. As there is a need to inject the liquid metal to the hollow channel of the fiber, the metal has to be liquid at room temperature. Thus, we have narrowed down to the use of Indium Gallium as the metal core for our stretchable fiber. The fiber then would be sealed at the ends, while fitting through thin wires for enabling electrical connectivity from the fiber core to the external circuits. Having the liquid metal fully-filled (with little gap) within the core fiber enables a conductive path from one fiber end to the other. The fiber itself is about 3 mm in diameter.

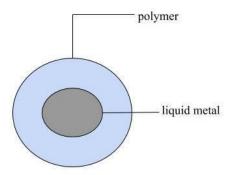


Figure 5: Cross-section view of the conductive fiber, the walls are made of polymer while the center core has been filled with liquid metal.

The raw data the fiber would provide is voltage difference depending on the strain on the fiber. As the fiber is stretched, resistance of the fiber increases as its length increases and its cross-sectional area decreases (See equation 1). If this fiber were to be placed across the chest, the movement of the diaphragm should be seen from the change in resistance in the fiber. Breathing in would cause the chest to rise, stretching the fiber, increasing the resistance. This fiber was connected to an Arduino to record the voltage difference when undergoing stress, and it was sensitive enough to detect respiratory rate. The fiber was placed over a shirt, across the chest for testing.

$$R = \frac{\rho L}{A} \quad {\text{$\frac{\rho$ = resistivity}{L$ = length}$}\atop{A$ = cross sectional area}}} \quad (1)$$

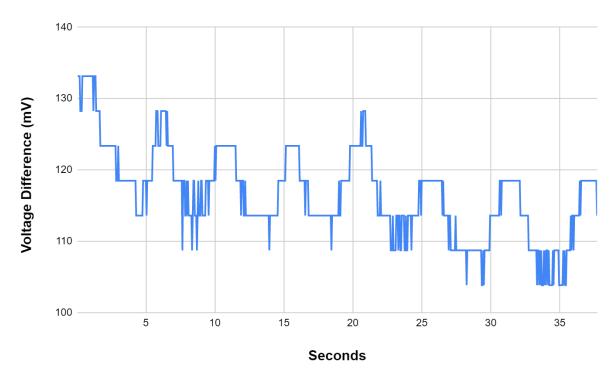


Figure 6: Data output from the conductive fiber across the diaphragm. Peaks indicate inhalation whereas the minimums indicate exhalation.

Results on Fiber Device 1:

In this test run, the data from the conductive fiber indicates the breathing rate of the test subject. The peaks indicate when the chest has risen, which indicates how the voltage difference is much larger when the resistance has increased. When the chest falls on an exhale, the voltage difference then decreases as the resistance changes back towards the norm. The frequency of these peaks also indicates how the breaths the patient takes is fairly consistent, and the data can indicate whether the breaths seem abnormal or not. This feature of the fiber was great, as it was proven that a lightweight wearable device can detect someone's respiratory rate. The ease of implementation for this fiber was also another upside. However, when taking the data with the conductive fiber, there was a lot of noise generated. In particular, the signal to noise ratio is low (signal peak is around 10 mV, while the noise level is approximately 5 mV, making the signal to noise ratio equals to a value of 2). It also did not perform the full function of listening to the sounds of the lungs. It was not sensitive enough to detect the low-amplitude sounds made from the body. It was sensitive enough though, that the fluctuation in the voltage difference would change drastically if there was any sort of movement in the body. This fiber would only be useful for someone sitting or standing perfectly still to detect their respiratory rate. Furthermore, the mindset of someone having a normal breathing pattern at all times throughout the day is unrealistic. Many people start breathing faster when exerting force or exercising, and when going to sleep, respiratory rate decreases. The next step was to look for a solution that included auscultation.

Device 2: Piezoelectric Fiber

After the development of the first device, there were some notable flaws to its performance. It did not allow for much flexibility in terms of function, and there was simply too much noise in the data to be able to interpret someone's respiratory rate while the user was moving. Furthermore, solely detecting the respiratory rate may not be enough to determine if there is a health problem. A better solution is to create a wearable device that can listen to the sounds the lung makes.

Piezoelectric materials are materials that accumulate or discharge electrical charge when undergoing mechanical stress. Because of their properties, they can detect minute changes in mechanical stress, even from sound waves. Due to their sensitivity, a fiber was developed to hear when the lung moves, determining if there are any abnormalities just by placing the fiber across a person's chest. The piezocomposite is then sandwiched between two carbon-loaded polyethylene (CPE) nanocomposite electrodes. CPE, exhibiting both an adequate electrical conductivity and a relatively high viscosity at the draw temperature, is able to collect charge carriers along the fiber cross-section and to confine the low-viscosity piezocomposite in the core to prevent its capillary breakup during drawing. Each of the two large-area CPE electrodes is in contact with two Cu wires (\sim 50 μ m) whose superior electrical conductivity ensures an excellent axial conductivity and a uniform electric field along the entire fiber length. This assembly is encapsulated within a SEBS cladding, an elastomeric thermoplastic that possesses excellent rheological properties and thus maintains the mechanical integrity of the resulting fiber. (Figure 7 and 8).

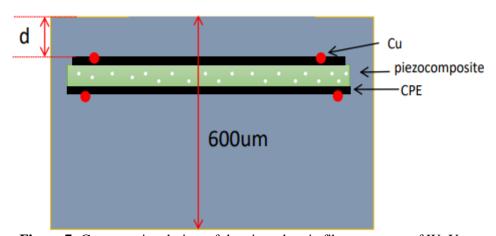


Figure 7: Cross-sectional view of the piezoelectric fiber, courtesy of W. Yan.

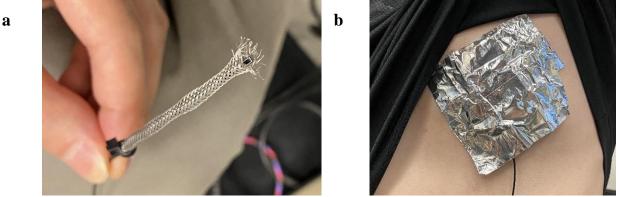


Figure 8: (a) Picture of the piezoelectric fiber encased in a stainless-steel mesh which grounds the outer surface of the fiber. (b) Piezoelectric fiber in use on a person's chest. Aluminum tape was used to hold the fiber in place.

Results on Device 2:

The piezoelectric fiber was placed against the chest of a patient and the voltage changes in the fiber was recorded. The waveforms that the fiber produced clearly indicates the heartbeat of the patient.

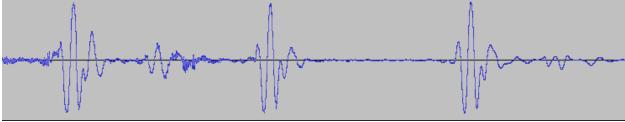


Figure 9: Sound Amplitude vs. Time (in seconds) Waveform of the heartbeat measured by the piezoelectric fiber after noise reduction and amplification steps. The fiber was placed on the heart. The heartbeat here is estimated to be 70 beats per minute.

As demonstrated from the graph (Figure 9) above, the fiber is sensitive enough to detect heartbeat when placed on the chest. We then proceed to place the fiber on the upper part of the ribs, where the lungs are located. The fiber was also placed on the side of the rib in an attempt to listen to the lungs from different angles.

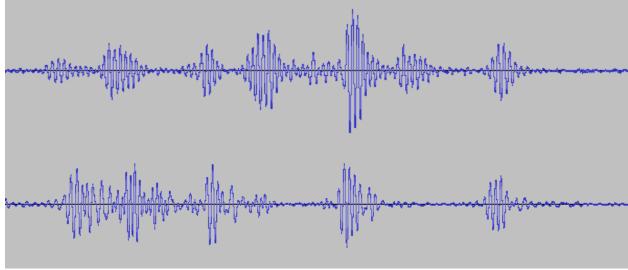


Figure 10: (**Top**) Waveform of the lung sounds with the piezoelectric fiber at the top of the ribs, under the heart. (**Bottom**) Waveform of the lung sounds with the piezoelectric fiber at the side of the ribs. Both waveforms are plotted by sound amplitude versus time (in seconds)

The signals from figure 10 are similar to each other. However, these signals seem to be the sounds of a heartbeat mixed in with the lung sounds. When listening to these waveforms, there is a consistent low frequency noise that resembles the heartbeat, and the noises surrounding the peaks become muffled by the heartbeat. It is possible that noise from the movement of the person could also be picked up which can add another source of disturbance. When comparing these signals with a commercial digital stethoscope (See figure 11), the waveforms from the piezoelectric fiber seem to have more noise. The commercial stethoscope clearly indicates heartbeat, but it is difficult to determine whether the lung noises are being recorded as the heart sound is the loudest. The Eko stethoscope actually listens to the lungs as well, but the amplitude is much smaller and the wave is spread out across a larger time period. Hence, it is not apparent in the waveform, but it is audible to the human ear when played back as an audio file.

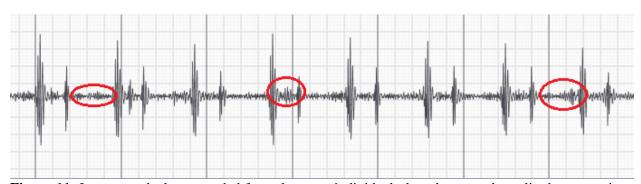


Figure 11: Lung sounds data recorded from the same individual plotted as sound amplitude versus time. The recording is done via a commercial stethoscope, and the estimated heartrate is 65 bpm. The circled locations indicate the lung sounds that are overwhelmed by the heart sounds. (Eko).

However, the breathing was more difficult to detect for two reasons: First, the heart was much louder than the lungs. The lung sounds have a higher frequency whereas the heart has a lower frequency sound wave. Lower frequency waves generally travel further than high frequency waves (Colwell). Second, the movement of the lungs is slower and more gradual when compared to strong impulse-like beats of the heart. Specifically, the generation of electricity from a piezoelectric is dependent on the mechanical impact (meaning how sharp the force vs time impulse is) rather than the magnitude of the absolute force itself. As such, this makes hearing of the lung sounds much more challenging than that of the heart sounds.

5. Discussion

The piezoelectric fiber was a much better solution than the conductive fiber because it was much more sensitive. The piezoelectric fiber is more sensitive because it is able to detect sound whereas the conductive fiber only detects strain. The conductive fiber needs to be under changes of strain to determine respiratory rate. The sensitivity of the piezoelectric fiber gave a much better platform for auscultation. The fiber was able to listen to the heartbeat of the patient, whereas the conductive fiber was only able to detect respiratory rates while the individual was not moving. The piezoelectric fiber can detect the heartbeat of the patient, even if the patient was moving. Due to the heartbeat overwhelming the noise from the lungs, it was difficult to determine whether the fiber can perform auscultation. Usually, a stethoscope can listen to the lungs quite clearly due to the shape of the diaphragm. The diaphragm is a hollow cylinder which allows the sound waves to be directed into the stethoscope, making the sounds in a specific direction louder. For the piezoelectric fiber, since it was the shape of a line, the fiber picked up sound across a larger area as opposed to the stethoscope.

For further studies, more development needs to be made on the piezoelectric fiber. The layout of the fiber will be important in directing a specific area on the body to be listened to. One change could be the shape of the fiber. The shape can resemble how the diaphragm in a stethoscope works. The fiber can be modified to be amplify the sound in a location of interest. A hollow channel will be created at the top of the fiber while the piezoelectric device will sit at the bottom of the fiber. The piezoelectric device within the fiber should be in direct interface with the chest due to the maximal vibration (See figure 12), while the channel operates as a sound amplifier by creating a larger surface area than the waves that move into the piezoelectric fiber. The sound waves have to travel more within the fiber, which will magnify the pressure waves, amplifying the sound (Kubin 2011). To test if this fiber design is indeed more sensitive to sound, FEM simulation via COMSOL can be performed as a future work.

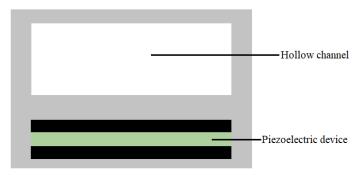


Figure 12: Cross sectional view of a potential shape change for the future study. The hollow channel at the top is an attempt to act as a sound-amplifying channel, resembling that in a bell stethoscope.

Also, additional tests need to be conducted to determine the best location to place the piezoelectric fiber. When doctors use stethoscopes, they usually listen to multiple locations, some being on the chest while other locations are located on the patients' backs. When listening to the lungs, it is actually easier to hear the sounds the lungs make from the back because the heart sounds will not be as overwhelming.

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Bibliography

- Block, V J, et al. "Continuous Daily Assessment of Multiple Sclerosis Disability Using Remote Step Count Monitoring." *Journal of Neurology*, U.S. National Library of Medicine, 28 Nov. 2016, www.ncbi.nlm.nih.gov/pmc/articles/PMC5292081/.
- "Bronchiolitis." *Mayo Clinic*, Mayo Foundation for Medical Education and Research, 15 Jan. 2020, www.mayoclinic.org/diseases-conditions/bronchiolitis/symptoms-causes/syc-20351565.
- Colwell, Catharine H. "Introduction to Sound." *PhysicsLAB*, dev.physicslab.org/Document.aspx?doctype=3&filename=WavesSound_IntroSound.xml.
- Erickson, Barbara. "Basics of Lung Sounds." *Easy Auscultation*, www.easyauscultation.com/course-contents?courseid=201.
- "FastStats Pneumonia." *Centers for Disease Control and Prevention*, Centers for Disease Control and Prevention, 20 Jan. 2017, www.cdc.gov/nchs/fastats/pneumonia.htm.
- Geddes, L.A. "Birth of the Stethoscope." *IEEE Journals & Magazine*, IEEE, 25 Jan. 2005, ieeexplore.ieee.org/document/1384105.
- Kahn, April. "Breath Sounds." *Healthline*, Healthline Media, 27 Feb. 2018, www.healthline.com/health/breath-sounds.
- Kubin, Paul. "Tools of the Trade: The Stethoscope and How To Use It." *Inside PA Training*, 20 Mar. 2011, www.mypatraining.com/stethoscope-and-how-to-use-it/.
- "Lung with Pneumonia." *VectorStock*, VectorStock Media, www.vectorstock.com/royalty-free-vector/diagram-showing-lung-with-pneumonia-vector-9914455.
- Parisien, Shelly. "Parts of a Stethoscope." *Nurselly*, Amazon, 14 Feb. 2020, www.nurselly.com/parts-of-a-stethoscope/.
- Wakai, Abel P. "Spontaneous Pneumothorax." *BMJ Clinical Evidence*, BMJ Publishing Group, 10 Mar. 2008, www.ncbi.nlm.nih.gov/pmc/articles/PMC2907964/.
- Welsby, P D, et al. "The Stethoscope: Some Preliminary Investigations." *The Stethoscope: Some Preliminary Investigations*, The Fellowship of Postgraduate Medicine, 1 Dec. 2003, pmj.bmj.com/content/79/938/695.full.
- Youngster, I, et al. "The Stethoscope as a Vector of Infectious Diseases in the Paediatric Division." *Acta Paediatrica*, John Wiley & Sons, Ltd, 7 Aug. 2008, onlinelibrary.wiley.com/doi/full/10.1111/j.1651-2227.2008.00906.x.