

Design Presentation:

Lung tissue culture chamber mimicking the blood flow and mechanical forces of air sacs within the lung

Problem Statement:

The main function of the lung is a rapid gas exchange. This process is achieved by an interaction between the circulatory system and the nervous system. The gas exchange occurs within the alveolus sacs within the lung, where on one side of the sac there is the blood flow from the circulatory system and on the other side is the desired air. The separation here is only a thin layer of tissue. This tissue is exactly what we are trying to mimic for the study of asthma. On one side of the tissue there are endothelium cells, which react with the blood, and on the other side there is epithelium cells, which react with the open air. So far the only devices made are for one side of the alveoli sacs. While this may be useful for the study of the reaction of cells, it does not paint a full picture of the reactions between these different cell layers.

Information/Motivation:

Asthma is one of the two known obstructive airway diseases. It is caused by hyperactivity to several different stimuli that produce inflammation; which then causes a narrowing of the airways. Such stimuli may include dust mites, pollens, smoke, pet-dander and many others. People with this disease make up about 5% of the population. These people can experience asthma attacks that range from minutes to hours and in severe cases even days. During these attacks breathing requires an extensive amount effort, due to this the victim may break out in a sweat, unable to talk, show signs of confusion, and take on a blue appearance. This is all due to the fact that the body is not getting the required amount of oxygen to operate normally. When an asthma attack occurs there are also many changes that occur on a molecular level. A type of white blood cell called the eosinophil is the suspected cause of tissue inflammation in the lungs. During a asthma attack eosinophilspass through the endothelium and into the matrix, after an allergen has contacted the epithelium. We are interested in the interactions these eosinophils make with the matrix as well as the epithelium. If we can produce a device, which is a correct representation of the gas exchange in the lung, we can understand these eosinophils and their role in asthma.

Design Descriptions:

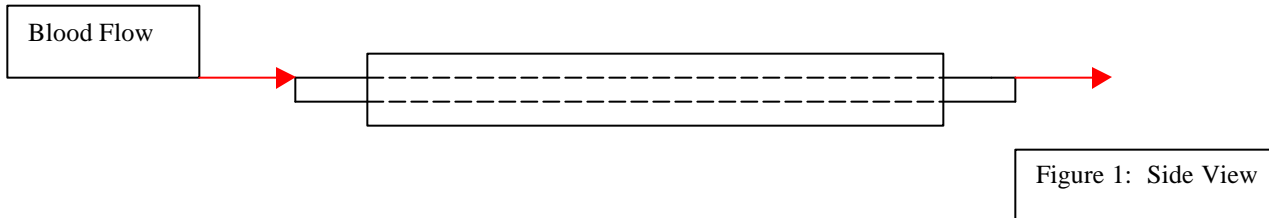
Several basic aspects that must be included in our design relate both of our devices. A space between the endothelial and the epithelial cells must be able to hold the interstitial fluid (matrix). The epithelial and endothelial cells must be attached to a permeable filter, which will act as a support. Above the endothelial cells there must be a way to allow blood to flow over the cells. Below the epithelial cells there must be a chamber for air to come into contact with the cells because this is where the allergens will be introduced into the system. The chamber must be able to be taken apart so that the

filters can be replaced, and have new cells grown. With these basic guidelines we were able to develop several solutions to the problem at hand.

The first design consists of three rectangular boxes that will create the tissue chamber. We titled this design the **Canal Design**.

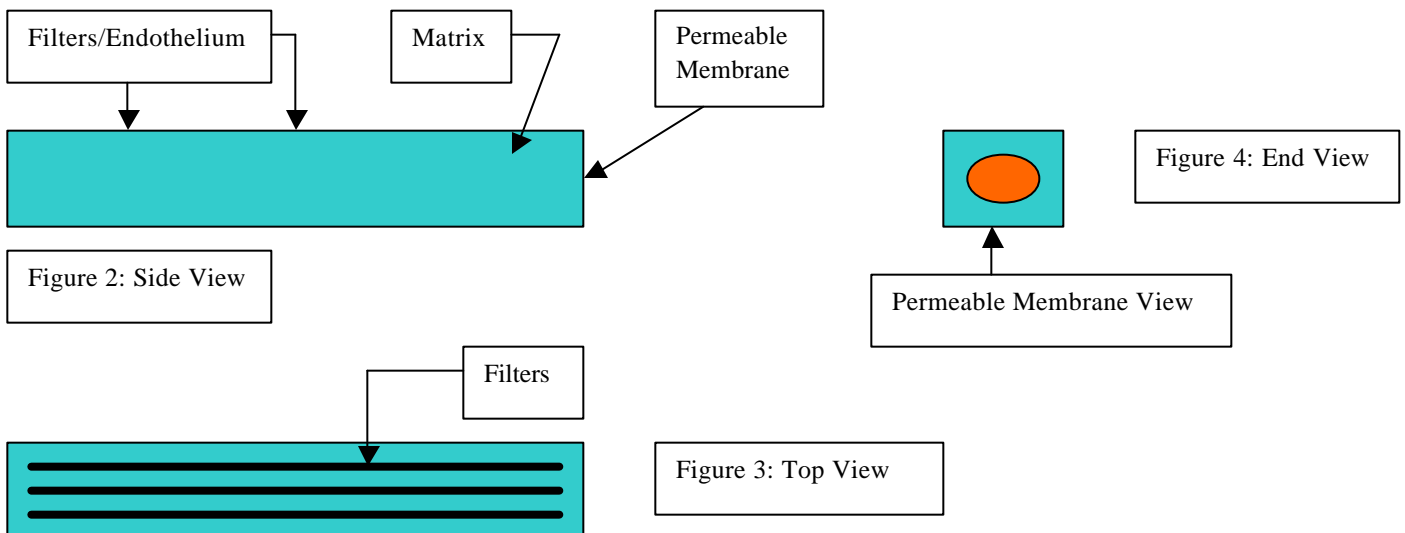
1st Piece:

The first/top piece consists of a tunnel like canal, which will serve as the blood flow over the endothelial cells. The main purpose here is to mimic the blood vessels surrounding the alveolar sac.



2nd Piece:

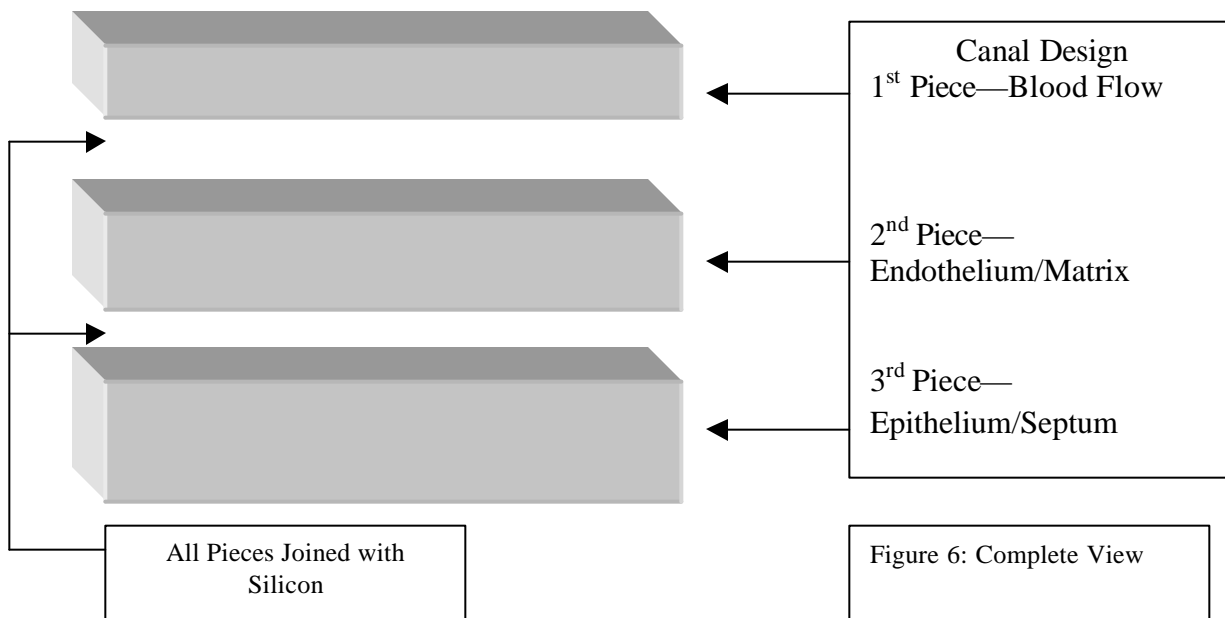
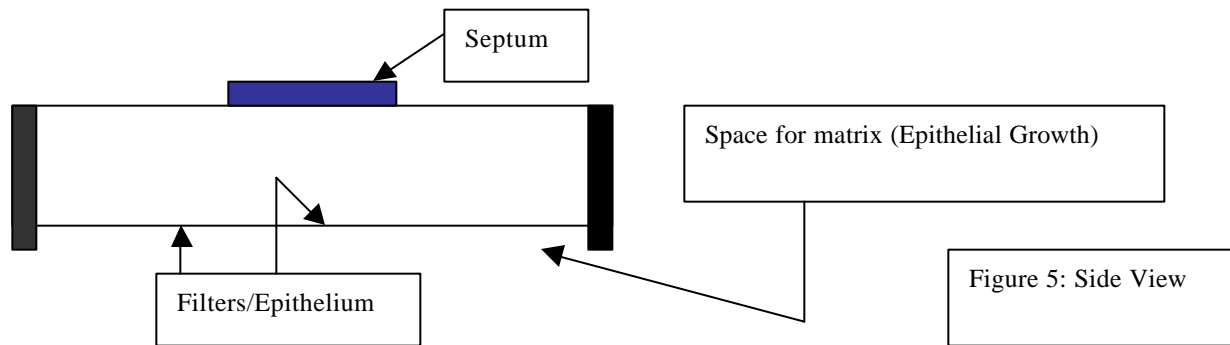
The next piece, endothelial section, consists of the following: The top is in the shape of a long canal type structure. On the base of this canal structure are a series of filters. These filters are long and narrow. This type of shape will allow the blood flow to have maximum contact area as well as maximum contact time. Directly below this canal, and still attached is another portion of our design, the matrix container. This container is a small area where the matrix will be held. A very important feature of this area of our device is that this liquid inside must be able to be accessed. To do this one side of the container is a membrane, which can be punctured with a needle or syringe to add or sample the fluid inside. The needle/syringe can be removed and the hole left will seal itself. This part is the most important part of the whole device because this is where the sample will be taken, and the sample has all the information, which we would like to study. It is very important that sampling will not disrupt the experiment; that is why we chose this special type of membrane. Samples can be taken and fluid can be introduced without taking the whole device apart. There will be no bottom to this piece because the epithelial piece, the next piece, will need to be directly attached to it.



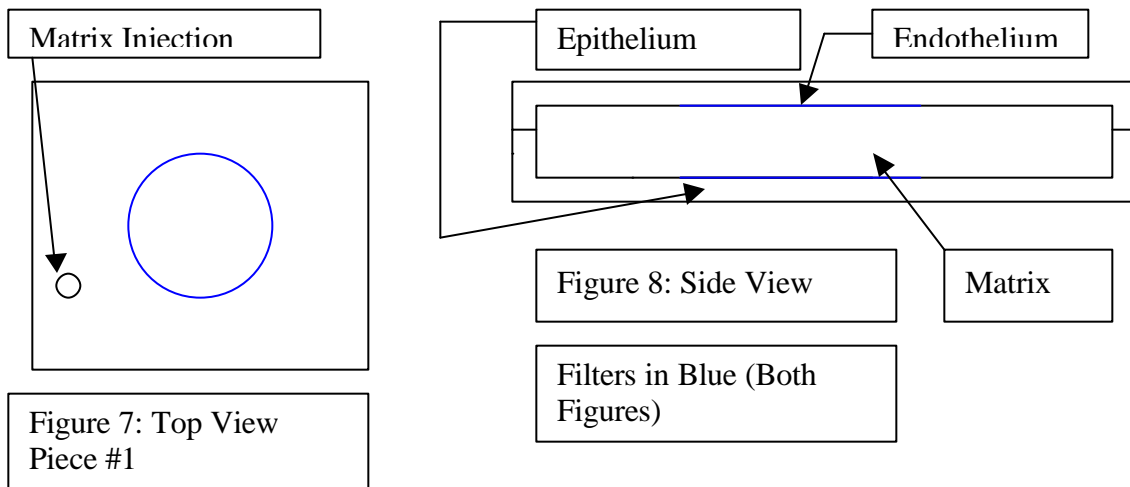
3rd Piece:

The last piece is the epithelium piece, which is designed to mimic the interior of the alveolar sac. What this part consists of is a filter, which when set on a level surface will be slightly raised. Around this filter are four walls, which will take the shape of a rectangle. A detachable cover will be the top to these four walls so the epithelial cells will be completely contained except for the septum, which is located in the center of the cover.

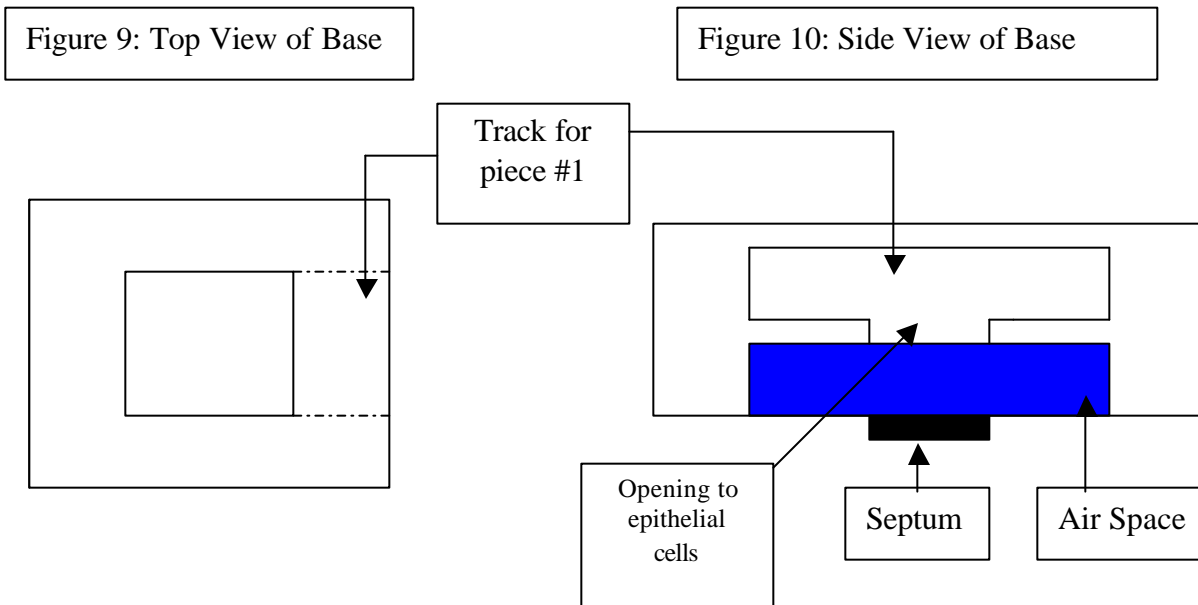
This final piece to the device is very unique. The cells, which grow on the filter, need three weeks to grow as well as the presence of matrix. Because of this the bottom filter is slightly raised. The area underneath is for the matrix when growing the epithelial cells. The epithelial device piece is simply put in a dish such as a lab dish where inside the dish a small amount of matrix is added. This way the epithelial cells are able to grow in the right orientation, which will give a correct representation of the whole device. Each of these pieces are fastened together using epoxy. We decided to use epoxy because we felt it was the best way to carry out the experiments. We needed to be sure the matrix area is completely sealed as well as the blood flow area to provide not only accurate results, but also a safe environment, which the experimenter is able to do his/her research.



The second design, which we called the **Base Design**, consists of two pieces that come together and slide into a base that would facilitate the air and blood flow. The pieces that snap together are nearly identical. Each is in the shape of a square and has a filter area located in the middle. The top filter area has the endothelial cells attached to it and the bottom piece has the epithelial cells attached to its filter area. After the two pieces are attached there is a space between them for the interstitial fluid (matrix). The attachment of these two pieces has several possibilities. There could be an actual mechanical bond formed by some sort of interlocking system. However, we feel that the ideal attachment would be through a silicon gel. The two pieces need to have a relatively large contact area between them to facilitate a strong bond. A silicon attachment would be strong enough for our purposes, easy to use and cost efficient. Once the pieces are held together there is the problem of how to inject the matrix in between them. A small hole placed on the topside of the endothelial (Figure 8) piece would allow the matrix to be inserted. This hole would have to be located near the edge of the piece so that it would be sealed as it was inserted into the base piece.



The base has a track for the other connected pieces to slide into. This is a simple mechanical system of interlocking grooves (Figure 9). Below the pieces that are slid into place, there is a cavity that is closed off except in two different places. There is an opening to the epithelial cell filter area, so that it could come into contact with the air containing the allergens. A septum at the bottom of the cavity is also necessary for injection of the allergens. Above the endothelial cells there is a system similar to the first design to allow for blood flow. It consists of a tunnel system that would be hooked up to a pump that circulates the blood.



The Tunnel for blood to flow through has been left out of the figures to simplify them. In Figure 10 it would fit directly above the track for piece #1 on the base.

There is a major problem that arises from this 2nd design. The manner in which it is connected together makes it all together too complicated. Because the endothelial and epithelial pieces are attached by silicon, they might come apart as they are slid into the base. There would have to be a rather tight fit between the base piece and the other two pieces, and this would cause friction in the system when inserting into base. If the levels of friction became too high the endothelial and epithelial pieces would come apart as they are slide into place. This is a large problem because in this system the matrix has to be injected before these two pieces are slid into the base. If they come apart as they are slid into position the matrix will spill out. Also the hole for the matrix injection may not form a tight seal to the base piece, this poses a problem because it can affect the results of the experiment.

We believe that the canal design is the best solution to this particular task. This design poses fewer problems then the other design we have proposed. Not only that, the overall idea behind the canal design seems much more ideal and efficient for what we are trying to accomplish. The canal for the blood to flow seems much more effective then blood passing over a circular area, the long rectangular filters provide much better contact with the direction the blood is moving, and the way to access the matrix seems to be the simplest way to take samples and introduce fluid.

A potential problem with the Canal Design is the size and shape of the filters. The rectangular shape of the filters maximizes the contact surface between the filters and the blood. However, the strength of the filters is an issue. If we increase surface area the strength of the filter will decrease. How big can we go till it poses a problem? A way to address this problem is maybe put breaks in the filter so instead of one big rectangle there

are a series of rectangles aligned end to end along the filter line. Another problem is the number of experiments that can be performed. In our design it is set up so one experiment can be performed at a time. What if the experimenter would like to do multiple tests and experiments with different allergens? A way to handle this problem is duplicating the device for instance four times, so there is a series of four different devices in one. This way the experimenter can put blood flow to each and perform different tests on each one. This would save a lot of cleaning and re-attaching filter time. A final problem we have discussed is the size of the device itself. We were originally going to decide to base it off of the size of the filters, but now our filters are in question as to how big or small we would like to make them. If the filters were of the long rectangle kind then we could reduce the width of the device, yet it must have enough width to provide a seal with the silicon. If the filters were of the circle kind, already used, then the device would have to be even wider. Once our questions on the filters are answered we can correctly and effectively assess this problem.