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# Generation of Pig Airways using Rules Developed from the Measurements of Physical Airways

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## Abstract

**Background:** A method for generating bronchial tree would be helpful when constructing models of the tree for benchtop experiments as well as for numerical modeling of flow or sound propagation in the airways. Early studies documented the geometric details of the human airways that were used to develop methods for generating human airway tree. However, methods for generating animal airway tree are scarcer. Earlier studies suggested that the morphology of animal airways can be significantly different from that of humans. Hence, using algorithms for the human airways may not be accurate in generating models of animal airway geometry.

**Objective:** The objective of this study is to develop an algorithm for generating pig airway tree based on the geometric details extracted from the physical measurements.

**Methods:** In the current study, measured values of branch diameters, lengths and bifurcation angles and rotation of bifurcating planes were used to develop an algorithm that is capable of generating a realistic pig airway tree.

**Results:** The generation relations between parent and daughter branches were found to follow certain trends. The diameters and the length of different branches were dependent on airway generations while the bifurcation angles were primarily dependent on bifurcation plane rotations. These relations were sufficient to develop rules for generating a model of the pig large airways.

**Conclusion:** The results suggested that the airway tree generated from the algorithm can provide an approximate geometric model of pig airways for computational and benchtop studies.

**Keywords:** Airway tree; Algorithm; Bifurcating plane; Generation; Pig

## Introduction

### Objectives

Realistic geometric models of the airways are essential for computational and experimental studies of fluid dynamics and acoustic propagation in the airways. Earlier studies of sound propagation in the airways and lungs suggested their utility for diagnosis of pulmonary conditions [1-6]. Sound propagation in the pulmonary system have been studied using animal [7-9] and benchtop [10,11] experiments. Numerical [12-15] models were developed and validated using animal experiments [16-18]. The objective of the current study is to develop an algorithm for generating pig airway trees with realistic geometry using measured values of branch diameters, lengths, bifurcation angles, rotation of bifurcating planes.

### Available information on airway geometry

Several studies [19-21] have documented human airway geometry, while some studies discussed the airway geometry in dog, rat, sheep and hamster [22-24]. Details of pig airway geometry are scarce or incomplete [25,26]. Since the morphology of animal airways can be significantly different from humans, approximating pig airway geometry by its human counterpart can lead to errors in both computational and numerical studies.

### Airway classification methods

Airways can be characterized by generations [27] and/or ordering schemes [20,21,28]. For instance, Weibel [27] categorized the airways by labeling each airway by a generation number (starting with generation zero at the trachea) that is increased by one at each branching. In this method, all bifurcations were assumed symmetric, where each parent airway bifurcates into two identical twins with a higher generation.

On the other hand, Horsfield [20,21] proposed an ordering scheme, where the peripheral conducting airways are assigned order 1 and the order increases by one at each bifurcation up from the peripheral airways towards the trachea. Strahler [28] adopted a similar ordering method where the parent branch is one order higher than its two children branches of the same order. On the other hand, if the two children branches are not symmetric or have different orders, the parent branch order is equal to the child branch with the higher order. Since these ordering methods start the numbering system at the peripheral airways, they would require a tree that contains at least some of these branches.

In the current study, generation numbering [27,29-31] will be used since the available airway trees deal with relatively larger airways that did not contain the terminal bronchioles.

There are several studies that described branching networks such as airway and vascular trees. Murray [32] used principle of minimum work to describe the branching network of the vascular tree. Murray assumed that the total power loss inside a blood vessel is summation of loss due

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to viscous drag and the power required to metabolically maintain the volume of blood and vessel tissue. This yielded a relation between the parent and daughter radii as well as, the relationship between branching angles and parent daughter radii known as Murray's law.

While the original Murray's law was derived for blood vessels, several studies [33,34] used that law to describe airway trees. Here, a generalized form of Murray's law where the exponent in the law varied [21,33-35] was used.

Kitaoka [34] proposed a branching network based on the premise that the fluid flow is proportional to the region it is supplying. The branching network was assumed to be dichotomous in nature, where airway diameters and branching angles are determined from relations provided by previous studies [32,35]. The length of a branch was set to be three times its diameter. The parent and daughters stayed in the same plane, which is called the branching plane. Branching planes for the consecutive generations were assumed to be perpendicular. Some supplementary rules were developed in this study to account for corrections in branching plane, branching angles, length to diameter ratio and rotation angle of successive branching to achieve a realistic branching patterns.

Tawhai [36] proposed a volume halving algorithm to develop the airway branching network. Stating with an initial airway branch and a lung region, a plane containing that branch and the center of mass of the lung region will split that region into two "halves". The daughter branches of the initial branch will then start from the parent end and grow in the direction of the center of mass of the halves. The daughter length is determined based on a fractional distance from the center of mass called "branching fraction". If the generated branch length is less than or equal to a predefined length limit, the branch is termed as a terminal branch. The branch diameters are assigned using Horsfield [20,21] orders. The branch angles were adjusted based on predefined angle limits.

Another method of generating a branching network is to use constrained constructive optimization (CCO) of a given tree volume [33,37,38]. Here, a perfusion lung volume is selected inside which the branching network will grow. The tree is required to fill the perfusion volume as evenly as possible without intersecting segments. The tree is optimized to have a minimum volume, with branches that follow the generalized Murray's law. In this method, the terminal branches are assumed to have the same terminal pressure and the total number of segments is about twice the number of terminal branches, which would be set by the user. A branching network created using CCO depends on the number of terminal segments. CCO algorithm can be used to grow terminal branches on top of a preexisting base tree which was extracted using image segmentation from CT or MRI [33].

## Available Information on Pig Airway Tree

To generate a pig airway tree model, the geometric features of pig airway tree are needed. The current study used the measurements of physical model of pig airway tree from previous studies [29-31] to develop rules that can be used to generate a realistic model of the pig airways. Table 1 summarizes the measured dimensions and angles of pig airway tree discussed in the previous studies [29-31].

For example, the logarithm of the diameter was found to be linearly proportional to airway generations and the branch length was linear up to generation 4 with the exception of generation 2. For generations higher than 4, the branch length varied between 5 to 12 mm without a clear trend. Most bifurcations were asymmetric where a parent branch bifurcates into two daughters of dissimilar diameters. The study showed that this bifurcation can happen in two different planes. The first plane is the one containing the trachea and mainstem bronchi. Major daughters tended to stay in that plan. When minor daughters approximately stay in this plane, the bifurcation is called an in-plane bifurcation. The second plane is perpendicular to the first and contains out-of-plane minor daughters. Previous study [29-31] found that the diameters and bifurcation angles for out-of-plane bifurcation were different than in-plane bifurcation cases.

In addition, branching angles were found to depend on rotation of bifurcation plane and appeared independent of generations.

## Parent Daughter Branch Relationship based on Generation of Airways

The difference in generation between two daughters is defined as "delta" similar to studies of human airways [21,36]. Since pig airway is predominantly monopodial, the relationship between delta and parent airway generation is expected to be different than human airways. In the current study, delta was different for in-plane and out-of-plane bifurcations as seen in Figure 1a and 1b. In Figure 1a, the relation between delta and parent airway generation may be represented with an approximate linear trend up to generation 10 and varied between 2 and 6 at higher generations without a clear trend. Please note that the delta for the tracheal bronchus is relatively high (i.e. delta≈11). While this value is not shown in the figure, it is included in the proposed algorithm. Figure 1b shows that delta for out-of-plane bifurcation followed an approximate linear trend.

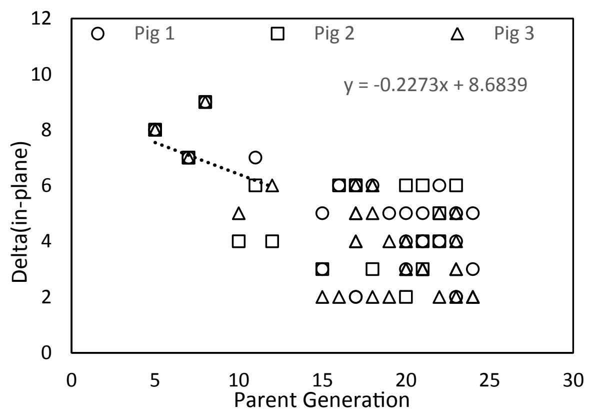


**Figure 1a:** Delta (in-plane) vs Parent Airway Generation.

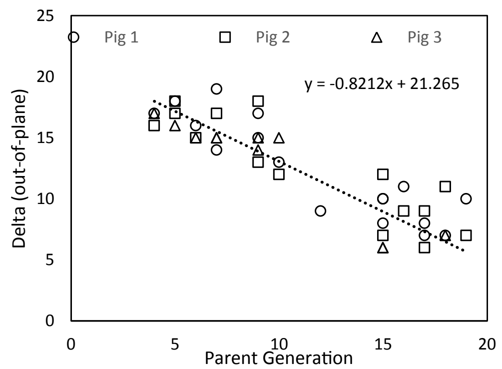


**Figure 1b:** Delta (out-of-plane) vs Parent Airway Generation.

The generation difference between a parent branch and a major daughter is defined as delta1 in the current study. Figure 2 shows delta1 against parent airway generation. Most of the delta1 values varied between 0 and 2 up to generation 10 and between 0 and 6 at higher generations.

## Pig Airway Generation Algorithm

To generate an airway tree, the starting point is the location of the proximal trachea and its direction vector. With this information, a cylindrical airway with tracheal diameter and length is generated and will serve as a parent.

Generally speaking, the algorithm uses the generation of each parent branch to determine the daughter generations from generation relations (delta1 and delta). Next, the bifurcation plane angle, bifurcation angles, and daughter diameters and lengths will be calculated.

More specifically, a unit vector ($n_1$) along the direction of parent branch is defined. Another unit vector ($n_2$) is then defined as the direction vector of the plane where the parent and daughter branch axes exist. In addition, a unit vector ($n_3$) that is perpendicular to both $n_1$ and $n_2$ is found by the cross product ($n_1 \times n_2$). $n_3$ will be in plane $n_2$.

Direction vectors for the major and minor daughters are then determined using the following equations

$$v_1 = n_1 + n_3 * \tan(\text{angle1}) \qquad (1)$$

$$v_2 = n_1 + n_3 * \tan(\text{angle2}) \qquad (2)$$

Where $v_1$ and $v_2$ are the direction vectors for major daughter vector for minor daughter and angle 1 and angle 2 are the bifurcation angles for major and minor daughters, respectively.

Figure 3 illustrates an example of a bifurcation where unit vectors for $n_1$, $n_2$ and $n_3$ are used to determine the direction vectors for major and minor daughter branches $v_1$ and $v_2$, respectively.

The major and minor daughters of are then generated as cylinders with their diameters and lengths along their respective direction vectors.

The end points of each branch are stored to be used as the starting points for the next branching. These recursive procedures repeated a number of times to generate a tree with a certain number of generations. The airway generation algorithm is also described in flow chart in Figure 4.

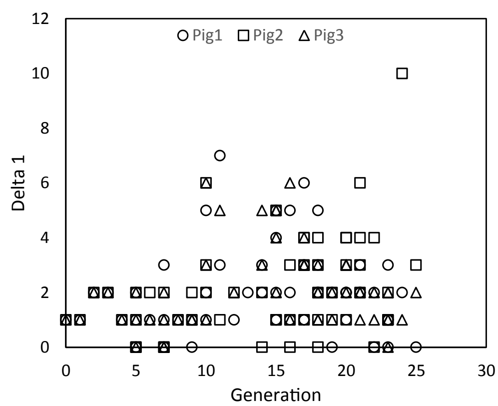


**Figure 2:** Delta 1 vs Parent Airway Generation.

This algorithm was used to generate the pig airway tree with 25 generations which is shown in Figure 5. Figure 6 shows the airway tree extracted from CT images of three pig lung. All three lung airway trees show similarity in terms of morphometry of the lung airways. The lungs show the monopodial morphology of pig airways. By comparing figure 5 and 6 it can be seen that the generated airway tree has comparable general features. Further studies would require to directly compare the detail morphology of the constructed and actual airways.

## Discussion

Realistic model of the pig airway tree is desired when performing computer simulations of flow or sound transmission in the pig airways.

| Diameter | Length | Angle 1 | Angle 2 | Bifurcation Plane Angle |
|---|---|---|---|---|
| log D = − 0.0438 ∗ *Generation* + 1.3094 . For Generation< 12 | *L* = − 7.51 *Generation* + 37.556 For Generation 0 to 4 except Generation 2. | 15° ± 2 for in-plane bifurcation | 45° ± 5° for both in-plane and out-of-plane bifurcation | Alternates between 0°, 90° and -90° with three successive bifurcations. |
| log D = − 0.0228 ∗ Generation + 1.0979 For 12 ≤ Generation ≤ 20 | L=10 mm at Generation 2 L = 8± 3 mm | 0° for out-of-plane bifurcation | | |
| log D = − 0.0418 ∗ Generation + 1.488 For Generation > 20 | For Generation > 4 | | | |

**Table 1:** Geometric features of pig airways [29-31].

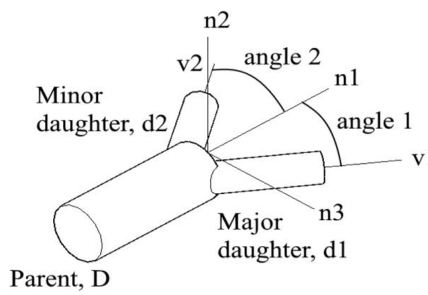


**Figure 3:** Parent and daughter branches along with their direction vectors.

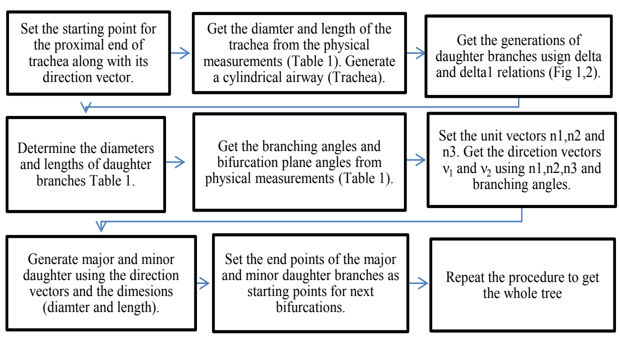


**Figure 4:** Pig airway tree generation algorithm.

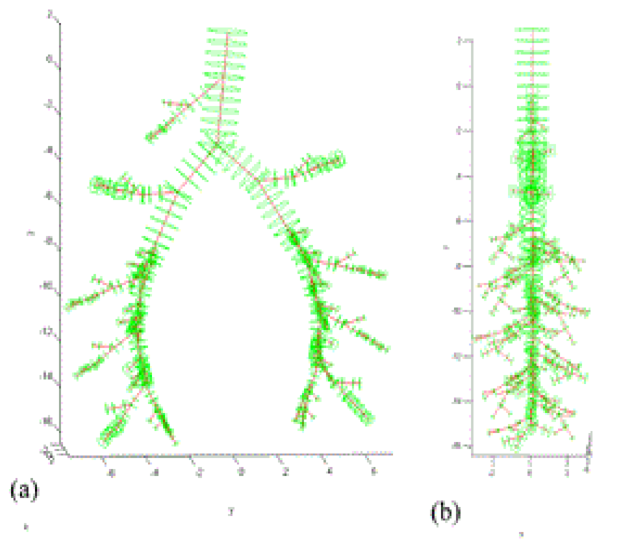


**Figure 5:** Pig airways tree generated from the algorithm (a) anterior view showing the in-plane branching (b) lateral view showing the out-of-plane branching.

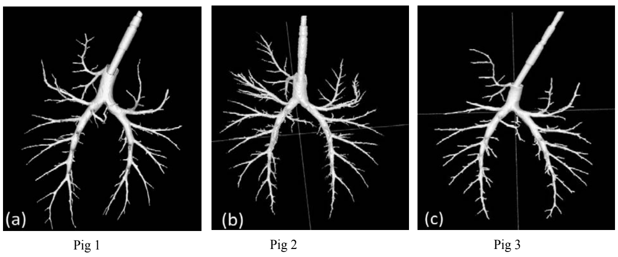


**Figure 6:** Pig airways that were extracted from CT images using automatic and manual segmentation. The airways are viewed from the anterior side [29-31].

There is little information on the pig airway geometry in the literature. Previous studies [29-31] were used to extract information on the length, diameters, branching angles and change of bifurcating planes of the pig airways using computed tomographic imaging along with segmentation software tools. The current study developed an algorithm based on these measurements to create a realistic pig airway tree. The tree generated from the algorithm was comparable to the geometry extracted from CT [29-31], which showed monopodiality, and is comparable to the dog lung airways [22]. The generated tree morphology also showed similarity with that reported in previous studies [17,26,33].

The information available from pig airway measurements is up to generation 25 only. Hence, the current algorithm was valid up to that generation. Several previous studies have provided quantitative measurements of the airway morphology but it appears that the current study is one of few early attempts to develop an algorithm capable of generating three-dimensional airway structures based on actual measurements.

Some previous studies [34,36] showed good agreement with human airways but didn't address pig airways, and hence their results cannot be directly being compared to the current study. It is worth mentioning that tree generated from the CCO depends on the number of terminal bronchioles and other input parameters that need to be chosen with care. Moreover, the algorithm doesn't account for monopodial geometries that is dominant in the airway morphology discussed in this study. Hence CCO may be a good candidate only for small airways.

Previous algorithms relied on either pure geometric relation [34,36] or theoretical analysis and optimization criteria [32,33,37]. Some of the geometric relations can be used to generate the large airways [34] while others would be mainly appropriate for adding airways to an existing tree of large diameters [36,37]. The current study proposes a pig airway generation algorithm based on empirical relations extracted from morphometry of actual pig airways. This approach is most appropriate for the large airways considered in the current study. The algorithm directly addresses the monopodial nature of the tree under consideration. Generating smaller airways may be achieved using other methods such as CCO, volume halving, etc. [36,37].

## Conclusion

The primary objective of the current study is to develop an algorithm that can create a realistic pig airway tree based on the empirical relations developed from the experimental measurements [29-31]. The generated tree showed similar in morphology and dimensions to the extracted geometries from previous CT. The generated tree may provide a good approximation of pig airways in computational and experimental studies of physical phenomenon of the airways. Since the airway geometry appears to be significantly different among species, using this algorithm is likely to introduce smaller geometric errors than approximating the pig geometry by that of other species including humans.

## Conflicts of Interest

The authors declare no conflict of interest.

## Ethic Approval

This study was approved by IACUC.

## Acknowledgment

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