Imaging the airways

Betsy Skrip

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ROCHESTER INSTITUTE OF TECHNOLOGY

A Thesis Submitted to the Faculty of
The College of Imaging Arts and Sciences
In Candidacy for the Degree of
MASTER OF FINE ARTS

IMAGING THE AIRWAYS

3D Modeling of a Complete Respiratory Airway for Use in
Computational Flow Dynamics Studies of Particle Deposition in the Lungs

Creation of an Educational Animation about the Respiratory System for
Use in the Human Visualization Project and CollaboRITorium

BETSY SKRIP
Medical Illustration

Date Approved: October 7, 2008
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Betsy Skrip Medical Illustration, Rochester Institute of Technology

ABSTRACT

The IMAGING THE AIRWAYS thesis project is a multidiscipline and multimedia endeavor consisting of two main parts: I. 3D Modeling of a Complete Respiratory Airway for Use in Computational Flow Dynamics Studies of Particle Deposition in the Lungs and II. Creation of an Educational Animation about the Respiratory System for Use in RIT’s Human Visualization Project and CollaboRITorium.

Part I involved collaboration with RIT’s Mechanical Engineering Department to construct a 3D model of one complete respiratory pathway, from the oral cavity to the site of gas exchange between the lungs and the blood. The project is a continuation of thesis work completed by Jackie Russo, MS Mechanical Engineering, Class of 2007 and Jessica Weisman, MFA Medical Illustration, Class of 2007. Russo and Weisman constructed a model of the upper respiratory tract, from the oral cavity to generation 5 (as defined by Des Jardins, 2007). Weisman also constructed a model of a respiratory acinus (generation 20-28).

Part I of the IMAGING THE AIRWAYS thesis project involved creating a Maya model of generations 6-19 to bridge the two existing models and creating a Maya model of the respiratory membrane to study nanoparticle translocation from the lungs to the blood. Part I of the project also involved creating promotional materials that were featured in the March 17-April 9, 2008 thesis show and at the 2008 Imagine RIT Innovation and Creativity Festival. The promotional materials consist of a 35” x 43” poster, a postcard, a website, and a one-minute promotional video.

Part II of the project involved creating a 5-minute animation about the respiratory system for use by RIT’s Human Visualization Project (HVP) and CollaboRITorium, as well as an HVP website.

INTRODUCTION

The IMAGING THE AIRWAYS project consists of two main parts, with the first part further separated into three sections.

Part I. 3D Modeling of a Complete Respiratory Airway for Use in Computational Flow Dynamics Studies of Particle Deposition in the Lungs

The main thesis project, conducted for RIT’s Mechanical Engineering Department under the direction of thesis supervisors Dr. Risa Robinson, Jim Perkins, and Glen Hintz, as well as professors Nancy Ciolek and Ann Pearlman.

Part I.1 Bronchi/Bronchiole Model

Modeling of the respiratory path between the upper tract and a respiratory acinus.

Part I.2 Respiratory Membrane

Modeling of the respiratory membrane at the cellular and molecular levels in
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order to visualize nanoparticle transport from the lungs into the bloodstream.

Part I.3 Promotional Materials
Creation of promotional materials for the project to educate the RIT community and other interested audiences.

Part II. Creation of an Educational Animation about the Respiratory System for Use in the Human Visualization Project and CollaboRItorium
An animation and website created for RIT’s Human Visualization Project and CollaboRItorium under the direction of thesis supervisors, as well as Dr. Richard Doolittle, Shaun Foster, and Dr. Jake Noel-Starr.

Part I.1 Bronchi/Bronchiole Model
Modeling of the respiratory path between the upper tract and a respiratory acinus.

ORIGINAL THESIS STATEMENT
The aim of this project is to create a 3D computer-generated model of generations 6-19 of a single respiratory airway.

The model will bridge existing computer-generated models created for use by the Mechanical Engineering Department: models extending from the oral cavity to generation 5 and a model of a single acinus (generations 20-28).

The end product of this project will be a complete model of a respiratory airway extending from the oral cavity to the alveoli.

The model will be constructed in Maya from published data of airway dimensions (e.g., papers authored by Weibel and Horsfield). The model will then be meshed to the two existing models to form one complete model.

The complete model will be imported into two computational flow dynamic engineering software programs (Fluent and Comsol) in order to study particle flow and deposition in the lungs.

Effectiveness and accuracy of the model will be evaluated based on comparisons to published data, such as that derived from biological specimens.

Current methods for creating an accurate model of the respiratory airways include scanning and creating casts from cadavers; however, these methods create only a static model. The main contribution of working in Maya is the ability to generate a modifiable model in which researchers can vary different parameters of the tract’s morphometry and examine the effects of those variations.

The ability to alter different parameters of an airway model will enhance research to better define the mechanics of breathing and changes in particle flow and deposition among different disease states, such as asthma and emphysema.

Maya also allows for the creation of a more organically shaped model than current engineering CAD (Computer-Aided Design) programs.

BACKGROUND
Over several years, Dr. Risa Robinson in RIT’s Mechanical Engineering Department and Dr. Richard Doolittle in RIT’s Allied Health Sciences Department have spearheaded student research to better understand the mechanics of breathing.

In 2006, two graduate students—Jackie Russo (MS Mechanical Engineering, Class of 2007) and Jessica Weisman (MFA Medical Illustration, Class of 2007)—designed their thesis projects to model parts of the respiratory system using 3D computer software. The models were then analyzed using engineering computational flow dynamics software in order to study fluid flow and particle deposition in the respiratory system.

Russo and Weisman produced the following models:

1. A model of the upper respiratory tract
   Created by Russo (2007) and Weisman (2007)
   This model consists of three models, each created using different methods: (1) the oral cavity, (2) the oropharynx, laryngeopharynx, and larynx, and (3) the trachea through bronchi generation 5.

2. A model of a respiratory acinus
   Created by Weisman (2007)
   This model was constructed using the same overall methods and consists of generations 20-28 (the respiratory bronchioles, alveolar ducts, and alveolar sacs).

Several systems exist for numbering the structures of the respiratory tree. Differences among these systems result in part because the number of branches beyond the bronchi differ among individuals and among the lungs’ regions. For this project, Des Jardin’s (2007) system was used, in which the structures are numbered as follows:

<table>
<thead>
<tr>
<th>Structure</th>
<th>Generation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trachea</td>
<td>0</td>
</tr>
<tr>
<td>Main stem bronchi</td>
<td>1</td>
</tr>
<tr>
<td>Lobar bronchi</td>
<td>2</td>
</tr>
<tr>
<td>Segmental bronchi</td>
<td>3</td>
</tr>
<tr>
<td>Subsegmental bronchi</td>
<td>4-9</td>
</tr>
<tr>
<td>Bronchioles</td>
<td>10-15</td>
</tr>
</tbody>
</table>
Terminal bronchioles 16-19
Respiratory bronchioles 20-23
Alveolar ducts 24-27
Alveolar sacs 28

Generations 0-19 are termed “conducting” structures, for they channel air from the mouth and nose to the respiratory acini (as well as in the opposite direction from the acini to the atmosphere). Gas exchange with the blood occurs within the respiratory acini, which each consist of generations 20-28.

Previous Research
In her study, 3D Reconstruction of a Female Lung Using the Visible Human Data Set to Predict Cigarette Smoke Particle Deposition, Russo utilized two upper respiratory models: one with the normal oral cavity model (meant to represent a non-smoker) and one with an oral cavity model in which the casting material was siphoned through a straw (representing the mouth structure of a smoker at the time of inhalation).

Russo’s procedure for importing the upper respiratory models into the computational flow dynamics software involves three main steps:

1. Importing the original models generated with Maya or 3D Doctor into VP-Sculpt for refinement and to combine the separate model components into one model.

2. Importing the VP-Sculpt models into Solid Works in order to convert the models from a surface texture to a closed volume. (The surface model represents the physical, hollow-interior airway, whereas the closed volume model represents the space inside the airway.)

3. Importing the Solid Works models into computational flow dynamics software, such as Gambit, Comsol, or Fluent.

Using Gambit, Russo calculated a higher air velocity and turbulence in the smoker model. For the particle deposition analysis, Russo injected 0.1-µm (micrometer), 1-µm, 3-µm, 5-µm, 9-µm, and 10-µm particles into both models and calculated deposition in five regions: the oral cavity, throat (i.e., the oropharynx, laryngeopharynx, and larynx), trachea, left main bronchi, and right main bronchi.

Russo found that over twice as many particles deposited in the smoker model than in the non-smoker model. Specifically, Russo found that in the smoker model, 45% of all particles deposited in the upper airway, and in the non-smoker model, only 21% of the particles deposited in the airway.

Russo’s results suggest that the greater air velocity and turbulence in the smoker airway somehow influence particle deposition. Russo hypothesizes that, instead of flowing smoothly along the contours of the airway as they would in a non-smoker, the particles in a smoker’s lungs become forcefully propelled into the airway walls, where they then remain.

Russo’s results further suggest that in a smoker, more particles are likely to become trapped in the upper airway, whereas in a non-smoker, more particles are likely to continue flowing to deeper parts of the respiratory system.

For future research, Russo proposes analyzing airflow and particle deposition in those deeper regions, such as in Jessica Weisman’s model of the acinus.

Therefore, the IMAGING THE AIRWAYS thesis project (specifically, Parts I.1 and I.2) sought to construct models of the deeper regions of the respiratory system and to combine them with Russo and Weisman’s models. This effort would thereby establish a complete pathway from the oral cavity (the site of gas exchange between the atmosphere and the lungs) to the respiratory membrane (the site of gas exchange between the lungs and the blood). To the best of our knowledge, such a model has never before been created.

Completing the pathway would involve creating a model of generations 6-19 (to connect the models of the upper respiratory tract and the respiratory acinus) and a model of the respiratory membrane (see Part I.2).

In order to provide more detail about the overall, collaborative modeling project and to establish a clearer understanding of the methods used to construct Parts I.1 and I.2, the following is a summary of the methods used to create the original model’s individual parts. (Note: These descriptions, with some variations, also appear on the IMAGING THE AIRWAYS website, http://www.betsyskrip.com/thesis.)

The oral cavity models
Created by Russo (2007)
The oral cavity models were made from a cast of a female student’s mouth. Aquasil Ultra LV Smart Wetting Impression Material was spooned into the student’s mouth and allowed to dry. For the non-smoker model, the mouth was left slightly open and at rest. For the smoker model, the casting material was also siphoned through a straw placed in the student’s mouth (in order to represent the mouth structure of a smoker at the time of inhalation).

After the impressions were made, they were scanned at a resolution of 0.003 inches using the Model Maker ZI40 3D Scanner with a
Romer Cimcore Infinite Arm. The arm attachment was used to trace over the surface of the casts and transferred the data into the computer to create a 3D model.

**The laryngopharynx, oropharynx, and larynx model**
*Created by Weisman (2007)*
The oropharynx, laryngopharynx and larynx model was based on dimensions taken from multiple sagittal and anterior medical photographs of cadavers and a partial cadaver cast of the throat.

The cadaver of an elderly woman was prepared, and silicone rubber was injected through the bottom of the trachea and through the mouth.

The casting material was then allowed to dry and removed from the cadaver. Sketches were made and used in Maya to create a 3D model.

**The trachea to generation 5 model**
*Created by Russo (2007)*
The trachea/bronchi model was created using slices of the thoracic cavity from the Female Visible Human Project. The slices were imported into 3D Doctor and converted to greyscale in order to increase contrast among the different anatomical structures. Outlines of the desired structures were then generated by the software based on those contrasts. Some boundaries were also drawn and refined by hand.

The software rendered a 3D surface model by connecting the defined outlines from all of the segmented images using polygon-based surfaces. The file was exported as an OBJ and imported into VP-Sculpt for further processing. VP-Sculpt was used to smooth the surface and to trim or delete incomplete branches. Specifically, branches beyond the 5th generation were trimmed off.

**The acinus model**
*Created by Weisman (2007)*
Dimensions of the acinus were obtained through scanning electron microscopy. The acinus from a male human lung was observed through a scanning electron microscope (SEM), and the dimensions of the respiratory bronchioles, alveolar ducts, and alveolar sacs were measured.

Sketches were made and used in Maya to create a 3D model.

**Present Research**
As previously mentioned, the upper respiratory model extends to only the 5th generation of branching. Branches beyond the 5th generation were indistinguishable on the Female Visible Human slices. Therefore another method was devised to create a model of generations 6-19 (subsegmental bronchi, bronchioles, and terminal bronchioles) to bridge the models of the upper respiratory tract and the respiratory acinus.

Without access to a human cast, the best solution was to use data published by Horsfield et al. (1971). The researchers created a resin cast of the respiratory tree from a male cadaver and measured the lengths, diameters, and angles of branching for all structures down to 0.7 mm in diameter. They then broke off a single branch to measure structures smaller than 0.7 mm in diameter.

For our model, the required Horsfield et al. (1971) data were organized into Table 1. A sketch was also made in order to visualize the correlation between the Des Jardins' (2007) branch generations and Horsfield et al.'s system of orders (Figure 1).

**Modeling in Maya**
Each branch was first modeled separately as a polygon cube with the correct length and width (which became the diameter once the model was smoothed). Edge loops were inserted at the top and bottom of each model to prevent reduction of the central diameter when the models were smoothed.
Horsfield et al.’s data provide the numerical values for each angle of branching, which they define as “the angle by which the line of the axis of the daughter branch deviates from the line of the axis of the parent branch.” In this system, the branches are categorized from top-down, with parent branches being a lower order number than their daughter branches.

However, Horsfield et al. (1971) do not indicate in which direction (right or left) each branch deviates from the parent axis. Several images were used as references in order to determine the directions, such as images from Pernkopf (1980) and Des Jardins (2007). However, differences existed among the different models, and many of the lower branches were either obscured by other branches or too small to discern.

In addition, Horsfield et al.’s data also do not include the branch angles’ deviation from the parent axis anteriorly or posteriorly.

Therefore, in order to estimate the branching angle directions, a model of the left lung was constructed in 3D Doctor, and the bronchi/bronchiole model was constructed to fit within the lower posterior lobe. Specifically, the individual branch models were placed inside of the lung model and adjusted to fit within the lower posterior region. The final directions and angles are listed in Table 2.

After the angles of branching were set in the x-axis for each individual branch model, the models were combined (Mesh > Combine). The bottom face of each parent branch was cut in the z-axis, and the two resulting faces were deleted, leaving UVs in the center of the two parallel edges. The face of the top of each daughter branch was also

Table I  Dimensions for the pathway supplying the lower posterior lobe of the left lung

<table>
<thead>
<tr>
<th>Branch Gen.</th>
<th>Order</th>
<th>Diameter (mm)</th>
<th>Length (mm)</th>
<th>Angle (°)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>23</td>
<td>5.50</td>
<td>10.20</td>
<td>32</td>
</tr>
<tr>
<td>7</td>
<td>22</td>
<td>3.90</td>
<td>7.60</td>
<td>30</td>
</tr>
<tr>
<td>8</td>
<td>21</td>
<td>4.80</td>
<td>10.00</td>
<td>32</td>
</tr>
<tr>
<td>9</td>
<td>20</td>
<td>3.30</td>
<td>8.93</td>
<td>30</td>
</tr>
<tr>
<td>10</td>
<td>19</td>
<td>3.37</td>
<td>8.00</td>
<td>30</td>
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<td>18</td>
<td>3.14</td>
<td>13.68</td>
<td>30</td>
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<tr>
<td>12</td>
<td>17</td>
<td>2.87</td>
<td>9.05</td>
<td>36</td>
</tr>
<tr>
<td>13</td>
<td>16</td>
<td>2.60</td>
<td>7.12</td>
<td>36</td>
</tr>
<tr>
<td>14</td>
<td>15</td>
<td>2.46</td>
<td>7.26</td>
<td>36</td>
</tr>
<tr>
<td>15</td>
<td>14</td>
<td>2.33</td>
<td>6.90</td>
<td>36</td>
</tr>
<tr>
<td>16</td>
<td>13</td>
<td>2.16</td>
<td>5.50</td>
<td>36</td>
</tr>
<tr>
<td>17</td>
<td>12</td>
<td>1.95</td>
<td>4.91</td>
<td>43</td>
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<tr>
<td>18</td>
<td>11</td>
<td>1.70</td>
<td>4.83</td>
<td>43</td>
</tr>
<tr>
<td>19</td>
<td>10</td>
<td>1.43</td>
<td>4.01</td>
<td>43</td>
</tr>
</tbody>
</table>

Figure 1  An initial sketch of the bronchi/bronchiole model comparing the order numbers to the generation numbers. The “a” and “b” designations were not used by Horsfield et al.; they were implemented to facilitate keeping track of the 27 branches.
deleted, and the top UVs on each daughter branch were then merged to their corresponding UVs on the bottom of the parent branch.

The combined, unsmoothed individual branch models are shown in Figure 2.

The overall model was then smoothed, and a rig was created with a joint at each point of bifurcation. The model was bound to the rig, and the joints were rotated in the z-axis (anteriorly or posteriorly) in order to fit the model within the boundaries of the lung model.

The history for the bronchi/bronchiole model was then deleted (in order for the model to keep its

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**Table 2: Angles of branching**

The individual branch models for each order were first positioned roughly within the lung model in order to estimate their directions of branching—either right (+) or left (-) from the parent branch from an anterior view. The final angles were then calculated by adding Horsfield et al.’s (1971) angles of branching to the calculated final angles of the parent branches. The final angles were then entered into the “Rotate x” field in Maya for each of the branch models.

<table>
<thead>
<tr>
<th>Order</th>
<th>Horsfield et al. angle (°)</th>
<th>Direction (+/-)</th>
<th>(Angle x direction) + final angle of parent branch (°)</th>
<th>Final angle (°)</th>
</tr>
</thead>
<tbody>
<tr>
<td>23a</td>
<td>32</td>
<td>-</td>
<td>-32 + 0</td>
<td>-32</td>
</tr>
<tr>
<td>22a</td>
<td>30</td>
<td>+</td>
<td>30 + (-32)</td>
<td>-2</td>
</tr>
<tr>
<td>21a</td>
<td>32</td>
<td>+</td>
<td>32 + (-2)</td>
<td>30</td>
</tr>
<tr>
<td>20a</td>
<td>30</td>
<td>-</td>
<td>-30 + 30</td>
<td>0</td>
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<tr>
<td>19a</td>
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<td>+</td>
<td>30 + 0</td>
<td>30</td>
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<td>18a</td>
<td>30</td>
<td>-</td>
<td>-30 + 30</td>
<td>0</td>
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<td>17a</td>
<td>36</td>
<td>+</td>
<td>36 + 0</td>
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<td>16a</td>
<td>36</td>
<td>-</td>
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</tr>
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<td>15a</td>
<td>36</td>
<td>+</td>
<td>36 + 0</td>
<td>36</td>
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<td>14a</td>
<td>36</td>
<td>-</td>
<td>-36 + 36</td>
<td>0</td>
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<tr>
<td>13a</td>
<td>36</td>
<td>+</td>
<td>36 + 0</td>
<td>36</td>
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<td>-</td>
<td>-43 + 36</td>
<td>-7</td>
</tr>
<tr>
<td>11a</td>
<td>43</td>
<td>+</td>
<td>43 + (-7)</td>
<td>36</td>
</tr>
<tr>
<td>10a</td>
<td>43</td>
<td>-</td>
<td>-43 + 36</td>
<td>-7</td>
</tr>
<tr>
<td>19b</td>
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<td>+</td>
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<td>11b</td>
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<td>+</td>
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<td>79</td>
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<td>-43 + 0</td>
<td>-43</td>
</tr>
<tr>
<td>9b</td>
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<td>+</td>
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<td>79</td>
</tr>
<tr>
<td>8b</td>
<td>50</td>
<td>-</td>
<td>-50 + (-7)</td>
<td>-57</td>
</tr>
<tr>
<td>7b</td>
<td>50</td>
<td>+</td>
<td>50 + 36</td>
<td>86</td>
</tr>
</tbody>
</table>
shape once the rig was removed. The rig was deleted, and the model was exported as an OBJ to be imported into VP-Sculpt.

Figures 3 and 4 show the final model from the anterior and side views.

Figure 3 lists the joints and their angles of rotation (in Maya) in the z-axis.

**3D Doctor Lung Model**

The model of the left lung was constructed in 3D Doctor using slices from the thoracic region of the Female Visible Human Project (VHP), similar to Jackie Russo’s methods for constructing the trachea/bronchi model.

For approximately 600 slices, boundary lines were hand-drawn around the edges of the left lung, as well as around the trachea and discernible bronchi (Figures 6 and 7). The computer then generated a 3D model from the stack of boundary lines, and the model was saved as an OBJ file and imported into Maya.

In order to ensure that the bronchi/bronchiole model and the lung model were approximately the same scale, Russo’s (2007) trachea/bronchi model was used as a guide. The 3D Doctor model was scaled in Maya so that its trachea and bronchi portions fit directly over Russo’s model. The two models were then scaled so that the 6th generation branch of the bronchi/bronchiole model fit to the 5th generation branch of Russo’s model, and so that the 19th generation branch reached the bottom edge of the lung model (leaving some space for generations 20-28).

The lung model, trachea/bronchi model, and bronchi/bronchiole model (with rig) are shown in Figure 8.

<table>
<thead>
<tr>
<th>Joint</th>
<th>Angle (°)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>-27.295</td>
</tr>
<tr>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>-16.437</td>
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<tr>
<td>5</td>
<td>31.400</td>
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<td>-4.887</td>
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<td>7</td>
<td>-18.957</td>
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<td>6.272</td>
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<td>0</td>
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<td>25.688</td>
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<td>13</td>
<td>0</td>
</tr>
<tr>
<td>14</td>
<td>0</td>
</tr>
</tbody>
</table>
Figure 6  In 3D Doctor, boundaries (green lines) were drawn around the edges of the lungs, as well as around the trachea and discernible bronchi, for approximately 600 Female Visible Human Project slices.

Figure 7  A screen shot from 3D Doctor with the list of slices (top left), the boundary outline from an anterior view (bottom right), and the boundary outline from a side view (bottom left). At this stage, boundaries for only the top portion of the lung were completed.

CONCLUSIONS

Creation of the bronchi/bronchiole (generations 6-19) model provided valuable experience in problem solving, as multiple challenges were overcome:

- where to obtain data since the lower generations are not discernible in the VHP slices, and no cast of those structures was available for SEM analysis
- how to arrange the branches and angle them anteriorly and posteriorly, since the Horsfield et al. (1971) article does not provide such data.

The project was also a reinforcement of modeling skills using Maya and a learning experience using 3D Doctor.

After the bronchi/bronchiole model was completed in Maya, it was exported as an OBJ file and successfully imported into VP-Sculpt. Current RIT students in Mechanical Engineering and Medical Illustration will connect the model to the upper respiratory and acinus models and conduct computational flow dynamics (CFD) studies with the complete airway model.

To the best of our knowledge, this model will be the first model of a
complete respiratory pathway—one that extends from where oxygen enters to where gas exchange occurs with the blood.

Future plans with the complete airway model include studying the effects of changes in lung morphometry due to certain disease states, such as asthma. In an asthmatic, the airways become contracted; in Maya, the dimensions of the airway model components can be altered (e.g., diameters reduced) to represent the airway of an asthmatic.

Knowledge of how airflow and particle deposition compare between asthmatic and healthy airways would aid in the treatment of asthma, including the design of more effective inhalation therapy methods.

Future plans also include using more of Horsfield et al.’s data to construct a pathway model for each lobe of the left and right lungs. CFD research with such models would show how and where air flows and particles deposit not only within each pathway, but also throughout the respiratory tree. Mechanical Engineering researchers would also be able to determine the transition point (i.e., the point at which particles stop moving by convection and begin moving by diffusion) for each lobe.

Also, once more of the airways are constructed, a 3D printout of the entire model will be generated for demonstration purposes.
**ORIGINAL THESIS STATEMENT**

Gas exchange in the lung requires the diffusion of molecules across an extremely thin membrane, known as the blood-air barrier. With a thickness of only 500 nm (nanometers) or less, this membrane represents the interface between a capillary lumen and a pulmonary alveolar air space.

Other 3D models of the respiratory system do not extend beyond the alveolar level (~250,000 nm in diameter). The goal of this project is to continue this visual reduction to the nanoscale level (less than 100 nm), in an effort to model cellular and molecular detail of the respiratory membrane’s five main components: (1) surfactant (a lipid monolayer), (2) surface lining fluid, (3) alveolar epithelial cells, (4) basement membrane, and (5) endothelial cells.

Recent research has shown that nanoparticles (particles less than 100 nm in at least one dimension) can cross the respiratory membrane; however, the mechanisms of transport are not well known.

In order to understand the possible health effects and medical applications of nanoparticle inhalation, use of virtual and real models will help to define these mechanisms of transport.

In particular, respiratory membrane models created in Maya will serve as models in a computational flow dynamic engineering software program used in common practice to study particle deposition.

**BACKGROUND**

Research for the IMAGING THE AIRWAYS thesis project was initiated in Summer 2007. An extensive literature review about the respiratory system was conducted, and several articles of current interest were selected as references. Specifically, articles were chosen concerning nanoparticle translocation across the respiratory membrane.

According to Orberdorster et al. (2005), “Berry et al. (1977) were the first to describe the translocation of NSPs (nanosized particles) across the alveolar epithelium.” Berry et al. (1977) reported that 30 minutes after injecting 30-nm colloid gold particles into the tracheas of rats, the particles were found within platelets of the alveolar capillaries.

In more recent studies with rats and humans, UFPs (ultrafine particles) have been shown to cross from the lungs into the systemic circulatory system to reach the liver, heart, spleen, lymph nodes, kidneys, and bone marrow (Orberdorster et al. 2005).

Nanoparticles, NSPs, NPs, and UFPs

According to McShane (2006), “No standard definitions have been established for the terms UFPs and nanoparticles, which has led to some confusion because the words are often used interchangeably.” From the articles researched, four terms were encountered: nanoparticles, NSPs (nanosized particles), NPs (engineered nanoparticles), and UFPs (ultrafine particles). All four terms refer to particles with diameters <100 nm. However, the origin of the particles differ.

NPs are manufactured, or engineered, particles, created through the growing field of nanotechnology. Knowles (2006) defines nanotechnology as: “the design, characterization, production, and application of structures, devices, and systems by controlling shape and size at the nanometer scale.” Further, Orberdorster et al. (2005) state that the term NP “includes only spherical [particles]; other engineered nanosized structures will be labeled according to their shape, for example, nanotubes, nanofibers, nanowires, nanorings, and so on.”

UFPs are created unintentionally as by-products of natural and anthropogenic processes. Gwinn and Vallyathan (2006) state that the term ultrafine “is frequently used to describe nanometer-size particles that have not been intentionally produced but are the incidental products of processes involving industrial, combustion, welding, automobile, diesel, soil, and volcanic activities.”

Nanoparticles and NSPs are general terms that include NPs and UFPs. Knowles (2006) defines nanoparticles as particles that are “found widely in the natural world as products of photochemical and volcanic activity, created in plants and algae, and from products of combustion, food cooking, and diesel exhaust; also manufactured particles such as metal oxides (titanium dioxide, zinc oxide); used in cosmetics, textiles, paints, targeted drug delivery systems, and sunscreens.”

Health Effects of Nanoparticles

The physical and chemical properties of a material differ between the macroscopic and nanoscale levels. In particular, nanoparticles have a much larger surface area per unit mass, which is considered to make them more reactive. According to Orberdorster et al. (2005), “This
increased biologic activity can be either positive and desirable (e.g., antioxidant activity, carrier capacity for therapeutics, penetration of cellular barriers for drug delivery) or negative and undesirable (e.g., toxicity, induction of oxidative stress or of cellular dysfunction), or a mix of both."

Harmful effects of UFPs to the respiratory system and extrapulmonary organs have already been documented through studies with humans, rats, and in vitro cell cultures. Adverse respiratory and cardiovascular effects resulting in morbidity and mortality have been associated with UFPs in air pollution (Orberdorster et al. 2005; Gwinn and Vallyathan 2006). In laboratory experiments, UFPs have induced inflammatory responses in rats and in vitro cell cultures, and caused oxidative stress to in vitro cell cultures, resulting in changes to gene expression and cell signalling pathways (Orberdorster et al. 2005).

While such effects may be undesirable for normal cells, they could be utilized through NPs for anticancer treatments and gene therapy applications. Also, because NPs can be coated with biological micromolecules such as antibodies and proteins and can travel to target organs from the respiratory system, they are being developed for drug delivery and as in vivo and in vitro immunofluorescent probes (Gwinn and Vallyathan 2006).

The potential for NPs to cause adverse health effects still exists, however, particularly for NPs that may be released into the environment through manufacturing pollution and degradation of products through normal use and disposal. According to McShane (2006), "...the current state of knowledge concerning the exposure risks associated with nanotechnology are poor.” Gwinn and Vallyathan (2006) state: “One major challenge facing industry and government is the lack of information on the possible adverse health effects caused by exposure to different nanomaterials.” Therefore, as Yacobi et al. (2007) summarize, “Further knowledge about the mechanisms by which particles injure, interact with and/or are transported across the alveolar epithelium is thus of considerable importance for understanding health effects related to inhalation of ultrafine [and engineered nano-] particles in ambient air.”

**Mechanisms of Transport**

While numerous studies have shown that nanoparticles cross the respiratory membrane to enter the bloodstream and extrapulmonary organs, many studies also state that little is known about how nanoparticles cross the respiratory membrane:

- Berry et al. (1977): “The pathways by which inhaled metallic particles cross the gas exchanging surface in the pulmonary alveoli (where only the finest particles are deposited), must be identified in order to study the action of those contaminants on the respiratory system and on the body generally. The mechanism of this migration still remains uncertain and controversial.”

- Churg (2000): “The determinants of particle uptake remain poorly defined...It is still impossible to provide any generalized explanation of the marked differences in uptake seen with different types of particles, and little is known of the mechanisms of this process.”

- Hoet et al. (2004): “The literature on the translocation of very small particles from the lung into the blood circulation is limited and often conflicting.”

- Geiser et al. (2005): “To date, the mechanisms by which UFPs penetrate boundary membranes...are largely unknown.”

- Gwinn and Vallyathan (2006): “...currently the process of UFP translocation is poorly understood...”

- Rothen-Rutishauer et al. (2006): “So far, little is known about the interaction of nanoparticles with lung cells, the entering of nanoparticles, and their transport through the blood stream [sic] to other organs. ...The entering mechanisms for nanoparticles into cells are still not yet known.”

Such statements indicate a significant need for research about nanoparticle mechanisms of transport across the respiratory membrane. Therefore, it was decided for the IMAGING THE AIRWAYS thesis project to create a model of the respiratory membrane using available data and to study fluid flow and particle movement through the model using CFD (computational flow dynamics) analysis.

Maya models were created of the respiratory membrane’s five main layers: surfactant (a lipid monolayer), surface lining fluid, an alveolar Type I epithelial cell (with lipid bilayer and caveolae), basement membrane (made of proteins perlecain, laminin, entactin, and collagen IV), and an endothelial cell (with lipid bilayer and caveolae).

However, challenges existed to using the model in Mechanical Engineering CFD studies:

(1) **Mechanisms of transport through or between cells**

Numerous methods have been proposed for how nanoparticles move across cell boundaries. Examples include:
• diffusion
• caveolae transport (transcytosis)
• receptor-mediated transcytosis
• movement between cellular tight junctions

Diffusion and movement through cellular tight junctions could easily be studied through CFD analysis. However, the current model represents only a representative section of an alveolar Type I cell and an endothelial cell; therefore, another model would have to be constructed in order to include cellular tight junctions. Further, CFD cannot easily be used to study transcytosis because the process involves biological and chemical factors, including caveolae movement along cytoskeletal elements.

(2) Properties of basement membrane proteins
Although the basement membrane proteins were modeled based on available data, the representations are more iconic than literal. Even space-filling, ball-and-stick, and surface models are representations of the spaces occupied by electrons, and do not represent molecules as literal solid structures. Therefore, in order to run CFD analysis through the basement membrane model, we needed to learn more about the chemical properties of the individual proteins (such as polarity and other factors that could influence interactions with nanoparticles).

(3) Properties of nanoparticles
Different nanoparticle properties, such as size, charge, surface chemistry, and concentration of particles may influence which mechanism of transport is used. Therefore, for our study, we would need to learn more about the properties of certain types of nanoparticles.

Moving Forward
In order for our research to be credible, we would need to work with experts in biology, chemistry, and nanotechnology—people who could not only generate new data for us to work from, but to also help us interpret existing data.

With these concerns in mind, a meeting was established in the Fall 2007 quarter with Dr. Gunter Orberdorster, Professor of Environmental Medicine at the University of Rochester and author of numerous papers about nanotoxicology. Dr. Orberdorster was shown the respiratory membrane model; however, he confirmed that much information is lacking in the scientific community in terms of understanding how nanoparticles cross the respiratory membrane.

The decision was eventually made to change the focus of the thesis research from nanoparticle translocation across the respiratory membrane to completing the respiratory pathway model using data that was known to exist. Other Mechanical Engineering students could then follow Russo’s (2007) methods for conducting the computational flow dynamics studies, and Russo’s data could be compared with the newly generated data.

Research using the respiratory membrane model would be conducted when more resources and background data became available. In the meantime, the model was used for promotional materials about the IMAGING THE AIRWAYS project and in the Human Visualization Project animation about the structure of the respiratory system.

THE BODY OF WORK

Over Summer 2007, Maya models were constructed of the respiratory membrane’s five main components: surfactant (a lipid monolayer), surface lining fluid, an alveolar Type I epithelial cell (with lipid bilayer and caveolae), basement membrane (made of proteins perlecan, laminin, entactin, and collagen IV), and an endothelial cell (with lipid bilayer and caveolae).

The models were constructed from available data and are to scale.

Table 3 lists the dimensions of each respiratory membrane component and the references from which the data was obtained. Table 4 shows some of the models and their relative sizes, and Figure 9 shows the basement membrane model. Figure 10 shows the complete respiratory membrane model in scale compared to a model of one red blood cell, and Figure 11 labels the components of the complete respiratory membrane model.

Orientation of the basement membrane components
The basement membrane models were organized according to descriptions by Crouch et al. (1991) and from an illustration of a basement membrane by David Goodsell (2000).

The entactin models were placed to link the collagen IV models to the laminin models where the short arms of laminin intersect.

The core protein of the perlecan models were placed within the basement membrane meshwork, with the heparan sulfate chains extending along the surface of the basement membrane adjacent to the epithelial cells. According to Crouch et al. (1991), the heparan sulfate chains form a negatively charged barrier that prevents the passage of negatively charged molecules greater than 3-5 nm in diameter.

The perlecan models were arranged in groups of three, according to the

The laminin models were connected by the globules at the ends of the four arms. The models were rigged with a Maya joint system in order to bend them around the other basement membrane protein models.

**Future Work**

In the current model, the heparan sulfate chains extend only toward the alveolar Type I epithelial cell. Future work with the model should involve creating a second layer of perlecan models oriented in the opposite direction, with the heparan sulfate chains facing the endothelial cell.

The collagen IV models were originally arranged with bonds between the globules of two molecules and between the N-terminus of four molecules. However, the models were rearranged in order to better simulate the greater density of collagen IV molecules beneath the meshwork of entactin, laminin, and perlecan, as illustrated by David Goodsell (2000).

As shown in Figure 9, the collagen IV models are still arranged with bonds between two globules; however, the ends of the models are no longer arranged in groups of four. Future work with the model should involve using the collagen IV models in their original orientation.

The orginal, rigid arrangement of collagen IV was based on a diagram by Crouch et al. (1991); however, the authors state that their model represents “the most extended structure, which is likely to be very much condensed via lateral aggregation.” Therefore, the original collagen IV models could be modified, such as with a Maya joint system, in order to create a more condensed collagen IV meshwork.

Future research could also involve using protein models from the Protein Data Bank (PDB) and other public-domain molecular imaging sites. At the time the IMAGING THE AIRWAYS protein models were constructed in Maya, no complete models of the proteins were found on the PDB, only specific domains of those proteins.

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**Table 3 Dimensions used to create the respiratory membrane model**

<table>
<thead>
<tr>
<th>Structure</th>
<th>Dimensions</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory Membrane</td>
<td>thickness = 0.5 µm (500 nm)</td>
<td>Fawcett (1986)</td>
</tr>
<tr>
<td>Basement Membrane</td>
<td>thickness = 80 nm</td>
<td>calculated*</td>
</tr>
<tr>
<td>Surfactant</td>
<td>thickness (length of lipid) = 3.5 nm</td>
<td>lipid bilayer thickness/2</td>
</tr>
<tr>
<td>Surface Lining Fluid</td>
<td>thickness = 15-20 nm</td>
<td>Patton (1996)</td>
</tr>
<tr>
<td>Alveolar Type I epithelial cell</td>
<td>diameter = 81 µm (81,000 nm)</td>
<td>Patton (1996)</td>
</tr>
<tr>
<td></td>
<td>thickness = 0.2 µm (200 nm)</td>
<td>Fawcett (1986)</td>
</tr>
<tr>
<td>Endothelial cell</td>
<td>length = 36 µm (36,000 nm)</td>
<td>Patton (1996)</td>
</tr>
<tr>
<td></td>
<td>thickness = 200 nm</td>
<td>Simionescu (1991)</td>
</tr>
<tr>
<td>Caveolae</td>
<td>opening diameters ≈ 40 nm</td>
<td>Patton (1996)</td>
</tr>
<tr>
<td></td>
<td>internal diameters ≈ 50-100 nm</td>
<td>Patton (1996)</td>
</tr>
<tr>
<td>Lipid Bilayer</td>
<td>thickness (from polar head to polar head) = 7-8 nm</td>
<td>Campbell and Reece (2002)</td>
</tr>
<tr>
<td>Entactin</td>
<td>length ≈ 20 nm</td>
<td>Rohrbach and Timpl (1993)</td>
</tr>
<tr>
<td>Perlecan</td>
<td>core protein length = 80 nm</td>
<td><a href="http://www.uku.fi/anatomicalPG/perlecan.htm">www.uku.fi/anatomicalPG/perlecan.htm</a></td>
</tr>
<tr>
<td>Perlecan Heparin Sulfate Chains</td>
<td>thickness = 3-4 nm</td>
<td>Rohrbach and Timpl (1993)</td>
</tr>
<tr>
<td></td>
<td>length = 50 nm</td>
<td>Rohrbach and Timpl (1993)</td>
</tr>
<tr>
<td>Laminin</td>
<td>long arm length = 75 nm</td>
<td>Hay (1981)</td>
</tr>
<tr>
<td></td>
<td>3 short arm lengths = 35 nm</td>
<td>Hay (1981)</td>
</tr>
<tr>
<td></td>
<td>arm diameters = 2 nm</td>
<td>Hay (1981)</td>
</tr>
<tr>
<td></td>
<td>globule lengths = 5-7 nm</td>
<td>Hay (1981)</td>
</tr>
<tr>
<td>Collagen IV</td>
<td>length = 300 nm</td>
<td><a href="http://www.answers.com/topic/collagen?cat=health">www.answers.com/topic/collagen?cat=health</a></td>
</tr>
<tr>
<td></td>
<td>diameter = 1.5 nm</td>
<td><a href="http://www.answers.com/topic/collagen?cat=health">www.answers.com/topic/collagen?cat=health</a></td>
</tr>
<tr>
<td>Red Blood Cell</td>
<td>diameter = 7 µm (7,000 nm)</td>
<td>Knowles (2006)</td>
</tr>
</tbody>
</table>
### Table 4: Maya models of respiratory-membrane components

<table>
<thead>
<tr>
<th>Component</th>
<th>Diameter (nm)</th>
<th>Magnified view</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lipid bilayer</td>
<td>7</td>
<td><img src="image" alt="Lipid Bilayer" /></td>
</tr>
<tr>
<td>Nanoparticle</td>
<td>20</td>
<td><img src="image" alt="Nanoparticle" /></td>
</tr>
<tr>
<td>Entactin</td>
<td>20</td>
<td><img src="image" alt="Entactin" /></td>
</tr>
<tr>
<td>Perlec an</td>
<td>50</td>
<td><img src="image" alt="Perlec an" /></td>
</tr>
<tr>
<td>Heparan sulfate</td>
<td>80</td>
<td><img src="image" alt="Heparan sulfate" /></td>
</tr>
<tr>
<td>Laminin</td>
<td>110</td>
<td><img src="image" alt="Laminin" /></td>
</tr>
<tr>
<td>Collagen</td>
<td>300</td>
<td><img src="image" alt="Collagen" /></td>
</tr>
</tbody>
</table>

**Figure 9**: The basement membrane model (view from below, as the joining of three perlec an molecules can be seen)

**Figure 10**: The respiratory membrane model and a model of a red blood cell, to scale
Figure 11 Complete model of the respiratory membrane
CONCLUSIONS

Creating the respiratory membrane model honed valuable research skills, as well as modeling skills in Maya.

The respiratory membrane model and its use in the Human Visualization Project animation were significant first steps into this area of research, not only for RIT researchers, but also for the scientific community at large. As previously stated, little is known about the mechanisms by which nanoparticles cross the respiratory membrane. However, piecing together what data is currently available has allowed for the creation of a model that will serve as the foundation for RIT’s future studies about the respiratory membrane. In fact, such research is being conducted over the Summer 2008 quarter, where the model was successfully imported into VP-Sculpt.

Again, to the best of our knowledge, this model is the first model of the respiratory membrane—one that includes all layers and their components (i.e., surfactant; surface lining fluid; an alveolar epithelial cell with lipid bilayer and caveolae; the basement membrane with proteins perlecain, laminin, entactin, and collagen IV; and an endothelial cell with lipid bilayer and caveolae).

The model will not only be used for CFD analysis, but also serves as a visual aid for helping researchers to better understand the structure of the respiratory membrane.
IMAGING THE AIRWAYS

PART I.3 Promotional Materials

Creation of promotional materials for the project to educate the RIT community and other interested audiences.

ORIGINAL THESIS STATEMENT

No written proposal was submitted for Part 1.3 of the project. However, it was discussed with thesis advisors that the promotional materials, featured in the March 17-April 9, 2008 thesis show, would be a poster, a website, and a video.

BACKGROUND

The poster, postcard, website, and video were inspired and created through assignments in two classes:
1. An independent study in Nancy Ciolek's Information Design class
2. Ann Pearlman's Digital Video class

The Information Design class greatly helped to reinforce the principles of good design, such as structure (e.g., alignment through use of the grid system), emphasis (e.g., of words and images with use of color, size, and style), and information flow. Principles were reinforced with examples from innovators in information design, such as Edward Tufte, as well as through class critiques, both throughout the design process and on project due dates.

The Digital Video class was an invaluable introduction to Final Cut Pro and helped to reinforce the principles of filming and documentary design, such as digital-video-camera use, lighting, sound, storyboarding, titling, and editing. Virginia Orzel, an RIT alum and currently an independent filmmaker, also assisted (outside of class) with aspects such as image enhancement (e.g., size and color correction).

THE BODY OF WORK

Promotional materials for the IMAGING THE AIRWAYS thesis project consist of a poster, a postcard, a website, and a one-minute video. These materials were presented in the March 17-April 9, 2008 thesis show in the Bevier Art Gallery. The poster, website, and video were also presented at Imagine RIT, May 3, 2008.

Images associated with the upper respiratory and acinus models were acquired from a PowerPoint designed by Jackie Russo for her thesis defense. All other research images were created from Parts 1.1 and I.2 of the IMAGING THE AIRWAYS thesis project.

THE POSTER

Figure 12
Dimensions: 35” x 43”
Media: Illustrator, Photoshop

The IMAGING THE AIRWAYS poster was designed in Professor Nancy Ciolek's Information Design class. Many design principles were applied, such as:
• alignment of text and images through use of the grid system
• establishment of information hierarchy through use of font size and color
• establishment of relationships among pieces of information through use of color (e.g., all models created as part of the IMAGING THE AIRWAYS thesis project are highlighted in orange-red to match the title along the left side of the poster)
• information flow (e.g., the complete pathway model is the largest and most prominent image, drawing attention first to the center/upper left of the poster; the eye is then drawn around the poster in a clockwise direction.)

THE POSTCARD

Figures 13-14
Dimensions: 4.25” x 6”
Media: Illustrator, Photoshop

The postcard was designed specifically to advertise the March 17-April 9, 2008, thesis show and for visitors to take. The design of the front of the postcard mimics the design of the poster.

THE WEBSITE

Figures 15-29
Media: Flash, Illustrator, Photoshop
http://www.betsyskrip.com/thesis

The IMAGING THE AIRWAYS website was first designed as a PowerPoint in Professor Nancy Ciolek's Information Design class. The images, text, and design elements were then transferred into Flash.

The design for the original PowerPoint also influenced the design for all of the IMAGING THE AIRWAYS promotional materials. The colors, fonts, project logo, and other elements are consistent among the website, poster, postcard, and video.

The website buttons were designed using Photoshop and Illustrator. Some button logos were created in Photoshop by altering the original images (i.e., isolating the models from their backgrounds and making the models solid white). All other logos were created in Illustrator either with the pen tool or with Wingding and Apple Symbols characters.
Figure 12  IMAGING THE AIRWAYS Poster  35" x 43"  Illustrator, Photoshop
Figure 13  IMAGING THE AIRWAYS Postcard (front)
4.25” x 6”  Illustrator, Photoshop
IMAGING THE AIRWAYS

3D Modeling of a Complete Respiratory Airway for Use in Computational Dynamics Studies of Particle Deposition in the Lungs

March 17-April 9, 2008

Bevier Gallery
Rochester Institute of Technology
College of Imaging Arts and Sciences
James E. Booth Building 7A

OPENING RECEPTION
FRIDAY, MARCH 21, 2008
5:00-7:00 PM

(585) 475-2646
Mon-Fri 9:00 am - 4:30 pm
Mon-Thurs 7:00 pm - 9:00 pm
Sat 1:00 pm - 4:30 pm
Sun 2:00 pm - 4:30 pm

Figure 14 IMAGING THE AIRWAYS Postcard (back) 4.25” x 6” Illustrator
Figure 15: IMAGING THE AIRWAYS Website: Homepage

WELCOME

The following project is a collaboration that spans across various departments and graduating classes.

The end-product, for now, is a model of one complete respiratory pathway, from the mouth (where air is inhaled) to the respiratory membrane (where gas exchange occurs with the blood).

My contributions to this project have been:

1. to model the bronchial path between the upper respiratory tract and a respiratory acinus, two models that were created last year

2. to model the respiratory membrane at the cellular and molecular levels in order to visualize nanoparticle transport into the bloodstream

3. to create promotional materials for the project to educate the RIT community and other interested audiences
Figure 16 IMAGING THE AIRWAYS Website: Anatomy 780 x 600 px Flash, Illustrator, Photoshop
Figure 17  IMAGING THE AIRWAYS Website: Model

3D Modeling of a Complete Respiratory Airway for Use in Computational Flow Dynamics Studies of Particle Deposition in the Lungs

- Oral Cavity
- Larynx
- Trachea
- Bronchi (Generations 0-5)
- Bronchioles (Generations 6-10)
- Acinus (enlarged to show detail)

780 x 600 px  Flash, Illustrator, Photoshop
Figure 18  IMAGING THE AIRWAYS Website: Oral Cavity Model  780 x 600 px  Flash, Illustrator, Photoshop

The oral cavity model was made from a cast of a student's mouth. Aquasil Ultra LV Smart Wetting Impression Material was spooned into the student's mouth and allowed to dry while the mouth was slightly open and at rest.

After the impressions were made, they were scanned at a resolution of 0.003 inches using the Maker Z140 3D Scanner with a Romer Cimcore Infinite Arm. The arm attachment is used to trace over the surface of the object, which translates into the computer to create a 3D model.
**Figure 19** IMAGING THE AIRWAYS Website: Larynx Model

**MODELER:** Jessica Weisman

The oropharynx, laryngopharynx and larynx model was based on dimensions taken from multiple sagittal and coronal medical photographs and a partial cadaver cast of the throat. The cadaver of an elderly woman was prepared, and silicone rubber was injected through the bottom of the trachea and through the mouth. The casting material was then allowed to dry and removed from the cadaver. Sketches were made and used in Maya to create a 3D model.
The trachea/bronchi model was created using slices of the thoracic cavity from the Visible Human Project. The slices were imported into 3D Doctor and converted to grayscale in order to increase contrast among the different anatomical structures. Outlines of the desired structures were then generated by the software based on those contrasts. Some boundaries were also drawn and refined by hand.

The software rendered a 3D surface model by connecting the defined outlines from all of the segmented images using poly-edges and imported into the polygon-based surface. The file was exported as an OBJ and imported into 3D Studio Max. Sculpt was used to smooth the surface and to refine and complete branches specifically. Branches beyond the 5th generation were extruded off.

Figure 20 IMAGING THE AIRWAYS Website: Trachea Model 780 x 600 px Flash, Illustrator, Photoshop
Figure 21  IMAGING THE AIRWAYS Website: Bronchi Model

**3D Modelling of a Complete Respiratory Airway for Use in Computational Flow Dynamics Studies of Particle Deposition in the Lungs**

**MODELER:** Betsy Skrip

The model of bronchi generations 6-10 and bronchiole generations 10-19 was created in Maya.

The dimensions were obtained from the 1971 research paper Models of the human bronchial tree by Keith Horsefield, Gladys Dart, Don E. Olson, Giles E. Filley, and Gordon Cumming.

A model of the left lung was created using 3D Design and slices from the thoracic region of the Visible Human Project (VHP). The bronchi/bronchiole model was placed to fit in the lungs model and oriented to fit in the lower posterior lobe.

**780 x 600 px    Flash, Illustrator, Photoshop**
Figure 22  IMAGING THE AIRWAYS Website: Acinus Model  780 x 600 px  Flash, Illustrator, Photoshop
Figure 23  IMAGING THE AIRWAYS Website: Maya to CFD  780 x 600 px  Flash, Illustrator, Photoshop
The next model to be created is the airway of an asthmatic. Bronchioles in asthmatic suffers are constricted, thereby reducing air flow. Creation of this model will involve altering the geometry of the healthy-state airway model.

Using data from Models of the human bronchial tree, we plan to eventually create a complete model of the entire respiratory tract. This would involve modeling one complete pathway in all lobes of both the left and right lungs.

Other 3D models of the respiratory system do not extend beyond the alveoli. The goal of this project, which was started in summer 2007, is to continue this visual reduction to the nanoscale level (less than 100 nm) and model cellular and molecular detail of the respiratory membrane.

more about the respiratory membrane...

Figure 24 IMAGING THE AIRWAYS Website: Future Work  780 x 600 px  Flash, Illustrator, Photoshop
Figure 25  IMAGING THE AIRWAYS Website: Respiratory Membrane  780 x 600 px  Flash, Illustrator, Photoshop
Figure 26  IMAGING THE AIRWAYS Website: Thesis Show  780 x 600 px  Flash, Illustrator, Photoshop
Figure 27: IMAGING THE AIRWAYS Website: Video

- 3D Modeling of a Complete Respiratory Airway for Use in Computational Flow Dynamics Studies of Particle Deposition in the Lungs
- Watch a short video about the project.

Dimensions: 780 x 600 px
- Flash, Illustrator
Figure 28  IMAGING THE AIRWAYS Website: Poster

Dimensions 35” x 43”
File Size 2.5 MB
Download PDF

780 x 600 px  Flash, Illustrator, Photoshop
Figure 29  IMAGING THE AIRWAYS Website: Mentors and Modelers  780 x 600 px  Flash, Illustrator, Photoshop
IMAGING THE AIRWAYS

THE VIDEO
Title: IMAGING THE AIRWAYS Promotional Video
Duration: 1 min
Medium: Final Cut Pro
http://www.betsyskrip.com/thesis
(Movie section)

The IMAGING THE AIRWAYS Promotional Video is a “sneak peek” at the overall thesis work, meant to attract people’s attention and interest. The video does not fully explain the research or the images presented. However, the video is contained within the website where such information can be obtained and does summarize the project, condensing all of the most important information into a one-minute, visually and aurally aesthetic presentation. Specifically, images of the models and segments from interviews with Dr. Doolittle and Dr. Robinson were carefully selected to highlight the most important aspects of the thesis research.

The video presents:
• the project’s purpose
  Dr. Doolittle explains that the project involves looking at particle deposition in the human lung; Dr. Robinson explains that the model will be a pathway from the upper airway to the site of gas exchange.

• the models
  Models of the airway, respiratory membrane (Figure 32), and alveolar sacs with capillaries (Figure 33) are featured.

• how the models were created
  Images from 3D Doctor are shown (Figure 30); they are explained elsewhere on the website.

• significant aspects of the project
  Dr. Doolittle highlights the model of the basement membrane; Dr. Robinson states that the project is the first to create a complete model of the airways from the atmosphere to the site of gas exchange.

Methods
The video was created in Professor Ann Pearlman’s Digital Video class using Final Cut Pro. Many methods had been learned in previous class assignments (e.g., principles of digital-video-camera use, lighting, sound, storyboarding, titling, and editing). Some methods, however, were learned specifically through creation of this video:

• Overlapping animations
  Still images were animated in Final Cut by keyframing image properties such as location, scale, and opacity. The animations were then overlapped with each other or with still images. Examples include the nanoparticle moving across the respiratory membrane (Figure 32, left) and the project logo moving with the acinus model (Figure 33, right).

• Importing QuickTime movies
  The movie of the alveolar sacs (Figure 33) is a QuickTime file imported into Final Cut Pro. Discovery of this method for bringing Maya- and Flash-generated animations into Final Cut made creation of the HVP and CollaboRITorium animation possible.

• Importing a QuickTime movie into Flash
  Once the video was completed in Final Cut, it was exported as a QuickTime file and imported into the Flash website. Importing involves converting the QuickTime file to an FLV (Flash Video) file. Learning this method facilitated importing the HVP and CollaboRITorium animation into the HVP website.

Figure 30 Images from 3D Doctor
Figure 31  Interviews with Dr. Richard Doolittle and Dr. Risa Robinson

Figure 32  Left, nanoparticle crossing respiratory membrane; right, basement membrane proteins

Figure 33  Acinus QuickTime file imported into Final Cut Pro
CONCLUSIONS

The Poster and Postcard
Creation of the poster and postcard as part of Professor Nancy Ciolek’s Information Design class was an invaluable learning experience in the principles of design. Projects following the thesis project have been greatly influenced by the experience and knowledge gained through the Information Design class.

The Website
Design principles were reinforced through creation of the website as well, which was first designed as a PowerPoint presentation in Professor Ciolak’s Information Design class. The PowerPoint was created before the poster; therefore, designing the PowerPoint was also a worthwhile experience in gathering and summarizing information for presentation to a specific audience and inspired the style for all of the project’s promotional materials.

Creating the website reinforced skills in Flash, as well as in Photoshop and Illustrator (particularly with designing the buttons). The procedure for importing a QuickTime movie into Flash as an FLV (Flash Video) file was also learned.

The Video
Creation of the promotional video in Professor Ann Pearlman’s Digital Video class was an invaluable experience in learning Final Cut Pro and, again, worthwhile practice in summarizing information. The knowledge gained using Final Cut Pro allowed for the creation of the Human Visualization Project animation.
II. Creation of an Educational Animation about the Respiratory System for Use in the Human Visualization Project and CollaboRITorium

ORIGINAL THESIS STATEMENT

In previous quarters, Maya (a 3D computer graphics program) was used to create models of the respiratory tract and the respiratory membrane’s five main components: (1) surfactant (a lipid monolayer), (2) surface lining fluid, (3) alveolar epithelial cells, (4) basement membrane, and (5) endothelial cells.

In the Spring 2008 quarter, an animation will be made using the previously created models in order to educate viewers about the respiratory system and about current studies in nanoparticle transport across the respiratory membrane into the bloodstream.

The work will be projected in RIT’s CollaboRITorium, a specialized classroom designed by RIT students. The CollaboRITorium features four large (wall-height) screens whose orientation can be changed to form a cube, making the learning experience immersive. The work will also be available online as part of RIT’s Human Visualization Project website.

The project will be created through two independent studies: the animation and website will be created through collaboration with professor Shaun Foster from the Computer Graphics Design Department; projection in the CollaboRITorium will be accomplished through an independent study in Dr. Jake Noel-Storr’s Honors class Frontiers of Science II, a course in which “students explore a topic of current research on campus through interactions with faculty and research groups while learning about aspects of science communication and presentation and developing a digital interactive, immersive, science learning experience.”

This project will help to greatly enhance my skills with Maya, particularly in texturing and creating realistic environments. Such a large-scale teaching project will also test and greatly increase my medical illustration skills—particularly the art of organizing and presenting information in easy-to-understand, easy-to-navigate, and attractive formats.

BACKGROUND

The Human Visualization Project (HVP)
The HVP is a collaboration to create an interactive model of the human body and an online learning platform available for students and teachers both within and outside the RIT community. The project will consist of models and animations of the body’s systems (e.g., skeletal, muscular, cardiovascular, respiratory, urinary, endocrine, and digestive), both at the macroscopic and microscopic levels.

The team spans different graduating classes and disciplines: Biological Sciences and Chemistry (College of Science), Medical Illustration (College of Imaging Arts and Sciences), Computer Gaming and Information Technology (College of Computing and Imaging Sciences), and Mechanical Engineering (College of Engineering).

The CollaboRITorium
The CollaboRITorium is an immersive learning environment and an incubator for the design of new technologies, designed by RIT students and faculty.

Spearheaded by Dr. Jon Schull in Information Technology and his class Innovation and Invention, the project currently features three immersive DOMEs (Digital Omnidirectional Multimedia Environments). Each DOME consists of four screens that can be folded into a cube. Viewers stand inside of the cube as images are projected onto each of the four walls, thus creating an immersive environment.

Furthermore, most images and animations projected in the cubes are interactive. Using a Wii remote, viewers can navigate through a virtual landscape or an educational game and rotate, zoom, and pan through 3D models.

Independent Studies
The IMAGING THE AIRWAYS animation and revised Human Visualization Project website were created in the Spring 2008 quarter through two independent studies:

1. A three-credit independent study with Shaun Foster from the Computer Graphics Design Department
2. A one-credit independent study in Dr. Jake Noel-Storr’s Honors class, Frontiers of Science II.

For the animation, several new methods using Maya were learned and implemented through working with Shaun Foster:

- use of the Paint Effects tool and manipulation of the resulting models to create the bronchial tree (Figure 38)
- the creation and animation of glowing edges (e.g., the texture on the human figure) using a ramp shader
- the creation of metallic-looking surfaces for the basement membrane proteins using an environmental ball shader (Figures 51 and 53)
- video compression using the
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H.264 codec

Professor Foster also provided valuable feedback about the aesthetics, pace, and understandability of the animation at its various stages of development.

The Frontiers of Science II class required students to research a topic of their choice and develop content to present their research in the CollaboRITorium classroom (A-400).

Work completed as part of the independent study included:
• creating an interactive platform (i.e., the revised Human Visualization Project website) to feature the animation
• designing part of the animation to extend to all four walls of the cube.

THE BODY OF WORK

Animation and website at:
http://www.betsyskrip.com/hvp
(Note: The animation is located in the Respiratory section.)

THE ANIMATION

Duration: 5 min
Media: Flash, Final Cut Pro

The HVP and CollaboRITorium animation is a video to educate viewers about the structure and function of the respiratory system and about current research (i.e., nanoparticles and the respiratory membrane model). Unlike in the thesis promotional video, the images in the animation are explained through narration.

The animation illustrates gas exchange at the macroscopic level (Figures 36 and 37) and microscopic level (Figure 44) and guides viewers through this visual reduction in size.

The video contains six main sections:
1. Introduction
2. \( \text{O}_2 \) and \( \text{CO}_2 \) Exchange
3. The Respiratory Membrane
4. Current Research
5. The Basement Membrane
6. Summary

Methods
The overall animation consists of many smaller animations created in Maya and Flash. These short animations were exported from Flash as QuickTime files and imported into Final Cut Pro, where they were arranged and compiled with narration and music.

Introduction
The animation first provides an orientation of the lungs inside the human body (Figures 34 and 35). The lung models were created in Maya in Summer 2007 using Netter illustrations (Netter, 1979) as references. The model of the human body was purchased by the Human Visualization Project and has been used in other student animations for the HVP. The larynx model was created by Weisman (2007), and the trachea/bronchi model was created by Russo (2007).

To visually explain the inhalation of oxygen and exhalation of carbon dioxide, the thoracic wall and lungs were animated in Maya to expand and contract (Figures 34 and 35), and colored layers were animated in Flash to highlight the path between the atmosphere, lungs, and body (Figures 36 and 37). The expansion and contraction were achieved with the flare nonlinear deformer in Maya. The path highlights were achieved in Flash by animating shapes placed on masking layers.

The animation next shows the bronchial tree—a model created in Spring 2008 using a tree Paint Effects brush in Maya. The settings on the brush were altered to increase the number of branches and to eliminate any flowers, leaves, and other botanical features except buds. Buds were kept to represent the alveolar sacs, and their size and color were altered to increase their prominence.

Once the bronchial tree model was created using the Paint Effects brush, it was converted to polygons, and faces were deleted to make the overall structure fit the shape of the lungs. Specifically, the bronchial tree model was placed inside the lung model in Maya, and any branches extending outside of the lung model were trimmed off.

\( \text{O}_2 \) and \( \text{CO}_2 \) Exchange
A green highlight at the edges of the bronchial tree (Figure 39) helps to introduce the alveolar sacs—a model created in Summer 2007 in Maya. Animated masking layers were again used in Flash to show the flow of \( \text{CO}_2 \)-rich blood to the sac and \( \text{O}_2 \)-rich blood away from the sac (Figure 41).

The Respiratory Membrane
The respiratory membrane section features artwork made in Summer 2007: a cross-sectional view of an alveolus and a capillary made in Illustrator, and a Maya model of a red blood cell (Figures 42, 43, 44, and 45).

The cross-sectional Illustrator drawing first appears directly over an alveolus and capillary on the 3D model, thus establishing the relationship between the two views. The cross-sectional drawing then enlarges to feature the respiratory membrane, whose parts are highlighted (using Flash) as they are named in the narration. Flash text and arrows illustrate the movement of \( \text{O}_2 \) and \( \text{CO}_2 \) across the membrane (Figure 44).
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Current Research
In order to illustrate a nanoparticle crossing the respiratory membrane and entering the bloodstream (Figures 45 and 46), a buckyball model was obtained from the public-domain site www.3dchem.com. The file was saved as a PDB (Protein Data Bank) file and opened in Chimera, the University of California San Francisco’s Molecular Modeling System. From Chimera, the model was exported as a VRML and imported into Cinema 4D.

The model in Figure 45 was rendered in Cinema 4D as a PNG and animated in Final Cut Pro. The model in Figure 46 was exported from Chimera as an FBX and imported into Maya, where it was parented to the rear red blood cell to flow through the blood vessel. The blood-vessel animation was created in Winter 2007 as an assignment in the class 3D Bio and Organic Forms II. The buckyball model was acquired in Spring 2008.

The nanoparticle in Figures 47 and 49 appears as a solid sphere, as it was created before knowledge of other molecular imaging sites (such as 3dchem.com) was gained. As described for Part I.2, the respiratory membrane model components were constructed in Maya and are to scale (based on available data).

In the animation, the layers of the respiratory membrane model are explained nonverbally. An image of the respiratory membrane model was animated in Final Cut Pro to overlap the Illustrator diagram (Figure 50). Therefore, layers of the respiratory model (i.e., surfactant, alveolar epithelial cell, basement membrane, and endothelial cell) lay directly over their corresponding layers in the Illustrator diagram—layers that were identified earlier in the narration.

The Basement Membrane
The basement membrane model (Figures 48 and 51) of proteins collagen, laminin, perlecan, and entactin was created in Summer 2007. The metallic-looking surface (Figure 51) was created using a technique taught by Professor Shaun Foster.

The technique involves taking a photograph of a reflective surface (e.g., a garden globe), cropping and coloring the photograph in Photoshop, and applying the image to an Environmental Ball shader in Maya. The Environmental Ball shader is then connected to the color, specular color, and reflected color inputs of a Phong shader.

CollaboRITorium animation
For the CollaboRITorium animation, the basement-membrane fly-through was constructed to span all four screens of the DOME. The process was learned in Summer 2007 from Julia Lehman, MFA Medical Illustration, Class of 2007. Four cameras were created in Maya and rotated at 90° from each other.

The cameras were then grouped, and the group was animated to move throughout the basement membrane model. JPEGs were rendered from each camera and imported into four separate QuickTime files. The four QuickTime files were then assembled into one QuickTime file using the following procedure:

1. Adding one QuickTime file to another
For three of the files, all of the frames were selected and copied. In the fourth file, the playhead was set to the beginning of the movie, and the frames from videos 1-3 were pasted into it (Edit > Add To Movie).

2. Positioning the movies
In the fourth file, the positions of all four files were altered by going to Window > Show Movie Properties, selecting the Resources tab, selecting the file names, and then, under the Visual Settings tab, changing the “offset x” value for each file by the file widths. For example, because each video was 800 pixels wide, the offset x values were:

- video 1  offset x = 0
- video 2  offset x = 800
- video 3  offset x = 1600
- video 4  offset x = 2400

The resulting video, therefore, was 3200 pixels wide, with the four separate videos aligned horizontally (Figure 53).

In Summer 2007 it was found that, in order for the four images to line up properly, the shutter angle of the Maya cameras must be set to 90 and the angle of view set to 97 (Figure 52). This formula worked with the lung model, but was not successful with the respiratory membrane model (Figure 53). Larger angles of view were tried, but to no avail. The reason for this misalignment is currently unclear; however, the CollaboRITorium team will be working on the file over the Summer 2008 quarter to resolve the issue.

Narration and Music
The animation was narrated by Ryan Fuller, a first-year graduate student in RIT’s Electrical Engineering Department. The narration was recorded using Soundtrack Pro and imported into Final Cut Pro as AIFF files.

All music was acquired from Garage Band. The files were imported into iTunes, saved as AIFF files, and imported into Final Cut Pro.
Figure 34
Exterior surface of lungs (exhalation)

Figure 35
Exterior surface of lungs (inhalation)

Figure 36
Oxygen moving from the lungs to the body

Figure 37
Carbon dioxide moving from the body to the lungs

Figure 38
Bronchial tree

Figure 39
Green highlight to indicate branch ends (like leaves)
**Figure 40**
A single alveolus of an alveolar sac

**Figure 41**
Capillaries carrying CO$_2$ to and O$_2$ away from the sacs

**Figure 42**
Cross section of an alveolus and a capillary

**Figure 43**
The respiratory membrane (highlighted in yellow)

**Figure 44**
O$_2$ and CO$_2$ crossing the respiratory membrane

**Figure 45**
A nanoparticle crossing the respiratory membrane
Figure 46
*A nanoparticle flowing in the blood with red blood cells*

Figure 47
*A nanoparticle and caveolae in an alveolar epithelial cell*

Figure 48
*Basement membrane proteins*

Figure 49
*A nanoparticle and caveolae in an endothelial cell*

Figure 50
*3D model of the respiratory membrane*

Figure 51
*Basement membrane proteins*
Figure 52. Different angles of view for the cameras in Maya affect how images from the four cameras align. The above images of the lung model each consist of three images, rendered in Maya by three cameras set at 90° from each other. These images were assembled in Photoshop to test which angle of view was needed for the images to align properly.
(a) The angle of view for the cameras was set at 90°. The angle of view is not wide enough, therefore a harsh line of contrast (seam) results where part of the model is missing (i.e., in an area neither of two cameras was able to capture).
(b) The angle of view was set at 95°. More of the model was captured, but a line of contrast is still discernible.
(c) The angle of view was set at 97°. No lines of contrast are visible.

Figure 53. Although the angle of view was set to 97° for the respiratory membrane fly-through, lines of contrast are still visible.
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THE HVP WEBSITE
Medium: Flash
http://www.betsyskrip.com/hvp

The design for the HVP website was inspired by another HVP website created in Summer 2007 by Randall Church (Figure 54), http://www.rit.edu/~ez-viz/adobe. Church’s site was designed specifically to document the Summer 2007 research. The site also features all other student animations created for the HVP as of that summer.

The new HVP website (Figure 55) not only features the respiratory animation (Figure 56), but also organizes the other student animations into their respective systems (skeletal, cardiovascular, respiratory, urinary, endocrine, and digestive). Thumbnail buttons (Figure 57) and a slideshow (Figure 58) were created by taking screen shots of the animations on the Summer 2007 site and altering the image sizes in Photoshop.

CONCLUSIONS

The Animation
Many skills were learned and reinforced through creation of the animation:
• script-writing and storyboarding
• using input and output connections in Maya to create attractive surface textures
• animating with Flash
• stitching Flash animations together with Final Cut Pro
• working with a narrator and recording in a soundproof booth using Soundtrack Pro

Methods for creating a four-panel QuickTime movie for display in the CollaboRIT orium were also learned and applied. Although setting the angle of view to 97 for each of the four Maya cameras did not produce a seamless image for the respiratory membrane fly-through (Figure 35), the CollaboRIT orium team will be analyzing the files to devise a solution.

The HVP Website
Creating the HVP website was another valuable reinforcement of Flash web design skills, including importing video. The experience also reinforced information design skills, as it involved reorganizing much of the information on the Summer 2007 HVP site into a new format.
Figure 55  HUMAN VISUALIZATION PROJECT Website: Homepage  800 x 600 px  Flash, Photoshop
Figure 56  HUMAN VISUALIZATION PROJECT Website: Respiratory section  800 x 600 px  Flash, Photoshop
Figure 57  Thumbnail buttons created by taking screen shots of the animations on the Summer 2007 HVP site and altering the image sizes in Photoshop.

(a) Skeletal animations created by Erin Topley, Multidisciplinary Studies and Corrine Grande, Biology.

(b) Endocrine animations created by Britney Peters, BFA Medical Illustration, Class of 2007.

(c) Heart animation created by Nathan Skinner, Jamestown Community College, Class of 2007. Hemoglobin animation created by Laura Garell, MS Bioinformatics, Class of 2007 and Paul Yacci, MS Bioinformatics, Class of 2009.

(d) Liver animations created by Thomas Nowaki, MFA Medical Illustration, Class of 2006.

Figure 58  The above images were created by taking screen shots of the animations on the Summer 2007 HVP site and altering the image sizes in Photoshop. The images were then compiled into a slideshow in Flash for the Human Visualization Project website.

(a) Pancreas animation created by Britney Peters, BFA Medical Illustration, Class of 2007. (b) Kidney animation created by Katie Tower, BFA Medical Illustration, Class of 2006 and Mylissa Kowalski, BFA Medical Illustration, Class of 2006. (c) Liver animation created by Thomas Nowaki, MFA Medical Illustration, Class of 2006. (d) Hemoglobin animation created by Laura Garell, MS Bioinformatics, Class of 2007 and Paul Yacci, MS Bioinformatics, Class of 2009. (e) Insulin animation created by Britney Peters, BFA Medical Illustration, Class of 2007.
OVERALL CONCLUSIONS

The IMAGING THE AIRWAYS project was an invaluable experience toward earning a Master of Fine Arts degree in Medical Illustration. Many skills were learned and reinforced, creating a strong foundation for a career in the discipline and in the arts in general. Overall, the project helped to strengthen several abilities that are critical to being a Scientific/Medical Illustrator:

• The ability to locate and interpret available data and images and to use one's imagination and critical thinking skills to create artwork that is unique. To the best of our knowledge, the complete respiratory pathway model and the respiratory membrane model are the first of their kind and will help to advance current research about the respiratory system.

• The ability to collaborate with researchers, understand their research, and create artwork that meets their needs and vision.

• The ability to problem-solve and to find new ways of working that are more efficient and produce better-quality results.

• The ability to organize information into different types of presentations that span across the media (i.e., print, web, and video).

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• Jackie Russo, MS Mechanical Engineering, Class of 2007: Created the oral cavity model and the trachea to bronchi generation 5 model; supplied images for Part I promotional materials
• Jessica Weisman, MFA Medical Illustration, Class of 2007: Created the larynx and acinus models
• Julia Lehman, MFA Medical Illustration, Class of 2007: Established a formula for creating a four-panel animation for display in the CollaboRIT orium
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• Ryan Fuller, narrator for the 3D Modeling of the Respiratory System animation
• Donald Arday, School of Art Department Chairperson

REFERENCES


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<th>Role</th>
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<td>Chief Advisor</td>
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