POLITECNICO MILANO 1863

SCUOLA DI INGEGNERIA INDUSTRIALE E DELL'INFORMAZIONE

Executive Summary of the Thesis

Simulating Aeration at Birth: building an Open-Source Newborn Lung Model

Laurea Magistrale in Biomedical Engineering - Ingegneria Biomedica

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1. Introduction

During pregnancy, the fetal airways are filled with a fluid known as fetal lung fluid, which is essential for the development of airway. Consequently, at birth, the respiratory system must expel this fluid to allow aeration. Preterm infants may not be able to adequately achieve lung aeration at birth autonomously. The application of a positive pressure waveform at the airway opening can support them. However, the best pressure strategy for promoting lung aeration without damaging the fragile lung is still unknown. Model simulation can help in the definition of such a strategy.

Anatomical morphometric models of the adult lung have been extensively developed starting from the asymmetric model of Horsfield (fig. 1). They were used in the literature to enhance our understanding of pulmonary pathologies and to guide treatments. In contrast, anatomical morphometric models of the newborn lung are largely absent. It's not sufficient to simply scale down models developed for adult lungs to fit newborn lungs. Newborn lungs are not merely smaller versions of adult lungs; they exhibit significant differences in morphometric characteristics, airway wall structure, and tissue composition and properties. These differences must be considered when developing or adapting mathematical models to accurately represent the functioning of newborn lungs.

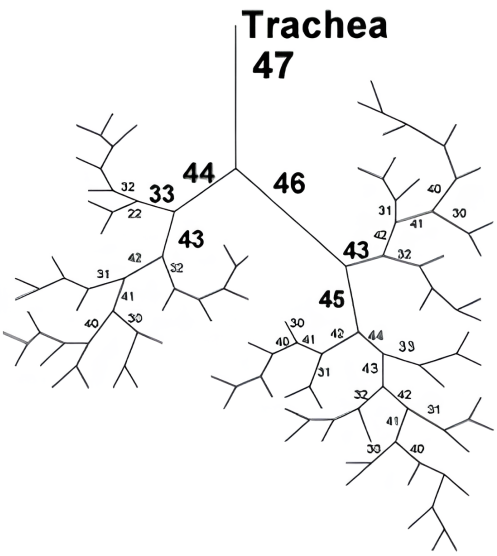


Figure 1: The dichotomous bronchial tree.

Aims of this projects are:

Generate a model from neonatal CT scans to optimize the generation of airways, ensuring they adhere to the morphometric characteristics at various ages.

- Develop an open-source mechanical model that allows for the simulation of mechanical properties along with fluid dynamics.

2. Model Development

An anatomically coherent 3D lung model is combined with a mechanical model of the airways and acini, able to simulate changes in the mechanical properties of the airways when the lung fluid is replaced by air entering the lungs.

The sequence for model development is reported in fig. 2. We extracted a 3D surface mesh of lung lobes and airway centrelines from a lung CT of a newborn. We implemented a statistical method, previously described for adult lung models, able to generate distal airways that were not visible on the CT. We adapted the method for the newborn lung.

We implemented a mechanical model of the airways and acini whose parameters are dependent on the airway's lengths and diameters and the presence of fetal fluid, fetal fluid-air interface, or air in the airway. We exploited an open-source solver for differential equations to simulate the network.

Morphology generation process is required as it is not possible to obtain high generations (aka small airways) using standard high-resolution CT[1]. This is performed by «Chaste» an open-source C++ library for computational physiology. The «Chaste» User Project required for airways and lobar segmentations to calculate the distal airways.

In order to perform simulation it is required to use an efficient differential equation solver. Julia Programming Language[3] has «`DifferentialEquations.jl`», which is very efficient and includes all available solvers (even C and FORTRAN ones)[2, 5]. «`ModelingToolkit.jl`»[4] is also required: it is a package for model design and instantiation. It allows for prototyping components easily, using macros and a Domain-Specific Language optimized for such purpose. Lung model is made out of modules at various hierarchical levels: from the lowest ones at the level of the electrical component to the highest ones emulating acini and airways (see their schematics in figs. 3 and 4).

Simulations are executed starting from a subtree (see fig. 5), as the full circuit (comprising over 50k modules) requires more memory space than typically available on a common laptop.

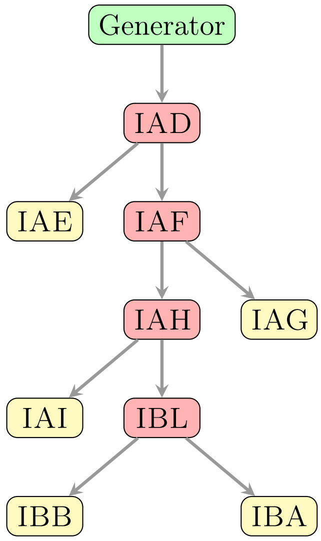


Figure 5: The simulated subtree. Airways are represented in red, acini in yellow.

3. Conclusion and Future Developments

We developed an anatomical morphometric model of the newborn lung. Using a CT scan of a newborn infant, we extracted the centreline and the lobe surfaces (see fig. 6).

We then reconstructed the anatomy of the missing airways using a statistical algorithm originally proposed for adult lungs, which we adapted for the newborn lung. This algorithm assigned airway diameters based on proportions measured in the newborn lung (see fig. 7).

We implemented a mechanical analog of the airway and acini in Julia. This model accounts for changes related to aeration at birth, allowing the simulation of the flow of fetal fluid toward the periphery as air enters the airways. The model incorporates changes in resistance (R) and compliance (I), as well as capillary pressure developed in the airways at the fluid-air interface. Testing on a subset of the anatomical tree yielded consistent results (see figs. 8 and 9), demonstrating the model's ability to simulate the phenomena involved in lung aeration. Future developments will include simulating the entire airway tree and analyzing the time required for full network simulation.

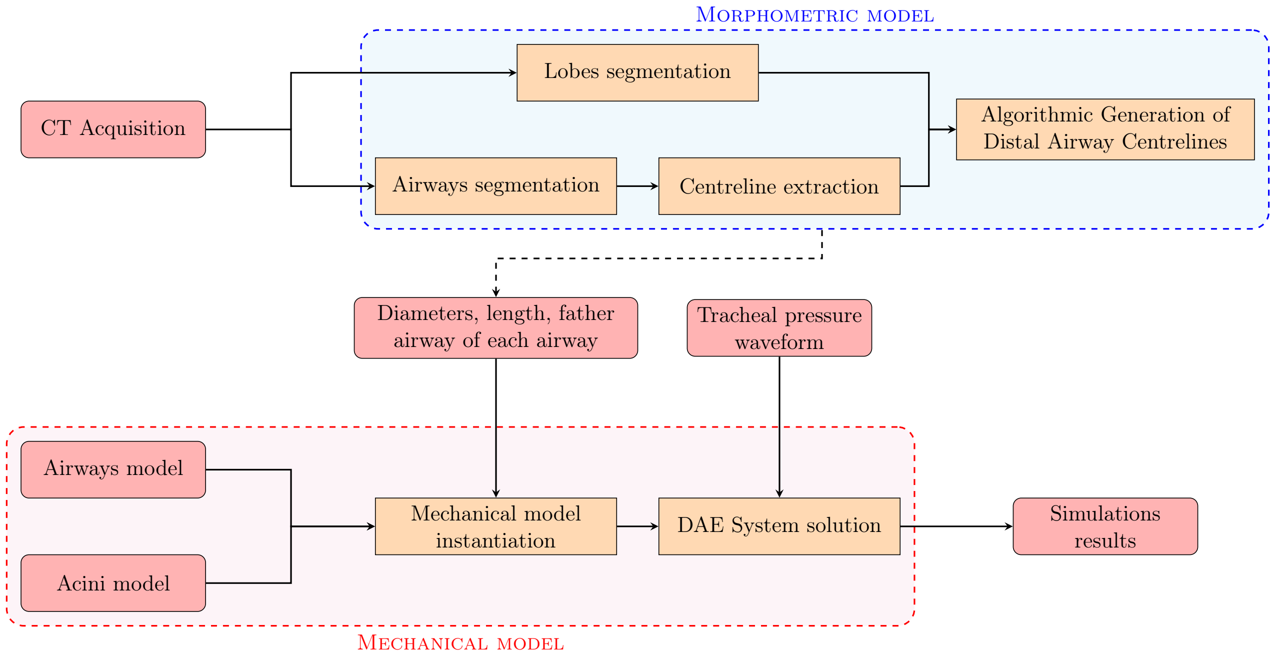


Figure 2: Data pipeline. The process begins with a *patient-specific image* (i.e. CT) of a premature newborn. The extracted data, comprising *two segmentations*, are then processed to obtain an anatomical surrogate of the airway tree. This is necessary due to scanner resolution not allowing for the discrimination and localization of small branches. From the resulting morphometric model, the *mechanical parameters* can be derived, which are essential for generating an accurate simulation model. Finally, a numerical solver for differential equations provides the final output.

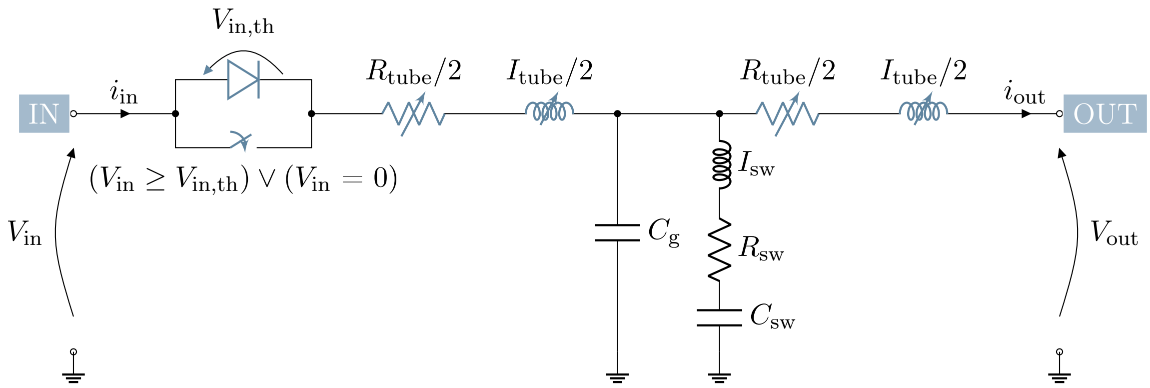


Figure 3: Airway equivalent circuit. In blue: all current integral-dependent components.

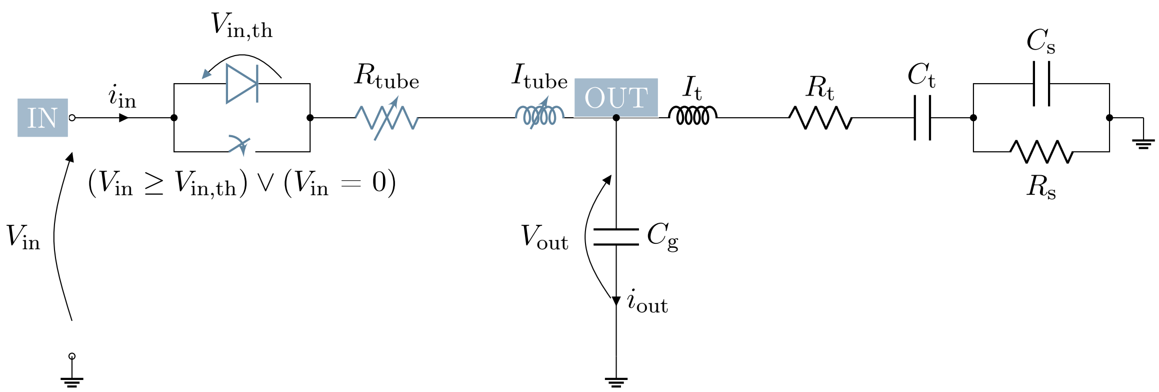


Figure 4: Acinus equivalent circuit. In blue: all current integral-dependent components.

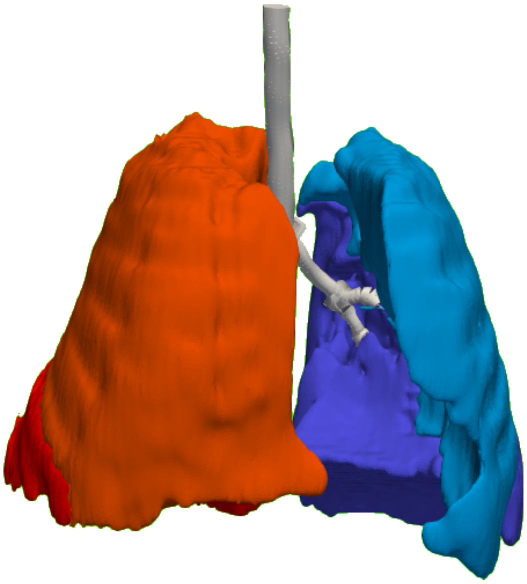
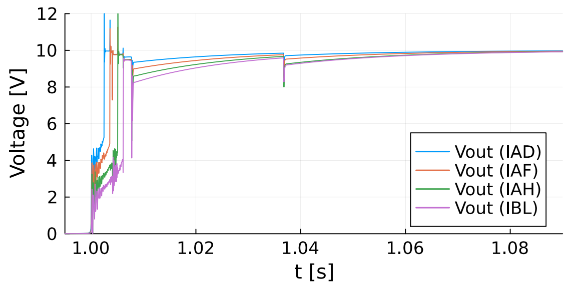
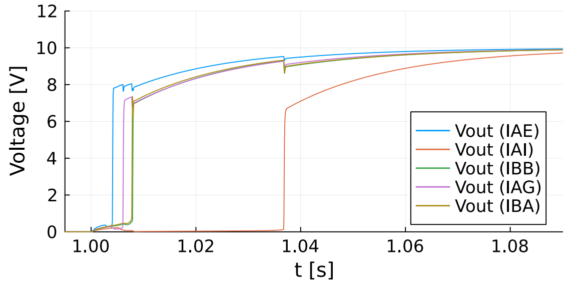


Figure 6: Major Airways and Lobes segmentations. Cyan: Upper Left Lung; Blue: Lower Left Lung; Orange: Upper Right Lung; Red: Lower Right Lung.



(a) Airways voltages



(b) Acini voltages

Figure 8: (Electrically equivalent) mechanical simulation for acini and airways. The step amplitude is 10V.

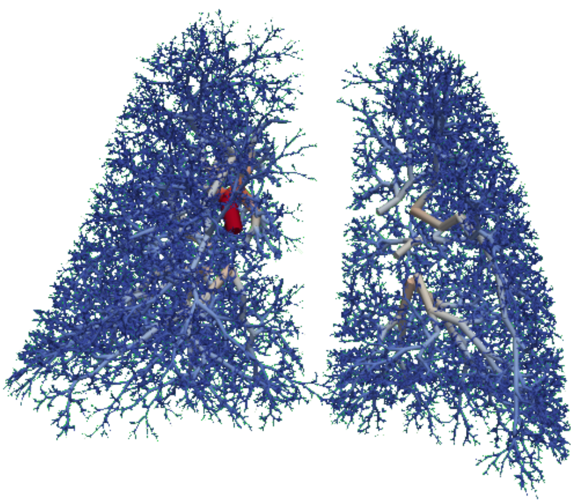
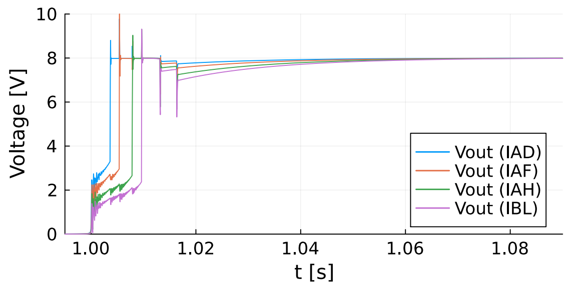
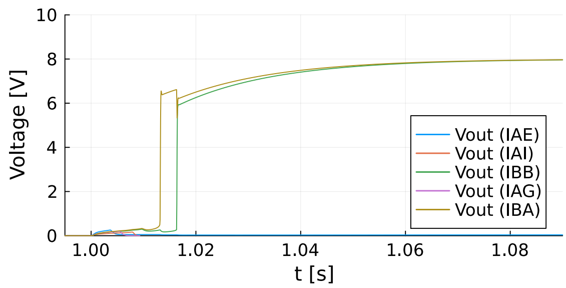


Figure 7: Complete Airways generated by Chaste User Project (major airways are here excluded). They are color-coded by their radii.



(a) Airways voltages



(b) Acini voltages

Figure 9: (Electrically equivalent) mechanical simulation for acini and airways. The step amplitude is 8V.

References

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