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A REDUCED-ORDER ELECTRICAL MODEL FOR AIRFLOW AND GAS TRANSPORT IN PULMONARY AIRWAYS

by
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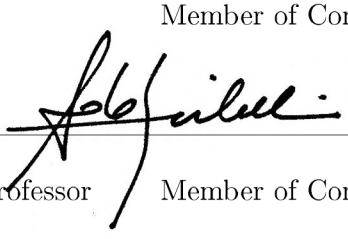

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An Abstract of the Thesis of

Ali Taher Yehya for Master of Engineering
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Title: A Reduced-Order Electrical Model for Airflow and Gas Transport in Pulmonary Airways

In this thesis, a reduced-order electrical model for the advection-diffusion equation is presented. It is derived from the cable theory with some modifications.
The model is used as a part of a bigger lung model to simulate oxygen and carbon dioxide concentrations distributions along pulmonary airways down to the alveoli, and it can be extended to model species concentrations in the pulmonary capillaries.
The objective of this model is to accurately simulate oxygen and carbon dioxide concentration distributions along airways in time, while at the same time reducing simulation time, and conserving the critical properties necessary for optimizing lung performance, such as maximizing the alveolar surface area and minimizing airways resistance through branching.
The lung model is composed of three submodels: (i) mechanics model, (ii) a model for species transport in airways, (iii) and in the alveoli, and it can be coupled to other models such as cardiovascular model.

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Symbols

A	Area
C	Capacitance or Compliance
D	Diffusion Coefficient
J	Diffusion Flux
L	Length
P	Pressure
q	Flux
Q	Charge
Q_{in}	Inward Volume Flow Rate
Q_{out}	Outward Volume Flow Rate
r	Radius
R	Resistance
u	Velocity
U	Voltage

V	Volume
$\dot{V}$	Volume Flow Rate
μ	Viscosity
φ	Species Concentration

Chapter 1

Introduction

Respiration is the process by which our body gets oxygen and removes carbon dioxide. Oxygen is an essential component for cells to live and function properly. Therefore respiration is critical for the human body.
Modeling the respiratory mechanism is an essential step for studying and understanding many pulmonary diseases.
Our model is a reduced order model (1-D) for the flow of air in the pulmonary airways, which models the pressure, velocity, and species concentration distribution along these airways.
Chapter two presents some previous models for the human lung.
Chapter three describes the physiology of the respiratory system.
Chapter four describes the architecture of the reduced order model.
Chapter five presents some simulation results of the presented model.

1.1 Motivation

Modeling the lung is essential in order to study pulmonary diseases, and also to predict the effects of changes of lung properties on lung performance. In fact, a good lung model is a replacement for the experimental study of the lung, since it eliminates the difficulties and costs associated with experimental studies.

1.2 Problem Statement

Modeling species trasnport in pulmonary airways in three dimensions is time consuming. Therefore we need a reduced order model which accurately models species transport in pulmonary airways.

The model should predict oxygen and carbon dioxide concentrations in space and time starting from the trachea down to the alveolus.

Chapter 2

Literature Review

2.1 Mechanics of Lung

Various models are reported in the literature including the Bogaard et al[2] model developed for patients with chronic obstructive pulmonary disease, and the Van Genderingen et al[17] model for HFOV of neonates suffering from IRDS. In this model, shown in Fig. 2-1(a), the endotracheal tube is modeled as a non-linear resistance in series with an inertance, and the rest of the respiratory system modeled as a resistance, inertance, and a non-linear compliance in series. The static nonlinear model presented in [17], expressing relationship between the mean airway distal pressure pressure and the alveolar volume in neonatal lung, is given by

$$\begin{aligned} V_{alv} &= 0 \quad \text{for} \quad \overline{p}_{aw} < p_{open} \\ V_{alv} &= C_{alv}\overline{p}_{aw} + V_0 \quad \text{for} \quad p_{open} < \overline{p}_{aw} < p_{tr} \\ V_{alv} &= p_{tr}C_{alv}\left((1+\beta) - \beta e^{-\frac{\overline{p}_{aw}-p_{tr}}{\beta p_{tr}}}\right) + V_0 \quad \text{for} \quad \overline{p}_{aw} > p_{tr} \end{aligned} \tag{2.1}$$

where $\beta = \frac{1}{2}$, $p_{tr} = 20$ cmH2O, $p_{open} = 5$ cmH2O, V_0 is the volume of an open alveolus at ambient pressure. The model describes three regimes based on the value of the mean airway pressure: (i) atelectatic alveoli for which the mean airway pressure is less than the open pressure (assumed to have a normal distribution among the alveoli), (ii) linear regime with constant compliance, and (iii) a nonlinear regime for

mean airway pressure larger that 20 cmH2O capturing the reduction in compliance for overdistention. The lung compliance is further enhanced by accounting for the number of recruited alveoli.

Pillow et al[15] presented a similar model, shown in Fig. 2-1(b), that incorporates two alveolar compartments instead of one, with different resistances and compliances. The model additionally includes compliance of the central airways and proximal compartment (albeit small $C_h = 0.011$ mL/cm H_2O) and a minimal resistance attributed to the section between the tip of the tracheal tube and the carinal junction ($R_c = 1$ cm H_2O.s/L.) The tissue resistance was neglected in accordance with the constant phase model at HFOV while constant (frequency independent) values of the tissue compliances were apparently used.

An integrated model of the respiratory system of a normal human subject executing the forced vital capacity maneuver is presented by Liu at al in [7]. The model integrates nonlinear airway/lung mechanics covering the full range of lung volumes, pulmonary blood flow, and gas exchange. The lung mechanics model, presented in Fig. 2-1(c), divides the lung into the following compartments: (i) mouthpiece, (ii) upper airways, (ii) collapsible airways, (iii) small airways, and (iv) the alveolar compartment. The model is characterized by the following: (i) constant lung tissue resistance, (ii) a non-linear compliance, expressed as dependence of the elastic recoil pressure (Δp_{el}) on alveolar volume and mean intrapleural pressure, (iii) small airways resistance dependent on alveolar volume and mean intrapleural pressure, (iv) collapsible airway region, included to match airflow during forced expiration, of volume and resistance dependent on transmural pressure, and (v) a rigid upper airway region with nonlinear flow-dependent resistance. The model parameters for lung mechanics (in addition to its building blocks) were based on Golden et al[4] and Olender at al [14], for pulmonary circulation from Milnor[11], and for pulmonary gas transport from Flumerfelt et al[3]. The blood circulation model employed in [7] considers the pulmonary vascular resistance to be made up of (i) a proximal pre capillary arteriolar resistance, (ii) pulmonary capillary resistance, and (iii) a distal post capillary venous resistance. The model lumps the pulmonary capillaries as a single tubular

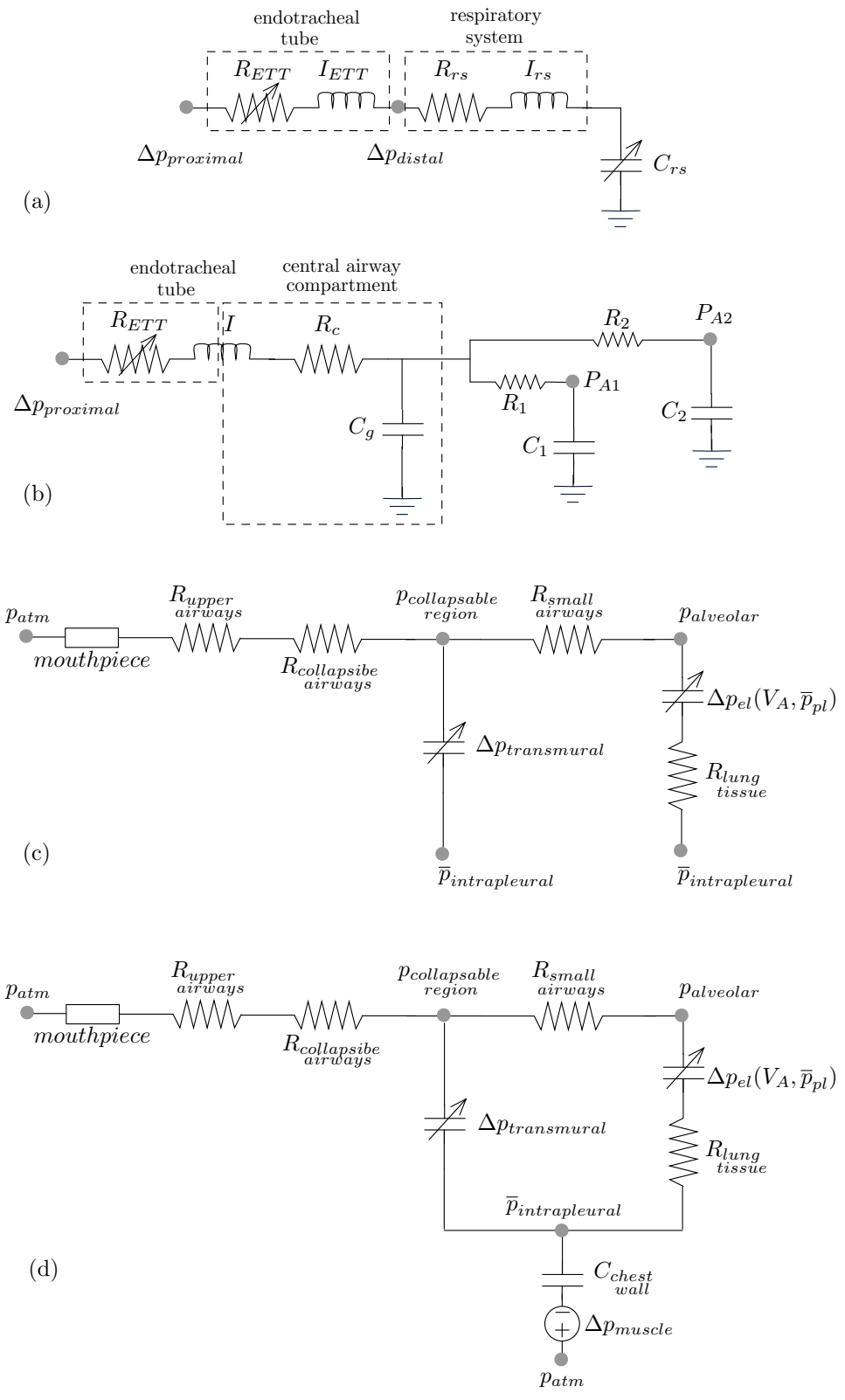


Figure 2-1: Lung mechanics models: (a) van Genderingen et al[17], (b) Pillow et. al.[15], (c) Liu et al[7], (d) Athanasiades et al[1].

compartment of constant length and variable volume. The gas exchange model used in [7] , adapted from Flumerfelt et al[3], accounts for gas exchange in the constant volume dead space, variable volume collapsible space, and alveolar compartments. The inspired air is assumed to be instantly at body temperature and fully saturated with water vapor. The model is based on solving the species conservation laws. The gas exchange model in [7] treats the blood in pulmonary capillaries as a uniform homogenous phase (masking the discrete constituents: plasma and erythrocytes) and assumes equilibrium conditions for the reactions thus allowing use of the empirical dissociation curves to relate the partial pressure to the species concentration. Blood flow and species transport in the capillary are assumed to be in the in the axial direction only. Gas transport across the alveolar-capillary membrane is modeled as a diffusion process with a specified constant diffusion capacity. A simplified linearized model of [7] is presented in [13], where the rigid upper airway and two lower airways each connected to an alveolar compartment are considered for the lung mechanics. Effects of various inspiratory flow waveforms during mechanical ventilation and regional disparities on expired gas species, among other performance indicators, are investigated. Athanasiades et al[1] extended the model of [7] to include the effect of the chest wall compliance (Fig. 2-1(d)) and replaced the pressure-volume mechanical model with a viscoelastic model of the form $P = ae^{kV} + b$. Athanasiades et al[1] employed their model to estimate the work of breathing and identify where and when it is expended. The model of [7] was later applied to the analysis of the Valsalva maneuver in [8]. It was later integrated in whole body gas exchange cardiopulmonary models in [9] and [10] .

2.2 Modeling the advection diffusion equation

Kennedy et al.[6] modelled the convection-diffusion equation using the transmission line modelling (TLM) method.

The method works well for steady state solutions, for a range of Peclet numbers.

However, for transient cases, the method exhibits numerical diffusion and convection. Shafaq et al.[16] proposed a method for modelling the convection-reaction-diffusion equation using electric circuits. The method, called the lumped-component circuit method (LCM), is similar to the TLM method but with the inductance being zero. The LCM models the convection-reaction-diffusion equation with low to moderate Peclet numbers, but for large Peclet numbers the method might fail to model the convection-reaction-diffusion equation.

Chapter 3

Lung Physiology

The main goal of respiration is to provide the body with oxygen and remove carbon dioxide.
This is accomplished through:

- Ventilation
- Diffusion across alveolar membrane
- Blood Circulation

3.1 Lung Mechanics

Normally, the lung expands and contracts mainly though the movement of the diaphragm, which contracts downward during inspiration causing the lung to expand and pulling air in, and relaxes during expiration causing the lung to contract and pulling air out [5].
The lung is surrounded by a fluid called the pleural fluid, which functions as a lubricant between the lung and the thoracic cavity. The pressure in this fluidic region is called the pleural pressure, which varies between -5 centimeters of water at the beginning of inspiration, and about -7.5 centimeters of water at the end of inspiration [5] .

Transpulmonary pressure is the difference between alveolar pressure and pleural pressure.

Lung compliance is how much the lung expands for a unit increase in transpulmonary pressure. It is around 200 ml/cmH_2O [5].

Compliance is caused by two main reasons: the elasticity of lung tissue, and the surface tension caused by the alveolar fluid on the alveolar walls. Where the first reason accounts only for one third of the toal lung elasticity, whereas the surface tension accounts for the other two thirds [5].

3.2 Gases Trasnport Across the Alveolar Membrane

Each alveolus is surrounded by a vast number of capillaries that form a sheet of blood flow to promote the exchange of oxygen and carbon dioxide. This exchange occurs as diffusion through a $\sim 0.6\mu$m thick pulmonary membrane across a difference in partial pressure between blood side and alveolar side. Typically oxygen partial pressure is higher in the alveolus while carbon dioxide partial pressure is higher on the blood side so that oxygen diffuses from the alveoli to the capillaries and carbon dioxide diffuses from the capillaries to the alveoli. Of the oxygen captured by the blood, 97% is bound to the hemoglobin in the red blood cells that flow in a single file in the capillary. The concentration of oxygen bound to hemoglobin can be related to its partial pressure in blood through the empirical dissociation curve. Several effects such as blood acidity and chemical composition may alter the saturation capacity of hemoglobin through a leftward or rightward shift in the dissociation curve. Carbon dioxide can be transported in blood in three different ways: dissolved in the plasma, as bicarbonate ions, and forming the carbamino-hemoglobin complex. Interactions between oxygen and carbon dioxide with hemoglobin through chemical reactions promote the delivery of oxygen to the blood and expulsion of carbon dioxide to the alveoli[5].

Chapter 4

Model Architecture

The model consists of two submodels: the first submodel is a momentum circuit which models the distribution of pressure and velocity along the airways, and the second submodel is a species concentration circuit that models the distribution of species concentration along these airways.

4.1 Momentum Circuit

The momentum circuit is used to model the lung mechanics. It is a combination of resistors and capacitors, where esistors are used to model the pressure drop along the airways, and capacitors are used to model the capacitance of the alveoli.

4.1.1 Governing Equations

Navier-Stokes equation along the axial direction in a pulmonary airway is:

$$\rho\left(\frac{\partial u_x}{\partial t}+u_r\frac{\partial u_x}{\partial r}+\frac{u_\theta}{r}\frac{\partial u_x}{\partial \theta}+u_x\frac{\partial u_x}{\partial x}\right)=-\frac{\partial P}{\partial x}+\rho g_x+\mu\left[\frac{1}{r}\frac{\partial}{\partial r}\left(r\frac{\partial u_x}{\partial r}\right)+\frac{1}{r^2}\frac{\partial^2 u_x}{\partial \theta^2}+\frac{\partial^2 u_x}{\partial x^2}\right] \tag{4.1}$$

Neglecting gravity, and the inertia term, and assuming fully developed flow and constant axial velocity, equation 4.1 reduces to the following equation:

$$0=-\frac{\partial P}{\partial x}+\mu\frac{1}{r}\frac{\partial}{\partial r}\left(r\frac{\partial u_x}{\partial r}\right) \tag{4.2}$$

Integrating equation 4.2 we get the following relation:

$$\Delta P = \frac{8\mu L}{\pi r^4}\frac{dV}{dt} \tag{4.3}$$

where P is the pressure, μ is the viscosity of air, L and r are respectively the length and the radius of the airway, and V is the volume.

Defining the resistance R as:

$$R = \frac{8\mu L}{\pi r^4} \tag{4.4}$$

Then the relation between the pressure P and the volume flow rate $\dot{V}$ in an airway is:

$$\Delta P = R\dot{V} \tag{4.5}$$

4.1.2 Electrical Model

Equation 4.5 models the resistive behaviour of the airways, as it relates the pressure drop in an airway of radius r and length L to the volume flow rate $\dot{V}$ in that airway. Moreover, to model the compliant behaviour of the lung tissue we use a capacitor with capacitance C which is defined as:

$$C = \frac{TV}{\Delta P_{TP}} \tag{4.6}$$

where TV is the tidal volume of the lung, and ΔP_{TP} is the change in transpulmonary pressure, which is the difference between alveolar pressure and intrapleural pressure. Combining equation 4.5 and equation 4.6 we get the following equation:

$$\frac{V(t) - FRC}{C} = -R\dot{V} - P_{ip}(t) + P_{ip_0} \tag{4.7}$$

The electric equivalent of the mechanics model os presented in figure 4-1 for one-compartment model, where $C = \frac{TV}{P_{ip,max} - P_{ip,min}}$, and $U = P_{ip}(t) - P_{ip_0} - \frac{FRC}{C}$. (See Appendix A)

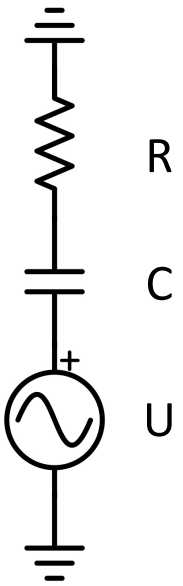


Figure 4-1: One-compartment electric model equivalent for the mechanics model

Variable	Equivalent Variable
Pressure (Pa)	Voltage (V)
Volume Flow Rate (m^3/s)	Current (A)
Volume (m^3)	Charge (C)

Table 4.1: Variables and their equivalents in the mechanics model

4.2 Modeling the Advection-Diffusion Equation

The advection-diffusion equation in its simple form is:

$$\frac{\partial \varphi}{\partial t} + u\frac{\partial \varphi}{\partial x} = D\frac{\partial^2 \varphi}{\partial x^2} \tag{4.8}$$

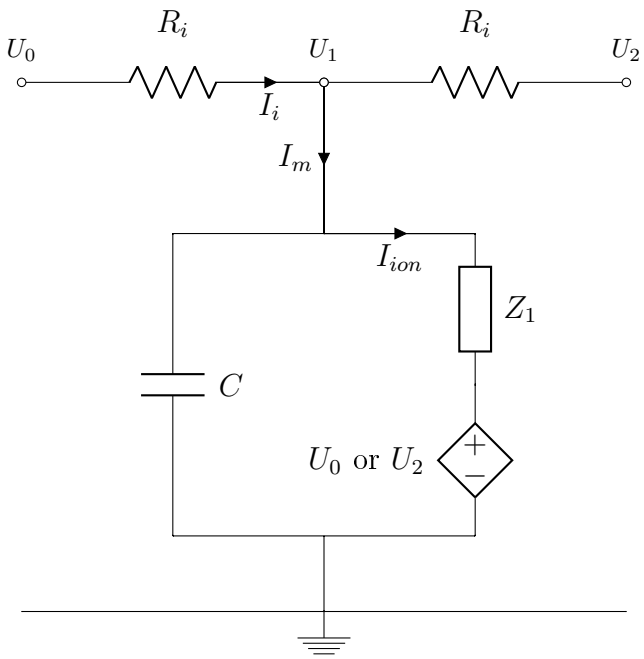
In order to find an equivalent circuit to the advection-diffusion equation, we have resorted to a modified version of the Cable theory model.

Cable theory models the distribution of membrane potential (or electrical current propagation) along a passive dendritic tree.It is expressed by the following equation:

$$C\frac{\partial U}{\partial t} + F(U) = R_i\frac{\partial^2 U}{\partial x^2} \tag{4.9}$$

where U and F are continuous functions of space and time, represented by x and t respectively. $F(U)$ can be represented as the ionic current per unit length of membrane cylinder noted as I_{ion}.

Our modifications, presented in the circuit below, consist of the following: setting the dendritic membrane potential outside of the cell, noted U_e, to ground, and zeroing out the resistance in the extra-cellular space between the center of two unit cells, and finally introducing a dependent voltage source that will either represent the voltage of previous or next dendrite. This will in effect allow us to implemet the upwind scheme in the model.



Now $I_{ion} = \frac{U_1 - U_0}{Z_1}$

Our equation becomes:

$$C\frac{\partial U}{\partial t} + \frac{U_1 - U_0}{Z_1} = \frac{1}{R_i}\frac{\partial^2 U}{\partial x^2} \tag{4.10}$$

Note that if we set $Z_1 = \Delta x/u$ we get $u\frac{(U_1 - U_0)}{\Delta x}$, which represents the advection term in the advection-diffusion equation.

4.3 Species Circuit for Airways

4.3.1 Governing Equations

Applying the conservation of species to a control volume in the airway (shown in Fig. 4-2) we get the following equation:

$$V\frac{\partial \varphi}{\partial t} = \varphi_{in}\dot{V}_{in} - \varphi_{out}\dot{V}_{out} + A_{in}J_{in} - A_{out}J_{out} \tag{4.11}$$

where φ is the concentration in mol/m^3, V is the volume in m^3, $\dot{V}$ is the volume flow rate in m^3/s, A is the area in m^2, and J is the diffusion flux in mol/m^2s defined as:

$$J = -D\frac{\partial \varphi}{\partial x} \tag{4.12}$$

where D is the diffusion coefficient in m^2/s.

Rearranging equation 4.11 and letting $\Delta x \to 0$ we get the following equation:

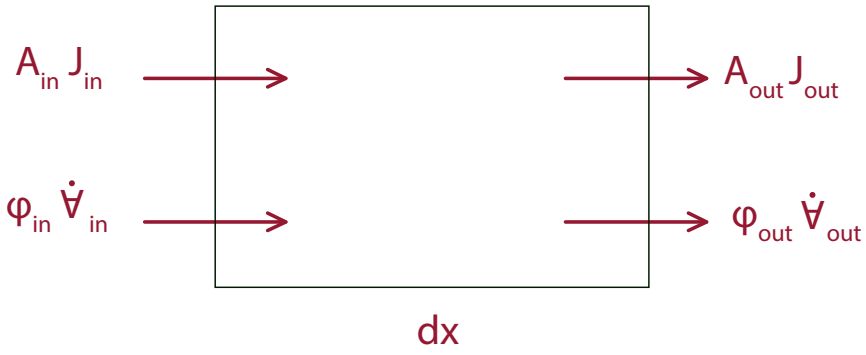


Figure 4-2: Control volume in an airway

$$A\Delta x\frac{\partial \varphi}{\partial t} + \frac{\Delta \varphi}{1/\dot{V}} = \left[-\left(\frac{\Delta \varphi}{\Delta x/AD}\right)_{in} + \left(\frac{\Delta \varphi}{\Delta x/AD}\right)_{out} \right] \tag{4.13}$$

4.3.2 Electric Model

This model is derived from the convection-diffusion equation, and it models species concentration distribution along the airways.

Equation 4.13 can be written as:

$$C_1\frac{\partial \varphi}{\partial t} + \frac{\Delta \varphi}{R_1} = -\frac{(\Delta \varphi)_{in}}{R_2} + \frac{(\Delta \varphi)_{out}}{R_3} \tag{4.14}$$

Variable	Equivalent Variable
Concentration (mol/m^3)	Voltage (V)
Molar Flow Rate (mol/s)	Current (A)
Number of moles (mol)	Charge (C)

Table 4.2: Variables and their equivalents in the species concentration model

where $C_1 = A\Delta x$, $R_1 = 1/|\dot{V}|$, $R_2 = (\Delta x/AD)_{in}$, and $R_3 = (\Delta x/AD)_{out}$
If we model the concentration φ as voltage U, equation 4.14 becomes:

$$C_1 \frac{\partial U}{\partial t} + \frac{\Delta U}{R_1} = -\frac{(\Delta U)_{in}}{R_2} + \frac{(\Delta U)_{out}}{R_3} \tag{4.15}$$

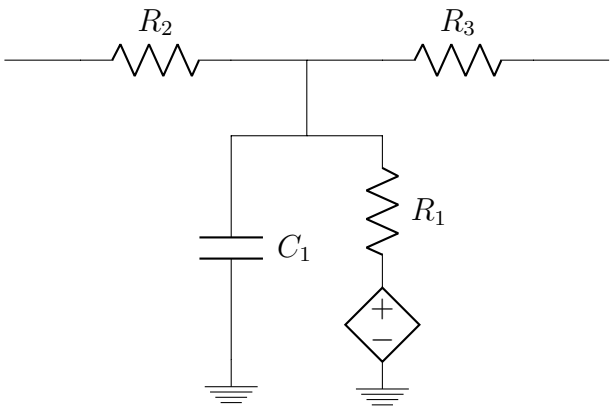


Figure 4-3: Electrical equivalent to the advection diffusion equation in the airways

The model in Fig. 4.3.2 is equivalent to one control volume, therefore to model a complete airway multiple electric blocks are to be used in series as shown in Fig. 4-4
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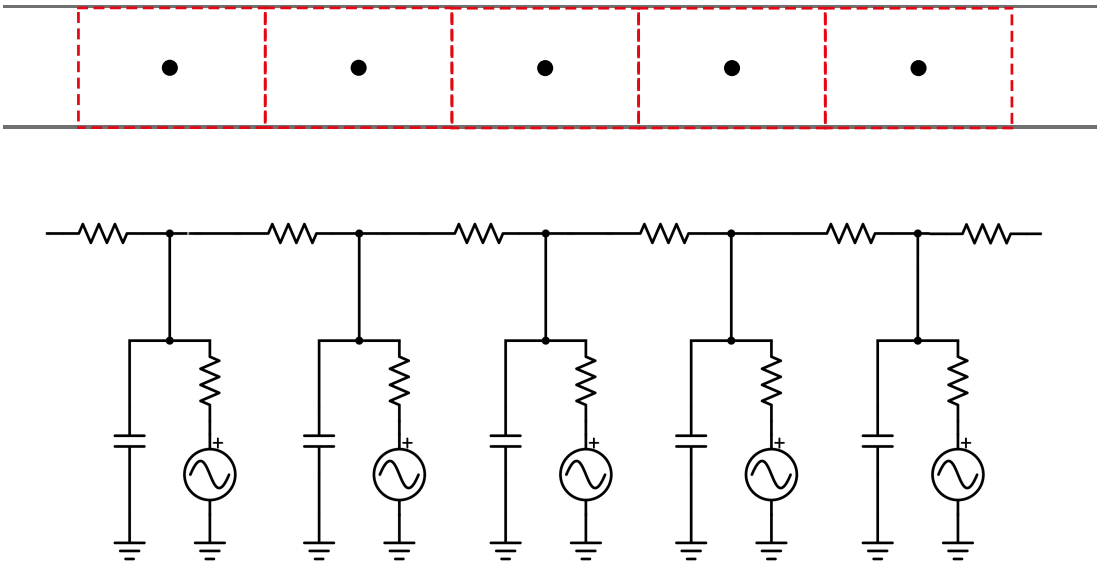


Figure 4-4: Electric equivalent for the advection-diffusion equation in an airway

4.4 Species Circuit for the Alveolus

4.4.1 Governing Equations

The transport equation in the alveolus is:

$$\frac{\partial(V\varphi)}{\partial t} = \varphi_{in}\dot{V}_{in} + A_{in}J_{in} - A_{out}J_{out} \tag{4.16}$$

which is:

$$V(t)\frac{\partial\varphi}{\partial t} + \varphi\frac{\partial V}{\partial t} = \varphi_{in}\dot{V}_{in} + A_{in}J_{in} - A_{out}J_{out} \tag{4.17}$$

Since the alveolus is so small, we can assume that the concentration at inlet is

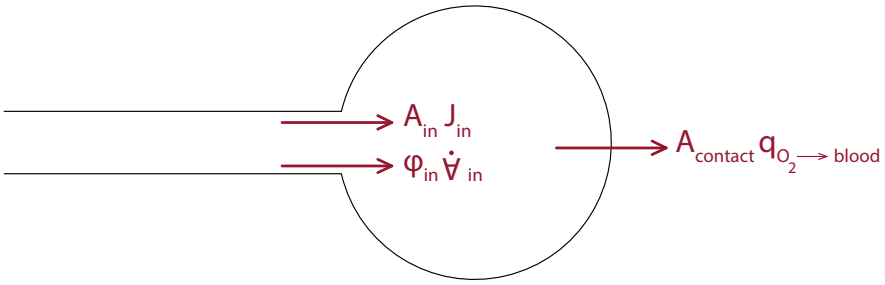


Figure 4-5: Control volume in the alveolus

approximately the concentration in the alveolus, therefore: $\varphi = \varphi_{in}$, and since $\frac{\partial V}{\partial t} = \dot{V}_{in}$, then $\varphi\frac{\partial V}{\partial t} = \varphi_{in}\dot{V}_{in}$. Therefore, the transport equation in the alveolus reduces to:

$$V(t)\frac{\partial\varphi}{\partial t} = A_{in}J_{in} - A_{out}J_{out} \tag{4.18}$$

which is:

$$V(t)\frac{\partial\varphi}{\partial t} = -A_{in}D\left(\frac{\partial\varphi}{\partial x}\right)_{in} + A_{out}D\left(\frac{\partial\varphi}{\partial x}\right)_{out} \tag{4.19}$$

As $\Delta x \to 0$, we can write A.4 as:

$$V(t)\frac{\partial\varphi}{\partial t} = -A_{in}D\left(\frac{\Delta\varphi}{\Delta x}\right)_{in} + A_{out}D\left(\frac{\Delta\varphi}{\Delta x}\right)_{out} \tag{4.20}$$

Rearranging the above equation, we get:

$$V(t)\frac{\partial \varphi}{\partial t} = -\left(\frac{\Delta\varphi}{\frac{\Delta x}{AD}}\right)_{in} + \left(\frac{\Delta\varphi}{\frac{\Delta x}{AD}}\right)_{out} \tag{4.21}$$

Note that for the alveolus, A_{out} is the contact area between the alveolus and blood capillaries. The model for this equation is shown in Gig. 4-6. Concerning $V(t)$, it is the volume of the alveolus, which is variable in time. Therefore we get its value from the momentum circuit. The volume in the momentum circuit is equivalent to the charge Q in the capacitor. Knowing that $Q = CU_c$, where C is the capacitance of the capacitor, and U_c is the voltage across it. Therefore $V(t) = C\Delta P$, where C is the compliance of the lung tissue (around 200 ml/cmH2O), and ΔP is the transpulmonary pressure.

Equation 4.21 for oxygen is:

$$V(t)\frac{\partial \varphi}{\partial t} = -\left(\frac{\Delta\varphi}{\frac{\Delta x}{AD}}\right)_{in} - A_{contact} q_{O_2 \rightarrow blood} \tag{4.22}$$

where the last term is defined in [12]

$$q_{O_2 \rightarrow blood} = \frac{D_{O_2,water}}{k_H^{cc}} \frac{\varphi_{O_2,alv} - \frac{P_{O_2,b}}{RT}}{h(t)} \tag{4.23}$$

For carbon dioxide, equation 4.21 is:

$$V(t)\frac{\partial \varphi}{\partial t} = -\left(\frac{\Delta\varphi}{\frac{\Delta x}{AD}}\right)_{in} - A_{contact} q_{CO_2 \leftarrow blood} \tag{4.24}$$

where the last term is defined in [12] as:

$$q_{CO_2 \leftarrow blood} = \frac{D_{CO_2,water}}{k_H^{cc}} \frac{\varphi_{CO_2,alv} - \frac{P_{CO_2,b}}{RT}}{h(t)} \tag{4.25}$$

Concerning the values of oxygen and carbon dioxide partial pressures in blood, we have two choices: we either set an average value for each one in blood, or we couple

the alveolus model to the capillary model which will be explained in the next section.

4.4.2 Electrical Model

Similar to the electrical model for the advection-diffusion equation in an airway, equation 4.22 can be written as:

$$C\frac{\partial \varphi}{\partial t} = -\frac{(\Delta\varphi)_{in}}{R_1} + \frac{(\Delta\varphi)_{out}}{R_2} \tag{4.26}$$

where $C = V(t)$, $R_1 = (\Delta x/AD)_{in}$, and $R_2 = \frac{h(t)k_H^{cc}}{A_{contact}D_{O_2,water}}$ for oxygen, and $R_2 = \frac{h(t)k_H^{cc}}{A_{contact}D_{CO_2,water}}$ for carbon dioxide.
If we model the concentration φ as voltage U, equation 4.26 becomes:

$$C\frac{\partial U}{\partial t} = -\frac{(\Delta U)_{in}}{R_1} + \frac{(\Delta U)_{out}}{R_2} \tag{4.27}$$

The model for equation 4.27 is shown in Fig. 4-6, where $U_b = \frac{P_{O_2,b}}{RT}$ for oxygen, and $U_b = \frac{P_{CO_2,b}}{RT}$ for carbon dioxide, U_a is the concentration of species in the alveolus, and U_l is the species concentration in the last control volume of the airway just before the alveolus.

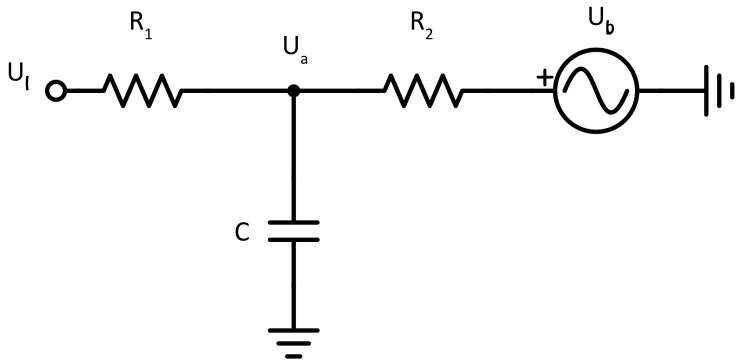


Figure 4-6: Electrical equivalent of the advection-diffusion equation in the alveolus

4.5 Species Circuit for the Capillaries

4.5.1 Governing Equations

The transport equation in a capillary (see Fig. 4-7) is:

For oxygen:

$$V\frac{\partial \varphi}{\partial t} = \varphi_{in}\dot{V}_{in} - \varphi_{out}\dot{V}_{out} + A_{in}J_{in} - A_{out}J_{out} + A_{contact}q_{O_2 \rightarrow blood} \tag{4.28}$$

and for carbon dioxide:

$$V\frac{\partial \varphi}{\partial t} = \varphi_{in}\dot{V}_{in} - \varphi_{out}\dot{V}_{out} + A_{in}J_{in} - A_{out}J_{out} + A_{contact}q_{CO_2 \leftarrow blood} \tag{4.29}$$

(yes it is plus sign for the last term in equation 4.29, see its value in equation 4.25, normally it will be a negative value).

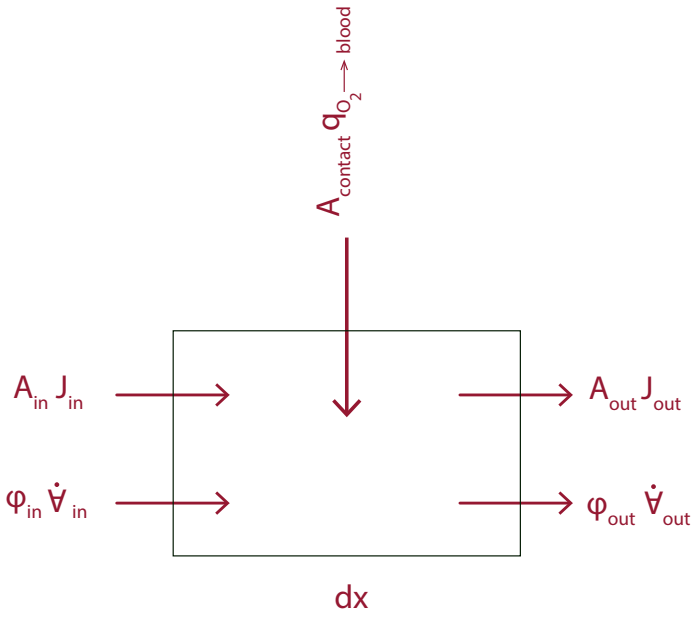


Figure 4-7: Control volume in blood capillary

Rearranging 4.28 and 4.29 gives:

$$V\left(\frac{\partial\varphi}{\partial t}+u\frac{\partial\varphi}{\partial x}\right)=-A_{in}D\left(\frac{\partial\varphi}{\partial x}\right)_{in}+A_{out}D\left(\frac{\partial\varphi}{\partial x}\right)_{out}+A_{contact}q_{O_2\rightarrow blood} \quad (4.30)$$

$$V\left(\frac{\partial\varphi}{\partial t}+u\frac{\partial\varphi}{\partial x}\right)=-A_{in}D\left(\frac{\partial\varphi}{\partial x}\right)_{in}+A_{out}D\left(\frac{\partial\varphi}{\partial x}\right)_{out}+A_{contact}q_{CO_2\leftarrow blood} \quad (4.31)$$

where $A_{contact}$ is the contact area between the alveolus and the capillary control volume, which is equal to Wdx, where W is the contact area per unit capillary length, assumed to be equal to capillary diameter.

$q_{O_2\rightarrow blood}$ and $q_{CO_2\leftarrow blood}$ were defined before. For the capillary model we have two more equations to implement, these equations relate the concentrations of oxygen and carbon dioxide in blood to their partial pressures.

The two equations are derived from the oxygen-hemoglobin dissociation curve and the carbon dioxide dissociation curve [12]:

$$O_{2,b}=f\left(P_{O_2,b},P_{CO_2,b}\right)=O_{2,b|S=100\%}\frac{K_0P_{O_2,b}^n}{1+K_0P_{O_2,b}^n} \quad (4.32)$$

where $O_{2,b|S=100\%}=201ml/L$

$$CO_{2,b}=f\left(P_{O_2,b},P_{CO_2,b}\right)=462e^{0.00415P_{CO_{2,b}}}-340e^{-0.0445P_{CO_{2,b}}}+0.62(97.5-S) \quad (4.33)$$

with $S=100\frac{K_0P_{O_2,b}^n}{1+K_0P_{O_2,b}^n}$.

Equation 4.32 is implemented in our model by finding the expression of $P_{O_2,b}$ as a function of $O_{2,b}$. Similarly, equation 4.33 is implemented by finding the expression of $P_{CO_2,b}$ as a function of $CO_{2,b}$. These two expressions will be used to express the values of the dependent voltage source in the alveolus model, which is U_b in Fig. 4-6. And setting the current source value (which is ' i ' in Fig. 4-8) to be equal to the current flowing through R_2 in Fig. 4-6.

4.5.2 Electrical Model

As $\Delta x \to 0$, equation 4.30 can be written as:

$$A\Delta x \frac{\Delta\varphi}{1/\dot{V}} = -\left(\frac{\Delta\varphi}{\Delta x/AD}\right)_{in} + \left(\frac{\Delta\varphi}{\Delta x/AD}\right)_{out} + A_{contact} q_{O_2 \leftarrow blood} \tag{4.34}$$

Equation 4.34 can be modelled as:

$$C\frac{\Delta U}{R_3} = -\frac{(\Delta U)_{in}}{R_1} + \frac{(\Delta U)_{out}}{R_2} + i \tag{4.35}$$

where $C = A\Delta x$, $R_3 = 1/|\dot{V}|$, $R_1 = (\Delta x/AD)_{in}$, $R_2 = (\Delta x/AD)_{out}$, and $i = A_{contact} q_{O_2 \leftarrow blood}$ as shown in Fig. 4-8.

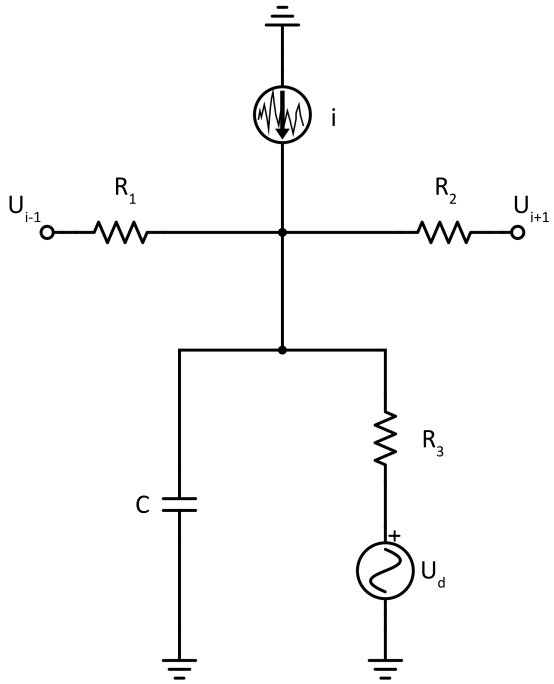


Figure 4-8: Electrical equivalent for the advection-diffusion equation in the capillaries

4.6 Complete Model

To model the entire lung, we have to find the equivalent for the species concentration circuit. Fig.4-10 and Fig.4-11 show the transition from the actual circuit to the equivalent circuit.

As seen in these two figures, collapsing is done only horizontally at each generation. In these figures each generation was divided into 3 divisions (3 blocks) just as an example here.

In the equivalent generations (for example in Fig. 4-11, starting from the 4th generation), the values of these components will be as follow:

$$R_{equivalent} = \frac{R}{2^k} = \frac{\Delta x/DA}{2^k} = \frac{\Delta x}{2^k DA} \tag{4.36}$$

$$Z_{equivalent} = \frac{Z}{2^k} = \frac{1/\dot{V}}{2^k} = \frac{1/\left(\frac{\dot{V}_{last}}{2^k}\right)}{2^k} = \frac{1}{\dot{V}_{last}} \tag{4.37}$$

$$C_{equivalent} = C * 2^k = 2^k A \Delta x \tag{4.38}$$

Where $\dot{V}_{last}$ is the flow rate in the last actual generation (in the example in Fig. 4-10 it is the third generation). And k is the generation index starting from the last actual generation as zero. For example in Fig. 4-11 : $k_{4th} = 1, k_{5th} = 2, k_{6th} = 3$.

4.7 Reynolds and Peclet Numbers for Adults and Infants

Table 4.3: Peclet and Reynolds Numbers for an adult

Generation Number	Reynolds Number	Peclet Number

1	1520	678
2	1821	812
3	1517	676.8
4	1090	486
5	722	322
6	454	202.6
7	276	123
8	163	72.8
9	95	42.2
10	54	24.1
11	30	13.6
12	17	7.58
13	9.4	4.19
14	5.16	2.3

15	2.8	1.256
16	1.5	0.68
17	0.8	0.367
18	0.44	0.197
19	0.24	0.106
20	0.13	0.056
21	0.067	0.02998
22	0.036	0.0159
23	0.019	0.0084
24	0.0099	0.0044

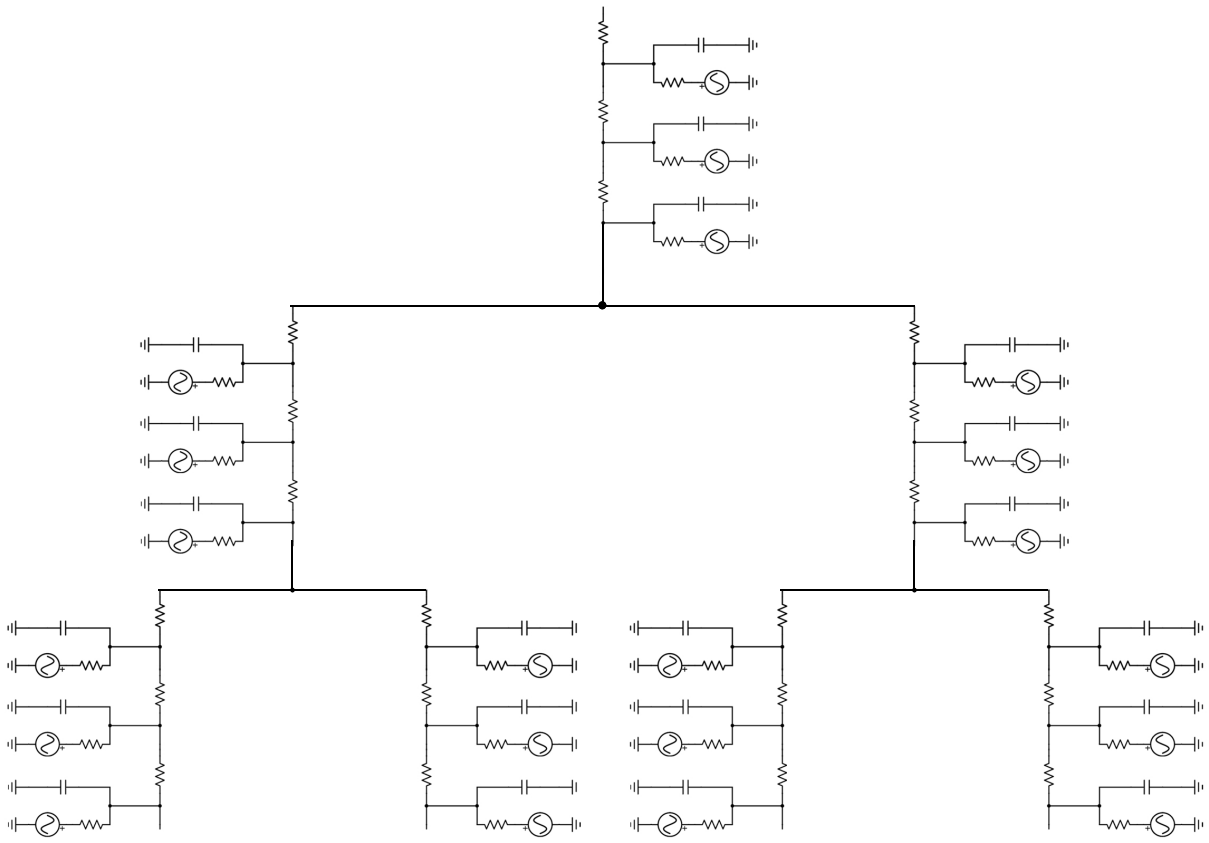


Figure 4-9: Branching of the electrical model

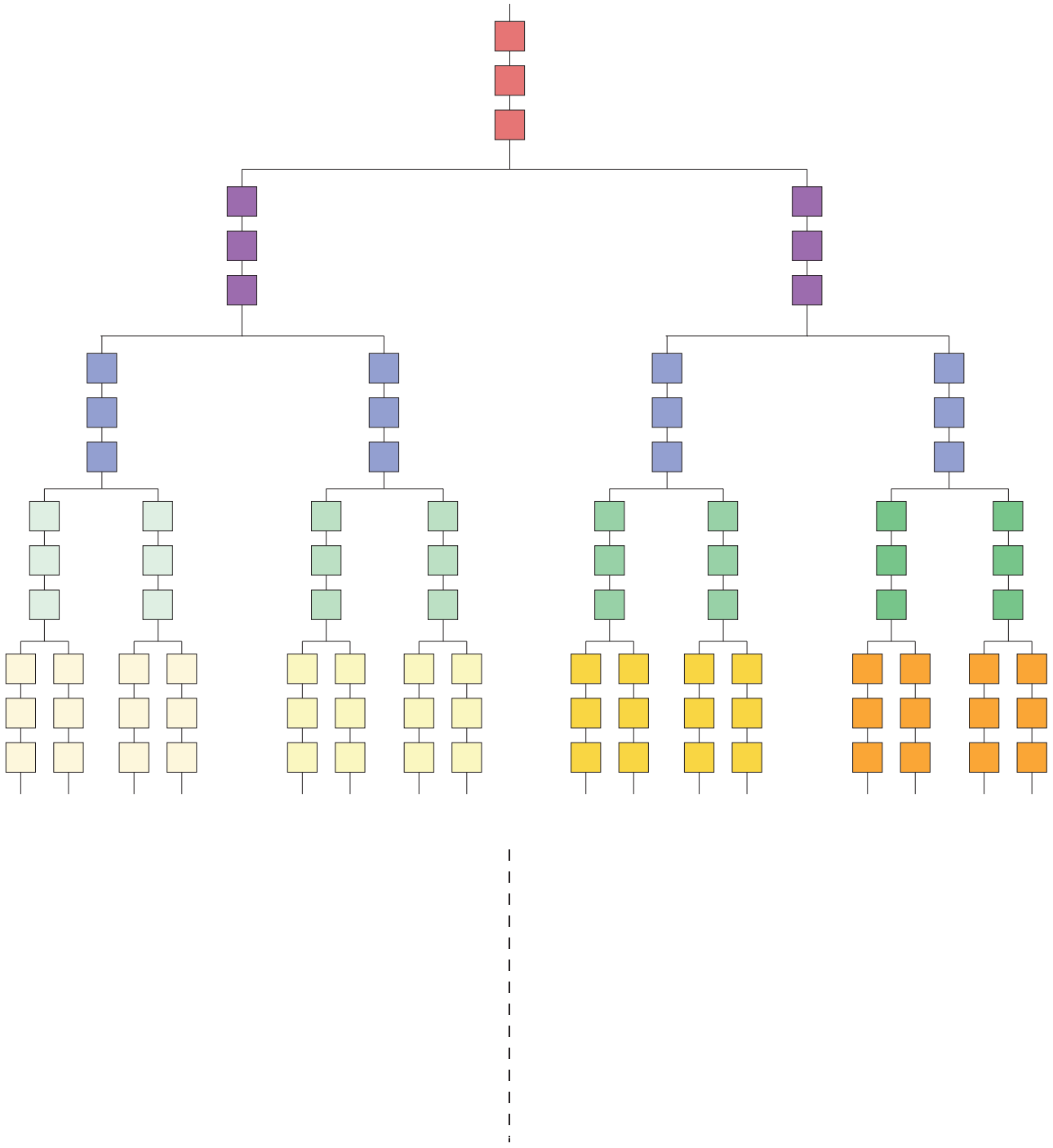


Figure 4-10: Four-compartment actual model

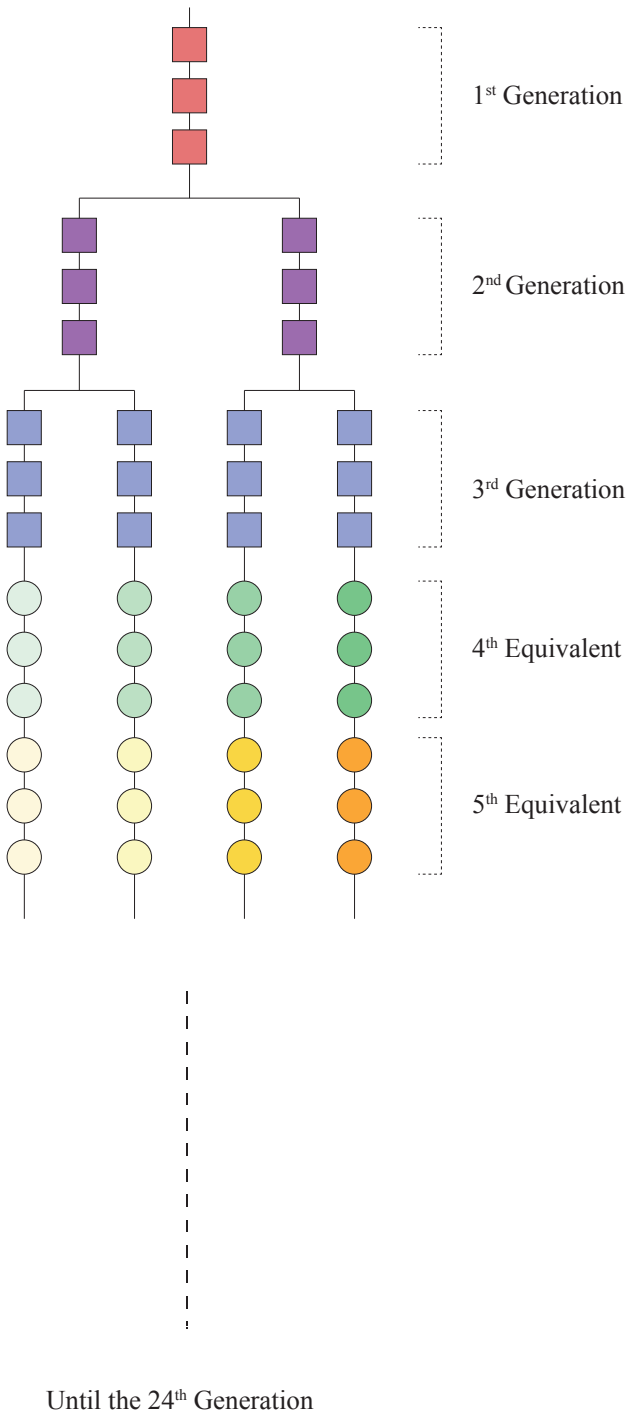


Figure 4-11: Four-compartment equivalent model

Table 4.4: Peclet and Reynolds Numbers for an infant

Generation Number	Reynolds Number	Peclet Number
1	884.8	394.7
2	571.4	254.9
3	377	168.3
4	239	106.8
5	167.5	74.7
6	109.7	48.9
7	67.86	30
8	45.8	20.4
9	27.7	12.4
10	15.2	6.8
11	8.4	3.7
12	4.7	2.11
13	2.4	1.09
14	1.29	0.57
15	0.67	0.3
16	0.35	0.16

Chapter 5

Results

5.1 Methodology

In order to simulate our model, we resorted to a circuit simulator called Ngspice.
The simulator reads the electric circuit as a netlist, which is basically a text file describing the connectivity of the simulated electric circuit.
In order to obtain the netlist file for our model, we developped a MATLAB code which takes as input: the number of compartments of the lung, and the density of divisions (i.e. number of divisions per unit length), with the option of manipulating other parameters such us the dimensions of airways, compliance of the lung tissue, frequency of respiration, and many other parameters.
A chart showing the flow of information is shown in Fig. 5-1

5.2 Model Validation

In order to validate our model, we compared our results with 2D simulation results from ANSYS Fluent.
A simple simulation was performed for the first lung generation (i.e. the trachea), with a length of 100 mm and a diameter of 16 mm
Boundary conditions at the inlet were: atmospheric pressure (i.e. zero gauge pressure), and constant species concentration of $8.567\, mol/m^3$. Whereas the outlet bound-

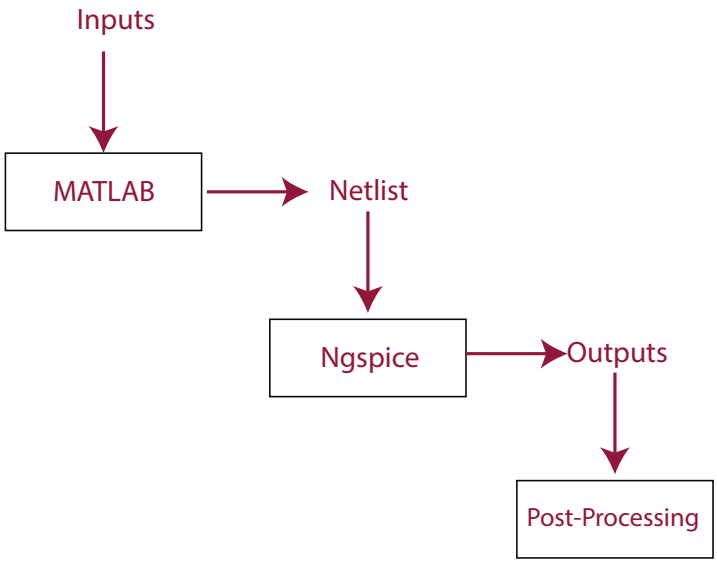


Figure 5-1: Methodology

ary conditions were: sinusoidal velocity with an amplitude of 1.74 m/s, and a species concentration of 5 mol/m^3 .

Results are shown in Fig. 5-2 and 5-3.

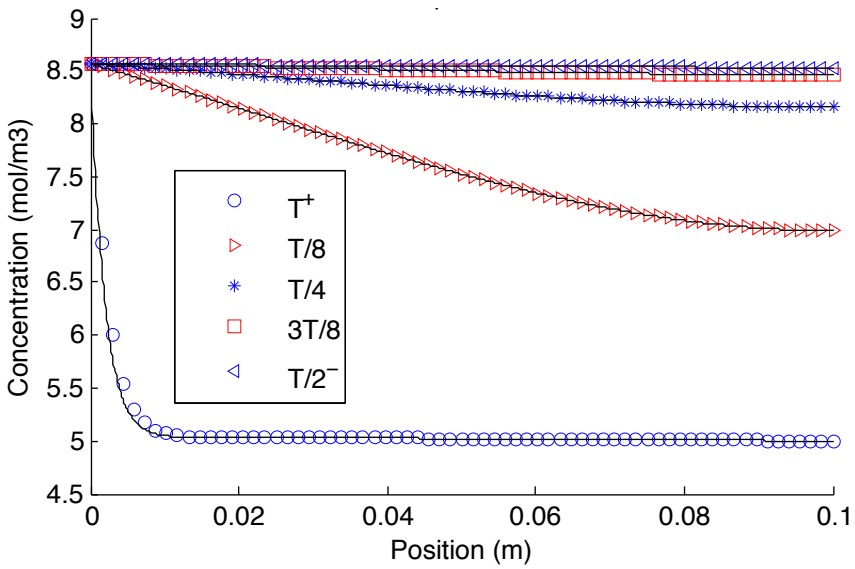


Figure 5-2: 2D vs 1D - Pe = 0.0933 - Inspiration

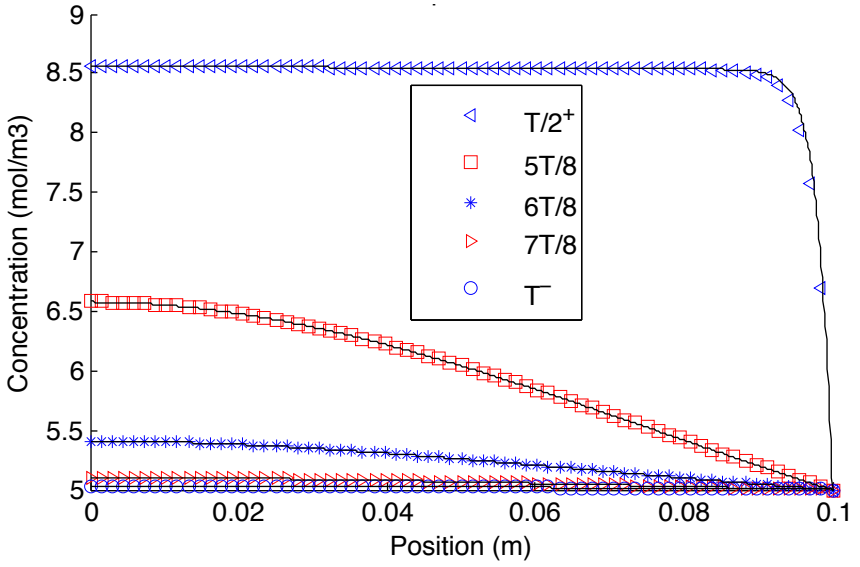


Figure 5-3: 2D vs 1D - Pe = 0.0933 - Expiration

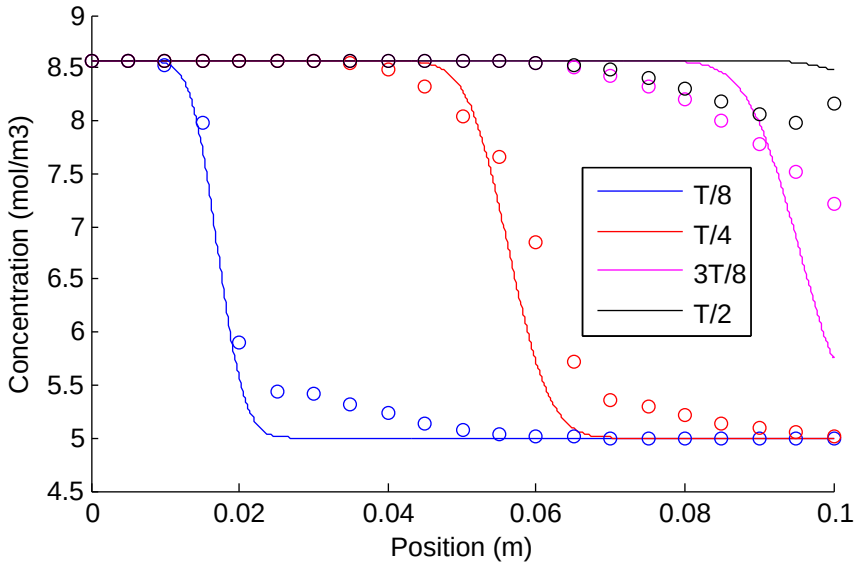


Figure 5-4: 2D vs 1D - Pe = 93 - Inspiration

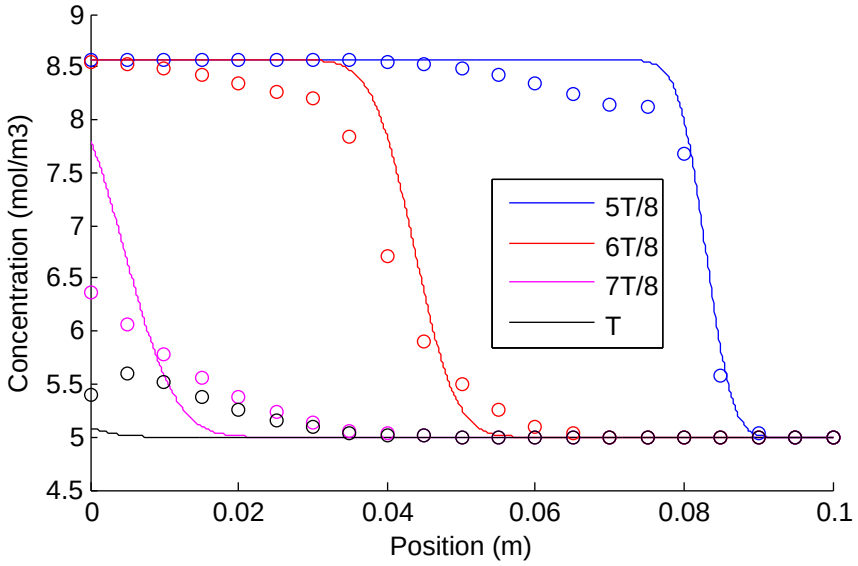


Figure 5-5: 2D vs 1D - Pe = 93 - Expiration

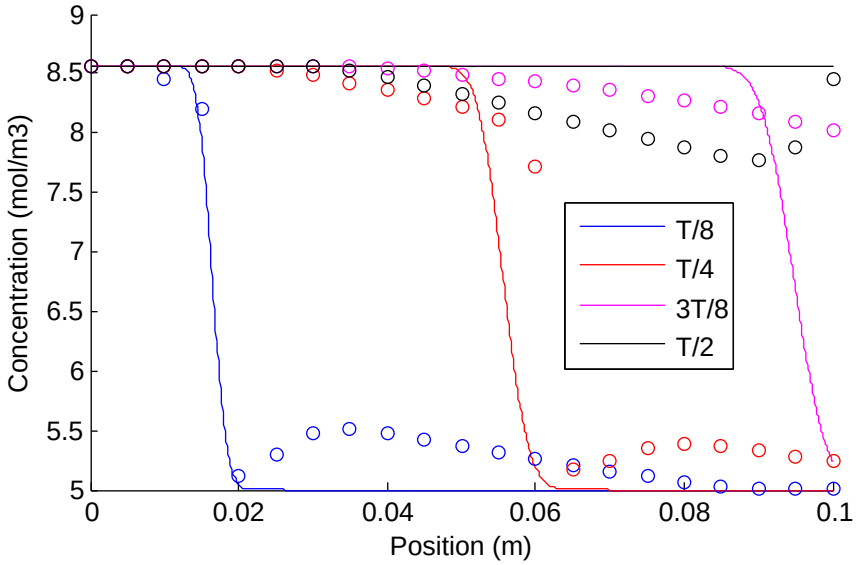


Figure 5-6: 2D vs 1D - Pe = 793 - Inspiration

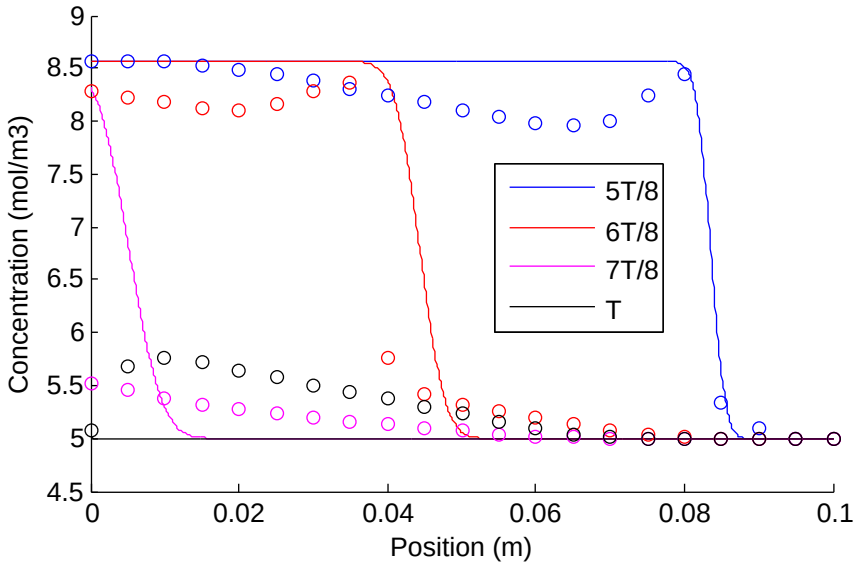


Figure 5-7: 2D vs 1D - Pe = 793 - Expiration

It can be seen that our 1-D model models exactly the 2-D flow for low peclet number, but as Pe number goes higher our model results deviate from the 2-D simulation results. Moreover, the more turbulent the flow is, the more accurate is our model. The reason for that is that our 1-D model is equivalent to a 2-D plug flow, so as the flow goes turbulent, it resembles more a plug flow, which means that there is no significant change in velocity in the radial direction. Whereas for a laminar flow, the velocity profile is parabolic, which means that the velocity is maximum at the center, and zero at the boundary. Therefore for a laminar flow, the maximum transport of species by convection is at the center, and it is minimal at the boundary. But when Pe number is low, radial diffusion compensates any concentration gradient along the radial direction, which means that the concentration along the radial direction is almost uniform for low Pe number.

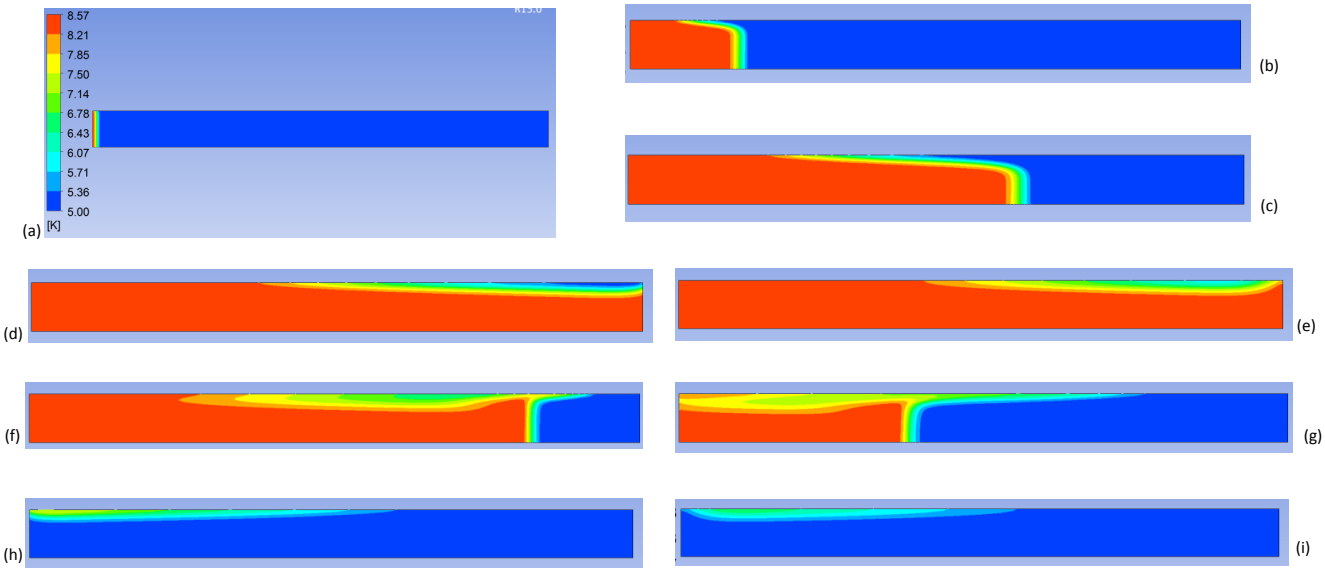


Figure 5-8: 2D species concentration contours for high peclet case Pe = 793 , Re = 1774. (a) T/40 (b) T/8 (c) T/4 (d) 3T/8 (e) T/2 (f) 5T/8 (g) 6T/8 (h) 7T/8 (i) T

5.3 Simulation Setup

A simulation of an adult's lung (with a constriction at one branch in the 4th generation) was run with the following parameters values:

- Frequency of respiration = 0.2 Hz
- Inspiration time = $T/3$
- Expiration time = $2T/3$
- Tidal volume = 500 ml
- Lung compliance = 166.667 ml/cmH_2O
- Number of compartments = 8
- Number of generations = 24
- Density (resolution) = 1000 divisions/meter
- 4th Generation Diameter = 2.7895 mm

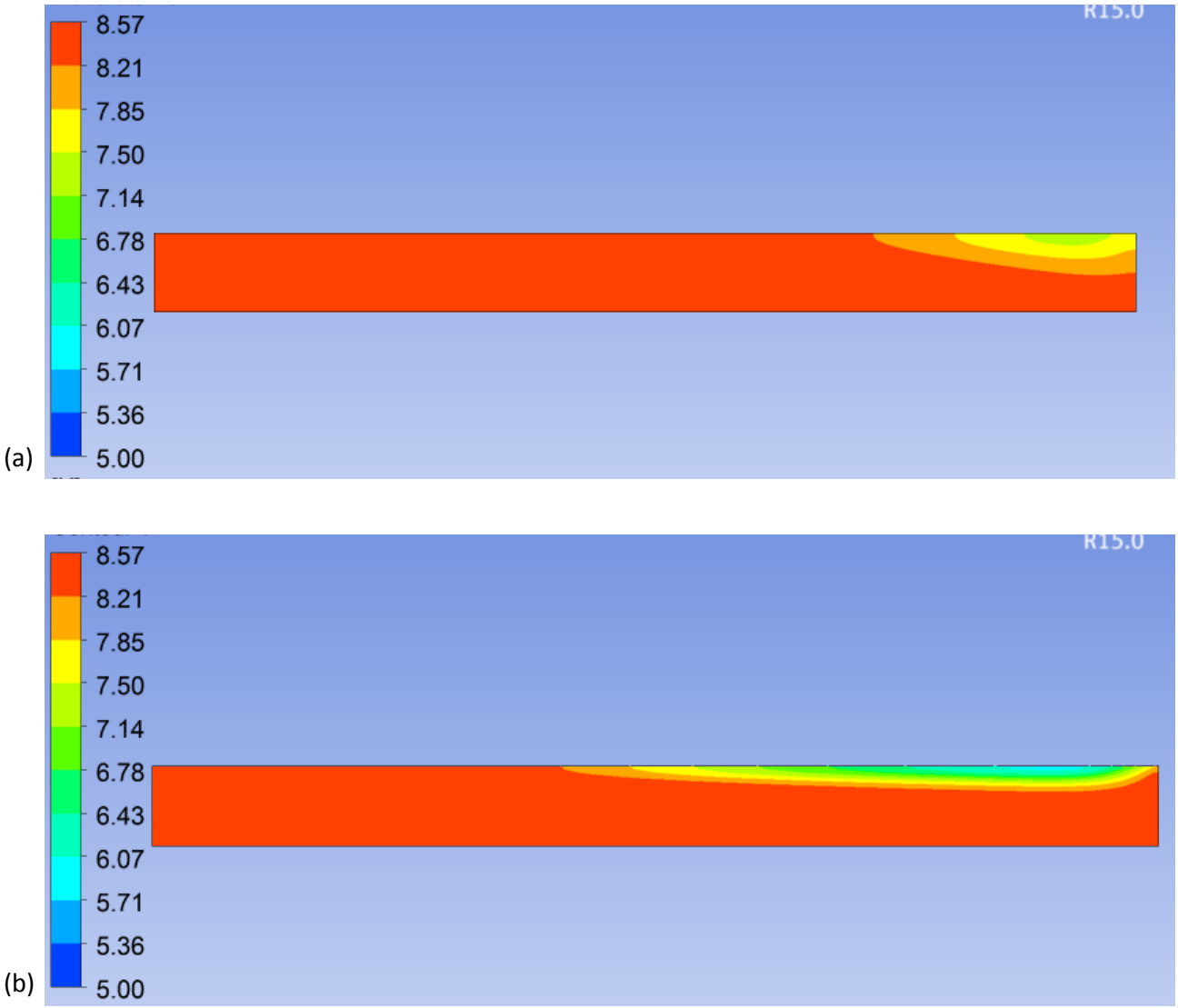


Figure 5-9: 2D species concentration contours for high and moderate peclet cases. (a) Pe = 93, Re = 1774 (b) Pe= 793, Re = 1774

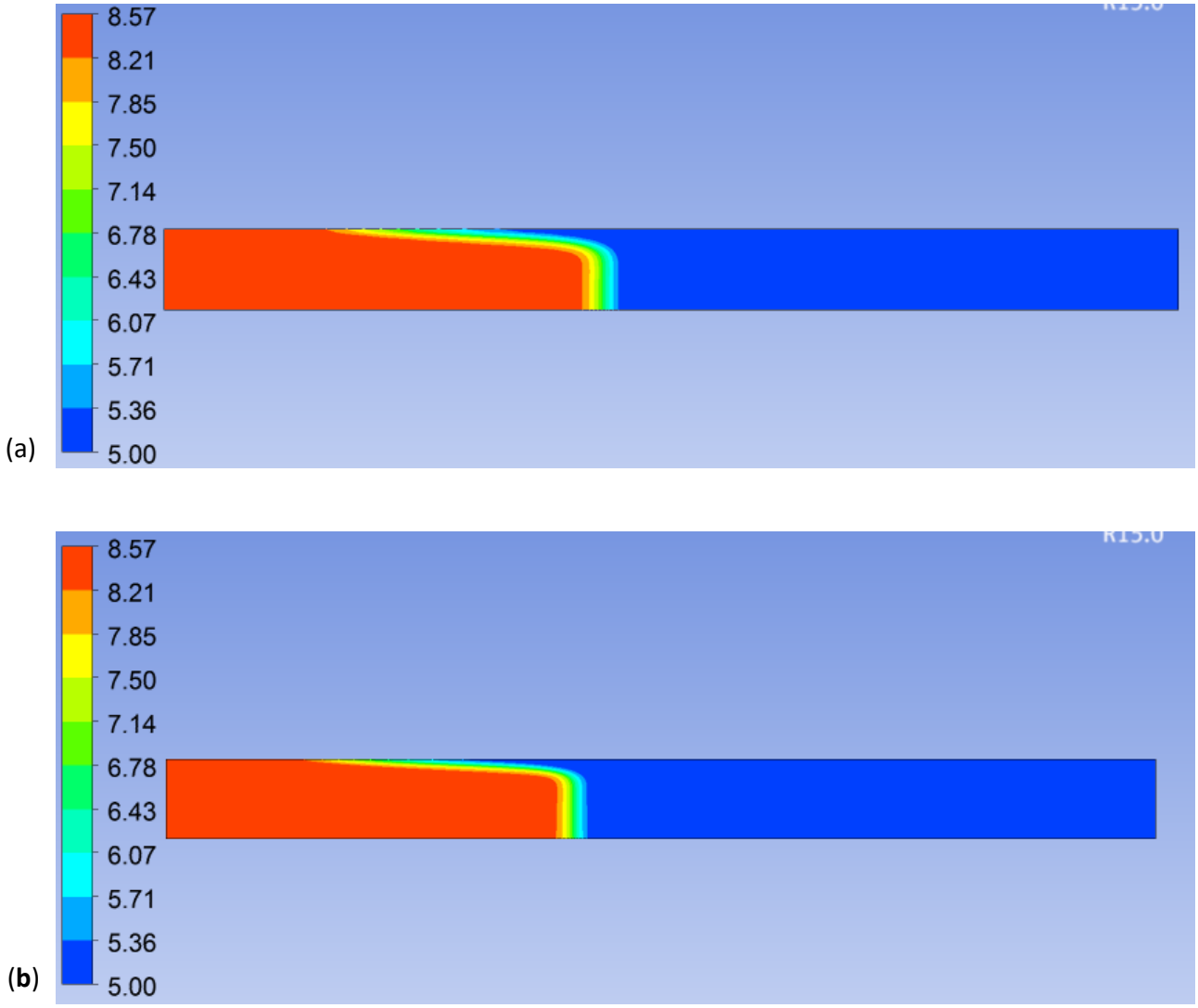
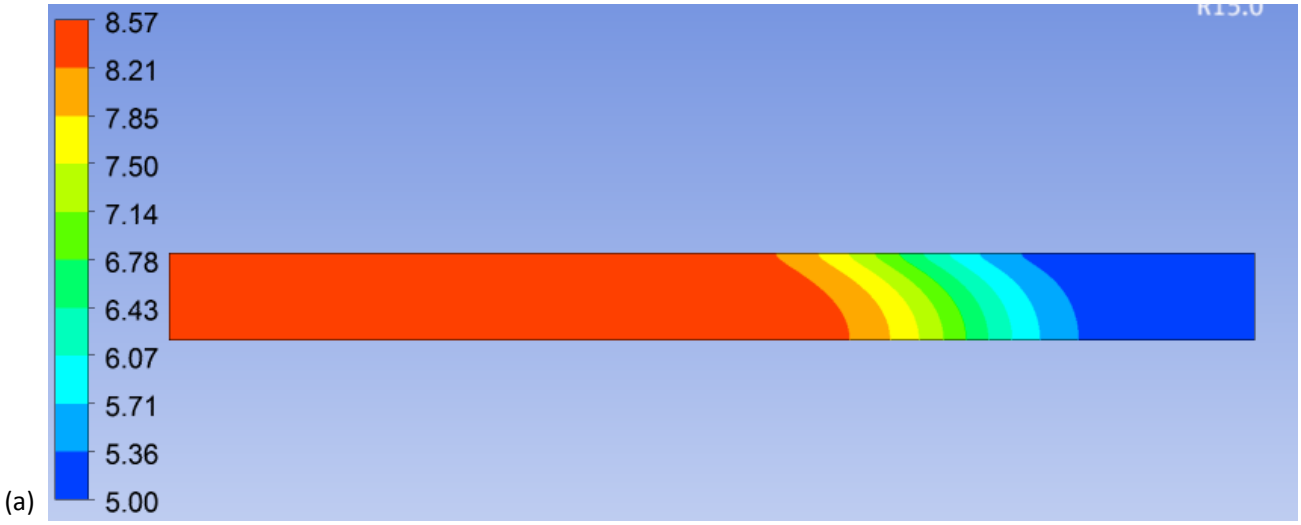


Figure 5-10: 2D species concentration contours for laminar and turbulent cases. (a) T/5, Pe = 793, Re = 1774 (b) T/8, Pe= 1823, Re = 4078



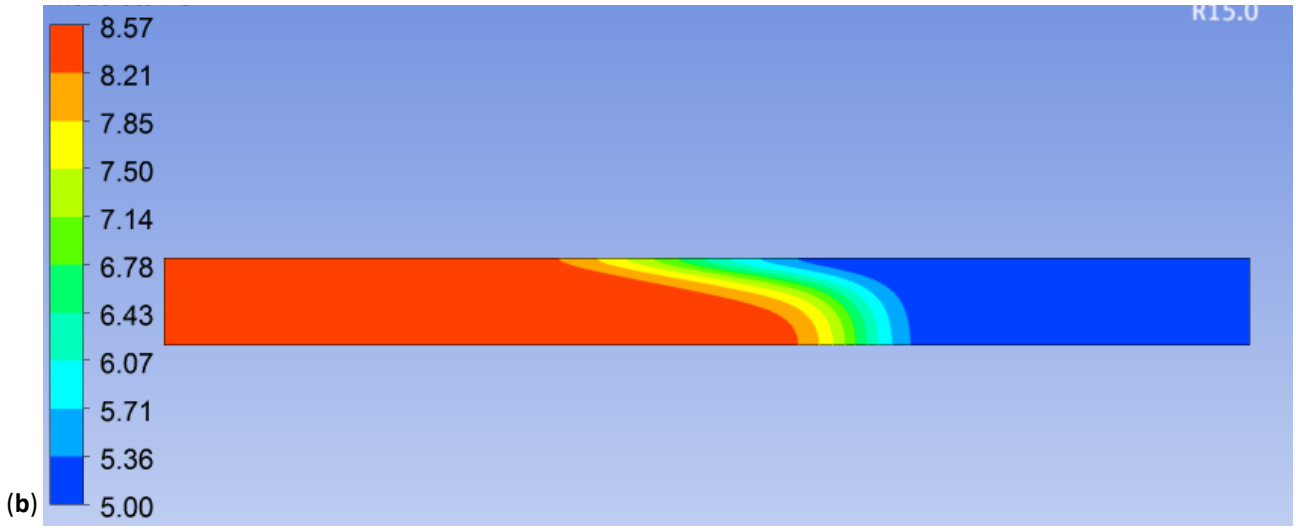


Figure 5-11: 2D species concentration contours for laminar and turbulent cases. (a) T/8, Pe = 93, Re = 7136 (b) T/4, Pe= 93, Re = 1774

- Constricted Branch Diameter = 1 mm

Boundary condition for oxygen in atmospheric air (at the entrance of the trachea) was set to 8.567 mol/m^3.

Pleural pressure is assumed to vary between -5 cmH_2O and -8 cmH_2O during inspiration as shown in Fig. 5-12.

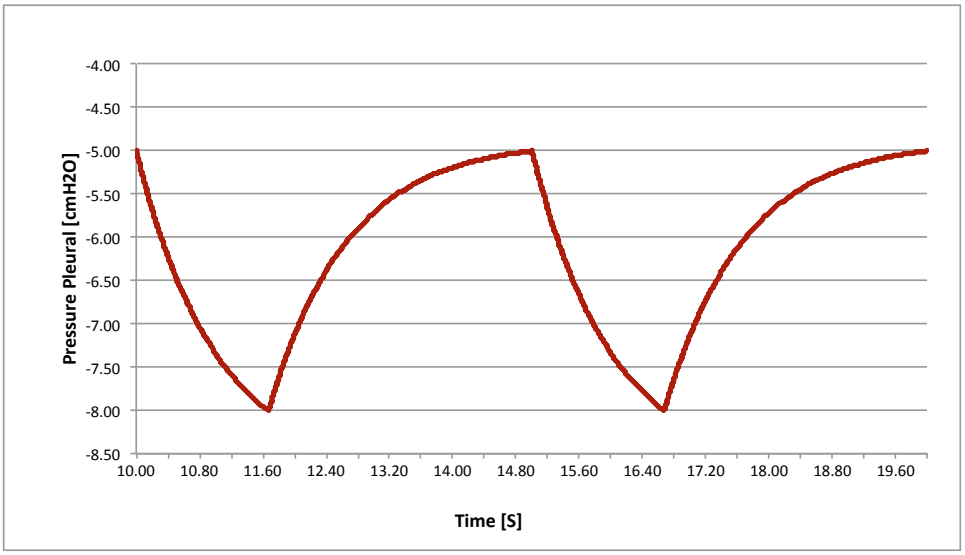


Figure 5-12: Pleural pressure vs time

5.4 Simulation Results

Results of the simulation are presented in the following figures.

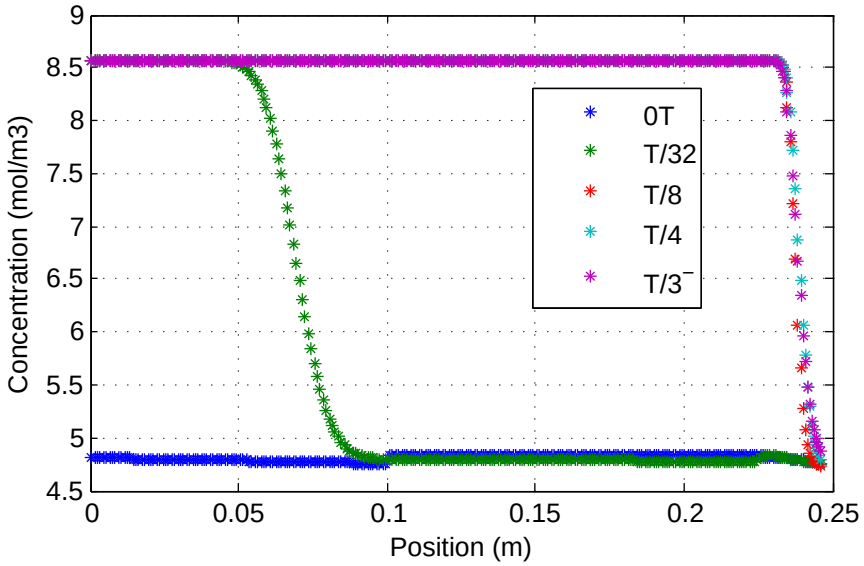


Figure 5-13: Oxygen concentration for all generations vs position at different times during inspiration - Normal Branch N

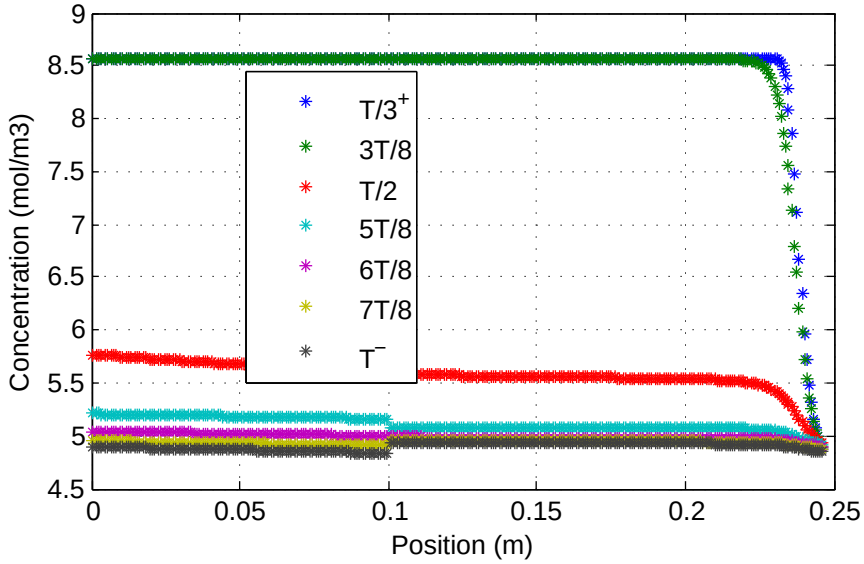


Figure 5-14: Oxygen concentration for all generations vs position at different times during expiration - Normal Branch N

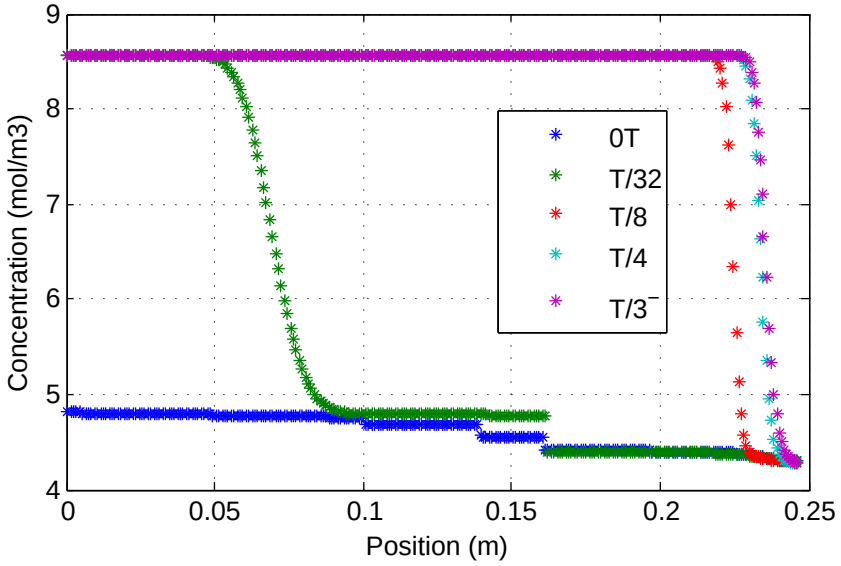


Figure 5-15: Oxygen concentration for all generations vs position at different times during inspiration - Abnormal Branch A

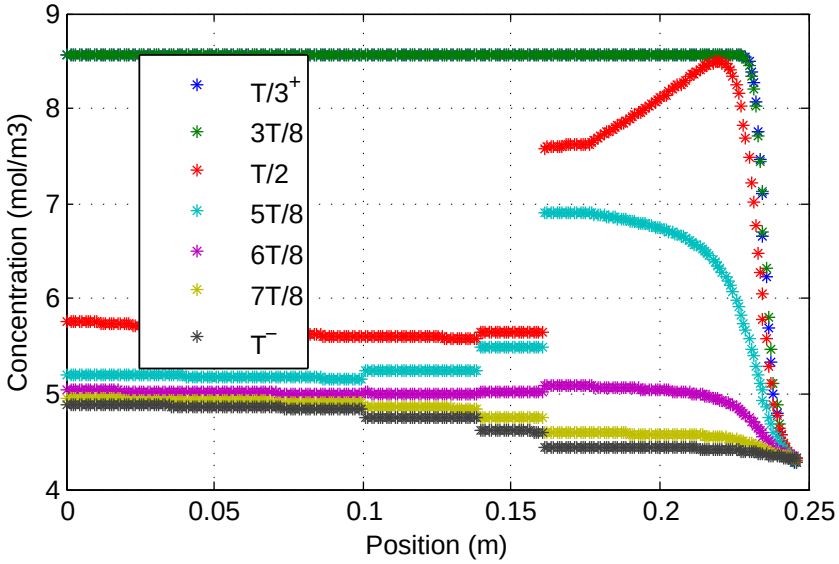


Figure 5-16: Oxygen concentration for all generations vs position at different times during expiration - Abnormal Branch A

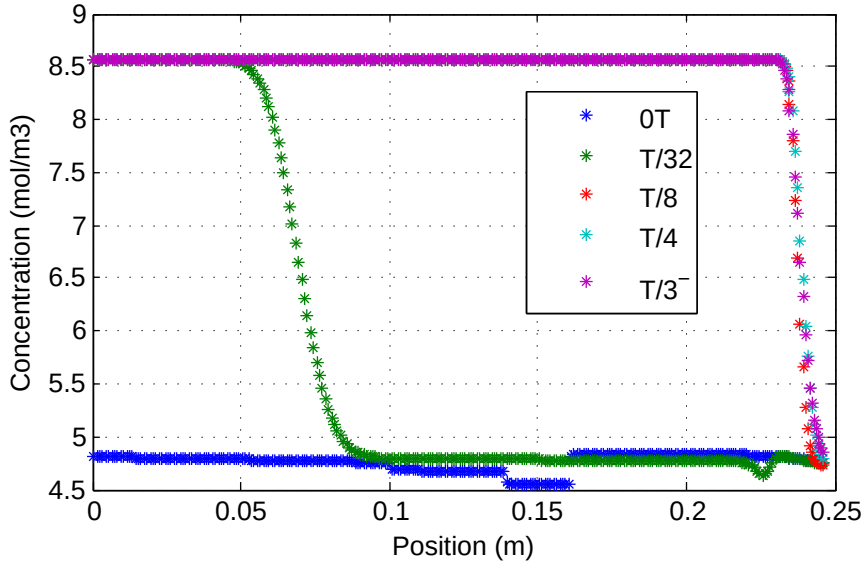


Figure 5-17: Oxygen concentration for all generations vs position at different times during inspiration - Branch B

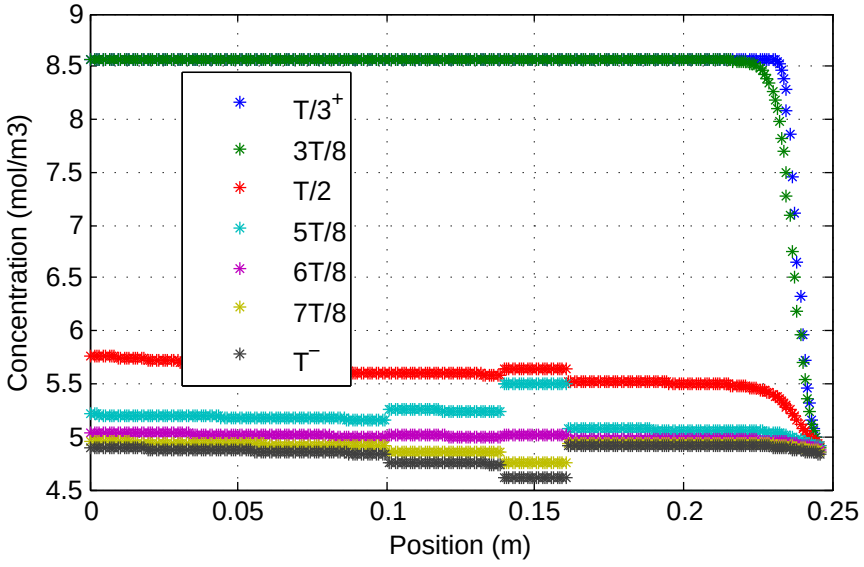


Figure 5-18: Oxygen concentration for all generations vs position at different times during expiration - Branch B

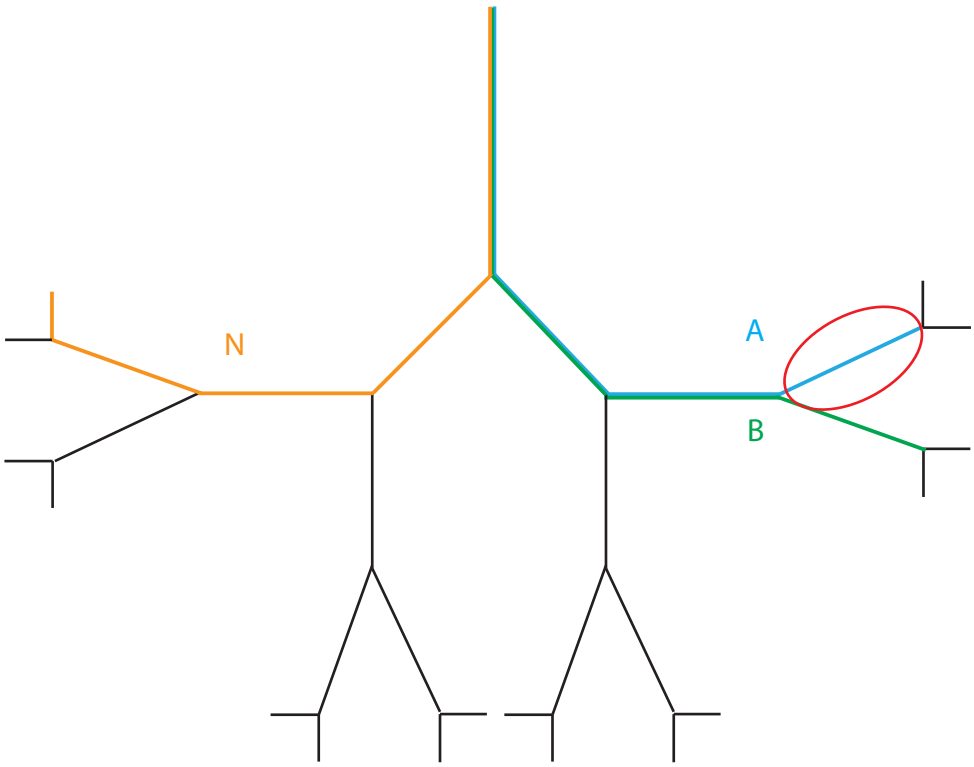


Figure 5-19: Pathways N, A and B

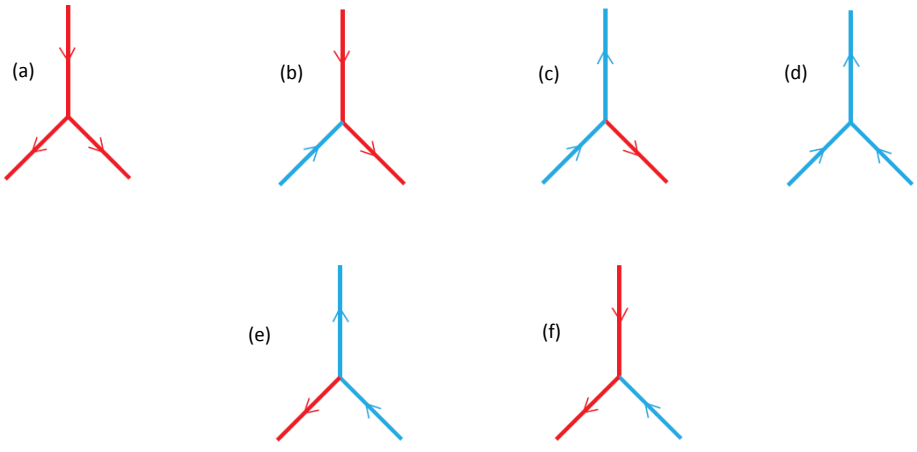


Figure 5-20: Flow cycle for the case of constriction

Chapter 6

Conclusion

We presented a method to model the advection-diffusion equation through electrical circuits. The method was shown to be accurate for low Peclet numbers, and works for transient and steady state solutions.

Also, we used this method to build a model that simulates gas transport through pulmonary airways down to the alveoli.The model conserves the critical properties of the lung and capillaries, these properties are essential for opimizing the process of ventilation, like maximizing surface area, and minimizing resistance through branching, while at the same time reducing simulation time and giving accurate results.

The model lets us collapse the whole lung into a desired number of compartments.

Some applications of the model are to simulate the effect of some changes in lung properties on lung performance, to study scenarios for pulmonary diseases, to simulate the transport of gases, other than oxygen and carbon dioxide, in airways and through the alveoli.

The model can be coupled with a model of the cardiovascular system to have a full model that simulates gases transport starting from the trachea, and ending in tissue cells.

In the future, higher order schemes will be implemented in the model, and oxygen and carbon dioxide transports are to be simulated simultaneously to get accurate species fluxes across the alveolar surface.

Appendix A

Derivation of the Mechanics Model

The model simulates the resistive behavior of the airways and the compliant behavior of the alveoli.
The pressure drop across an airway is:

$$\Delta P = R\dot{V} \tag{A.1}$$

The pressure drop across the alveolar membrane is related to the alveolar volume through the following relation:

$$dV = CdP_{TP} \tag{A.2}$$

Integrating equation A.2:

$$V(t) - V_0 = C(P_{TP}(t) - P_{TP0}) \tag{A.3}$$

Transpulmonary pressure is defined as:

$$P_{TP} = P_{alv} - P_{ip} \tag{A.4}$$

Substituting equation A.4 in equation A.3 we get the following equation:

$$V(t) - V_0 = C[P_{alv}(t) - P_{ip}(t) - (P_{alv0} - P_{ip0})] \tag{A.5}$$

Note that the subscript 0 is used in the above equations to refer to a reference state, which we chose it to be the end of expiration, where P_{alv0} is equal to 0, and V_0 is equal to FRC.

The alveolar pressure is equal to the difference between atmospheric pressure and the pressure drop from the trachea inlet to the alveolus. The latter is defined in equation A.1. Therefore:

$$P_{alv} = 0 - R\dot{V} \tag{A.6}$$

$$\frac{V(t) - FRC}{C} = 0 - R\dot{V} - P_{ip}(t) - (0 - P_{ip_0}) \tag{A.7}$$

Rearranging equation A.7:

$$\frac{V(t)}{C} + R\dot{V} + P_{ip}(t) - P_{ip_0} - \frac{FRC}{C} = 0 \tag{A.8}$$

To get the value of C and P_{ip_0} we take two conditions: the end of inspiration and the end of expiration.

At the end of inspiration: $V = FRC + TV$, $\dot{V} = 0$, and $P_{ip} = -8\ cmH2O$.

At the end of expiration: $V = FRC$, $\dot{V} = 0$, and $P_{ip} = -5\ cmH2O$.

For $FRC = 2500\ ml$ and $TV = 500\ ml$, we get $C = 166.667\ ml/cmH2O$, and $P_{ip_0} = -5\ cmH2O$.

Appendix B

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