Modeling, Simulation, And Visualization Of 3d Lung Dynamics

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MODELING, SIMULATION, AND VISUALIZATION OF 3D LUNG DYNAMICS

by

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ABSTRACT

Medical simulation has facilitated the understanding of complex biological phenomenon through its inherent explanatory power. It is a critical component for planning clinical interventions and analyzing its effect on a human subject. The success of medical simulation is evidenced by the fact that over one third of all medical schools in the United States augment their teaching curricula using patient simulators. Medical simulators present combat medics and emergency providers with video-based descriptions of patient symptoms along with step-by-step instructions on clinical procedures that alleviate the patient’s condition. Recent advances in clinical imaging technology have led to an effective medical visualization by coupling medical simulations with patient-specific anatomical models and their physically and physiologically realistic organ deformation.

3D physically-based deformable lung models obtained from a human subject are tools for representing regional lung structure and function analysis. Static imaging techniques such as Magnetic Resonance Imaging (MRI), Chest x-rays, and Computed Tomography (CT) are conventionally used to estimate the extent of pulmonary disease and to establish available courses for clinical intervention. The predictive accuracy and evaluative strength of the static imaging techniques may be augmented by improved computer technologies and graphical rendering techniques that can transform these static images into dynamic representations of subject specific organ deformations. By creating physically based 3D simulation and visualization, 3D deformable models obtained from subject-specific lung images will better represent lung structure and function. Variations in overall lung deformations may indicate tissue
pathologies, thus 3D visualization of functioning lungs may also provide a visual tool to current diagnostic methods.

The feasibility of medical visualization using static 3D lungs as an effective tool for endotracheal intubation was previously shown using Augmented Reality (AR) based techniques in one of the several research efforts at the Optical Diagnostics and Applications Laboratory (ODALAB). This research effort also shed light on the potential usage of coupling such medical visualization with dynamic 3D lungs. The purpose of this dissertation is to develop 3D deformable lung models, which are developed from subject-specific high resolution CT data and can be visualized using the AR based environment.

A review of the literature illustrates that the techniques for modeling real-time 3D lung dynamics can be roughly grouped into two categories: Geometrically-based and Physically-based. Additional classifications would include considering a 3D lung model as either a volumetric or surface model, modeling the lungs as either a single-compartment or a multi-compartment, modeling either the air-blood interaction or the air-blood-tissue interaction, and considering either a normal or pathophysical behavior of lungs. Validating the simulated lung dynamics is a complex problem and has been previously approached by tracking a set of landmarks on the CT images.

An area that needs to be explored is the relationship between the choice of the deformation method for the 3D lung dynamics and its visualization framework. Constraints on the choice of the deformation method and the 3D model resolution arise from the visualization framework.
Such constraints of our interest are the real-time requirement and the level of interaction required with the 3D lung models. The work presented here discusses a framework that facilitates a physics-based and physiology-based deformation of a single-compartment surface lung model that maintains the frame-rate requirements of the visualization system.

The framework presented here is part of several research efforts at ODALab for developing an AR based medical visualization framework. The framework consists of 3 components, (i) modeling the Pressure-Volume (PV) relation, (ii) modeling the lung deformation using a Green’s function based deformation operator, and (iii) optimizing the deformation using state-of-art Graphics Processing Units (GPU). The validation of the results obtained in the first two modeling steps is also discussed for normal human subjects. Disease states such as Pneumothorax and lung tumors are modeled using the proposed deformation method. Additionally, a method to synchronize the instantiations of the deformation across a network is also discussed.
To my Amma, Appa, Uma, Rama, Arun and Nikila who have supported me all the way since the beginning of my studies, and in loving memory of my grandparents.

To my friends, who have kept my spirit alive!

To all those who believe in the spirit of learning.
ACKNOWLEDGMENTS

It is said that guru (preceptor and advisor) is greater than god, devotion to guru is more meritorious than that of god. If we ask why, the answer is that god has not been seen by any one, but the guru is present here and now before us. If a guru who is immaculate and pure, full of wisdom and steadiness of vision completely free from weakness were available to us, the mental peace in search of which we pray to god is at our reach by devotion to the preceptor. The guru has the same great and auspicious qualities that god possesses, namely, blemish-less purity, truth, devoid of deceit or dissimulation, complete control of the senses, infinite compassion and wisdom. The only difference is that we are able to see the guru by our eyes, while god is invisible. Hence if we begin to develop devotion to the guru clinging to his holy feet we will gain with ease all the benefits that we expect from god with effort.

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LIST OF ACRONYMS

3D Three Dimension
AR Augmented Reality
CAD Computer Aided Design
CMA Capacitance Matrix Algorithms
CPO Control Packet Object
CPU Central Processing Unit
CRPG Central Respiratory Pattern Generator
CT Computed Tomography
FEM Finite Element Method
FFD Free Form Deformation
FLOPS Floating Point Operations
FPS Frames Per Second
FRC Functional Residual Capacity
GF Green’s Function
GPU Graphics Processing Unit
HMD Head Mounted Display
MCAT Multi-resolution Computer Aided Tomography
MRI Magnetic Resonance Imaging
NURBS Non-Uniform Rational B-Spline
PV Pressure-Volume
RMS Root Mean Square
<table>
<thead>
<tr>
<th>Acronym</th>
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<tr>
<td>SHT</td>
<td>Spherical Harmonic Transformations</td>
</tr>
<tr>
<td>TLC</td>
<td>Total Lung Capacity</td>
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<tr>
<td>TV</td>
<td>Tidal Volume</td>
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CHAPTER ONE : INTRODUCTION

Medical simulations that demonstrate the anatomical and physiological aspects of human body are important tools for both guiding medical physicians towards the correct course in complex medical procedures and for training medical students effectively. Real-time Visualization is necessary for medical simulation applications for its users to visually perceive the dynamics of the physiology and anatomy involved. Technological advances in computer graphics and visualization environments lead to an increased interest in such visualization paradigm with computer generated 3D objects. Moreover, technological advances in the optical projection enable us to further increase the effectiveness of augmented reality techniques, an advanced visualization framework. Such visualization environments significantly help perceive the time-dependent dynamics of the physiology under complex physical conditions. Such dynamics can be represented by coupling computer generated 3D medical models with deformation methods.

One anatomical component of particular interest is the lung physiology. Human lungs are the key anatomical organs that take part in the exchange of oxidation gases. In this process, lung expands and contracts based on the flow of air inside it and the exchange of gases. A visual analysis of the lung’s shape dynamics may be an effective tool for understanding the physiology of breathing. However obtaining patient-specific tissue properties which are key requirements for modeling the dynamics of lungs accurately, is a significant limitation. In this section, we provide some of the basic concepts of deformation and its relation to its applications and their requirements.
1.1 Motivation

Envision a world where medical physicians, trainees and patients can visualize and perceive three dimensional (3D) lung dynamics instead of analyzing two-dimensional images. Imagine being able to superimpose deforming 3D lung models onto a human subject in order to learn and predict lung dynamics under different physical breathing conditions of that subject.

The research discussed in this dissertation facilitates real-time visualization of lung dynamics beyond the current framework of understanding by allowing the users of the environments to visualize, perceive and analyze 3D lung dynamics of either a specific human subject or a general lung model.

A schematic representation of the environment is as shown in Figure1.1. The proposed research work investigates the technical challenges involved in developing a deformation framework that caters to the needs of real-time visualization environments. The work presents a framework for visualizing deforming models by combining physically-based deformation methods and real-time stereoscopic visualization. A method to non-invasively obtain the lung tissue properties of patients is also presented. This method further helps in accurately predicting lung deformations under dynamic conditions. The 3D models of particular concern are anatomical datasets based on visible human dataset and human subject data obtained from medical imaging equipments.[1]
1.2 AR-based Stereoscopic Visualization

Between the extremes of real life and synthetic life lies the spectrum of Mixed Reality (MR) in which views of the real world are combined in some proportion with views of a virtual environment. A subclass of the MR systems is formed by Augmented Reality (AR) systems. Combining direct stereoscopic 3D graphics, AR describes that class of systems that consists primarily of a real environment, with graphic enhancements or augmentations superimposed over the real environment.[2] Furthermore, the augmentations are modified (translated, rotated and deformed) in real-time in order to correspond to the changes in the real world.

1.3 Deformation Methods

Deformation methods have been used in a range of application areas such as Animations,[3] Image analysis, [4] and Computer-aided Design.[5] It is a broad area of research involving wide-reaching issues related to 3D data representation, modification and its interaction. These issues are generally addressed considering the real-time and physical accuracy constraints involved.
The type of deformation methods range from simple algorithms such as 3D interpolations (key framing) to complex physically-based algorithms that take into account the physiological and mechanical factors. With respect to medical simulations, deformations of great importance are the physically-based deformations. Physically-based real-time deformations are generally obtained by a detailed modeling of the mechanics involved in the deformation, which also take into consideration the real-time constraints of the deformation. Some of these approaches are applied for realistic deformation of computer-generated virtual humans and realistic deformation of synthetic materials and human tissues.

A key aspect of physically-based deformations arises from its ability to model both normal and diseased lung deformations. The latter can be modeled by introducing variations in the deformations that reflect changes in the physiology, breathing control and external conditions. Two particular cases of our interest are pneumothorax and lung tumors. Pneumothorax refers to the presence of air in the pleural cavity.[6] Death in this case can be as quick as 30 minutes. Federal regulations also prevent patient imaging for extreme cases of pneumothorax. The proposed framework for lung dynamics, when extended to model pneumothorax can significantly help in guiding clinical trainees to improve their methods. Lung tumors are dead hardened tissues inside lungs, which create breathing dis-comfort.[7] The presence of lung tumors creates variations in the lung breathing. The proposed framework of lung dynamics, when extended to model lung tumors may significantly help in guiding clinical trainees on treatment procedures.
The technical limitations for visualizing physically-based deformations arise mainly from the fact that the real-time requirements of the visualization inversely affect the physical accuracy of the simulation. While the computational complexity of deforming and rendering 3D models requires the models to be small, the physical accuracy of the dynamics requires the 3D models to be large. However, recent developments in hardware-accelerated graphic methods provide scope to alleviate the scenario by increasing the computing speed.

1.4 Dissertation Outline

Chapter 2 gives an overview of related works done in the areas of deformation methods and lung physiology modeling. To provide the necessary background for further discussions, section 2.1 starts with a brief description of the fundamental concepts behind deformation of 3D models. The usage of deformation as an operator for an application is clearly explained. A description of the general approaches for 3D data representation is then presented. It is followed by a discussion on geometrical modeling of deformation in section 2.2,[5] and physical modeling of deformation in section 2.3.[3] The Lagrangian equation of motion and kinematics using differential equations and an Eulerian approach for the simulation of those differential equations for kinematics is explained in Section 2.4 and 2.5.[8]

Chapter 3 explains the efforts undergone in modeling lung physiology. Section 3.1 explains the general physiology and anatomical information related to human lungs. Section 3.2 discusses the control of breathing by the medulla oblongata. Section 3.3 explains the modeling efforts undergone in modeling the gas-exchange process in lungs. Specifically, gas-laws that affect the
breathing are discussed. Section 3.4 explains the initial efforts undergone by Pedley in representing the 3D lung dynamics using electrical circuit representations.[9] Section 3.5 discusses the mechanical representation of 3D lungs by Grodins. Section 3.6 explains an initial 3D modeling effort of lung dynamics by Metaxas using Finite Element Methods (FEM), which extends the electrical circuit representation discussed in section 2.4.[10] Section 3.7 explains the modeling efforts by Tawhai on an FEM based bronchial tree structure.[4, 11] Section 3.8 discusses the modeling efforts undergone in representing volumetric lung deformations that encapsulates the FEM based bronchial tree.[12] Section 3.9 discusses the related work done in modeling parenchymal deformation movements.[13, 14] Section 3.10 presents an alternative approach for obtaining 3D lung simulations by modeling the abdominal torso movements.[15] Section 3.11 explains the modeling of lungs using 4D (Non-Uniform Rational B-Spline) NURBS and its validation using patient-data by Segars et al. [16]. It then explains the modeling of lungs using warping functions and their verification using MRI-tagged patient-data by Krishnan et al. [17]. Section 3.12 explains the efforts undergone in extracting high-resolution 3D lung models.[1] Section 3.13 presents a discussion on some of the key physiological factors that reflect on the lung deformation.

Chapter 4 presents an introduction on the proposed framework and is divided into two sections. Section 4.1 presents an outline of proposed method of deforming 3D lung models.[18] Section 4.2 presents an outline of the visualization system used.[19]

Chapter 5 presents the proposed method of modeling the pressure-volume relation using motor drive of breathing and the muscle mechanics.[20] Section 5.1 presents an introduction of the
biomathematical formulations and the control of ventilation. Section 5.2 discusses the related work involved in formulating the first-order differential PV relation as a biomathematical formulation for diagnostic purposes. Section 5.3 discusses a second-order differential PV relation to formulate the PV relation for visualization purposes. Section 5.4 presents the results of PV curves parameterized from both human subject data and the data used by the peers. The flexibility of the method in simulating variations in the PV relation for modeling breathing variations is also demonstrated in this section. Finally section 5.5 provides a discussion on the future work that needs to be undertaken for the application of this model. Section 5.6 concludes the chapter.

The physics and physiology-based deformation of lungs form the main topic of this chapter 6 and is detailed in sections 6.1-6.5.[21-23] Section 6.1 discusses the lung morphology as observed from the 4D HRCT scans. Section 6.2 presents a discussion on the modifications done to the 3D polygonal lung model extracted from the HRCT scan, in order for the model to be deformable. The mathematical model of the deformation method is discussed in section 6.3. Section 6.4 discusses the validation of 3D lung dynamics using 4D HRCT datasets. Finally, section 6.5 discusses pre-computing the lung deformation for a given orientation in order to obtain real-time deformations. Section 6.6 concludes the chapter.

Chapter 7 discusses a method for optimizing the 3D lung dynamics in order to be visualized in a stereoscopic AR framework.[24] Section 7.1 presents an overview of the Graphics Processing Units (GPU). Section 7.2 presents an overview of the method proposed using GPU. Section 7.3 then discusses the mathematical model of the proposed method. It is followed by a discussion on
the SH coefficients of the applied force in section 7.4. Section 7.5 discusses the lung deformation results. Section 7.6 presents a discussion on the limitations of the proposed method and extensions that can be done to this method. Section 7.7 concludes the chapter.

Chapter 8 presents a discussion on the case studies done using the proposed 3D lung dynamics. Specifically, we consider two disease states: Pneumothorax, and Tumor-influenced lungs. We first discuss the changes that occur in the lung deformation for pneumothorax, (section 8.1) and tumor-influenced lungs (section 8.2).[25, 26] It is followed by a discussion on the subsequent breathing variations in the PV curve caused by the above-mentioned disease states (section 8.3). Finally, we discuss in section 8.4 an extension to the lung dynamics framework: a distributed lung dynamics framework that would allow geographically separated experts to interact for training and diagnostic purposes.[27, 28]

Chapter 9 concludes the research with a discussion section on the future work in the proposed components.
CHAPTER TWO: LITERATURE REVIEW- DEFORMATION METHODS

In this section we discuss recent methods adopted for deforming 3D models. Deformation methods aide in applications related to Animations, and Computer aided Design (CAD) by changing the shape of the 3D object.[5] This change in shape could be done either periodically or based on external control factors that depend on the application. While in applications related to animations, real-time deformation methods are given importance, in application related to CAD, interactive control in change of shape with high level of detail is given importance. The level of accuracy in the deformation required in each of these application areas differs from one another. The real-time requirements are addressed mainly in specific cases such as 3D scientific visualization and interaction, which applies to both animation and CAD applications.

The choice of a deformation method affects the other requirements or constraints of the application. The method, which is computationally expensive affects the real-time requirement of the application. Similarly the method whose mechanical compliance is less, affects the accuracy requirements of the application. An efficient approach to deform a 3D object would consider the requirements of a given application and optimize the deformation operator accordingly.

A deformation method can be used for both global and local changes in shape. A global change in shape deals with a relatively uniform change in position of every element of the object. A simple example would be to an increase in volume of a parametric object such as a cube. A local change in shape would also include unrelated change in every element of the object. A simple
example would be an increase in volume of an elastic object such as a balloon. Such local deformations can be seen in the animation of 3D models in computer games. The difference is from the level of detail at which the change in shape can be viewed. In our discussion we always consider the deformation as a local deformation.

In this chapter we shall first analyze the computer generated virtual model representations in section 2.1. We shall then analyze the deformation methods for those model representations and their related works in section 2.2 and 2.3. The importance of model representation and the choice of the deformation method are then discussed in section 2.4. Finally, the steps involved in the physical simulation are discussed.

2.1 3D Data Representations

A 3D medical dataset can be collected using commercially available 3D scanning techniques such as magnetic and optical trackers, and medical imaging techniques such as Computed Tomography (CT) and Magnetic Resonance Imaging (MRI).[16] The collected data is pre-processed for obtaining smooth surfaces using softwares such as Surfviewer, Geomagic studio, [29] etc. The collected 3D data can either be a volumetric model or a surface model. A volumetric 3D model has points (voxels) in the whole volumetric region of the 3D model thus filling its complete space. A surface 3D model has points only on the surface or boundary of the 3D model.[5]
The 3D data needs to be represented in such a way that deformation steps can be computed with efficient memory access. Thus the computer generated 3D virtual data can be fitted to a parametric equation or directly represented using regular data structures.[30] A parameterized representation of a 3D model is obtained by developing an equation for approximating all the points (positions) in the 3D representation. The equations can be a function of a set of control points as seen in parametric curves and splines. The regular data structures are naïve representations of the 3D model. The simplest regular data structure is an array of points. A linked list representation of the data is considered to be apt for representing the polygons in the object as a nodal net. Specialized data structures such as Winged Edge data structure are developed in order to get representations that are efficient in model transformations.[5]

A 3D model is said to be rigid when it does not undergo any deformation and undergoes shape variations that involve only translations, and change in its orientation. A non-rigid model can undergo local deformations as well as translation and change in orientations. For our discussion we always consider a 3D model as a non-rigid model.

The steps of a deformation method deal with changes applied to the parametric and regular data structures of a 3D model in order to create 3D shape changes. A simplest choice of deformation would be simple operations on these data structures, such as an addition of a constant to the every element of the data structure. The material deformation parameters are then associated to each element (point) of the 3D data to obtain the required change in shape, in order to fit the model representation. These material deformation parameters are based on the type of deformation method used and further discussed in the next section.
We will now discuss two important categories of deformation methods.[5] The deformation methods fit grossly into two sub-divisions namely the geometric and the physical modeling. Geometric deformation methods mainly provide interactive controls to the shape of a 3D object, while the physically-based methods provide a way to include the mechanics of motion. The sub-division comes from the fact that a given change in shape for an object can be represented as an answer to either “what was the change” or “what caused the change”. We now continue our discussion in describing these two deformation categories.

### 2.2 Geometric Modeling

A geometric model is also referred to as a non-physical representation. This is a technique used by 3D model designers to design complex surfaces of 3D objects. Early efforts in developing such representations arose from the field of Computer Aided Geometric Design. A description of geometric representations was summarized by Solomon.[5]

A 3D curve is considered as a basic geometric primitive for developing 3D surface and volumetric models. The representation of a curve is in the form of either an array of points or a parametric equation which can be obtained by fitting the array of points using Lagrange’s polynomial equation or Newton’s polynomial equation.[31] Some of the initial curve-based representations include Bezier and B-spline curves and surfaces. In both methods, a point on a curve is represented as a function of a set of control points.
In Bezier curves, the Bernstein (cubic) polynomials are generally used to specify the weights for each of the control points, in order to compute the position of a single point in the curve. It is done by computing a weighted distance of the curve point from each control point. These control points are either outside or on the actual curve (end control points) obtained from them. The number of control points used to compute the position of a curve point minus one is referred to as degree of the curve. Figure 2.1a and b show an illustration of a deformation of Bezier surface patch with a degree of 3.

B-Splines were introduced in order to represent curves with improved control of shape. In this approach, every control point also has associated weights that compute a point in the curve. The control points lie always outside the actual curve for a degree greater than 2. The weights were not based on the barycentric distance but on the polynomial equations which are referred to as Knots. Figure 2.2a and b illustrate the deformation of a B-spline surface patch with a degree of 3. A modification to B-Splines in which each control point is associated with a constant weight is referred to as NURBS. This method provides non-uniform meticulous control for the design of the curve.
Figure 2.1 A Bezier surface patch (a) denoted by red and blue lines created by control points connected by white lines. The deformation of the Bezier surface patch is computed by displacing the control points and shown in (b).

Figure 2.2 A B-Spline surface patch denoted by red and green lines created by control points connected by white lines. (b) A sample deformation of B-Spline surface patch by displacing the control points.
Parabolic blending methods such as Catmull-Rom curves consider an implicit equation of a parabola as a representation of a curve and the blending is obtained by modifying the parameters of the parabolas involved using Bernstein polynomials for assigning weights to different parabolas.[5]

A special case of geometric deformation system is Free-form deformation (FFD) whereby a unit space is considered as the basic geometric primitive. A given 3D object space is divided by a regular lattice and by modifying the lattice points we modify the space between the lattice and thus the graphic primitive of the 3D object. The modification of the lattice points is however user-controlled, as seen in the previous geometric modeling representations.

Geometric models being flexible in deformations are limited by the fact that the deformation is limited by the expertise and patience of the user. The system has no prior assumptions on the nature of the objects being manipulated. Also the basic primitive of these models were required to be interpreted as vertices for them to be displayed or rendered.

### 2.3 Physical Modeling

Physically based methods were introduced in the field of computer graphics in order to alleviate the daunting task of modeling complex deformations.[32] These methods involve realistic simulation of complex physical processes. A physical representation involves coupling of mechanics of motion that defines the deformation with the 3D data of the object. It is essential to thus understand how a physical 3D object deforms when some force is applied on it.
A physical modeling method of deformation mainly consists of two levels of integration of mechanics (i) spatial and (ii) temporal. A spatial integration takes into account the effect of the material of the 3D model on the deformation. A temporal integration takes into account the variations in a deformation during a sequence of deformations and is further explained in section 2.4.

Any physical elastic object has a potential energy and strain energy associated with it. The strain energy is the energy stored in the body because of the deformation the body underwent. The strain energy is proportional to the change in shape of the object. The potential energy of the system is a constant and the strain energy is 0 when the object is rigid. The potential energy and strain energy vary when the object is non-rigid. The deformation is computed by the change in potential energy of surface points of a non-rigid object. The total potential energy of a deformable 3D physical object is denoted by \( \Pi \). It is formulated as

\[
\Pi = \Lambda - \Delta, \quad (2.1)
\]

where \( \Lambda \) is the total strain energy of the deformable object and \( \Delta \) is the work done by the external forces in deforming the object.

The individual components of the equation (2.1) is now expanded as follows: The work done by the external forces accounts for the concentrated loads applied at discrete points on the object, loads distributed over the body and loads distributed over the surface of the object. The strain energy is represented in terms of a volumetric representation of the object. It is derived from the integral expression over the volume of the material stress \( \sigma \) and strain \( \varepsilon \).
\[ \Lambda = \int_0^{Volume} \sigma^T \varepsilon dV = \int_0^{Volume} \varepsilon^T D \varepsilon dV, \quad (2.2) \]

where \( D \) is a matrix which relates the stress and strain components for an elastic system. The components of this matrix are defined by material strain parameters in either linear or non-linear form. In the linear form, only the diagonal elements of the matrix are possibly set to non-zero values. In the non-linear form, all the elements of the matrix are possibly set to non-zero values.

The strain is related to a given displacement vector \((u,v,w)\) of a position of 3D data point and is given as a vector of six values. This vector is represented as

\[ \varepsilon = \{ \varepsilon_{xx}, \varepsilon_{yy}, \varepsilon_{zz}, \varepsilon_{xy}, \varepsilon_{yz}, \varepsilon_{zx} \}. \quad (2.3) \]

The components of this vector are further expanded as,

\[ \varepsilon_{xx} = \frac{du}{dx}, \]
\[ \varepsilon_{yy} = \frac{dv}{dy}, \]
\[ \varepsilon_{zz} = \frac{dw}{dz}, \]
\[ \varepsilon_{xy} = \frac{du}{dy} + \frac{dv}{dx}, \]
\[ \varepsilon_{yz} = \frac{dv}{dz} + \frac{dw}{dy}, \]
\[ \varepsilon_{zx} = \frac{dw}{dx} + \frac{du}{dz}. \quad (2.4) \]

An explanation of these components can be given based on the theory of elasticity and is described in [33]. The work done \((\Delta)\) by the external force is computed as the dot product of the applied force \((f)\) and the material displacement \((d)\), integrated over the object volume.

\[ \Delta = \int_0^{Volume} d.f dV. \quad (2.5) \]
Having expanded the components of the equation (2.1) in equations (2.2-2.5), we continue our discussion in simulating the equation (2.1). There are two ways in which equation (2.1) can be simulated. In the first approach, the equation can be computed as it is. Such a computation will create instabilities in the form of mechanical vibrations, and so the deformation will be required to be re-computed until the deformation stabilizes. This approach is generally referred to as a dynamic approach. In the second approach, the derivative of potential energy is set to 0 and is then solved for the deformation. Such a computation will immediately provide a final deformation. This approach is generally referred to as a static approach.

An equilibrium shape of an object is the one that the total strain energy stabilizes for an external force. It is essential to calculate the equilibrium shape as most of the deformations render the physical object in an equilibrium shape. The system potential energy reaches a minimum when its derivative with respect to the material displacement is 0. The conditions for the existence of equilibrium displacement however need to be verified.

Physical modeling methods are classified into (a) Discrete modeling, (b) Continuous modeling and (c) Approximate Continuous modeling. This classification is done based on how the 3D virtual model is modified or discretized in order to compute equation (2.5).

2.3.1 Discrete Representation

Discrete modeling methods associate the mechanics of motion to the nodes and edges of 3D polygonal models. With respect to modeling the elastic deformations, the mass-spring system is
a prominent discrete modeling method that has been used widely and effectively in the field of animation.[34, 35] A given 3D object is represented by a set of mass points connected by springs. Such a representation is shown for a sample chain connection using a software, KineticKit in Figure 2.3. Forces are applied on nodes of the 3D object. Springs are assigned their respective elastic spring constants based on their linear or non-linear representation. The deformation is obtained when some known force is applied on a node. The node as it displaces, pulls its neighboring nodes which are connected by springs. The movement of every node exerts a pull on its neighboring nodes thus creating a sequence of shape changes.

Mass-spring systems are simple physical model with well understood dynamics. They are well suited to parallel computation as well, due to the local nature of the interactions between nodes. They have demonstrated their utility in animating deformable objects that would be very difficult to animate by hand.

Figure 2.3 A mass-spring model that represents a 3D lattice of mass nodes connected by springs.
A significant amount of effort has undergone in developing facial animations, using mass-spring systems. The goal of these applications is to model subtle human facial expressions in applications ranging from computerized expression of the American Sign Language to storytelling. The face was modeled as a two-dimensional mesh of points warped around an ovoid and connected by linear springs. Muscle actions were represented by the application of a force to a particular region of nodes, inducing node displacements that propagate outward to adjacent nodes.[36] This approach was expanded by Waters, who developed more sophisticated models for node displacements in response to muscle forces. In Water's approach, muscles directly displaced nodes within zones of influence, which were parameterized by radius fall-off coefficients, and other parameters.[37]

Terzopoulos and Waters were the first to apply dynamic mass-spring systems to facial modeling.[38] In their method a three-layer mesh of mass points were developed which represents three anatomically distinct layers of facial tissue: the dermis, a layer of subcutaneous fatty tissue, and the muscle layer. The upper surface of the dermal layer forms the epidermis, and the muscles were attached to rigid bones below and to the face above. Like the earlier work in facial modeling, the actuating muscles corresponded to actual muscles in the human face. The facial model had 6500 springs, and was animated at interactive rates. A technique to generate facial models for particular individuals from a radial laser-scanned image data was then developed by the same group. The scanned data provided a texture map for the top layer of the mesh and the initial geometry of the mesh.[39]
Different spring constants were used to model the different layers based on tissues properties. Because some of the tissues are incompressible, and because the standard mass-spring model cannot easily enforce this constraint, additional forces were applied to mass points in order to maintain constant volume. These forces were computed by comparing the volumes of the regions between the nodes to their rest volumes. This work thus used hand-crafted models of a generic face. Real-time animation was achieved with a simplified two-layer skin model and an Euler integration method. [39]

Mass-spring models of facial tissue were also used to predict the post-operative appearance of patients whose underlying bone structure has been changed during cranio-facial surgery. Spring stiffnesses for the system were derived from tissue densities recorded by 3D Computed Tomography (CT) imaging.[35]

Mass-spring models were combined with free form deformations to animate the embedded objects.[34] By changing the spring stiffness matrix to correspond to vibrational modes such as twisting, scaling, and shearing at specific times in the animation sequence, they obtained whimsical but physical behavior of the animated objects. This approach was also used for modeling muscles in human character animation.[38]

Terzopoulos et. al.. described a mass-spring model for deformable bodies that experience state transitions from solid to liquid.[40] Each node had an associated temperature as well as a position, and the spring stiffness between nodes were dependent on temperature. A discretized form of the heat equation was used to compute the diffusion of heat through the material, and the
changes in nodal temperatures. Increased temperatures decrease the spring stiffnesses; when the melting point was reached, the stiffness was set to 0, severing the bond.

Tu and Terzopoulos have used mass-spring systems with full dynamics to generate “artificial fish.” The fish model comprises 23 mass points and 91 springs connecting these mass points. The hydrodynamic forces required for the movement of the fish inside water were created by muscle actuation. An implicit Euler integration method was used for added stability in the presence of large forces. Aquatic plants were also modeled with mass-spring systems.[41]

Desbrun et al. proposed a stable and efficient algorithm for animating mass-spring systems. In this approach the equation of motion is solved using a predictor-corrector approach. It works by computing the displacement for an applied force as a rapid estimation and its subsequent iterative correction. This method has shown to obtain interactive realistic animation of any mass spring network.[42]

Mass-spring systems, though widely used, have some drawbacks. The discrete model is a significant approximation of the true physics that occurs in a continuous body. The lattice is tuned through its spring constants, and proper values for these constants are not always easy to derive from measured material properties. In addition, certain constraints are not naturally expressed in the model. For example, incompressible volumetric objects or thin surfaces that are resistant to bending are difficult to model as mass-spring systems. These systems also exhibit a problem referred to as “stiffness” which can occur when spring constants are large. Large spring constants are used to either model objects that are nearly rigid, or model hard constraints due to
physical interactions, such as a non-penetration constraint between a deformable object and a rigid object. Stiff systems are problematic because they have poor stability, requiring the numerical integrator to take small time steps, even when the interesting modes of motion occur over much longer time intervals. The result is a slow simulation.[43]

2.3.2 Continuum Representation

Continuum models are solid models with mass and energies distributed throughout. Two types of continuum model representation are discussed in this chapter: (i) Finite Element Methods (FEM), and (ii) Green’s Functions (GF).

2.3.2.1 Finite Element Methods (FEM)

FEM is a prominent continuum model that has been widely used in the area of engineering design. In this approach we divide the object into a set of elements and approximate the continuous equilibrium equation over each element. The elements can be represented as a node or a group of nodes as shown in Figure 2.4. The displacement of nodes is subjected to constraints at the node points and the element boundaries so that the continuity is achieved. The method of computing displacement is split into two parts. In the first part the displacement of nodes inside an element is computed. It is done by using a polynomial interpolator function among the nodes in the element. In the second part, the effect of displacement of nodes in one element on another node in the boundary of another element is computed. It is done by using the formulation given in equation (2.1) at an element level. This approach provides a reduced computational complexity when compared to mass-spring systems.[44]
The usage of a polynomial interpolator is explained as follows. A shape function is a value assigned to every node in the element. This value is assigned with reference to any point in the element and so for every reference point, there is a different value given to the boundary nodes of an element. Any property at the reference point is given by the weighted sum of the property at the boundary nodes with the weights being the shape functions at the boundary nodes. A 3D displacement vector in FEM can be represented using shape functions as follows:

\[ u = HU, \]

where \( H \) is a \( 6 \times 3N \) interpolation matrix and \( U \) is a set of vectors that represent the displacement of neighboring nodes of \( u \). Third order cubic hermite polynomials are generally employed for representing this interpolation matrix. The strain can thus be formulated as

\[ \varepsilon = BU, \]

where \( B \) is a \( 6 \times 3N \) interpolation matrix. Based on equation (2.2), each row of \( B \) is a derivative of \( u \). Let \( D \) be the matrix that relates the stress and the strain. Thus the strain in the element can be re-formulated as

\[
\Lambda = \int_{0}^{Volume} \varepsilon^T D \varepsilon dV = \int_{0}^{Volume} U^T B^T D B U dV = U^T \left( \int_{0}^{Volume} B^T D B dV \right) U = U^T K U. \quad (2.8)
\]

Substituting the expansions of the work done (equation (2.5)) and the strain in the element (equation 2.8) in the total potential energy expansion (equation (2.1)) we solve for the displacement vector \( U \). A static FEM is obtained by differentiating the potential energy expansion with respect to \( U \) and equating it to 0. The static FEM is written as

\[ KU = F, \]

(2.9)
where $K$ is considered as the stiffness matrix and $F$ is the applied force. Solving equation (2.9) for a known applied force and the stiffness matrix gives the displacement vector $U$ for all the boundary nodes in an element. In order to calculate for all the nodes in the object, a matrix formulation of equation 2.9 is done and is solved using Gaussian elimination techniques.[45] From equation 2.9 it is clear that the accuracy in estimating $K$ forms a key factor in accuracy in the deformation. It can also be seen from equation 2.7 that the assignment of shape functions also forms a key factor in accuracy of deformation.

FEM was used for shape editing in computer-aided design by Celniker et al.[46] They used 2D triangular surface elements and Hermite polynomials functions as interpolation functions to model the 3D displacements of the triangle vertices for deforming surfaces. User-controlled external forces are applied to edit the object shape.

FEM was also widely used for modeling muscle movements and deformations. Chen et al. used a 20-node cubiodal element with parabolic interpolation functions to model deformation of human muscles.[47] For muscles, external forces were applied where tendons connect the muscles to rigid, moving bones. A small number of elements per object were used (2 elements per muscle, 4 elements for a plastic head model) and the object geometry was embedded into the rest state of the elements. When forces were applied, object vertex displacements are calculated from the FEM node displacements. Gouret et. al. used FEM to model interactions between the soft tissues in a human hand and a deformable object. They used 3D elements with linear interpolation functions and a dynamic formulation to animate the interaction.[48]
Bro-Nielsen, Cotin et al. applied FEM for modeling human tissue deformation for surgical simulation.[49] They used a tetrahedral element with linear interpolation functions. In order to accomplish real-time simulation, they performed a number of pre-processing steps. Bro-Nielsen partitioned the problem into interior and surface points and solved for deformations only at surface points. This was achieved using matrix condensation techniques.

Cotin et. al. investigated a method for obtaining real-time object deformations.[50] For every surface node, they pre-calculated and stored the deformations of all node points and the applied force at the given node when it is subjected to an infinitesimal load. During the simulation, the applied forces were expressed as linear sums of these infinitesimal loads, and the stored displacements and applied forces were superimposed to estimate the object deformation. The methods used by Bro-Nielsen and Cotin greatly improved the speed of the simulation with the cost of significant pre-processing and reduced flexibility for objects whose shape or topology change significantly.[49]

Finite element methods provide a more physically realistic simulation than mass-spring methods with fewer node points, hence requiring the solution of a smaller linear system. The usage of interpolators inside an element results in smaller computations as compared to mass-spring methods. However, applied forces must be converted to their equivalent force vectors, which can require numerically integrating distributed forces over the volume at each time step. This can lead to significant pre-processing time for finite element methods. For any change in topology of the object during the simulation, the mass and stiffness matrices must be re-evaluated during the simulation.
2.3.2.2 Green’s Functions (GF)

Elastostatic Green’s functions represent a particular case of deformation when the second derivative of the displacement with respect to the Cartesian coordinate axis is equal and opposite to the applied force.[51] It can be written as,

\[
-\frac{\partial^2 u}{\partial x^2} = f(x),
\]

(2.10)

where \(f\) is the applied force. This case of deformation is observed under three conditions: (i) the displacement is continuous and has a continuous first derivative, (ii) the dilation of displacement is zero, and (iii) the applied force function \(f\) is continuous over the entire surface.

It is important to not only solve equation (2.10) for the displacement but also to find its relation to the applied force. This relation helps in computing the change in displacement for a change in
applied force. A feature of equation (2.10) that enables us to achieve this goal is linearity, as
reflected in the superposition principle. Let $x$ and $y$ represent a list of vertexes in a volumetric 3D
model. If $u_i(x)$ is a solution for an applied force $f_i(x)$ then there exists a solution $(Au_i(x)+Bu_j(x))$
for an applied force $(Af_i(x)+Bf_j(x))$ with $A$ and $B$ being arbitrary constants. In practice, the
superposition principle allows us to decompose complicated data into possibly simpler parts, to
solve each of the simpler boundary value problems and then to reassemble these solutions to find
the solution of the original problem.

A solution of displacement for a given applied force is given by the following form of
representation.

$$u(x) = \frac{\text{Volume}}{0} g(x,y) f(y) dy,$$

(2.11)

where $g(x,y)$ is referred to as a Green’s function (GF). It is to be noted that the GF is not
explicitly known. However one can obtain a great deal of useful information about the GF. First
we point out that $g(x,y)$ has a very simple physical interpretation as the force applied at $x$ when
the only source is a concentrated unit source located at $y$. This physical interpretation has been
used for modeling articulated deformations by Pai.[52]

In recent years, linear elastostatic GF models (LEGFM) have been shown to strike an attractive
trade-off between realism and speed.[53] The models are physically based and are accurate
approximations of small-strain elastic deformations for objects in equilibrium. In practice, they
are an appealing model for simulating deformable materials that are relatively stiff (with respect
to the applied forces) and tend to reach equilibrium quickly during continuous contact. The
linearity of the model allows for the use of extremely fast solution algorithms based on linear superposition that support real-time rendering and stable force feedback. The use of these techniques in interactive simulation was advanced by Bro-Nielsen and Cotin,[49] Cotin et al.,[50] and James and Pai,[53] who demonstrated real-time interaction with deformable models in applications such as force feedback surgical simulation and computer animation. Reality-based active measurement techniques also exist for acquisition of LEGFMs.[52]

The key to the fast simulation technique is a data-driven formulation based on precomputed GFs. GFs provide a natural data structure for subsuming details of model creation such as numerical discretization or measurement and estimation. The benefit of linearity is that the response to any set of boundary values can be quickly reconstructed by a linear combination of precomputed GFs. In this way, these solution techniques can be used to obtain the solution for any set of applied constraints by using the GFs in combination with a collection of matrix updating methods (related to the Sherman–Morrison–Woodbury formula) which is referred as Capacitance Matrix Algorithms (CMAs).[53] The CMAs achieve their fast visualization speed at the expense of storing $O(n^2)$ elements of the large dense GF matrices that can be accessed in constant time.[51]

The applicability of the elastostatic deformation of any 3D model depends on the required type of deformation and the material properties assigned to each node. As we envision modeling the human lung deformations we continue our discussion on analyzing the lung physiology and modeling done by peers.
2.3.3 Approximate continuum models

These models are physically motivated but adhere less strictly to the laws of physics than continuum models. “Snakes” or Active Contour Model is a method that is widely used in contour identifications.[54] Snakes are 1D deformable curves that are often used to define and deform contours. In this model the basic primitive is a point on a curve. These points undergo two kinds of deformation, namely stretching and bending. Every point is also associated with two weight parameters that correspond to the force applied for each type of deformation. The displacement of every point is computed by minimizing the two forces applied at every point. It finds wide application in tracking motions inside a video.

2.4 Significance of Model Representation and Deformation

From the above discussion on continuum models it can be seen that the choice of the element level is a key factor in calculating the force applied on it. An element level can vary from a point to a polygon. As the level goes towards being a point, calculating the applied force \( F \) becomes an overhead, since the element boundary interaction is complex. Although it is simpler to represent an element as a polygon, it is not possible to calculate deformation for high-definition models obtained from 3D digitization, due to its high polygon count. Also \( F \) varies with deformation and computing the solution for every deformation is computationally expensive.

In summary, we discussed how the concept of deformation is seen in terms of animation. We discussed some of the approaches for implementing the equation of motion defined by some of the peers.
In this section we discuss the time-based integration of deformation, which is of great importance for applications related to animations. The motion dynamics for any moving particle is referred to as the Lagrangian equation of motion and is given as

\[ F_{T[i]} = F_{E[i]} + MA[i-1] - D[i]V[i-1], \]  

(2.12)

where \( i \) and \( i-1 \) are discrete time instants, \( M \) is the mass of the particle, \( A[i-1] \) is the acceleration of the particle at time instant \( i-1 \), \( D[i-1] \) is the damping component (e.g. coefficient of viscous drag) of the object at time instant \( i-1 \), \( V[i-1] \) is the velocity involved at time instant \( i-1 \), \( F_T[i] \) is the total force resulting on the object at time instant \( i \), and \( F_E[i] \) is the step increase in the force applied on the particle at time instant \( i \). Traditionally the coefficient of viscous drag is generally set to a constant value. Also the maximum magnitude for the coefficient is equal to the mass of the moving particle.

From the physics of the phenomenon, the values of \( A[0] \) and \( V[i] \) are set to 0. The time-step \( (\Delta) \) is set to 1. The position of the particle \( V[i] \) at a time instant \( i \) may be calculated as

\[ V[i] = V[i-1] + V[i-1] \times (\Delta i) + 0.5 \times A[i-1] \times (\Delta i)^2, \]

(2.13)

with

\[ A[i] = \frac{\text{Force}_{\text{Total}}[i]}{M}, \]

(2.14)

and

\[ V[i] = V[i-1] + A[i-1] \times (\Delta i). \]

(2.15)

The position of the particle \( x[i] \) at time instant \( i \) is given as

\[ x[i] = x[i-1] + V[i] \times (\Delta i) + A[i] \times (\Delta i)^2. \]

(2.16)
Equation (2.19) can also be obtained from the Taylor series expansion of a differential variable at the next time instant. The key advantage of this differential representation is that the damping component can be estimated from a known sequence of particle position and $F_E[i].$

$$D[i] = (F_E[i] + MA[i-1] - F_T[i]) / Vd[i-1].$$

(2.17)

In this chapter we have thus discussed the physically-based methods for representing the 3D models and the methods for simulating the physically-based deformation. We now continue to discuss the different deformation methods used for modeling the lung dynamics.
CHAPTER THREE: LITERATURE REVIEW- LUNG DYNAMICS

Respiration is the biological process of the controlled oxidation of metabolites for the production of useful energy by living organisms. In this section we present the related works undergone in modeling lung dynamics for understanding its role in the respiration. We start our discussion by presenting the basics of lung physiology and effect of air constituents on the behavior of lungs. It is followed by a discussion on the research efforts undergone in modeling lung mechanics. These research efforts are mainly based on either a physically-based deformation system or a geometrically-based deformation system. We first present the initial works done on modeling the effect of air constituents by Pedley using an electrical analogue.[9] We then present the model given by Grodins on representing the lung mechanics using a mechanical analogue.[55] Each of these methods consider steady-state values of partial pressures of gases and simulate the pressure and volume of air inside lungs.[9] We then present an improved electrical analogue model given by Kaye that are coupled with 3D lung models and accounts for a specific patho-physical condition (pneumothorax).[10] It is followed by a discussion on the 3D bronchial and parenchymal models, which are then integrated to form a 3D deformable volumetric lung model. We then investigate the geometric 3D models of human lungs given by Segars,[16] and Krishnan.[17] We conclude this chapter with a discussion on the physiological observations on human lungs that affects the deformation.
3.1 Functionality of Human Lungs

Breathing is an automatic, rhythmic, centrally regulated mechanics process of respiration by which the contraction and relaxation of the skeletal muscles of the diaphragm, abdomen and rib cage cause gas to move into and out of the respiratory units inside the lungs.[56] The lungs of a normal living adult weigh 900-1000g, of which 40 to 50 % is blood. At the end of expiration, the gas volume is about 2.4 liters and is known as functional residual capacity (FRC). At the end of a normal inspiration the gas volume is about 2.9 liters. While at the end of maximal inspiration the gas volume is about 6 liters and is known as total lung capacity (TLC). The inhalation and exhalation of air occurs at 11 to 14 times a minute.[57] The internal surface of human lungs is made of a large number of alveoli and the total surface area is approximately 1 m²/kg body weight at FRC. This vast area fulfills the need for distributing the pulmonary blood flow into a very thin film in such a manner that even under stressful circumstances the gas-exchange can be accomplished.[57]

During growth and development, the lung conforms to the shape of the pleural cavities in such a manner as to minimize structural stress. At FRC the lungs are about 24 cm high, narrowing at the top and at the bottom. With breathing, the lung expands in all directions as the chest cavity expands. If the apex of the pleural cavity is the fixed reference point, then during inspiration all parts of the lung, even the topmost portion, move downward. The downward movement can be seen not only by the descent of the diaphragm, but also by the descent of the tracheal bifurcation.[57]
The airways through the air to flow into lungs are made up of a set of branchings. There exist two types of conducting branched airways: bronchi and bronchioles. The bronchi form the initial set of conducting branched airways with branchings from 0 to 13. Since these conducting airways do not generally participate in gas exchange, their portion of each breath is referred to as anatomic dead space. Their combined length and cross-sectional area is such that the dead space represents about 30% of each normal breath, while resistance to airflow is low. The bronchi decrease in diameter and length with each successive branching. The cartilage support also gradually disappears. All subsequent airways are called bronchioles. The bronchioles form the rest of the conducting branched airways with branchings from 14 to 30.[58] The bronchioles are embedded directly into the connective tissue framework of the lung so that their diameter depends on lung volume. The principal function of the lung is to distribute inspired air and pulmonary blood so that the exchange of oxygen ($O_2$) and carbon-di-oxide ($CO_2$) between the alveolar gas and the pulmonary capillary blood occurs efficiently. The exchange is accomplished with a minimal expenditure of power used in breathing.[57] The pulmonary artery carries venous blood from the heart, which is also contained within the thoracic cavity. This artery also divides repeatedly, the smallest vessels being capillaries in intimate contact with alveoli. Carbon dioxide leaves the blood and enters the alveoli, ultimately leaving the body by way of the respiratory airways; oxygen goes in the opposite direction and, after entering the pulmonary capillaries from the alveoli by diffusion, is carried to the left heart and on to all part of the body by the bloodstream.[56]

Healthy lungs inhale 10000 liters of air per day and during exercise they enable 2.5 liters of oxygen per minute to be exchanged through the blood-gas interface. This level of activity
requires a finely tuned system of airways to direct the gas to the respiratory membranes. Unlike other body surfaces, such as skin, the non-abrasive nature of the inhaled medium does not ordinarily result in a need for a high rate of continuous cell replication. The filtration of damaging particles en route by the nasal and upper respiratory tract epithelia may not be complete especially when small particles such as carcinogenic fibers and chemicals are inhaled. Damage resulting from such particles results in cells death. The epithelial cells of the lung possesses mechanism that can replace these dead cells. Extensive research work has been undergone in stimulating these epithelial cells for cell replication.

A brief account of these replicative cells (also known as stem cells) are as follows: The three types of replicative cells are (1) the basal cells of the bronchi, (2) the clara cells of the bronchiole and (3) type II pneumocyte of the alveoli. Of particular importance is the epithelium of the alveoli. They are mainly populated by the type I and II pneumocytes. The former constitute 86% of the alveolar surface area by virtue of their shape and mainly contributes to the gas exchange. The latter, which are secretory cells, occupies the corners of the alveoli and mainly contributes to the alveolar morphology.

Lung damage to these replicative cells can be classified into two origins: (1) mineral particles, and (2) chemical compounds. Mineral particles reach different levels of the lung based on their size and shape. Dust particles are filtered by the conducting airways and removed by mucociliary action. In contrast, roughly spherical particles that are below 5 micrometers in diameter can penetrate the alveoli and may become lodged there with much potential for long-term damage. Most of these cells are indigestible and result in the death of the cells and the formation of
fibrosis. More importantly, dusts reaching the type II pneumocytes may promote the release of excess amounts of surfactant which can fill the alveoli. Type I cells are exquisitely sensitive to these dust particles. It was also shown in an animal study that these particles since their exposure to the animals were retained by the animals in their lungs for over a year. Thus the presence of these dust particles in the alveoli leads to cell death of type I pneumocytes and the cell replication process is initiated by the type II pneumocytes. Chemical compounds such as nitrogen dioxide or the supra normal oxygen affect the alveolar epithelium which subsequently leads to the death of type I pneumocytes. Upon return to normal conditions the epithelium recovers during which the type II cells rise dramatically without a concomitant rise in the type I cells. Thus the gas exchange process of the alveoli is significantly reduced. Based on the level of exposure to these chemical compounds the damage to type I pneumocytes occurs. Additionally the presence of high levels of type II pneumocytes in the alveolar epithelium leads to the creation of cell tumors. [59]

3.2 Control of Breathing

The inspiration is caused by coordinated neural influences from the respiratory control centers in the brain step during an active phase of breathing. It causes the diaphragm and external intercostal muscles to contract.

The motor drive of breathing is managed at the highest level by a network of neurons that extends between the medulla-oblongata and the muscles of the thoracic cavity.[60] The medulla oblongata is an enlarged continuation of the spinal cord extending up into a large bulge under the
1. brain stem. On either side of the medulla oblongata is an oval swelling from which a large bundle of nerve fibers arises and passes up into the cerebellum. Because of its location, all ascending and descending nerve fibers connecting the brain to the spinal cord must pass through this anatomical structure. The motor drive of breathing controls the respiratory rhythm and the adaptation to physical conditions. The network of neurons drives the muscles and tissues of the respiratory pump thereby controlling the respiratory rhythm, magnitude and the adaptation to physical conditions. The respiratory rhythm is generated by the Central Respiratory Pattern Generator (CRPG), which is formed by synaptic connections of neurons generating a specific firing pattern in the medulla. The outputs of the CRPG in this simplified model are the phrenic nerve activation and the intercostal nerve activation. While the phrenic nerve activation controls the diaphragm movement, the intercostal nerve activation controls the intercostal muscles movement. These activations innervate the muscles of the thoracic region and the motor units of the respective muscles. The combined output of these activations causes the change in shape of the thoracic cage, which subsequently leads to the decompression of air into the lungs and a decrease in pressure inside lungs. This decrease in pressure leads to the flow of air inside lungs. The relation between the change in pressure and the change in volume is represented by the pressure-volume (PV) relation of lungs. The PV relation reflects key respiratory parameters of the subject such as lung tissue properties [14] and also indicates the presence of changes in pulmonary mechanics.[61] Ventilation and the movement of air are dependent on the airway and tissue resistance of the lungs during breathing. These mechanical factors subsequently affect the lung physiology.
The variations in the motor drive based on changes in physical conditions are made possible by receptors that sense changes in breathing conditions.[62] These receptors are generally classified into mechano-receptors and chemo-receptors. The mechano-receptors carry information from the tissues to the medulla-oblongata regarding the muscle tension and extension. The chemo-receptors send signal information from the blood-brain barrier to the medulla-oblongata on the chemical content of the blood. However the signals sent by these receptors in one breathing cycle do not cause any signal change in that breathing cycle. Within a modeling and simulation context, modeling the neural drive effects on the pulmonary structures is possible, although extremely complex. For the problem of modeling the role of the motor drive on the physiology of breathing, it suffices to model the summary output of the motor response. The added benefit of this approach is that existing patient data represented by Pressure-Volume curves is available to drive the modeling process.

3.3 Effect of Gas-Laws on Breathing

Variations in the breathing air constituents lead to changes in the breathing. For modeling such breathing variations, it is essential to understand the gas exchanges between alveoli and blood capillaries in the lungs, transport of gases in the cardio-vascular system, and absorption or release of gases by body tissue. In this section we discuss the effect of air on breathing, based on gas laws. It is followed by a discussion on the steady-state quantities in the respiratory system.[9]
Gas laws predict the manner in which the air being a mixture of gas constituents, dissolve in blood inside lungs. There are three key gas laws that are taken into consideration when modeling air behavior, namely (i) Dalton’s law (ii) Ostwald solubility coefficients and (iii) Henry’s law.

Dalton’s law for gas mixtures expresses the fact that gas mixtures have a total pressure equal to the sum of the partial pressure of components. Thus normal dry air at sea level is made up of oxygen ($O_2$), nitrogen ($N_2$), carbon dioxide ($CO_2$) and water vapor ($H_2O$), with

$$P = PO_2 + PN_2 + PCO_2 + PH_2O = 760 \text{ mm Hg}, \quad (3.1)$$

where $P$ is the total pressure, $PO_2$ is the partial pressure of oxygen, $PN_2$ is the partial pressure of Nitrogen, $PCO_2$ is the partial pressure of carbon-di-oxide, $PH_2O$ is the partial pressure of water vapor. It is to be noted that the partial pressure of water vapor increases with temperature. The presence of increased water vapor results in reduced partial pressure of other gases, with total pressure remaining unchanged. This variation affects the alveolar partial pressures of oxygen and carbon-di-oxide which subsequently affects breathing.

The Ostwald solubility coefficients for a given fluid (usually blood) and a given gas is the volume of gas at body temperature that dissolves in a liter of the fluid. An experimental analysis of solubility coefficients of blood is done using an anesthetic called halothane. It was found that 2.3 litres of halothane anesthetic dissolves in 1 liter of blood at BTPS, and the Ostwald coefficient is thus 2.3. Some Ostwald solubility coefficients for the gases found in air are detailed in [9].
The Ostwald coefficient for inert gases is defined as the volume of gas (at body temperature) dissolved in a unit volume of the fluid solute when the partial pressure of the dissolved gas is 760 mm Hg. The effective solubility is quite different for an active gas such as oxygen, which combines readily with the hemoglobin in red blood cells. The amount of oxygen thus taken up is much larger than what is dissolved and is nonlinearly related to its partial pressure. This fact is further explained by Henry’s law which states that gases do not react with the solvent but go into solution in proportion to their partial pressure. Two key measurements that are to be analyzed are (i) ventilation and (ii) perfusion. Ventilation refers to the rate and depth of breathing. Perfusion refers to the volume flow rate of blood to each part of the lung. The process of breathing balances these two measurements for efficient breathing. [57]

3.4 Electrical Circuit Representation of Lung Dynamics

A fluid circuit model diagram of the mechanics of this system, by combining the air pathways that are anatomically in parallel into a single conduit is as presented by Pedley. A schematic representation of this model is given by Pedley and is as shown in Figure 3.1. The flow of current inside this circuit is equated to the flow of air inside the lungs. The Inertance (second-order flow derivative) of gas are neglected in this model. Approximated values of capacitances and resistances, which are based on the steady-state quantities of gas exchange are used for the resistances and capacitances.
The overall compliances (inverse of resistance) which are based on a combination of the effects of chest-wall elasticity and the compressibility of air are assumed to be linear and to include an unstressed volume. The pressure produced by the chest and diaphragm muscles is assumed to vary sinusoidally. This method however does not model the respiratory muscles. This pressure is applied to the compliances of trachea, bronchi and alveoli that are within the chest cavity. The final flow in this model is the algebraic sum of the flow of current from one end to another. A detailed explanation of the method is also given by Rideout.[63]

### 3.5 Lumped Lung-Thorax Model

This model forms one of initial efforts in understanding the respiratory mechanics and has provided the basis for most of the work in this area.[55] It is most convenient to describe the dynamics of the ventilatory apparatus in terms of the equivalent piston pump shown in Figure
2.2. Its essential components are the inspiratory and expiratory muscles that provide the energy to drive the piston and the elastic and resistive elements against which they must work.

In this model, the lungs and the thorax are considered as a single equivalent resistive element. When the inspiratory muscles apply a force to expand the lung-thorax, the elastic tissues act as a spring and thus oppose the motion which is due to the internal viscosity. Finally the flow of gas through the tracheo-bronchial tree is opposed by resistive force generated by gas viscosity. The equation of motion is simply a statement of the physical principle that the driving force must be equal to the sum of the opposing forces at every instant. The equation of motion for the respiratory pump is given as

\[
(R_{LT} + R_g) \times \frac{dV}{dt} + \frac{1}{C_{LT}} \times V = P_M ,
\]  

(3.2)

Figure 3.2 (a) A mechanical model that represents the lung respiration. (b) A circuit model of the lung respiration which is the same as the mechanical model (Courtesy Grodins et al. [55]).
where $R_{LT}$ is the viscous resistance of the lungs, $R_g$ is the viscous resistance of the gas, and $C_{LT}$ is the compliance of the lungs-thorax. An equivalent electrical analogue of the mechanical setup is as shown in Figure 3.2b.

### 3.6 FEM Lung Surface Model

This model aims in producing realistic, animable models of the human body, by representing the physiological behavior of the human lungs using FEM methods. A simplified lung and chest cavity is modeled and simulated for normal quiet breathing and during pneumothorax. Initial effort towards this objective was done by Decarlo et al.[64] In this model, lung was treated as a single compartmental model. A 3D FEM lung model was considered for the deformation.

![Figure 3.3 A general illustration of the proposed lung representation by DeCarlo (Courtesy DeCarlo et al. [64]).](image)
The material parameters and the force applied on each element is hand-crafted to attain the required deformation. This attempt presented the scope to model patho-physical conditions using deformation methods. Figure 3.3 shows a general illustration of the proposed lung model. The method proposed by Kaye et al extended the previous model.[10] The force applied on each node was based on four forces namely the (i) force balance across the diaphragm, (ii) force balance across the abdominal wall, (ii) force balance across the common junction, (iv) force balance across the lungs. Figure 3.4 shows a general illustration of the proposed lung model. A 3D FEM model is generated from the medical data and is deformed. The resolution of 3D lung model is reduced for obtaining the deformation in real-time.

A specific patho-physical condition namely the tension pneumothorax is simulated using this 3D FEM model. It is done by piercing the 3D model and subsequently modifying the force balance equations. These pressure equations also affect the position of the mediastinum thus modifying the overall lung position. The simulation of pneumothorax is however not validated from the deformation perspective.
3.7 FEM Bronchial Model

It is known that the conducting airways bifurcate (divide into two daughter branches) repeatedly to supply around 30,000 respiratory units distributed within two irregularly shaped lung cavities. Meshes for the conducting airways and pulmonary arteries and veins were constructed within the lobe mesh, using a bifurcating-distributive algorithm. The algorithm generates an airway pattern by repeatedly bifurcated the bronchi pathway until the bifurcations significantly occupy the host volume. This airway mesh is then used as a template for generating blood vessel models. The bronchiole pattern generated by this algorithm inside each lobe is as shown in Figure 3.5.
The space unfilled by airway bifurcations is then filled with sponge-like elements which represent the parenchyma. The lung parenchyma was modeled as a space-filling three-dimensional (3D) Voronoi mesh, with generated geometry consistent with the alveolated airway structure. Pulmonary capillaries were generated over the alveolar model, as a 2D Voronoi mesh.\cite{4}

These structural models have been compared extensively with morphometric data to verify that their geometry is representative of the pulmonary system. The models were designed to be integrative: they relate multiple structural systems within the same individual, and their use as computational meshes allows application of spatially distributed properties.
Subject-specific geometric models are key tools in understanding the experimental results between the regional air-flow and the airway structures inside the lung. Additionally, disease states such as emphysema can be better understood and treated using the subject-specific airway structures. Thus a mathematical model of the subject-specific model would greatly benefit image-based guided applications such as Bronchoscopy.

An approach to obtain a Finite Element model of the bronchial tree was discussed by Tawhai. In this approach both human and sheep bronchial tree were extracted from multi-detector x-ray CT imaging system, which showed the cross-sectional area of the airway branchings. Volume meshes were then fitted to the lung lobes of both the human and sheep images. The airway branching model discussed at the start of this section was then employed to fill the volume meshes. The resultant airway branching models are subject-specific and are anatomically-based.

3.8 FEM Volumetric Lung Model

In this model, a computational model that represents the functional components of the pulmonary system such as alveoli and parenchyma is presented. This model aims to incorporate interactions between the lung’s subsystems by means of a hierarchy of structural and functional models.[12] A 3D volumetric lung model is created from detailed imaging-based data, along with a wide range of functional information from medical experiments. Advances in computed tomography imaging technology provide high-resolution data. Realistic finite element models are the subsystems that are hand-crafted from these high-resolution models. Segmented human lung lobe data are fit to high-order volume elements.
These lobes are then combined with the FEM based bronchial tree in order to form a FEM based volumetric lung model. Figure 3.6 illustrates a 3D volumetric lung model which includes the 3D FEM based bronchial tree.

### 3.9 Parenchymal Models

Parenchymal tissues are the set of fibers connecting the large airways, intricate vasculature and the pulmonary interstitium. These tissues were modeled in the FEM based volumetric model as generic tissue structures. However, such fibers mainly constitute two key types of elastic tissues: (i) Collagen, and (ii) Elastin. While the Collagen expands by 1%-3% during inhalation, the elastin expands more than 250%. A representation of such tissue structures was proposed using a string-spring representation shown in Figure 3.7. While the springs \((k_1 \text{ to } k_n)\) represented the elastin, the strings \((l_1 \text{ to } l_n)\) represented the collagen. The elastic coefficients for the springs were obtained from canine lung tissues. Such a representation mathematically corresponds to a second order differential equation.
Figure 3.7 A sequence of string-spring pair representations for parenchymal tissues (Courtesy Maksym et al. [14]).

This parenchymal representation was also used in modeling the static pressure-volume relationships of lungs. The proposed model was verified by using canine (dog) lung tissues. Pathological processes such as lung tumor affect the normal mechanical properties of these elastic lung tissues. A method to track the parenchymal tissue movements would help in understanding the behaviour of such tissues. A non-rigid deformation algorithm is thus coupled with imaging systems such as Magnetic Resonance Imaging (MRI) in order to model the parenchymal deformation. A linear elastic behavior of murine lungs (mouse lungs) is modeled using FEM in order to correlate two sequential MRI images $I$ and $J$, which were assumed to undergo a diffeomorphic fluid deformation. Specifically, one of the MRI images $I$ was deformed in order to obtain its deformed image $K$. The correlations between $J$ and $K$ were verified using shape and intensity details in the MRI images. The Jacobian of the 2D deformation fields revealed the local volumetric changes observed in the MRI images.

### 3.10 Torso Model

Human torso models, represent the human upper-body and its internal organs. These organs can be modeled either as rigid (e.g. rib-cage) or non-rigid (e.g. liver). In this approach the lung is
considered as a single-compartmental model inside the thoracic cage and the lung deformation is indirectly modeled, by deforming all the other organs in the torso. Such a physical torso simulation allows fine control over the subtleties of the movement and can encapsulate a range of behaviors in a single representation that can generate novel motion immediately without the need for additional recording. The breathing movement was considered as a signature movement of the human body. The muscles of the organs and the rib-cage are modeled using a mass-spring damper system. Each of the organs are then coupled with the volume preservation rules. The method of lung simulation is illustrated in Figure 3.8. The respiratory movement is activated by deforming the rib-cage along the anterior-posterior direction and the diaphragm along the cranio-caudal direction. This activation is controlled by a generic neuro-muscular activation mechanism. The organs that lie in the abdomen undergo subsequent deformation. Some of the drawbacks of this mechanism lie in the approximation of the lung deformations. In this approach the sliding behavior of the lung in the pleural space is not taken into account. Moreover, the rhythmic CRPGs are simplified into generic neuro muscular activations.
Figure 3.8 Respiratory movement of the torso is simulated with rib-cage and diaphragm movement coupled with the 3D deformable organs of the abdominal region. The blue arrows indicate the movement of the rib-cage and diaphragm. The green arrows indicate the abdominal movement. (Courtesy Zordan et al. [15]).

3.11 Geometric Lung Models

In this sub-section we discuss the modeling efforts undergone in representing lung surface models as a NURB surface and using special warping functions.

3.11.1 3D NURB Models

The geometric solids for the diaphragm, heart, ribs, and lungs (as shown in Figure 3.9a) were created from Multi-resolution Computer-aided Tomography (MCAT) data and deformed through manipulation of its control parameters. [16] The NURB surfaces for the lungs and body outline
were constructed from medical data. Expansion and contraction of the thoracic cage were then associated with the displacement of control points of spline models for its expansion and contraction. A general illustration of such a rib-cage motion is as shown in Figure 2.3.7b. The changes both the lung phantoms underwent were spline-interpolated over time to create time continuous 4D respiratory models. The geometry-based anatomical models of heart and ribs, and spline-based lung phantoms simulate effects of respiratory motion on myocardial spectroscopic images. Such respiratory models were shown to be effective tools for analyzing effects of respiratory motion.

Figure 3.9 A 3D illustration of geometric models of anatomical organs including the torso in the (a) anterior and (b) posterior orientations. (Courtesy Segars et al. [16])
Figure 3.10 An illustration of rib-cage movement during inspiration in (a) front view and (b) side view (Courtesy Segars et al. [16]).

3.11.2 3D Warped Models

A unique method to determine regional lung ventilation invasively is proposed by Krishnan et al.[17] In this study, lungs of two sheep were imaged utilizing a multi-detector row CT while maintaining the lungs at different lung inflations in prone and supine positions. To obtain estimates of regional volume change, static CT volume images were obtained from the sheep in the prone and supine positions. Six weeks before the study, eighty metal markers (1 mm in diameter) were implanted within the lungs of the sheep. Images were acquired using a multi-detector row CT scanner (model MX8000 Quad Scanner; Philips, The Netherlands) at multiple static lung inflations (airway opening pressures of 0, 8, 24, and 32 cm H₂O). Each volumetric image set contained 350 to 550 slices, with a slice thickness of 1.3 mm, a slice spacing of 0.65
mm and a reconstruction matrix of 512 X 512 pixels. In-plane pixel size was approximately 0.5 X 0.5 mm.

Analysis of cross-sections was then performed on the subjects. A warping function was used to map lung regions at different lung volumes based on a set of user-defined landmarks, and validated the warping functions using a set of implanted metal markers. The change in Hounsfield units within smaller lung regions was then used to calculate the percentage air content and regional ventilation.

### 3.12 High-resolution 3D Lung Model and Analysis

In this section we mainly discuss the two methods used for obtaining high-resolution 3D lung models. The first method is using x-ray CT analysis and the second method is using a combination of CT and cryosection imaging of anatomy (e.g. Visible Human project). X-ray CT serves as a comprehensive test for the anatomical state of the lung. The two quantities measured are the air-blood-tissue density and volume, which are extracted in the CT images from the local intensity. These measured quantities are then related to the regional lung mechanics.[65]

The CT imaging approach however requires meticulous volume control of the lungs over a period of time. It is caused by relatively slower scanning speed of x-ray CT when compared to the human breathing speed. Such scanning artifacts are of particular importance in tracking lung tumors and their motion.[7, 66]
Modern CT scanners have scan apertures which permit gated imaging during continuous respiration. Two important approaches of using such CT scanners are (i) volume-gated imaging, and (ii) retrospective gated imaging. Volumetric-gated imaging is a method in which known volume changes are induced in lungs and the scanning process is done over a sequence of breathing cycles. In each breathing cycle, only a few 3D slices are imaged. This helps in avoiding any artifacts induced by the controlled breathing of the human subject.[67] Retrospective gating is a method in which a slow helical scan of the lungs is taken with smooth breathing. The images are then analyzed in three dimension and placed at desired fourth dimension (time). This method currently has the disadvantage of high radiation dosage for the patient.[68]

The Visible Human project aims to create a complete anatomically detailed 3D normal male and female human model. The anatomical cross-sections were used at 1 mm intervals which coincided with the CT’s axial images. The anatomical organ shape was then extracted from every slice by using a contour detection algorithm such as Snakes. These contours were then combined to form the required anatomical shape. A detailed description of the process is as explained by Ackerman.[1]

### 3.13 Physiological Facts Related to Lung Dynamics

In this section, we summarize the three specific physiological facts that affect the behavioral properties of the deformation and are needed to be accounted for modeling the lung dynamics. They are (1) anatomical constraints, (2) anisotropic tissue surfaces and (3) low viscosity of air. It
has been previously discussed that the movement of the lungs is constrained by the thoracic cage. The ribcage along with the spinal cord and mediastinum form a closed cylinder inside which the lung deforms.[16] The space between the thoracic cage and the lungs forms the pleural space. This space is filled with pleural liquid which forms a lubricated damping medium. The expansion of the thoracic cage is controlled by the medulla. Initial models for this control were based on minimizing energy consumption by the breathing mechanism. [56, 58] The presence of lubricated damping by the pleural liquid and medullar control of the tissue movement concludes that the normal lung deformations do not vibrate, from a mechanical perspective. This theory is biologically supported by Mead.[69]

There is a variation in the internal tissue behavior caused by the regional expansion of the alveoli and by the branching pattern of airways. Initial observations of the anisotropic nature of these internal tissues come from air-blood barrier thickness analysis.[70] While the lung wall is considered to be isotropic, internal tissue structure can make the macroscopic properties of the lung wall anisotropic. The possible shape abstractions of alveoli are (i) hollow cylindrical shape, (ii) truncated conical shape and (iii) spherical shape.[71] The spherical shape was found to be the best shape approximation of alveoli. The direction of alveoli expansion is thus radial outward. Since the alveoli fill the lung volume, the direction of expansion of the lung is also radial outward. The viscosity of air at sea-level is low.[72] This low viscosity of air prevents it from creating rotational movements when it flows through the lung bronchioles.
CHAPTER FOUR: PROPOSED FRAMEWORK

The focus of our research is to visualize accurate lung dynamics in an AR environment. Such integration may form an effective tool for training clinical technicians on medical procedures,[19] and also for developing guiding systems for treatment procedures such as in radiation oncology. The technical challenges in accomplishing such a visualization arises from (i) real-time issues of the AR based visualization, and (ii) physical accuracy of the 3D lung dynamics. Specifically, the framework for the visualization of 3D lung dynamics in an Augmented Reality (AR) environment must satisfy both the visualization paradigm and the level of accuracy required by the application domain.

Section 4.1 presents the components of the framework for modeling 3D lung dynamics. A brief description of the inter-connectivity between each of the components is described in this section. A description of the visualization system is given section 4.2. The visualization requirements are described in this section.

4.1 Framework for 3D Lung Dynamics

The real-time issues of the visualization and deformation are taken into account by using state-of-the-art Graphics Processing Units (GPU). The technical challenges of designing and visualizing a medical simulation for lung morphology arise from its computational complexity. Specifically, in an AR environment the position and orientation of the patient are updated by the tracking sensor every 16 ms. Such update requires deforming and rendering 3D lung models at 30-66 times per second[30]. Additionally, the increase in the 3D lung deformation computations
caused by changes in the patient position and orientation in an AR environment were not discussed. This subsequently limits the usage of high-resolution 3D lung models for real-time deformation and visualization.

This proposed framework for modeling the 3D lung dynamics is composed of two components: (i) a pressure-volume (PV) data of a human subject, and (ii) modeling real-time 3D lung deformations. The second component is optimized by a real-time optimization of the deformation computation using GPU.

4.1.1 Pressure-Volume Relation of Human Lungs

A method to parameterize the PV relation is presented in this dissertation. From a modeling and simulation perspective, such an approach allows us to model the PV relations of both normal and disease states (e.g. Chronic Obstructive Pulmonary Disease & Dyspnea). The method takes into account both the control of ventilation and the muscle mechanics. Such an approach allows us to simulate PV curves in different breathing conditions, which can then drive the simulation of 3D lung dynamics for medical visualization applications. The PV relation is represented using both a second-order differential equation that represents the increase and decrease in volume, and a non-linear control function that represents the summary muscle resistance. The control function is given as a linear summation of products of control parameters and a set of basis functions. The basis functions allowed us to steer the control function, which accounts for variations in the breathing condition. The proposed method can be inversed in order to estimate the values of control parameters from human subject data. Results showed that a set of five
control parameters might define accurately the PV relation system. The associated PV relation shows less than 1% RMS difference with the normal human subject data. The clinical data include four PV curves obtained from normal human subject data. The PV curves are parameterized and the mean of the control constants associated with each of the parameterized PV curves is then computed, in order to represent the mean normal PV curves. The parameterized PV curve can then be modified to simulate breathing conditions in normal and disease states. We can then simulate a change in the motor drive for breathing, caused by the tumor inside the lungs. The method is further discussed in Chapter 4 of this dissertation.

4.1.2 3D Deformable Lung Model

A method to obtain changes in 3D lung shape in a physically and physiologically accurate manner is discussed in this dissertation. Within the context of computer animation, a Green’s function (GF) based deformation is chosen since it has been observed that lung deformations do not undergo vibrations. The total number of nodes on each of the 3D high-resolution lung models is approximately 400,000. Such a large number of nodes facilitate effective modeling of both normal and patho-physical lung deformations. Also, a Young’s modulus (the ratio between the stress and strain of a node) is first associated to every node of the 3D lung model based on the lung’s regional alveolar expansion. A unit force is then applied on each node and the transfer function matrix was computed using an iterative approach. The method is validated using the 4D HRCT images of a normal human subject. The method is further discussed in Chapter 5 of this dissertation.
The applied force is normalized so that the sum of the applied force magnitude on all the nodes is equal to a unit increase in volume. A unit increase in volume is set as the ratio between the tidal volume of human lungs (i.e. 500 ml) and the product of the deformation steps per second (i.e. 66.66 steps/sec) multiplied by the ventilation rate of inhalation or exhalation (normally 5 sec/breathing).

### 4.1.3 GPU-based Lung Deformation

A method to speed-up the computation process of the proposed deformation system is presented in Chapter 6 of this dissertation. For simulation purposes we consider an Nvidia GeForce4 Go5200 and their CG-based vertex shaders. A per-vertex approach for deforming and rendering 3D lung models is considered. A method to optimally compute the matrix-vector multiplication in a GPU during run-time is presented. Specifically the matrix-vector multiplication is represented in steps, which can be partially pre-computed off-line. The columns of the transfer function matrix is pre-computed (as discussed in section 4.1.2) and represented using Spherical Harmonic Transformations (SHT) coefficients. These coefficients are obtained from orthonormal decomposition of the transfer function matrix using SHT. This property of SHT allows us to represent the transfer matrix using a minimal number of SH coefficients. The vertex position of each node in the lung model along with the SHT coefficients are transferred into the GPU’s vertex array. For a given applied force, the displacement are computed in the vertex shader program executed in the GPU. While the 3D models is rendered using a point-based rendering approach, a comparison of the frame rate per second (FPS) in using point-based rendering and polygon-based rendering was discussed. Additionally, the number of SHT coefficients used for
representing the transfer function row is very less as compared to the number of coefficients used for shape approximation. The proposed method coupled with the per-vertex nature of the SH coefficients allowed us to use GPU for improving computational-speed.

4.2 AR-based Visualization System

The AR based interactive visualization system is aimed at applications such as emergency support and surgical planning. The visualization system allows the visualization of the virtual 3D deformable lung models overlaid on the patient body in an effort to improve the medical planning process. The planner and other medical personnel remotely located may be involved in the surgical planning procedure and may visualize the 3D lung model while seeing and interacting with each other in a natural way (Figure 4.1a). Moreover, they are able to participate in the planning procedure by pointing and drawing diagrams in correspondence with the 3D lung model. Figure 4.1b shows the super-imposition concept: the virtual 3D model of the lung overlaid on the patient’s thoracic cage. Such an advanced planning tool has the potential to: Involve local and remote planning personnel in the surgical planning procedure, opening new ways of collaboration and interaction, and the local planner can actually “see” the anatomical model (patient specific data) superimposed on the patient and improve the surgical plan.
Figure 4.1 (a) Surgical planning personnel interacting with 3D models, and (b) User’s view of the virtual 3D model of the lungs as he/she interacts with participants in (a).

The system integrates a 3D visualization device with an optical tracking system and a Linux-based PC. With the exception of the 3D visualization device, the framework was integrated using commercially available hardware components.

4.2.1 Visualization Device

To see the 3D model, the planner and the other users wear lightweight head-mounted displays (HMDs) [30] (Figure 4.2a). A key component in the reduction of weight in the optical design for the HMD is the optimal integration of diffractive and plastic optics as well as various emerging optical materials that may be used to compensate for optical aberrations responsible for image degradation. Optics as light as 6 grams per eye has been achieved for an horizontal field of view as large as 70 degrees with an organic 0.6 inch diagonal 600 X 800 pixels macro-display.
Figure 4.2 Collections of Light Emitting Diodes (LED) as tracking probes: (a) Optical see-through HMD developed through an interdisciplinary research effort at ODALab UCF (Courtesy- NVIS inc. for the opto-mechanical design) and a custom designed semispherical head tracking probe, (b) patient tracking probe.

4.2.2 Tracking System

To superimpose the 3D virtual models at the correct location with respect to the patient, we need to track, in real–time, the relative position of the visualization device or planner’s head and the patient’s thoracic cage [73]. The pose (i.e., position/orientation) of the planner's head, and the patient’s thoracic cage are determined using an optical tracking system (i.e., Polaris Northern Digital) and two custom built tracking probes [74] illustrated in Figure 4.2(a, b).

A key step in the accurate registration of the virtual lungs over the patient is the calibration procedure. In this step, the patient is positioned in the intubation posture. Magnetic Resonance
Imaging (MRI) data of the relative position of the mandible, selected landmarks with respect to the larynx, trachea, and the clavicle were collected in this posture. The inclusion of mandible, larynx and trachea in the above step allows us to track the position of the intubation tube (through the mouth and upper-airway), for medical procedures that require such support. The lung can be registered to the mandible and the upper chest landmarks (e.g. clavicle). From that point on, the lungs are kept in registration with the patient, based on the location of the upper chest landmarks, together with the position of the user. The tracking system is based on two tracking probes: one on the HMD to determine the planner’s head position and orientation, and a second on the chin of the HPS to determine its location. The tracking data obtained is currently updated at 60Hz. The tracking working volume is a cone having 1.5 meters in height and 0.5 meters in radius.
In this chapter we discuss a method for modeling the pressure-volume (PV) relation of the human lungs. This model extends the current literature of PV modeling efforts, by introducing the ability to induce breathing variations in PV curves. From a simulation and visualization perspective, this ability to account for breathing variations is important for modeling 3D lung dynamics. From a physics perspective, the model takes into account the Newtonian mechanics that is involved in the increase and the decrease of lung volume (a one-dimensional quantity) during breathing.

The chapter is further divided as follows: Section 5.1 presents an introduction of the biomathematical formulations and the control of ventilation. Section 5.2 discusses the related work involved in formulating the first-order differential PV relation as a biomathematical formulation for diagnostic purposes. Section 5.3 discusses a second-order differential PV relation to formulate the PV relation for visualization purposes. Section 5.4 presents the results of PV curves parameterized from both human subject data and the data used by the peers. The flexibility of the method in simulating variations in the PV relation for modeling breathing variations is also demonstrated in this section. Section 5.3 and 5.4 discusses the research contribution of the dissertation section on modeling the PV relation. Finally, section 5.5 provides a discussion on the future work that needs to be undertaken for the application of this model.
5.1 Bio-mathematical Formulation

Bio-mathematical formulations of the respiratory mechanics that describe the human lung have been developed as a set of balancing differential equations.[75] These equations were obtained by balancing the internal pressure components across the lung diaphragm, abdominal wall and rib cage. Based on experimental observation a first order differential relation was used for representing the balancing equations.[69] The values for the internal pressure components were obtained by subject measurement techniques such as estimating pleural pressure with esophageal balloon catheters. Mechanical and electrical analogues of these differential equations were then investigated in order to simulate the lung behavior which included functionalities such as ventilation and gas exchange aberrations. This method was further improved to model and visualize lung mechanical changes such as pneumothorax. The balancing equations in the first order differential equation form however simplify the combined effect of the elastic mechanics of the thoracic muscles, the lung tissues, and the control of ventilation. The thoracic muscles include the muscles of the abdominal region, the diaphragm, and the intercostal muscles. The elastic mechanics account for the change in the system impedance that subsequently lead to the airflow into the lungs during a single inhalation or exhalation [75].

A discussion on the control of ventilation and the role played by the CRPG was discussed as part of the lung physiology in section 3.2. A schematic diagram of the respiratory rhythm generation and its association with the lung mechanics is provided in Figure 5.1. The respiratory rhythm is generated by the CRPG formed by synaptic connections of neurons
generating a specific firing pattern in the medulla. The outputs of the CRPG in this simplified model are the phrenic nerve activation and the intercostal nerve activation. While the phrenic nerve activation controls the diaphragm movement, the intercostal nerve activation controls the intercostal muscles movement. These activations innervate the muscles of the thoracic region and the motor units of the respective muscles. The combined output of these activations causes the change in shape of the thoracic cage, which subsequently leads to the decompression of air into the lungs and a decrease in pressure inside lungs. This decrease in pressure leads to the flow of air inside lungs. The relation between the change in pressure and the change in volume is represented by the pressure-volume (PV) relation of lungs. The PV relation reflects key respiratory parameters of the subject such as lung tissue properties and also indicates the presence of changes in pulmonary mechanics. Ventilation and the movement of air are dependent on the airway and tissue resistance of the lungs during breathing. These mechanical factors subsequently affect the lung physiology.

Figure 5.1 Schematic diagram of the neuro-mechanical control of ventilation.
The variations in the motor drive are based on changes in physical conditions and are made possible by receptors that sense changes in breathing conditions. These receptors are generally classified into mechano-receptors and chemo-receptors. The mechano-receptors carry information from the tissues to the CRPG regarding pressure, airflow, lung volume, and the muscle tension and length. The chemo-receptors send information to the CRPG on the chemical status of the airway, instertial space, chemical content of the blood and the cerebrospinal fluid. The elastic mechanics of the muscles in the thoracic cage are known to be modified non-linearly by the motor drive for breathing. Thus modeling the control of ventilation as well as non-linearity of the elastic muscle and lung tissue mechanics is essential for accurately simulating dynamic breathing conditions. Alterations to the lung tissue lead to its thinning or thickening, which further lead to substantial changes in its elastic properties. Such alterations coupled with the subsequent variations in motor-drive are characteristic in disease states.

The first order differential equations must therefore take into account both the respiratory mechanical components and the control of ventilation. The change in muscle and tissue resistance coupled with the control of ventilation leads to a shift towards non-linear behavior.[64] The usage of the first differential equations of respiratory mechanical components is mathematically a simplistic model of these changes. Thus, the present study extends the respiratory mechanical-control model to include second order differential equations to account for the 3D modeling of the respiratory system. In this chapter, we present a method to formulate the PV relation accounting for the motor drive of breathing and muscle
mechanics. The formulation includes a control function that represents the non-linear muscle and tissue resistance. Additionally, a parameter for representing the motor drive for the control of breathing is also included in the control function. The proposed method aims at parameterizing a subject’s PV relation and steering these parameters to simulate variations in the lung deformations caused by an increased or a decreased resistance (e.g. Pneumothorax) and motor drive (e.g. Dyspnea).

In this chapter we discuss the representation of second order differential PV relation, a biomathematical formulation that we use for modeling the respiratory mechanics. The general form of the PV relation under normalized boundary conditions is shown in Figure 5.2. The Function Residual Capacity (FRC) on the lower bound and the Tidal Volume (TV) on the upper bound give the boundary values for the volume. The boundary values for the pressure are respectively given by the FRC pressure (RP) and the pressure at the end of expiration (TP).

Figure 5.2 A normalized PV curve (Pressure :1 unit = 0.1 cm H2O, Volume: 1 unit = 2 ml).
5.2 Related Works

There are three possible ways in which the PV curve can be parameterized or modeled, namely (i) Replicating the CRPG to compute the motor drive, (ii) Mono-exponential approximation for the PV relation, and (iii) Polynomial approximation to compute the integrated resistance. While the second method has been thoroughly investigated (section 5.2.2), the first and third methods remain components that can be coupled with bio-mathematical models of lung physiology for simulating the breathing variations of a subject. Also the second and third methods can be used to either create a PV curve given some input parameters or estimate those parameters from a subject’s PV curve. They are thus indicated by bi-directional flows in Figure 5.1.

5.2.1 CRPG replication models

The CRPG replication models, as their name indicate, replicate the biological CRPG using a combination of neurons whose roles are established by electro-physiological measurements. The CRPG replication methods capitalize on the fact that a direct influence of the tissue mechanics and motor drive can be seen in the PV relationship. Although modeling the PV relation specifically using a CRPG replication has not been attempted in the present report, it is worth mentioning the efforts undergone in providing a motor drive generation model. Initial models for neuronal control on respiratory rhythms and patterns, referred to as rhythmogenesis, were based on representing either involuntary control by neural networks or voluntary control by the cerebral cortex. The neural networks (feedback circuits) simulated the phrenic and
intercostal activations. The functionality of the involuntary control was found to be greatly dependent on the type of neural population and its respective firing patterns.

A hybrid model for the rhythmogenesis process was proposed by Rybak using a network of neuronal units generating specific firing patterns and a system level architecture of rhythms generation. A replicated CRPG model was coupled with a simple mathematical lung model using a tripartite model of neural control of movements. These methods greatly contribute to the understanding of respiratory motor neurons and their collective behavior. Modeling dynamic variations in firing patterns for obtaining different phrenic and intercostal activations requires meticulous control of the synaptic interconnections among a large population of neurons, which is computationally expensive. Therefore replicating the motor drive for dynamic activity levels of a subject using this technique has not been attempted. An alternative to modeling the CRPG is to parameterize the PV curves.

5.2.2 Mono-exponential Approximations

The first parametric equation that represented the PV relation during breathing was determined by Salazar. The method was based on curve-fitting the subject’s PV relation with a mono-exponential function (also referred to as a sigmoidal function) having two degrees of freedom. The power associated with the exponential component was referred to as the shape factor. The shape factor played a significant role in identifying patho-physical breathing. This method only modeled the volume range from 50% to 100% instead of modeling the whole volume range from RV to TV.
The mono-exponential PV relation was modified in order to obtain better insights into the physiological conditions. An exponential-sigmoid model for the PV relation with three degrees of freedom was suggested in order to analyze the static characteristics. However the volume range remained the same as for the mono-exponential method. The mean values of the parameters were computed for every breathing variation. A hyperbolic-sigmoid model for the average PV relation of the inhalation and exhalation, with five degrees of freedom was suggested. This model would analyze the gas distribution and the changes in the static PV curves with age for normal humans considering the whole range of the volume.

A sigmoid function was then proposed by Venegas. This method obtained better curve fitting with subject data and also considered the whole range of pressure and volume. In order to account for more variations in the PV relation, Narusawa proposed further modification to this sigmoid function.

Importantly, the above PV curve representations and methods do not take into account the muscle mechanics and the motor drive of breathing that are required to model the variations in PV curves for dynamic conditions. Thus further developing these methods for such a purpose cannot be considered for our work.
5.2.3 Polynomial Approximation Methods

PV curves are continuous in nature, thus methods that allow their parameterization are of interest in modeling their variations. Polynomial approximation methods are methods that play a significant role in accurately parameterizing continuous functions in terms of simpler continuous functions. These methods are based on the Weierstrass theorem that states that any continuous function can be “best” approximated using a group of continuous functions. These methods unlike the mono-exponential methods use more than one continuous function to parameterize the total function. They are defined as a linear equation using a set of basis functions and variable parameters. The usage of such approximation methods provides the possibility to include functionalities not only from a biological perspective but also from a mechanical perspective. A polynomial approximation method of significance is given by the Kolmogorov’s theorem, which represents a continuous function in terms of a group of continuous functions. The generality of this theorem was questioned and was then modified by Kurkova’s theorem. The Kurkova’s theorem states that any continuous function can be best approximated only by a group of sigmoidal functions using the formulation given by Kolmogorov’s equation. We have adopted this polynomial approximation method to parameterize the PV relation given that such an approximation can be steered with a high degree of freedom to model the PV relation. The usage of polynomial approximation methods unlike curve-fitting methods, allows us to solve for the polynomial’s coefficients using simultaneous linear equation solving methods in order to directly parameterize the PV relation which can then be used to simulate actual lung deformations.
5.3 Proposed Approach

In the proposed method the pressure-volume relation is represented as a second-order linear differential equation. We also account for the effect of the muscle mechanics and the motor drive of breathing in order to represent variations caused by physical tissue behavior. A control function, also referred to as the Damping curve, is included in the differential equation. This control function representing the summary of resistance is modeled using the polynomial approximation method. The basis functions used in this approximation represent a range of sinusoidal functions, and the associated control parameters to the basis functions are varied for creating variations in breathing patterns. The gas exchange aberrations and variations of temperature are not addressed in this paper. We are modeling a breathing environment of normal pressure and temperature conditions.

5.3.1 Mathematical Formulation of the PV Relation

The volume \( (V_t) \) at any discretized time instant \( t \) can be approximated as

\[
V_t = F(P_{dt}, V_{t-dt}, V'_{t-dt}, V''_{t-dt}), \tag{5.1}
\]

where \( F \) is a function that takes as inputs a constant step increase in pressure \( (P_{dt}) \) at \( t \) caused by the air flow, the volume \( (V_{t-dt}) \), and its first and second differentials with respect to time \( (V'_{t-dt} \) and \( V''_{t-dt} \) ) at time instants \( t-dt \). The volume \( (V_t) \) is thus a linear second-order differential function. When computing \( V_t \) without loss of generality, the step increase in pressure is set to a constant value and \( t \) is considered a continuous parameter within the range of 0 to 1.

A control function is now added to equation (5.1) in order to account for the changes in the resistance and motor drive of breathing. Furthermore without loss of generality we represent
this control function as a non-linear function during a single breathing cycle instead of a feedback function previously used in CRPG replications. This modification provides a control mechanism. Equation (5.1) written as

\[ V_t = F(P_{dt}, V_{t-dt}, V'_{t-dt}, V''_{t-dt}, f(t, L_0, ..., L_N)), \]

where \( L_0 \) to \( L_N \) are the control parameters and \( f \) is the control function. From a mathematical perspective, the control function acts as a steering tool for the PV curve. From a biological perspective, the control function relates the motor drive of breathing and the respiratory mechanics. The control function mimics the changes that occur in summary of respiratory resistance during breathing. For a given set of control constants, the control function generates a pattern discretized in time. This control pattern modifies the first derivative of the volume in equation (5.2) during inhalation or exhalation mimicking the damping component in motion dynamics.

5.3.2 Differential PV Relation

The differential equation for modeling the normalized PV relation is given by equation (5.2). Our approach is based on maintaining a mechanical analogy between Newton’s laws of motion in one dimension and the change in lung volume (a one dimensional quantity) during inhalation. For a step increase in pressure, the lung volume increases similar to a particle that moves when some force is applied on it. When the increase in lung volume stops at the end of inhalation or exhalation, just like the object stops, the force applied is zeroed. A method to simulate a particle motion using Newton’s laws of motion was explained in section 2.4. Following this analogy, the derivatives of the lung volume are associated with the derivatives
of the position of a particle moving in one dimension. Thus the step increase in pressure causes an increase in the second derivative of lung’s volume that leads to an increase in the first derivative of the volume (using Newton’s first law of motion). The increase in the first derivative of volume subsequently causes an increase in the lung volume itself (using Newton’s second law of motion). The control function which models the damping component is also represented within a normalized range (from 0 to 1).

5.3.3 Varying the Control Function

The proposed method for modeling the control of breathing is mathematically associated to the control function. This association (also shown in Figure 5.2) is explained by the relaxation of lung tissues, diaphragm, and intercostals muscles driven by the CRPG in order to facilitate smooth breathing under normal conditions with time. The normalized damping curve thus starts from 1 and reduces with the relaxation. The control function approximates the summary resistance. As previously stated, the solution for the continuous approximation of the summary resistance is given most generally by the Kurkova’s theorem. The theorem can be mathematically formulated as

\[
f(t, \rho_1, ..., \rho_N) = \sum_{j=1}^{N} \rho_j \left( \sum_{k=1}^{(N-1)/2} \psi_{kj}(t) \right),
\]

where \( \rho_j \) and \( \psi_{kj} \) are arbitrary continuous functions. Based on Weierstrass theorem it can be seen that the function \( \rho_j \) can be represented as a linear bounded function (a continuous function) of its parameter \( \psi_{kj} \). Such a function can be represented as,
\[ \rho_{j}\left(\sum_{k=1}^{(N-1)/2} \psi_{kj}(t)\right) = \chi_{j} \times \left(\sum_{k=1}^{(N-1)/2} \psi_{kj}(t)\right), \] 

(5.4)

where \(\chi_{j}\) is a constant value indexed by \(j\). These constants are referred to as control constants. The usage of control constants simplifies the function \(\rho_{j}\) and reduces the control function to a linear equation.

We model \(\psi_{kj}(t)\) as basis functions that represent the different harmonic frequencies of the rhythmic oscillations, also known as modes of vibration.\[44\] Such functions allow modeling the relaxation and contraction of muscles modulated by the mechanoreceptors. The values of \(\chi_{j}\) subsequently steer the rhythmic oscillations represented by \(\psi_{kj}(t)\). It has been shown that for rhythmic oscillations, which starts and ends at the same resting value (0) the harmonic frequencies have a polynomial decay. The \(\psi_{kj}(t)\) thus have a convergent representation. This polynomial decay also limits the number of control constants used, thereby providing a compact representation. General representations of such harmonic oscillations are trigonometric functions (with respect to the parameter \(t\)) that have the above properties of the basis functions. We can then write

\[ \psi_{kj}(t) = \sin^{q}(t \times \alpha / g(k, j)), \] 

(5.5)

where \(g\) is an arbitrary monotonic function whose minimum value is 0 and which increases with \(k\) and \(j\). \(\alpha\) and \(q\) are set as integer constants. The value of \(\alpha\) given in equation (5.5) is \(\pi\) in order to model only the positive range of sine function values. The polynomial decay of equation (5.5) depends upon the rate of increase of the monotonic function. Combining equation (5.3) and (5.5), we can write
\[
f(t, \chi_0, \chi_N) = \sum_{j=1}^{N} \sum_{k=1}^{(N-1)/2} (\sin(t \times \pi \div g(k, j)), \quad (5.6)
\]

or

\[
f(t, \chi_0, \chi_N) = \sum_{j=1}^{N} \sum_{k=1}^{(N-1)/2} (\chi_j^{2/q} \times \sin^2 \left( \frac{t \times \pi}{g(k, j)} \right)^{q/2}). \quad (5.7)
\]

Equation (5.7) represents a general formulation for modeling the control function using rhythmic oscillations. It can be seen that the value of the function \(f\) for increasing values of \(t\) will start from 0 and increase sinusoidally. It has been previously mentioned that the damping curve has its normalized initial value as 1 and decreases in a sinusoidal manner as the muscles relax. We set equation (5.7) to do the same.

Thus we introduce the following modification

\[
f(t, \chi_0, \chi_N) = \sum_{j=1}^{N} \sum_{k=1}^{(N-1)/2} 1 - (\chi_j^{2/q} \times \sin^2 \left( \frac{t \times \pi}{g(k, j)} \right)^{q/2}). \quad (5.8)
\]

The value of \(f\) in the above equation gets its maximum value when \(t\) is 0 (at the start of inhalation or exhalation). The values of \(f\) for increasing values of \(t\) are then normalized in order to fit in the range 1 to 0. In the above equation the muscle mechanics are represented by the control constants \(\chi_0\) to \(\chi_N\). The motor drive of breathing is represented by the value of \(q\), which in-turn represents the rate of non-linear increase of the basis function during inhalation and rate of non-linear decrease of the basis function during exhalation. Equation (5.8) is also a linear equation of \(t\). Thus linear equation solving methods can be used to solve for control constants from a subject data.
5.3.4 Implementation of the Control Function

It can be seen that the volume is computed at any instant $t$. The monotonic function $g$ that increases with values of $k$ and $j$ is an absolute value function [76], which may be of the form,

$$g(k,j) = (k \times j)^c,$$

(5.9)

where $c$ is a constant. For every respiratory phase, the values of the derivatives of the volume are initially set to 0. Let $T$ be the total simulation time taken for an inhalation or exhalation. The number of simulation time instants taken during each phase can be varied according to the ventilation rate. We also introduce a discrete time instant $i$ whose range is between between 0 and $T$ and which is related to $t$ as

$$t = \frac{i}{(T + T_{ext})},$$

(5.10)

where $T_{ext}$ is a constant set to 0 for normal breathing. From an implementation perspective, let an array $D$ indexed by $i$ by the control (damping) function. Let $M$ be a constant of proportionality. The damping $D[i]$ (also introduced in section 2.4.2) at any discrete time instant $i$ is thus given as

$$D[i] = M \times (\sum_{j=1}^{N} \sum_{k=1}^{(N-1)/2} 1 - (\chi_j \times \sin^q\left(\frac{i \times \pi}{(k \times j)^c \times (T + T_{ext})}\right))).$$

(5.11)

The effect of variation of $T_{ext}$ results in varying the hysteresis of the PV curve. A schematic diagram of the method for simulating a PV relation is as shown in Figure 5.3. Lungs for a given initial volume are subjected to an applied pressure. The increase in volume is computed using the method given in section 5.3.1 and 5.3.2. At each time instant the value of the damping is changed as given by equation (5.11). This PV relation is then normalized and scaled by given boundary values of pressure and volume shown in Figure 5.2. A range of
boundary values are given by West. There exists a unique solution for these simultaneous equations as the basis functions are linearly independent. Figure 5.4a shows a plot of the basis functions that represent the different frequencies of the oscillations in equation (8). The existence of linear independence among the basis is verified by their non-linearity in the difference among the different basis functions as shown in Figure 5.4b.

5.3.5 Parameterization of PV Curves

The parameterization of PV curves aims at estimating the control constants from a given PV curve. We consider as input, both the PV curves measured and presented previously by published reports and the PV curves that were recorded from adult human subjects. Published data includes an average of PV data for sheep and humans. The sheep and human data were collected using invasive methods. The mono-exponential functions were considered for an average of 28 human and dog PV data also collected using invasive methods. The sheep PV curves were at both normal (0 - 40 cm H₂O) and high (0 – 60 cm H₂O) atmospheric pressure breathing conditions.

The PV curves from recorded responses of human subjects were collected as follows: All subjects were adults. They were informed of the nature of the study prior to starting the experiment and consent obtained. The Institutional Review Board, University of Florida reviewed and approved this project. Four adult men with no history of pulmonary or cardiovascular disease participated in this study. At the beginning of the experiment, a standard
set of instructions was presented to the subject, informing them of their task. The subject was
told to respire as normally as possible. The subjects were seated comfortably in a chair. The
subject wore a nose clip and breathed through a mouthpiece connected to a non-rebreathing
valve. Care was taken to suspend the valve to eliminate the need for the subject to bite the
mouthpiece yet maintain an airtight seal. PM was recorded from a port in the center of the valve.
In esophageal pressure, Pes, was recorded. A thin-walled latex balloon (length of 10 cm, and a
diameter of 3.5 cm) was placed over a polyethylene catheter (i.d. = 0.14 cm). The balloon-
catheter was connected to a calibrated differential pressure transducer (Micro Switch, 14PC). A
topical anaesthetic (Citacaine 2%) was applied to the oropharynx before each experiment to
reduce the gag reflex, and the balloon was lubricated with 2% viscous xylocaine. Pes was
measured by advancing the balloon-catheter trans-nasally down the esophagus until the balloon
was in the middle third of the esophagus. During calibration, Pes sensitivity was adjusted to
zero. The subjects were also asked to close their eyes throughout the experiment to prevent eye
blinks and reduce visual distractions. The subjects inspired through the non-rebreathing valve
with a pneumotachograph placed between the mouthpiece and the mouth port of the valve. The
pneumotachograph was connected to a differential pressure transducer for the measurement of
airflow, V’. The volume was measured by electrical integration of the airflow signal. PM, Pes,
V’and V were digitalized and stored on computer disc for subsequent analysis. Pes-V curves
were obtained for quiet breathing and a slow vital capacity maneuver for each subject. The
cardiac artifact was removed by digital filtering of the Pes signal. The acquired PV curves were
analyzed using PowerLab ML866 with Chart software (version 5.0; ADInstruments) and
digitized at every 5 milliseconds.
Figure 5.3 A Schematic diagram representing the proposed method for approximating the PV relation.

Figure 5.4 (a) The values of the basis functions denoted by $j$. (b) The difference between basis functions for varying values of $j$. This graph points to the linearly independent basis functions.
The method of solving for the control constants is as follows. A given PV curve is first normalized to the range 0 to 1. For each phase (inhalation or exhalation) of the above curve, we consider a set of 100 sample points. A damping curve is created from these sample points using equation (A5) of section 2.4. A set of $N$ ($N=7$) sample points from this damping curve is considered. The control constants are solved from a set of $N$ simultaneous linear equations of equation (5/11). The value of $q$ (measure of motor drive) is set to 2 as it represents the simplest ramp function that linearly increases during inhalation and decreased during exhalation. The variations in the values of $q$ are later discussed in section 5.5.

5.4 Results

The ability to create parameterized PV curves from PV curves measured and presented by published reports and PV curves from recorded responses for adult human subjects are discussed in this section. Figure 5.5a shows an average of the PV curves for sheep lungs (Takeuchi) and the curve parameterized from this data using the polynomial approximation. The corresponding damping curve extracted from the data is shown in Figure 5.5b. The values of control constants are tabulated in Table 5.1. The subject measurements that formed the boundary values of PV curves are tabulated in Table 5.2.

Figure 5.6a shows an average of the PV curve for sheep lungs breathing under high pressure (Takeuchi) and the curve parameterized using the polynomial approximated. The corresponding damping curves for inhalation and exhalation are shown in Figure 5.6b. The values of control constants are tabulated in Table 5.1. The results show increased variations in
the resistance during inhalation as compared to exhalation. This variation in resistance is caused by the fact that during inhalation, air flowed into lungs at a faster rate caused by the pressure difference between the atmosphere and alveoli. There was a subsequent increase in damping at the end of the inhalation phase in order to resist the increased air flow. During exhalation a lowered tissue resistance allows a smooth air flow out of the lungs.

The comparison of the PV curve approximated from the human PV data reported by Colebatch, is shown in Figure 5.7a. The polynomial approximation allows modeling the complete volume range of human PV curves unlike mono-exponential curve-fitting methods used by Colebatch to fit the data. The values of control constants are tabulated in Table 5.1. The PV curve re-created using the proposed method from the mono-exponential PV curves of normal human lung breathing from Venegas is shown in Figure 5.7b. It can be seen that the data clearly overlaps the PV curve generated. The values of control constants are tabulated in Table 5.1.

The PV curves presented in Figure 5.5a, 5.6a, 5.7a and 5.7b match the corresponding PV curves with an RMS range of 1%, which reflects the achievable accuracy range of the polynomial parameterization method. The values of control constants (tabulated in Table 5.1) used in each of the normal breathing PV curves decrease with increase in their index. This decrease is caused by the polynomial decay in the frequency of the basis functions used. This decrease also experimentally supports the fact that the required number of control constants for re-generating normal PV curves remains finite. However, an exception to this observation was seen in Sheep’s breathing under high-pressure conditions (Row 2). The values of control
constants for inhalation converged faster than the values of control constants for exhalation. This indicates that any further variations in breathing conditions (patho-physical) would require more control constants for their re-generation.

The results of the parameterized human subject data are presented in Figure 5.8a-d. The PV curves obtained from these human subjects and the model parameterized PV curves for each subject are plotted. There was a close fit between the measured PV pattern over a tidal breath and the model PV prediction. The values of the control constants used for each of the PV curves are shown in Table 5.3.

5.5 Discussion

The simulation paradigm developed with this study includes prognostic capability with the design of a bio-mathematical model of lung dynamics that closely approximates the relationship between the biomechanics and the control of breathing. The ability to simulate, visualize and predict subject outcomes in various physical conditions has diagnostic and predictive applications. This report of second order derivation allows modeling of lung deformations that account for changes in thoracic muscle and tissue changes.

Results discussed in section 5.4 show a good correspondence between the PV curves obtained by the proposed approach with that of the results obtained from previous methods. We now discuss the ability of the proposed method to model variations in the breathing conditions, an essential requirement for the modeling and simulation of lung dynamics.
Figure 5.9a shows the ability of the proposed method to model variations in the PV relation with the variations in the motor drive. The PV curves were generated using control constants given in the first row of Table 5.1. It can be seen that for higher values of $q$, the shape of the PV relation becomes more sigmoidal. The correspondence of such experimental results with human subject data needs to be further analyzed. Figure 5.9b shows the ability of the proposed method to model variations in the hysteresis of the PV relation using the same control constants. This was done by increasing the value of $T_{ext}$ to higher values (e.g. 10, 20, 30). The value of $q$ was set to 2.0.

Table 5.1 Values of control constants computed from clinical data.

<table>
<thead>
<tr>
<th>Data</th>
<th>Values of Control Constants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Takeuchi (Figure 5a)</td>
<td>1.2, 0.9, 0.5, 0.3, 0.2, 0.1, 0.05</td>
</tr>
<tr>
<td>Takeuchi (Figure 6a)</td>
<td>Inhalation – 1.2, 0.3, 0.2, 0.1, 0.1, 0.05</td>
</tr>
<tr>
<td></td>
<td>Exhalation – 1.2, 1.2, 1.0, 0.7, 0.5, 0.3</td>
</tr>
<tr>
<td>Colebatch (Figure 7a)</td>
<td>0.65, 0.32, 0.14, 0.023, 0.045, 0.037, 0.031</td>
</tr>
<tr>
<td>Venegas (Figure 7b)</td>
<td>0.57, 0.46, 0.40, 0.35, 0.31, 0.30, 0.29</td>
</tr>
</tbody>
</table>
Table 5.2. Measurements for the boundary constraints.

<table>
<thead>
<tr>
<th>Measurements</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Functional Residual Volume</td>
<td>2400 ml</td>
</tr>
<tr>
<td>Tidal Volume</td>
<td>500 ml</td>
</tr>
<tr>
<td>Residual Pressure</td>
<td>0 cmH₂O</td>
</tr>
<tr>
<td>Tidal Pressure</td>
<td>10 cm H₂O (Human) &amp; 40 cm H₂O (Sheep)</td>
</tr>
</tbody>
</table>

Figure 5.5 (a) PV curve generated from sheep data from Takeuchi; (b) Damping curve extracted from Takeuchi data and used for generating the PV curve shown in (a).
Figure 5.6 (a) PV curve generated from sheep data from Takeuchi for higher pressure; (b) Damping curves used for generating the PV curve shown in (a).

Figure 5.7 (a) the PV curve generated from the data from Venegas. (b) the PV re-generated from the data from Colebatch.
Table 5.3 Values of control constants used for human subject data.

<table>
<thead>
<tr>
<th>Human Subject Data</th>
<th>Values of Control Constants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subject 1</td>
<td>2.0, 1.2, 0.2, 0.2, 0.15, 0.1, 0.08; q = 3</td>
</tr>
<tr>
<td>Subject 2</td>
<td>2.0, 1.18, 0.17, 0.2, 0.15, 0.1, 0.08; q = 3</td>
</tr>
<tr>
<td>Subject 3</td>
<td>2.0, 1.23, 0.2, 0.2, 0.15, 0.1, 0.08; q = 3</td>
</tr>
<tr>
<td>Subject 4</td>
<td>2.0, 1.15, 0.2, 0.2, 0.15, 0.1, 0.08; q = 3</td>
</tr>
</tbody>
</table>

Figure 5.8 PV curves generated from the subject data and the PV curves parameterized using the proposed method.
Figure 5.9 (a) the variations in the PV relation with variations in the value of \( q \) that represents the motor drive for breathing; (b) the variations in the PV relation with variations in the value of \( T_{\text{ext}} \).
In this chapter, we discuss the component, which computes the change in the 3D lung shape for a unit increase in volume using deformation methods, a key step in modeling lung dynamics. Such methods facilitate accurate deformation of a 3D lung model from its shape at the beginning to the end of the inhalation cycle. Of particular importance is modeling the shape change of high-resolution 3D models with a large number of elements (e.g. nodes, triangles).[1] Such high resolution lung models may be obtained from either Computed Tomography (CT) imaging and controlled mechanical ventilation,[67] or from the Visible Human data.[1] The large number of elements in these high-resolution 3D models contributes to computational complexity of the deformation computation and graphical rendering, therefore limiting the real-time capabilities of the application.

The proposed model of lung dynamics is based on the analysis of both pulmonary measurements to account for the physiology and CT imaging datasets to account for the morphology. The usage of both single and multi-compartmental models for lungs is discussed in chapter 3. Although the multi-compartment model for 3D lung dynamics [12] can be observed to be a more accurate model for 3D lungs, its visualization cannot be in real-time due to the high computational complexity induced by the collision detection among the lobes. The single-compartment model has the ability to satisfy the real-time requirement of the visualization system. Segars and Kaye have also previously validated the accuracy of the single-compartment model. Since our aim is to develop 3D real-time deformable lung models that can
be integrated with AR based medical visualization systems, we choose a single-compartment model for representing the 3D lung dynamics.

In order to achieve the challenging rate of deformation imposed by the AR framework, we present a physically-based deformation method that is combined with pre-computation. The proposed method of visualization can accommodate deformation of a high-resolution 3D human lung model. The usage of high-resolution models is needed in modeling both normal and patho-physical lung dynamics with high fidelity. The change in lung shape is modeled using an elastostatic deformation method. This deformation method has the following properties. First, it compensates for the lack of information about the lung tissue’s elastic heterogeneity by using an estimate of local tissue elasticity. Second, the method accounts for the fact that there are no contact forces at surface points, as commonly encountered in physically based deformation methods, given that the air is flowing and distributing everywhere inside the lungs.

The physics and physiology-based deformation of lungs form the main topic of this chapter and is detailed in sections 6.1-6.3. Section 6.1 discusses the lung morphology as observed from the 4D HRCT scans. Section 6.2 presents a discussion on the modifications done to the 3D polygonal lung model extracted from the HRCT scan, in order for the model to be deformable. The mathematical model of the deformation method is discussed in section 6.3. Section 6.4 discusses the validation of 3D lung dynamics using 4D HRCT datasets. Finally, section 6.5 discusses pre-computing the lung deformation for a given orientation in order to obtain real-time deformations.
6.1 Morphometric Analysis of 3D Lungs

3D lung deformations can be effectively understood by analyzing the 3D lung morphology obtained from CT imaging scans. The datasets have been collected as follows. Four CT scans of a normal subject lying in the supine position were obtained by Dr. Eric A. Hoffman from the University of Iowa.[74] Each scan was taken at a different time point during respiration with the lung volume held at approximately 5%, 40%, 75%, and 100% of the vital capacity. It was measured by a pneumotachometer and a high frequency balloon valve prohibited air flow at the mouth when lung volume reached the desired level on the expiratory limb.[67] The surfaces for the right and left lungs were computed from each scan and converted into 3D mesh models by using the segmentation functions from the Analyze software developed at the Mayo Clinic.[77]

Figure 6.1a and Figure 6.1b show the frontal and side view of the 3D lung models obtained in a supine position at the start of the inhalation (blue model) and at the end of the inhalation (brown model) cycle. In Figure 6.1a the cranio-caudal displacement of the lung base is shown to be greater than that of the lung apex. In Figure 6.1b the anterior-posterior displacement of the apex region of the lungs, which is minimal as compared to the base region of the lungs, is showed. Such non-uniform changes in lung dimension is caused by (1) the non-uniform change in the thoracic cavity dimension, (2) the heterogeneity of the regional alveolar expandability, and (3) the regional variation in the airflow caused by gravity. From the lung physiology it can be seen that the change in thoracic cavity dimensions is caused by the contraction of the diaphragm and the rotation of rib-cage during breathing, both of which can vary for every human subject. In Figure 6.1a and 6.1b, the base of the lungs shows no significant variations in the costal and crural...
diaphragm segments and thus the image data shows the uniform movements of the diaphragm segments. For our analysis, we thus consider the rate of change of costal and crural segments to be 0, as seen in the CT images, which allows us to focus on modeling the shape change induced by lung tissues.

It can also be observed from clinical data that there exists linearity in the change in lung dimensions with an increase in volume. Figure 2a represents the linear change in the dimensions of the lung’s bounding box (a box that exactly encloses the 3D lungs) with an increase in volume during a single breathing cycle. Figure 6.2b represents the linear change in the ratio of the lung volume and the bounding box volume as lung volume increases. The ratio is also seen to lie in a close range of 0.32-0.40.

A clinical analysis of the linearity in individual node displacements was presented in [74]. In summary, a set of landmarks were chosen and tracked in the sequence of 3D models obtained during a single breathing cycle. The magnitude of the landmark displacements was observed to be linear with an increase in volume. Thus the change in lung shape can be modeled as a linear function of the change in lung volume. The directional component of the nodal displacement was not reported. In this dissertation, the directions of the displacements of nodes in the surface of the 3D lung model is taken as a constant during a single breathing. The constant direction is motivated by two anatomical facts: (a) the radial and linear expansion of alveoli throughout a breathing cycle (based on morphometric analysis),[71] and (b) the pleural liquid that allows the lungs to slide during rib-cage rotation.[56] From a mechanical perspective the constant direction of nodal displacement is supported by the work minimization principle.[58].
Figure 6.1 (a) A frontal view of human 3D lung model at the start of inhalation (blue) and at the end of inhalation (brown) (b) A side view of human 3D lung model at the start of inhalation (blue) and at the end of inhalation (brown).

Figure 6.2 (a) The change in the length of the lung’s bounding box. (b) The ratio of lung volume to the change in bounding box volume.
6.2 3D Model Representation

We now explain the modifications applied to a 3D lung mesh model, then present the method for computing the magnitude of the node displacement. The input is a high-resolution mesh lung model that is to be deformed using the following modifications. For each link of the polygonal model, we add a node called a spring node. The spring node is used to damp the flow of applied forces between two mass nodes. A schematic representation of the mass-spring model together with the proposed model is shown in Figure 6.3a. Additionally, each node in this modified polygonal model is given an associated attribute representing its stiffness. These stiffness values are equivalent to the Young modulus, which represents the ratio of the stress applied to the strain experienced by the node.[33] These values are assigned based on the regional alveolar expansion.
of the human lungs.[56] In the proposed approach, force is applied on every mass node. A schematic representation of force application is as shown in Figure 6.3b. There are two ways in which the applied force for a mass node can be set. First, it can be estimated based on the orientation of the lungs since the air-flow inside the lungs is caused by the vertical pressure gradient. The computation of displacement of every node from this applied force is discussed in sections 6.3. Second, the applied force on every node can also be more accurately extracted using clinical data combined with the mathematical model discussed. This extraction of applied force from the clinical data is further explained in section 6.4.

6.3 Mathematical Model

We now explain the mathematical model that is used to compute the displacement of mass nodes for a given applied force. The elastostatic force (or the displacement) is computed using the following physical principle. A given amount of direct force that is applied on any node on the surface is transferred in part to the neighbors of that node in a particular ratio given by a transfer matrix. This transfer of force is caused by the elastic interaction, which causes the neighboring nodes to exhibit displacement. The transfer matrix contains the ratio with which the direct force is transferred between nodes. This principle is mathematically represented by the Green’s formulation.

Let $f[j]$ be the direct force applied on node $j$, and $\tau_{[j \rightarrow i]}$ be the transfer matrix element of the Green’s formulation that represents the transfer of force from node $j$ to $i$. The resulting elastostatic force $F[i]$ can be written as
\[ F[i] = \sum_{j=0}^{N} f[j] \times T[j \rightarrow i], \tag{6.1} \]

where \( N \) is the total number of nodes. Some of the key properties of the transfer matrix are as follows: The dynamics of air flow inside lungs follow fluid dynamic properties, which eliminate the contact force on each lung node. Such fluid flow properties allow the air to flow into regions of lower resistance. The variation in regional resistance to expansion is caused by the heterogeneous expansion of alveoli. While the transfer matrix is thus not symmetric as previously used in traditional methods, the summation of its elements for a given value of \( j \) is also set to 1.

\[ \sum_{j=0}^{N} T[j \rightarrow i] = 1. \tag{6.2} \]

Using equation (6.2), equation (6.1) can be expanded as

\[ F[i] = f[i] + \sum_{j=0, j \neq i}^{N} f[j] T[j \rightarrow i] - \sum_{j=0, j \neq i}^{N} f[i] T[i \rightarrow j]. \tag{6.3} \]

From equation (6.3), it can be seen that the elastostatic force is a summation of the force directly applied on a node \( i \) and the force received from its neighboring nodes, subtracted by the direct force of \( i \) transferred to its neighbors. Thus, for a known transfer matrix and applied force the displacement can be computed using equation (6.3). Equation (6.3) describes the force distribution that occurs in an elastic displacement of nodes. However, since the transfer matrix is not known, we consider a localized estimation of the transfer matrix elements, which is based on an elastic equilibrium caused by the laws of conservation of energy. Let \( T_{e}[j \rightarrow i] \) be the estimated transfer matrix element. The elastostatic force applied on surface nodes under elastic equilibrium can be represented as
\[ F[i] = F[i] \times T_e[i \to i] + \sum_{j=0, j \neq i}^{N} F[j] \times T_e[j \to i]. \]  

Equation (6.4) is an iterative equation, which represents the local balance among the forces acting on each node of an elastic surface, which in our case is a mesh lung model. In order to solve this equation an iterative solution is required. The initial value \( F[i] \) on the right hand side of equation (6.4) is substituted for \( f[i] \). The equation (6.4) is now re-written as

\[ F[i] = f[i] \times T_e[i \to i] + \sum_{j=0, j \neq i}^{N} F[j] T_e[j \to i]. \]  

Equation (6.5) is still an iterative equation as every neighbor of node \( i \) experiences a similar force distribution process. Additionally, every node receives an elastostatic force based on the elastic interaction among the nodes. Since in the real-world the lung tissues are thin, no vibrations are seen during lung deformations and the elastostatic force is assumed to reach its equilibrium in a negligible amount of time. Also, the lung deformations are observed to be linear with an increase in volume (as explained in section 6.1). For a known value of the estimated transfer matrix and applied force, the elastostatic force can be derived. The values of the transfer matrix \( T \) can be computed by equating the right hand side of equation (6.5) and equation (6.2) and by considering the magnitude vectors \( f \) and \( F \) as diagonal matrices. The elements of the transfer matrix \( T \) can thus be written as

\[ T[j \to i] = \left( \frac{F[j]}{f[j]} \right) \times T_e[j \to i]. \]  

We now proceed on solving equation (6.6) to estimate the elastostatic force for an initial estimation of the applied force. An iterative method to compute the elastostatic force starts with an initial estimation of the transfer matrix. Using estimation of the transfer matrix and the
applied force we compute the elastostatic force. The estimated transfer matrix \((T_e)\) is computed for every node pair \(j\) and \(i\). To estimate the transfer matrix, a regularly connected mesh, as observed in high-resolution 3D models, is considered. Let us consider an accumulator matrix \(TP\) used by the transfer matrix for storing intermediate computations. The transfer matrix from every node to every other node is initially set to 0 and then computed as follows. The transfer matrix from a node \(j\) to its immediate neighbor \(i\) is first computed by dividing the Young modulus of \(i\) by the summation of Young’s modulus of nodes in the immediate neighborhood of \(j\), and is given as

\[
T_e[j \rightarrow i] = TP[j \rightarrow i] + \left( \frac{S_i}{\sum_{l \in \text{cliqueof}(j)} \left( S_l \times \left( \frac{1}{\text{Dist}(l, j)} \right) \right) \ast \frac{1}{\text{Dist}(j, i)}} \right), \tag{6.7}
\]

\[
TP[j \rightarrow i] = T_e[j \rightarrow i], \tag{6.8}
\]

where \(S_i\) is the inverse of the Young modulus of the \(i^{th}\) node if \(i\) is a spring node. With respect to the mass node, the value of \(S_i\) is the Young modulus. The \(\text{Dist}(i, j)\) is a function that represents the Euclidean distance between the \(i^{th}\) and \(j^{th}\) node. The minimum value of \(\text{Dist}(i, j)\) is set to be 1. The \(\text{cliqueof}(j)\) represents the immediate neighboring nodes of \(j\). The transfer matrix is then propagated from \(j\) through \(i\) to other nodes until the contribution reaches 0 in the following manner: the transfer matrix from node \(j\) to a node \(k\), which is an immediate neighbor of node \(i\) and not an immediate neighbor to node \(j\) is given as

\[
T_e[j \rightarrow k] = TP[j \rightarrow k] + T_e[j \rightarrow i] \times T_e[i \rightarrow k], \tag{6.9}
\]

\[
TP[j \rightarrow k] = T_e[j \rightarrow k]. \tag{6.10}
\]

The value of \(T_e[i \rightarrow k]\) is computed using equation (6.7). Equation (6.9) is used for computing the transfer matrix for all nodes reachable from the node \(j\) along a forward path. Equations (6.7-
6.10) will always converge because the transfer matrix between any two nodes is always less than 1. The result of equations (6.7-6.10) gives an initial estimation of the transfer matrix.

To compute the elastostatic force, it is first initialized to the applied force. The force applied on a spring node is initially set to 0 since these nodes are used for damping the flow of force between two mass nodes. Two sets of accumulators for each node are introduced at each iteration time step $t$, which are named $Catcher^t$ and $Pitcher^t$, respectively. While the former provides the final value of the force that causes the displacement for a node, the latter indicates the force, which needs to be distributed to its neighbors if it is greater than 0. A schematic representation of the applied force and accumulators are shown in Figure 6.4. During a sequence of iterations denoted by $t$, a node $i$ of maximum $Pitcher^{t-1}$ is chosen and the force in that accumulator is distributed to other nodes as follows

$$Pitcher^t[j] = Pitcher^{t-1}[j] + Pitcher^{t-1}[i] \times T_e[i \rightarrow j], \quad (6.11)$$

$$Catcher^t[i] = Catcher^{t-1}[i] + Pitcher^{t-1}[i] \times T_e[i \rightarrow i], \quad (6.12)$$

$$Pitcher^{t-1}[i] = 0. \quad (6.13)$$

It can be seen that the $Pitcher^t$ accumulator reaches zero for all the nodes for higher values of $t$. Each node $i$ is either a mass node or a spring node. The elastostatic force $F[i]$ of a mass node $i$ in the model are given by the $Catcher^t[i]$ accumulator. The $Catcher^t[i]$ for a spring node $i$ is set to be the average of its two mass nodes for deformation purposes. The above equations are repeated in the same order until the $Pitcher$ accumulator of all the nodes becomes 0. Thus the iterative solution can compute the equilibrium displacement of each of the model nodes for a given applied force. A single row of the transfer function is shown in the two images. In Figure 6.5a and 6.5b, we show the local interaction that occurs among the lung nodes. In each of the images
a node in the 3D lung is chosen. The “white”ness of each pixel represents a normalized value of the force transferred from the chosen node (marked by the yellow arrow) to its neighborhood nodes. The higher the whiteness the higher is local elastic interaction. Figure 6.6 shows the convergence of the proposed method as compared to the exponential convergence of the mass-spring-damper model. The convergence of the proposed method is superior as compared to the mass-spring-damper model.

In Figure 6.5a, a node closer to the diaphragm is chosen, since they have very high alveolar expandability. In Figure 6.5b, a point closer to the apex of the lung is chosen since they have very low alveolar expandability. It can be seen that the node near the diaphragm has a higher elastic interaction, which stems from the regional alveolar expandability. It can also be seen from Figure 6.5a, that the neighborhood nodes that are farther away from the apex have a greater “whiteness”. This stems from the fact that the air flows towards the region of higher alveolar expandability which is thus towards the diaphragm.

This completes the computation of the elastostatic force that can be now used for animation of the lung model. Before we proceed with it, first we have to verify the validity of the iterative solution.
Figure 6.4 A schematic representation of the accumulators used for the iterative solution.

Figure 6.5 A kernel row (transfer function row) of a transfer function is as shown (in a white color) for (a) a node near the diaphragm, and (b) a node near the apex.
Figure 6.6 Convergence of the proposed method as compared to the exponential convergence of the mass-spring-damper model.

### 6.4 Validation Procedure

The validation procedure first focuses on the accuracy of the proposed mathematical model. It is then followed by the validation of lung deformations.

#### 6.4.1 Validation of the Proposed Mathematical Model

The latter can be used however to verify the accuracy of the deformation. Specifically, the mass-spring-damper model we chose was discussed in [79] and we simulated it using the Kineticskit source code’s graphical interface.[80] The same graphical interface is also used to simulate and compare the deformation method we proposed.
The mesh of the mass-spring-damper model was considered to have homogenous elastic properties. A force pattern similar to the expansion of lung models (bending force) was applied on each node of the mesh. The original mesh and the deformed mesh using the proposed method are shown in Figures 6.7a and 6.7b. The difference in the displacement using the two methods is less than 0.1% RMS. Figure 6.8a shows a 2D circular mesh with nodes (Blue spheres) of variable size. The lower the radius of the node, the higher is their Young’s modulus. This 2D mesh is deformed by applying a unit force on all the nodes along their radius. Using the proposed method of computation the 2D deformed mesh is as shown in Figure 6.8b. It can be seen that the radial displacement of nodes with lower Young’s modulus is less than 0.1% RMS, which illustrates the absence of fixed contact force on the nodes.

![Figure 6.7](image1.png) ![Figure 6.8](image2.png)

Figure 6.7 (a) A regular planar mesh of isotropic Young’s modulus. (b) the deformed shape of the regular mesh using the proposed method of deformation.
6.4.2 Validation of 3D Lung Dynamics

The validation of 3D lung deformations is done by: (i) validating the linearity in the direction of 3D lung deformation for every node using the proposed method, (ii) validating the 3D lung deformations, and (ii) estimating the applied force $f$ from the 4D HRCT dataset coupled with equation (6.5) and verifying that it correlates with the gradient of gravity caused by the orientation of the human subject. The relation of the air-flow and the gradient of gravity has been previously quantified by [74]. To deform the 3D lungs we start by computing the magnitude and direction of the applied force in order to deform a static 3D lung model from a lower tidal volume to a higher tidal volume.
We compute the directions of the displacement of the model nodes using 3D clinical data analysis while we compute the magnitude of applied force using equation (6.5). A sequence of three 3D lung models obtained from a normal human lung at 5%, 40%, and 75% tidal volume at supine position were considered for analysis. The supine position imposes no downward movement of the lung tissue at the apex and no forward movement at the posterior part of the lung. Thus the apex is chosen as the origin for the Z-axis, the posterior part of the lung as the origin for the Y-axis and the heart as the origin for the X axis. The surface node of these 3D models at various tidal volumes needs to be put in correspondence in order to compute the displacement of nodes. Although, various correspondences corresponding to different directions of deformation could be established, one direction for each node will yield a linear displacement when the lungs are expanding from 5% to 40% tidal volume and 5% to 75%. The correspondences are established by projecting a ray from a node of the 3D model at 5% tidal volume in a specific direction and performing a ray-triangle intersection analysis of that ray with the lungs at a higher tidal volume. The specific direction is estimated as follows: Let $\mathbf{min}$ and $\mathbf{max}$ be two vectors that represent the bounding co-ordinates of the lungs at 5% tidal volume. Let $\mathbf{p}_i$ be the position of node $i$ at 5% tidal volume, and $\mathbf{d}_i$ be a vector that represents the estimated direction of node $i$. Under the hypothesis that the direction of displacement is constant, the components of $\mathbf{d}_i$ may be simply modeled as first-order polynomials given by

$$d_iX = c_1 \times \left( \frac{p_i.X - \text{min}.X}{\text{max}.X - \text{min}.X} \right)^{c_2}, \quad (6.14)$$

$$d_iY = c_3 \times \left( \frac{p_i.Y - \text{min}.Y}{\text{max}.Y - \text{min}.Y} \right)^{c_4}, \quad (6.15)$$
\[
d_i.Z = c_5 \times \left( \frac{p_i.Z - \min.Z}{\max.Z - \min.Z} \right)^{c_6},
\]

(6.16)

where \( c_1, c_2, c_3, c_4, c_5, \) and \( c_6 \) are constants.

The choice of this first-order polynomials are now validated by ensuring that their use yields the correct lung deformation given by medical data within 1% root mean square (RMS) error. The required values for the constants must allow the displacement’s magnitude of every node to be linear with an increase in volume as previously observed in [74]. The constants were estimated by an exhaustive searching approach to choose their values that has the minimum RMS error. The searching approach may be described as follows. The initial value of the constants was set to be 0.01. We then computed different combinations of values for the constants, with the difference between two consecutive values of a constant set to 0.01. For each combination we computed the displacement of the surface nodes. The values of the computed constants that provided an RMS error of less than 1% are given in Table 6.1. Figure 6.9a and 6.9b shows the side view of the left and right lungs at 40% tidal volume (blue model) overlapped with the left and right lungs projected along the directions computed from equations (6.14-6.16) when expanding from 5% to 40% tidal volume (red model). Such results support not only the hypothesis that the direction of displacement of the surface nodes of a 3D lung model under normal breathing conditions can be modeled as a constant, but also that equations (6.14-6.16) present adequate representation of the direction of deformation.

The validation of 3D lung dynamics is now detailed. Figure 6.10a and 6.10b shows a side-view of the left and right lungs at 100% tidal volume (blue model) overlapped with the left and right
lungs projected along the same directions computed from equations (6.14-6.16) when the lung is expanding from 5% to 100% tidal volume. The magnitude of the displacement in this case was computed by linearly scaling the nodal displacement computed for a deformation from 5% to 40% tidal volume. For additional validation purposes, a medical expert from M.D.Anderson Cancer Center marked landmarks in the base of the lung (in an upright position) on both the actual left lung at 100% tidal volume and the simulated left lung at the same tidal volume. The landmarks on the simulated left lung differed from the actual left lung with a mean distance of 1.63mm and a SD of 0.52 mm.

The magnitude of the force applied on each node of the dataset is then computed using equation (6.5) with the displacement estimated from the above steps and the transfer function estimated using equations (6.7) and (6.8). The next step is to compute the magnitude of the applied force as a function of node position. The applied force on a node \( i \) is first normalized to fit within a range of 0 to 1 and then approximated using the following function

\[
f[i] = c_7 \times \left( \frac{p_i,X - \text{min}X}{\text{max}X - \text{min}X} \right) + c_8 \times \left( \frac{p_i,Y - \text{min}Y}{\text{max}Y - \text{min}Y} \right) + c_9 \times \left( \frac{p_i,Z - \text{min}Z}{\text{max}Z - \text{min}Z} \right),
\]

where \( c_7, c_8, \) and \( c_9 \) are constants, which are estimated by an exhaustive search approach with the constraint that the above function best fits the applied force computed from medical data. Using equation (6.18), the applied force of the given 4D lung dataset is modeled to satisfy an RMS error of less than 1%. The values of these constants are also tabulated in Table 1, which can be used for obtaining a physically-valid 3D lung deformation. It can be observed that the value of \( c_7 \) and \( c_9 \) are very less as compared to the value of \( c_8 \), which shows the effect of the gravity (along the Y axis) on the applied force. It must also be noted that the values of these constants
can be used in simulating 3D lung deformations in supine orientation for any 3D static lung model such as the Visible Human dataset. Such a simulation would yield a deformation similar to the 4D HRCT dataset. Datasets are now being collected on which a statistical analysis of these constants will be conducted in order to establish their range of variability across a given population, which in a first step will be normal subjects if such datasets can be obtained.

Figure 6.9 (a) A side view of a 3D left lung (a) and right lung (b) model at 40% tidal volume (blue color) and a 3D left lung model obtained by deforming the left lung at 5% tidal volume to 40% tidal volume (red color).
Figure 6.10 A side view of a 3D left lung (a) and right lung (b) model at 100% tidal volume (blue color) and a 3D right lung model obtained by deforming the right lung at 5% tidal volume to 100% tidal volume (red points) using the same direction of displacement used for Figure 6.9. The magnitude of the displacement in this case is computed by linearly scaling the nodal displacement computed for a deformation from 5% to 40% tidal volume.

Table 6.1 Tabulation of constants estimated from a normal human subject

<table>
<thead>
<tr>
<th>Lung</th>
<th>C1</th>
<th>C2</th>
<th>C3</th>
<th>C4</th>
<th>C5</th>
<th>C6</th>
<th>C7</th>
<th>C8</th>
<th>C9</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left</td>
<td>0.09</td>
<td>0.23</td>
<td>0.4</td>
<td>0.5</td>
<td>0.1</td>
<td>2.3</td>
<td>0.01</td>
<td>0.95</td>
<td>0.07</td>
</tr>
<tr>
<td>Right</td>
<td>0.09</td>
<td>0.22</td>
<td>0.39</td>
<td>0.51</td>
<td>0.11</td>
<td>2.2</td>
<td>0.01</td>
<td>0.96</td>
<td>0.05</td>
</tr>
</tbody>
</table>

**6.5. Real-time Deformations**

We now have discussed a physics and physiology-based method for modeling 3D lung deformations. Using this method we can now animate various single lobe 3D lung models in two
approaches. In the first approach we deform the 3D lung models for static subject orientations. In this case, the displacement of each node is pre-computed for a unit applied force, and for a given orientation of the patient. The pre-computed displacement is used for deforming 3D lung models in real-time across the whole breathing cycle using the linearity in displacement from lower to higher tidal volumes. Such an approach reduces the run-time complexity of deforming a 3D lung model to 3 additions per node. We also use state-of-the-art graphics processing units in order to avoid any rendering delays. Figure 6.11a shows the initial shape of a high-resolution 3D lung model obtained from the 3D HR-CT datasets of a normal human subject other than the one used in the analysis done in section 6.1. The unit increase in volume is set as the ratio of the tidal volume of human lungs (i.e, 500 ml), to the product of the deformation steps per second (i.e, 66.66 steps/sec) and the ventilation rate of inhalation or exhalation (normally 5 sec). For this increase in volume, the applied force for the lungs in the supine position is computed using equation (6.18). The deformed shape caused by inhalation is as shown in Figure 6.11b. The second approach of deformation accounts for multiple patient orientations and is discussed in chapter 7.

We now discuss the role played by the PV relation (discussed in chapter 5) in modeling the 3D lung dynamics and visualization. The PV relation, which provides the 3D lung volume under different breathing conditions, is now coupled with the 3D deformable model. Snapshots of 3D lung deformations driven by the PV curves shown in Figure 6.12a & 6.12b, are shown in Figure 6.12(b, c, e, and f). The PV curve shown in Figure 6.12a is modified, by changing the value of $q$ from 2 to 6, to form the PV curve shown in Figure 6.12d. Snapshots are taken with the deformed 3D lung model (red lung model) overlapping the un-deformed 3D lung model (grey lung model).
The lower the regional overlap the higher the visibility of the grey un-deformed lung model. Such variations in the overlap visually represent the change in lung shape caused by lung deformation. While Figure 6.12b and Figure 6.12e represent lung shape at a pressure of 5 cmH$_2$O, Figure 6.12c and Figure 6.12f represent lung shape at a pressure of 7 cmH$_2$O. It can be seen that the overlap between the deformed and un-deformed lung is lesser in Figure 6.12 compared to Figure 6.12e. This is caused by the fact that at 5 cmH$_2$O the PV shown in Figure 6.12a has approximately 100 ml of air, while the PV shown in Figure 6.12d has approximately 10 ml of air. However, the overlap between the deformed and un-deformed lung is higher in Figure 6.12c compared to Figure 6.12f. This is caused by the fact that at 7 cmH$_2$O the PV shown in Figure 6.12a has approximately 300 ml of air, while the PV shown in Figure 6.12d has approximately 400 ml of air. The run-time deformation takes $O(n)$ operations where $n$ is the number of nodes. The implementation system details are explained in Table 6.2.

### 6.6 Discussion

Through our research we aim to extend the thoracic simulation paradigm to include real-time visualization of 3D lung dynamics. This is achieved using the real-time pre-computation based approach for lung dynamics discussed in this dissertation, which closely models the change in 3D lung shape. Such an approach coupled with the PV relation, allows us to simulate normal 3D lung deformations.

The proposed method takes into account the deformation constraints imposed by the diaphragm and rib-cage (through the PV curve) on the lung’s air-volume and the regional alveolar
expandability on the regional lung shape. The above-mentioned physiological components can be individually varied in order to obtain physically-realistic variations of 3D lung deformation. For instance, pneumothorax, a pathophysical state in which the change in 3D lung deformations is caused by an external wound, is demonstrated using the proposed 3D lung deformations by varying the PV relation and static lung shape.[81] Similarly tumor-influenced lung dynamics, in which a change in 3D lung deformations is caused by the presence of lung tumor, is demonstrated using the proposed 3D lung deformations by varying the regional alveolar expandability.[82]

The choice of a single compartmental model enables visualization of high-resolution 3D lung deformations. The accuracy in the usage of single compartmental model has been validated by some of the peers. The validation however needs to be performed across a wide range of human subjects of various age and race. Additionally, the applicability of a single compartmental model to simulate diseased lung dynamics needs to be further validated. The simulated lung dynamics needs to be compared with 3D HRCT images of normal lung subjects with different breathing conditions.

The usage of a physically based deformation approach for lung deformations allows us to model lung deformations with variations in physics-based parameters. The usage of the regional alveolar expandability as one of the parameters allows the proposed method to account for the physiology of normal human subjects. The method can be extended by analyzing the regional alveolar expandability for human subjects across a wide range of age and race. An inverse analysis of the proposed method can also be used to estimate the alveolar expandability. Such
an analysis of physiology would facilitate modeling the 3D lung dynamics for a wide range of human population. Additionally, the variations in the air constituents also need to be included in the current method. One may note that the variations in the air constituents can lead to changes in the alveolar blood pressure, which subsequently alters the alveolar expandability. The proposed method can be expanded in order to address this aspect of the lung physiology.

The validation of the proposed method of deformation is discussed in section 6.4.1 and the simulated lung deformation in section 6.4.2. Through this validation we illustrate the method to obtain physically and physiologically based lung deformations. Additional validations can be done using HRCT data obtained from a higher number of normal and diseased human subjects under different breathing conditions. The validation can also be done by generating physically based deformable lung models using our human subject data as explained by the peers and comparing it with the proposed simulation method. The results of such a validation would discuss the feasibility of the proposed method in different breathing conditions of the human subject and will be discussed in the future.
Figure 6.11 The (output) deformation of a high-resolution lung model obtained from a normal human subject, using the proposed approach. (a) The lung at residual volume (i.e. before inhalation), (b) The deformed lung at the end of inhalation.

Table 6.2 Implementation system information.

<table>
<thead>
<tr>
<th>Implementation system information</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPU</td>
</tr>
<tr>
<td>GPU</td>
</tr>
<tr>
<td>Shaders</td>
</tr>
<tr>
<td>Op. System</td>
</tr>
</tbody>
</table>
Figure 6.12 (a-f). A 3D sequence of deformations generated using PV curves given in Figure 11a and 11d. The 3D shapes obtained during inhalation are shown at a pressure of 5 cmH\(_2\)O (Figure 11b & 11e), and 7 cmH\(_2\)O (Figure 11c & 11f) using each of the PV curves. In the above lung images, the deformed lung (red color) is overlapped with the un-deformed lung (grey color) in order to clearly show the shape change obtained at each of the pressures.
CHAPTER SEVEN : VISUALIZATION

The first two components of the proposed framework (discussed in chapter 4) have been addressed in chapter 5 and 6. The technical challenges of designing and visualizing a medical simulation for lung morphology using these two components arise from the computational complexity. Specifically, in an AR environment the position and orientation of the human subject are updated by the tracking sensor every 16 ms. Such update requires deforming and rendering 3D lung models at approximately 66 times per second[19]. This subsequently limits the usage of high-resolution 3D lung models for real-time deformation and visualization. A method to overcome this limitation was proposed in section 6.5, in which the 3D lung dynamics caused by the air-flow into the lungs were modeled using GF, pre-computed for an upright orientation, and simulated in real-time for the upright position. However, the changes in the 3D lung deformations for changes in the patient position and orientation in an AR environment were not accounted for.

The method presented in this chapter forms the third component of the proposed framework, which allows us to account for the breathing variations caused by the changes in the patient’s orientation. It extends the 3D lung dynamics previously modeled in [23] by off-loading the run-time deformation computations from the CPU to the GPU. Specifically, the deformation kernel is transformed into frequency-space coefficients using Spherical Harmonic (SH) transformations before being off-loaded to the vertex memory of the GPU. During run-time, the deformation is computed in the GPU as a dot product of the frequency-space coefficients. The end-result of such an approach allows the CPU to cater to the computational requirements of the AR
environment and the GPU to cater to the computational requirements of deforming and rendering the 3D model in this AR environment. Additionally, a method to approximate the SH coefficients of the airflow inside the lungs at any arbitrary orientation is discussed. The method and results discussed in section 7.3-7.5 are research contributions as part of this dissertation.

7.1 Graphics Processing Units

Modern GPUs perform floating-point operations (FLOPS) much faster than most CPUs. For instance, a 3-GHz Pentium 4 can theoretically issue approximately 6 billion FLOPS. A vertex program in NVIDIA GeForce 5600 Ultra achieves approximately 20 billion FLOPS. Similarly the memory bandwidth of a CPU is approximately 6 gigabits per second while a GPU has approximately 25 gigabits per second[83]. Programmable GPUs have been previously used for implementing both geometrically and physically-based deformation methods. The geometrically-based methods of particular importance were Key-framing and Vertex-skinning[84]. Key-framing allowed a cartoon artist to animate a 3D character (model) by interpolating among a set of intermediate 3D frame sequences. However by implementing this method in a GPU the intermediate 3D frames had to be stored[84]. Vertex-skinning allowed a cartoon artist to create animations by associating the movement of a node of a 3D model to the movement of a set of key nodes in the 3D model. These key nodes as a group were represented as a matrix (referred to as a bone matrix). The animation was reduced to a matrix-vector multiplication in a GPU[85]. Physically-based methods were implemented in a GPU using the “Render-to-Texture” feature. This feature, which is a multi-pass algorithm, allowed intermediate values of a computation to be stored into a texture memory in GPU, referred to as P-buffer[86]. This approach was used in
obtaining physically-based wave motions for fluid and cloud simulations,[87] and FEM computations [88] in a GPU.

7.2 Overview

We consider a per-vertex approach for deforming and rendering 3D lung models, which is a single-pass approach. We present a method to optimally compute the matrix-vector multiplication in a GPU during run-time. Specifically the matrix-vector multiplication is represented in steps, which can be partially pre-computed off-line. The columns of the transfer function matrix are pre-computed and represented using SH coefficients. These coefficients are obtained from orthonormal decomposition of the transfer function matrix using SH transformations[89]. The choice of using SH transformations for approximating the transfer matrix stems from its negative-exponential convergence, as opposed to a uniform convergence seen in other transformations such as wavelet transformations. This property of SH transformations allows us to represent the transfer matrix using a minimal number of SH coefficients. While the 3D models are rendered using a point-based rendering approach, [30] a comparison of the frame rate per second (FPS) in using point-based rendering and polygon-based rendering is discussed in the results section. Additionally, the number of SH coefficients used for representing the transfer function row is much less as compared to the number of coefficients used for shape approximation. This advantage of the proposed method coupled with the per-vertex nature of SH coefficient allow us to use GPU for improving the computation-speed.
In the proposed approach, we make use of a unique property of normal lung deformations. In our approach, the transfer function remains a constant until the tissue properties undergo irreversible damage[90]. Since lungs do not undergo irreversible damage under normal breathing conditions, the transfer matrix can be considered a constant. The transfer function matrix is pre-computed using the method proposed in chapter 5. The SH coefficients are transferred into the local memory of the GPU along with the 3D model before starting the simulation. The SH coefficients of the force applied on the 3D model are also pre-computed. During the simulation, 3D deformation is computed in GPU as a dot product of pre-computed SH coefficients of the applied force and the transfer function matrix. The method is computationally inexpensive when compared to the dot product of the transfer function matrix and the applied force for a high-resolution 3D model.

7.3. Mathematical Model

In this section we discuss the mathematical steps in the third component of the methodology adopted for simulating 3D lung dynamics. The surface nodes of the 3D lung model (as shown in Figure 7.1a) are represented using polar coordinates (as shown in Figure 7.1b). Such polar coordinates were obtained by projecting the nodes of the 3D lung model (Figure 7.1a) onto a spherical hull of large radius. It was observed that such an approach provided unique spherical coordinates for all the nodes of the 3D lung model. Any shape degenerations in the 3D lung model representing patho-physical conditions can be accounted for using conformal mapping methods, and is discussed in the future work.
Let $\theta_I, \vartheta_I$ represent the polar coordinate of node $I$ of the 3D lung model. At any instant during deformation a force is applied on each node. From the force we can determine the function $F(\theta_I, \vartheta_I)$ that best approximates the force[91]. Similarly, we can also determine the function $T(\theta_I, \vartheta_I, \theta_J, \vartheta_J)$ that best approximates the transfer function matrix of the 3D lung model, which represents the elastic interaction between node $I$ and $J$ associated with the deformation. The fundamental form of the transfer matrix is given in [51, 89]. Let $D(\theta_I, \vartheta_I)$ be the displacement of the node $I$. For simplicity in notation we denote $D(\theta_I, \vartheta_I)$ by $D(I)$, $F(\theta_J, \vartheta_J)$ by $F(J)$ and $T(\theta_I, \vartheta_I, \theta_J, \vartheta_J)$ by $T(I,J)$. $D(I)$ using GF can be written as,

$$D(I) = \sum_{J=0}^{N} F(J) \cdot T(I,J)$$ \hspace{1cm} (7.1)

where $N$ is the total number of nodes in the 3D lung model. To further reduce the complexity of the computation we approximate this function using SH transformations. We use SH transformations to modify the computations involved in the dot product on the right hand side of
equation (7.1). A finite set of SH coefficients are used for representing an array of numbers. Let \( y_{lm}(\theta_j, \varphi_j) \) represent the SH polynomials and \( y^*_{lm}(\theta_j, \varphi_j) \) be their conjugates polynomial at node \( J \) [92]. For simplicity in notation, we denote \( y_{lm}(\theta_j, \varphi_j) \) by \( Y_{lm}(J) \) and \( y^*_{lm}(\theta_j, \varphi_j) \) \( \times \sin(\theta_j) \) by \( Y^*_{lm}(J) \).

The applied force can be represented as

\[
F(J) = \sum_{l=0}^{n} \sum_{m=-l}^{l} F_{lm} \cdot Y_{lm}(J),
\]

where \( n \) specifies the total number of SH bands and is the square root of the total number of SH coefficients. The values of \( F_{lm} \) are the SH coefficients of the force where \( l \) and \( m \) are indexes for the SH coefficients and the SH polynomials. The SH coefficients can be computed from the applied force by the following relation.

\[
F_{lm} = \sum_{J=0}^{N} F(J) \cdot Y^*_{lm}(J).
\]

The \( I \)th row of the transfer function can now be given as

\[
T(J, I) = \sum_{l=0}^{n} \sum_{m=-l}^{l} T^{l}_{lm} Y_{lm}(J),
\]

where \( T^{l}_{lm} \) represents the SH coefficients of the \( I \)th row of the transfer matrix. We now write equation (7.1) by substituting the expansions of the applied force and the transfer function row given in equation (7.2) and (7.4), respectively. Thus equation (7.1) can be written as

\[
D(I) = \sum_{J=0}^{N} \left[ \sum_{l=0}^{n} \sum_{m=-l}^{l} F_{lm} \cdot Y_{lm}(J) \right] \left[ \sum_{J=0}^{N} \sum_{l'=0}^{n} \sum_{m'=l'}^{l'} T^{l'}_{l'm'} Y_{l'm'}(J) \right].
\]
\[ D(I) = \sum_{l=0}^{n} \sum_{m=-l}^{l} F_{lm} \cdot T_{lm}^{T} \cdot A, \quad (7.6) \]

where \( A \) is a constant representing the summation of the square of \( Y_{lm} \) for all values of \( J \) [93].

We now introduce the following modification to equation (6).

\[ D(I) = \alpha \sum_{l=0}^{n} \sum_{m=-l}^{l} (F_{lm} \cdot T_{lm}^{T} \cdot A), \quad (7.7) \]

where \( \alpha \) is a coefficient, which allows accounting for the finite value of \( n \). Further discussion on the choice of \( n \) and the corresponding value of \( \alpha \) are discussed in Section V. The SH coefficients of both the applied force and the transfer function matrix can be pre-computed and thus we need to compute only equation (7) during run-time in order to obtain deformation of the 3D model. The advantage of using SH coefficients is that it reduces the dot product of two arrays of variable length of non-zero values to a dot product of two arrays of fixed length of non-zero values. Since the SH coefficients of the transfer function matrix and the applied force are pre-computed, a significant amount of computation time is saved. Additionally the SH coefficients can be directly modified for any change in the 3D model’s level-of-detail which allows the method to comply with various application requirements.

We now summarize the method in three steps:

1. In the first step, the position, color and normal of a node in the 3D lung model and the transfer function matrix are transferred into the GPU’s vertex array. Since the GPU is a per-vertex processor, every row of the transfer matrix is associated with a node of the 3D model and is transferred into the vertex array as multi-texture coordinates.
2. The second step involves computing the SH coefficients of the applied force array using equations (8-9) for the current orientation of lungs. The AR steps in tracking the orientation of the patient or HPS is beyond the scope of this chapter and thus the orientation angles are obtained from AR components.

3. The third step of the method is the implementation of equation (7) in the GPU during every frame. We use a GeForce4 FX 5600 for rendering and deforming the 3D lung model. Specifically, we use a CG 1.1 based programmable vertex-shader, for the shading of the 3D model (cg_simple [84]) and implementing the dot-product of the per-vertex transfer matrix’s row and the applied force in the vertex shader.

### 7.4 SH Coefficients of the Applied Force

Having discussed the method to optimize the dot product, we now propose to compute SH coefficients of the applied force for different patient’s orientation in run-time by interpolating among a set of specified orientations. The origin of the coordinate system is set to be the centroid of the lung model. The orientation of the lung model is now represented in terms of the rotation angles along the $X$, $Y$ and $Z$ axes. Let $p_i, q_i$ and $r_i$ be the arrays of pre-computed SH coefficients for the applied force at rotation angle $i$ of $\pi/2$, $\pi$, $3\pi/2$, and $2\pi$ along the $X$, $Y$, and $Z$ axes, respectively. Let $a$, $b$ and $c$ be arbitrary values for current rotation angles for the 3D lung model. For such orientation, the SH coefficients for the applied force are computed by smoothly interpolating among $p_i$, $q_i$ and $r_i$. Let $a_0$, $a_1$, $b_0$, $b_1$, $c_0$ and $c_1$ be the angles of $i$ that form the closest lower and upper limits for $a$, $b$, and $c$, respectively. The SH coefficients of the applied force for the orientation $a$, $b$, and $c$ are now given by
\[ f^{abc}_{lm} = f^a_{lm} + f^b_{lm} + f^c_{lm}, \quad (7.8) \]

where

\[ f^a_{lm} = \frac{p_{lm}^{a_0} \times \cos(a - a_0) + p_{lm}^{a_1} \times \cos(a - a_1)}{3}, \]

\[ f^b_{lm} = \frac{q_{lm}^{b_0} \times \cos(b - b_0) + q_{lm}^{b_1} \times \cos(b - b_1)}{3}, \text{ and} \]

\[ f^c_{lm} = \frac{r_{lm}^{c_0} \times \cos(c - c_0) + r_{lm}^{c_1} \times \cos(c - c_1)}{3}. \quad (7.9) \]

### 7.5 Lung Deformation Results

In this section we first quantify the increase in speed obtained in using GPU-based deformations. Specifically, we show that when GPU-based deformations are used, an increase in the 3D model’s complexity, and the AR system’s computational complexity of the tracking and the registration components do not create a significant lag in simulation. We then discuss the graphic outputs obtained from the deformation approach.

The frame-rates per second (FPS) for the implementation system were computed using Nvidia’s benchmark program, *learning_VAR*,[94] and are reported in Table 7.1. It can be seen that the system provides a higher frame-rate with the GPU-based simulation (vertex array memory used in association with the vertex program[94]) compared to the CPU based simulation.

The mathematical computational requirements of using equation (7.1) and (7.7) are as follows. For high-resolution 3D lung models, it was observed that each row of the transfer function...
matrix has an average of 192 non-zero values. Thus the computation of deformation of a node, using equation (7.1), will undergo an average of 192 multiplications and 191 additions. In the case of using equation (7.7), we first compute the SH coefficients of the transfer function, which can be performed off-line since the transfer function for lungs is considered a constant. The SH coefficients of the applied force at pre-determined orientations can be computed from equation (7.3) off-line. For any orientation of the 3D lung model, the applied force is interpolated using equations (7.8-7.9). The deformation computation of equation (7.7) would be 4 vector (array of 4 floating-point numbers) dot products and 3 additions per node in the Nvidia’s GPU, which reduces the number of computations by approximately one-third.

The FPS observed during the 3D lung deformations are also traced using the learning_VAR program and are as detailed in Table 7.2. In this dissertation we have used a Nvidia’s shader, cg_simple,[84] to simulate lighting conditions. For simulation purposes, both generic point-based and polygon-based rendering approaches were considered. While the polygon-based rendering approach has been extensively discussed in the graphics field, the point-based rendering approach is currently being addressed for high-resolution rendering and tailored for VR/AR applications. Also for a point-based rendering approach the vertex size was set to be 5 for occlusion purposes. The relation between the vertex size and the FPS is later discussed in this section. It can be seen that the FPS observed for point-based rendering is much higher as compared to the polygon-based rendering, which stems from the low computational complexity of point-based rendering for data traversal, occlusion culling and lighting steps. In the case of a point-based rendering approach, it can be seen that the FPS for a GPU-based implementation of equation (7.7) is approximately 1/1.4 and 1/10 times the FPS of CPU-based implementation of
equation (7.7) and CPU-based implementation of equation (7.1), respectively. In the case of a polygon-based rendering approach GPU-based implementation of equation (7.7) is approximately 1/1.2 and 1/5 times the FPS of CPU-based implementation of equation (7.7) and CPU-based implementation of equation (7.1), respectively. Variations in the number of light sources (a rendering parameter) caused a reduction of approximately 2 FPS for each of the methods. Thus a GPU-based implementation of equation (7.7) can be used in conjunction with both point-based and polygon-based rendering approaches.

From the FPS numbers discussed in Table 7.2, it can be seen that for a GPU based deformation approach, the FPS get about half when rendering is changed from mono to stereo. This reduction in FPS numbers is caused by the fact that in the GPU based deformation approach the 3D lung model gets deformed for each eye (for a stereoscopic visualization). For a CPU-based deformation, the 3D lung model is deformed only once and rendered twice. Thus the FPS numbers in this case are not halved when rendering is changed from mono to stereo.

The GPU based deformation approach provides less improvement over the CPU based deformation approach when polygon-based rendering is used, which stems from the high data-structure traversal involved in a polygon rendering. Specifically, in a polygon-based rendering, each node is accessed approximately 4 times from the memory. A GPU based per-vertex deformation approach would thus compute the deformation at each of the four times, which overshadows the benefit of using the GPU. Thus a point-based rendering approach would be more suitable for high-resolution lung models in order to satisfy the requirements of the AR environment.
For the rest of the dissertation we use a point-based rendering approach. Figure 7.2a presents a comparison of the lung ventilation (volume change with time) visualized using a CPU-based implementation of equation (7.7) (2800+ AMD Athlon) with the ventilation visualized using a GPU-based implementation of equation (7.7) (Nvidia GeForce4 FX5600). For simulation purpose, a point-based rendering approach is considered to minimize the delays caused by the rendering process. It can be seen that there exists a difference (referred as Lag) between the lung ventilation with a GPU-based deformation (the red line in Figure 7.2a) and the lung ventilation with a CPU-based deformation using equation (7.7) (the yellow line in Figure 7.2a). The time lag can be explained from the off-loading of the deformation computations from the CPU to the GPU. Since we deform the 3D lung model at every frame, the time lag is directly related to the FPS. The CPU-based implementation of equation (7.7) has a time-lag of approximately 1.4 seconds per breathing cycle. The CPU-based implementation of equation (7.1) (the green line in Figure 7.2a) has a time-lag of approximately 13 seconds per breathing cycle. This lag in CPU-based deformation increases linearly with simulation time as shown in Figure 7.2b for both the CPU based implementation of equation (7.1) (the blue line) and (7.7) (the red line). These graphs support the computational speed-up results obtained from using the GPU.

The decrease in the FPS with an increase in the 3D model complexity is shown in Figure 7.3. We use a notation of “cx” to refer to the increase in the 3D model complexity by a constant c. With the increase in the 3D model complexity (0.25x, 5x, 1x and 2x) the CPU-based implementation of equation (7.7) had a decrease in the FPS since the number of SH coefficients does not increase with an increase in the total number of nodes. There also exists a significant
decrease in the FPS in the case of a GPU-based implementation of equation (7.7), which is caused by an increase in the number of data elements transferred from the vertex array for each rendering. Thus for higher model complexity, improved GPU with higher vertex array bandwidth would be required.

The accuracy in using SH transformation is shown in Figure 7.4. It was observed that the displacement of the nodes could be re-constructed using 16 SH coefficients with an accuracy of less than 1% RMS error, which translates to less than 1mm RMS error. An initial validation of the deformation obtained using CPU-based computation was discussed in [95]. The difference in this change in shape and volume was negligible when the GPU-based computation was compared to the change in shape and volume obtained using the validated CPU-based computation.

The scalability of the GPU-based computation approach was compared with the CPU-based computation and is shown in Figure 7.5. It can be seen that for an increase in the number of SH coefficients the FPS of the CPU-based computation approach decreased more than the GPU-based computation approach. Such scalability will be of importance for future work in modeling patho-physiological changes in breathing caused by disease states.

The variations in the vertex size and its effect on the GPU-based and the CPU-based computation are shown in Figure 7.6. It can be seen that for an increase in the vertex size the FPS of the CPU-based computation approach decreased more than that of the GPU-based
computation approach. The reduction in the FPS values for both approaches is caused by the increase in the occlusion culling computations.

The side-views of the lung dynamics in the upright and supine positions are shown in Figure 7.7a and 7.7b, respectively. Such visualization snapshots are taken during the inhalation phase with the deformed 3D lung model (red lung model) overlapping the un-deformed 3D lung model (grey lung model). The lower the regional overlap, the higher is the visibility of the grey undeformed lung model. Such variations in the overlap visually represent the change in lung shape caused by the lung deformation. The subtle difference in the deformation of the base of the lungs in the upright and supine positions can be seen. Specifically, the front side of the base region in the supine position displaces more when compared to the backside of the base region in the supine position, which is not observed in the upright position.

The usage of 16 SH coefficients used in the GPU-based implementation yields $\alpha$ to be 1.03 for lung deformations. For values more than 16 the value of $\alpha$ tends to 1. These sequences of images represent the shape change that will be viewed in AR.

Finally, Figure 7.8a represents a snapshot of the lung dynamics being visualized in an AR setup. The 3D lung model is in an upright orientation and is projected onto the ARC screen. Such 3D visualization can constitute a training platform for medics where a group of students or experts may visualize the 3D deforming lung model as if the layers of the body had been peeled off to reveal the lungs in its important anatomical structures. Furthermore a same view of the lung could also be given to each participant to train on a specific procedure such as needle insertion.
in the case of a pneumothorax. Figure 7.8b represents the lung dynamics when the 3D models are now superimposed over the HPS and visualized through a HMD. To take this camera view, the 3D models were hand-positioned over the HMD and their dynamic registration was left to future work.

**7.6 Discussion**

In this chapter we discussed a method to compute 3D lung deformations in a GPU for an AR environment that accounts for changes in the deformations associated with changes in the orientation of the patient or HPS. The physics and physiology based deformation operator for lung deformations allows us to model lung deformations with variations in physics-based parameters. The GPU-based deformation approach for lung dynamics discussed in this chapter closely models the change in 3D lung shape in real-time. Such an approach coupled with the PV relation allows us to visualize normal 3D lung deformations. Such visualization may play a significant role in assessing clinical interventions for a patient. The usage of high-resolution models in the visualization supports meticulous modeling of tissue-degnerations.

The creation of a deformation operator for lung dynamics was discussed in section 6.3. The usage of the regional alveolar expandability as one of the parameters allowed the deformation operator to account for the physiology of normal human subjects. The method can be extended, by analyzing the regional alveolar expandability for human subjects across a wide range of age, race and disease states. With respect to real-time 3D lung dynamics, such variations can lead to
an increase in the number of SH coefficients used for representing the deformation operator. The proposed method can be expanded in order to address this computational aspect.

The validation of the lung deformation was discussed in section 6.4. Through this validation we illustrated the method to obtain physically and physiologically-based lung deformations. Specifically, an estimate of the deformation kernel (transfer function) was made, which allowed us to compute the accurate displacement of each surface node using equation (7.1). In section 7.4 we showed the accuracy of the GPU-based deformation (using equation (7.7)) to represent the 3D deformed lung shape (using equation (7.1)).

We have discussed the advantages of the proposed method in terms of the time-lag and the FPS obtained using the proposed method in a GPU. Although the CPU–based deformation approach can be improved by using a heuristic frame-rate control method, the effectiveness of such a heuristic method needs to be carefully quantified under rapid breathing changes in the subject’s physical conditions and orientation. We are currently investigating these methods and will discuss its result in future work.

Finally, variations in rendering steps (occlusion culling, lighting, texture mapping etc) may also reduce the frame rates of the visualization system. In this dissertation we have used a Nvidia’s shader, *cg_simple*,[84] to simulate lighting conditions. Further investigation will be required in order to verify the FPS obtained using a combination of GPU-based deformation approach and state-of-the-art rendering algorithms for each rendering step that pertains to both point-based and polygon-based rendering approach.
Table 7.1 System benchmark using Learning_VAR

<table>
<thead>
<tr>
<th>Learning_VAR approach</th>
<th>FPS</th>
</tr>
</thead>
<tbody>
<tr>
<td>GPU-based computations</td>
<td>109.8</td>
</tr>
<tr>
<td>CPU-based computations</td>
<td>55.6</td>
</tr>
</tbody>
</table>

Table 7.2 Frame rates obtained for 3D lung deformations

<table>
<thead>
<tr>
<th>Approach</th>
<th>FPS – Point-based rendering</th>
<th>FPS – Polygon-based rendering</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mono</td>
<td>Stereo</td>
</tr>
<tr>
<td>CPU implementation of equation (7.1)</td>
<td>10</td>
<td>7</td>
</tr>
<tr>
<td>GPU implementation of equation (7.7)</td>
<td>148</td>
<td>75</td>
</tr>
<tr>
<td>CPU implementation of equation (7.7)</td>
<td>76</td>
<td>56</td>
</tr>
</tbody>
</table>
Figure 7.2 (a) Delay caused by the usage of CPU-based lung deformation using equation (7.1) (green) and equation (7.7) (yellow) and the subsequent optimization seen in a GPU-based lung deformation (red). (b) Demonstration of the increase in simulation lag with the usage of the CPU-based deformations of equation (7.1) (red) as opposed to equation (7.7) (blue). A point-based rendering approach is considered for the above results.

Figure 7.3 The increase in the slope of the time delay with an increase in the 3D model complexity (1x, 2x, and 4x). A point-based rendering approach is considered for the above result.
Figure 7.4 Comparison of the displacement of 3D lung nodes computed using equation (7.1) (dark blue) and equation (7.7) (light blue). The RMS difference in the displacement was computed to be less than 1mm.

Figure 7.5 Comparison of the FPS obtained for lung deformations using GPU-based implementation of equation (7.7) and CPU-based implementation of equation (7.7) for an increase in the number of SH coefficients used. A point-based rendering approach is considered for the above result.
Figure 7.6 Comparison of the FPS obtained for lung deformations using GPU-based implementation of equation (7.7) and CPU-based implementation of equation (7.7) for an increase in the vertex size (in mm). A point-based rendering approach is considered for the above result.

Figure 7.7 Visualization of 3D deformed lung shape (red color) overlapped with the undeformed lung (grey color) at the end of inhalation (a) in an upright position and (b) in a supine position.
Figure 7.8 Real-time 3D lung dynamics (a) when visualized through the HMD in an AR setup, and (b) when superimposed over a HPS and visualized through the HMD.
CHAPTER EIGHT : CASE STUDIES

In this chapter, we discuss some of the case studies where the proposed framework of lung dynamics has been applied. Specifically, we consider two disease states: Pneumothorax, and Tumor-influenced lungs. We first discuss the changes that occur in the lung deformation for pneumothorax (section 8.1) and tumor-influenced lungs (section 8.2). It is followed by a discussion on the subsequent breathing variations in the PV curve caused by the above-mentioned disease states (section 8.3). Finally, we discuss an extension to the lung dynamics framework: a distributed lung dynamics framework that would allow geographically separated experts to interact for training and diagnostic purposes.

8.1 Open and Closed Pneumothorax

Pneumothorax refers to the presence of air in the pleural cavity. Blunt chest trauma is the main cause of death in over 80% of all vehicular accidents in the United States,[96] and Pneumothorax is expected in 20% of all blunt trauma cases and is the leading preventable cause of death at accident scenes.[97] Mechanistic variants of pneumothorax include open (hole in the chest wall) and closed (hole in the viscera pleura or chest lining), which lead to different symptoms and treatment methods. One common concern with either type of pneumothorax is the development of tension pneumothorax, where the air in the pleural cavity constantly increases until the affected lung collapses and shifts other anatomical structures (e.g., mediastinum) thereby obstructing the venous return of blood from the head and upper body. Death from this type of pneumothorax could be as rapid as 30 minutes. Tension pneumothorax is one of the top three preventable medical emergencies facing soldiers in combat.[98]
Medical simulators such as the mannequin based trainer VIRGIL,[99] present combat medics and emergency providers with video based descriptions of patient symptoms along with step-by-step instruction on needle decompression procedures that alleviate tension pneumothorax. Other instructional simulations model the computationally expensive cardiopulmonary mechanics of pneumothorax using FEM techniques to capture the dynamic interactivity of the lung and chest wall system.[10, 64]. To improve the realism of such educational tools, we expand upon these techniques using a Green’s function based deformation of 3D lung models.

In this section, we focus on developing a medical simulation of closed and tension pneumothorax by modeling its physical symptoms using deformable high resolution 3D lung models obtained from human subjects. The simulation framework extends the lung dynamics framework to model pneumothorax influenced lung deformations. We consider a clinical parameter, the pneumothorax-index (i.e., the degree of lung collapse), as the input to the simulation. Specifically, such index constitutes a key parameter to the computation of the changes in size and shape of the affected lung. Once the index is obtained, the increase in ventilation rate and the change in the pressure-volume relationship of the affected lung are then computed. For tension pneumothorax, the air continuously flows into the pleural cavity and thus every exhalation is followed by the changes seen for a closed pneumothorax, until the affected lung collapses. The subsequent closure of pulmonary veins and resulting hyper expansion of the apposing lung is also seen.
8.1.1. General Physiological Description of Pneumothorax

The presence of air in the pleural cavity has its effect on the following factors: (a) the shape and volume of the affected lung and (b) the trans-pulmonary pressure and volume range of both lungs.\[6\] For an upright person experiencing a closed pneumothorax, a vertical downward displacement is seen in the affected lung which is caused by a layer of air which is concentrated near the apex of the pleural cavity.\[100\] The presence of air in the pleural cavity reduces the trans-pulmonary pressure range and the subsequent volume of air-flow into the affected lung. This change in volume of air-flow inside the lungs is equal to the amount of air entering directly into the pleural space. This change causes a decrease in the alveolar air intake during inhalation. Thus the ventilation (rate of air-flow) of both lungs increases in order to obtain a better oxygen inflow. Due to the increased ventilation the un-affected lung increases beyond its normal air volume in order to compensate. This added increase in the volume of un-affected lung varies from subject to subject. The changes of the mechanical aspects of the lung and chest wall system during pneumothorax conditions can be represented with a pressure-volume (PV) curve discussed in chapter 5. Specifically, the movement of the chest wall and abdomen are restricted by the external pressure caused by the air in the pleural cavity. Consequently, the lung compliance is functionally reduced. Therefore the pressure applied on the air inside the lung is not only that of the lung and the chest wall, it is also that of the external force. The additional muscular work performed during inspiration drives the flow of air into the lungs. Similarly during expiration, due to this increased recoil, the net collapsing pressure increases, thereby reducing the expiratory force on the part of the patient. The proposed model utilizes PV curve data to more accurately capture the mechanical changes caused by the pneumothorax.
8.1.2 Simulating Closed Pneumothorax

The 3D deformable lung models under normal breathing lung conditions are driven by the normal human pressure-volume (PV) curve. A ventilation rate of 12 breathing cycles per minute is taken as the normal breathing rate. We take as input the pneumothorax index, $I$, that conveys a degree of lung collapse. The value of this index ranges from 0 to 1. We assume that the volume of air in the pleural space is considered to be proportional to the ratio of the difference between the radius of hemithorax and the lungs, and the radius of the hemithorax; The change in volume of air inside an affected lung, $dV$ (a fraction in the range from 0 to 1) for a given index value, $I$, is given as

$$dV = (I)^{0.33}. \quad (8.1)$$

This change in size for the $dV$ computed is obtained by scaling down the 3D surface points of the model along their normals from the hilum, which is the entry point for air into the lungs. The modified 3D model is now displaced vertically from the apex so that it sits on the diaphragm.[100] We also assume that the vertical displacement of the lungs in an upright position is proportional to the lateral displacements of the lungs described in [100]. This vertical displacement ($A$) was shown (in [100]) to be,

$$A = \frac{(I \times 100 - 4.2)}{4.7 \times 2}. \quad (8.2)$$

Let $T_i$ and $T_e$ be the time taken for a single cycle of inhalation and exhalation respectively. The subsequent decrease in the time taken for one breathing cycle of the lungs ($dT$),[102] can be given as

$$dT = T \times dV, \quad (8.3)$$
and \[ T'_i = T_i - dT, \quad (8.4) \]

and \[ T'_e = T_e - dT, \quad (8.5) \]

where \( T'_i \) and \( T'_e \) are the modified time for a single cycle of inhalation and exhalation respectively, and \( T \) is the normal time taken for one breathing cycle.[101] The tidal volume of air flow into the affected lung \( (V'^{new}_1) \) during inhalation in one breathing cycle is set to be

\[
V'^{new}_1 = V'^{old}_1 \times (1 - dV). \quad (8.6)
\]

The tidal volume of the unaffected lung \( (V'^{new}_2) \) is set to be

\[
V'^{new}_2 = V'^{old}_2 + \alpha, \quad (8.7)
\]

where \( \alpha \) is a constant that refers to the increase in volume due to the extra effort in breathing. The range of values for \( \alpha \) can vary for every human subject between (0-2500 millilitres approximately) and a clinically accurate range is yet to be determined. For simulation purposes, the value of \( P \) and \( \alpha \) were set to 0.1 and 100ml, respectively. Figure 8.1a shows the shape of lungs in an upright position before inhalation. It can be seen that the patient’s left lung is lower in volume and is shorter than the right lung. Figure 8.1b shows the shape of lungs at the end of exhalation. It can be seen that the patient’s right lung is more expanded as compared to the normal lung, which is caused by the value of \( \alpha \).
8.1.3 Modeling Variations in Breathing Resistance

Disease states such as Pneumothorax lead to changes in the breathing resistance. It is thus important for the proposed PV relation to model these changes. In Chapter 3, the PV relation during inhalation and exhalation was represented using a second-order differential equation with a variable parameter. This parameter was further computed as a linear summation of products of a set of control parameters and trigonometric basis functions that represents the summary muscle resistance. The values of control parameters were extracted from patient’s specific clinical data.[103]

One key property of the control constants that we use is that they form a converging sequence and the rate of convergence is observed to be faster under higher drive conditions. We thus decrease the rate of convergence of control parameters for modeling more resistive breathing and increase the rate of convergence for modeling less resistive breathing. An increase in the rate
of convergence by first multiplying every parameter with its exponent. They are then divided by the exponent of the first parameter in order to keep the parameters in the same range of values. Similarly we decrease the rate of convergence during exhalation by multiplying every parameter with its logarithm and dividing it by the logarithm of the first parameter. Let $c_i$ be the array of control constants during inhalation and exhalation and let $d_i$ and $e_i$ be the modified control constants respectively. For a $dV$ amount of air entering the pleural cavity, a method to vary the control constants is given by,

$$d_i = C_0 \times \frac{e^{C_i \times \varphi \times dV}}{e^{C_0 \times \varphi \times dV}}.$$ \hspace{1cm} (8.8)

$$e_i = C_0 \times \frac{\log(C_i \times \varphi \times dV)}{\log(C_0 \times \varphi \times dV)},$$ \hspace{1cm} (8.9)

where $\varphi$ is a proportionality constant that relates the change in control constants to the amount of additional work. For demonstration purposes, the value of $\varphi$ is set to 0.1 for pneumothorax. The PV curve generated for the modified control constants, which simulate breathing conditions for pneumothorax is shown in Figure 8.2. For simulating pneumothorax, an increased resistance to breathing was taken into account during inhalation, and decrease resistance during exhalation. For simulating lung tumors, an increased resistance is taken into account during both the inhalation and exhalation. PV curve variations can thus be modified to simulate pathophysical conditions. The validation of these simulated PV curves based on the data collected from human subjects is currently in progress.
8.1.4 Simulating Tension Pneumothorax

Tension pneumothorax is a condition where the air enters into the pleural cavity and does not leave the cavity optionally. Let \( t \) be the number of breathing cycles since the onset of pneumothorax. We now represent \( \dot{V}_p \) as the volume of air flow into the pleural cavity at the \( t^{th} \) breathing cycle. The inflow of air into the pleural cavity for an inhalation is set as,

\[
\dot{V}_p = V_p \times e^{-\tau},
\]  

(8.10)

where \( \tau \) is a constant which controls the rate of air-flow inside the pleural cavity. The negative exponential component represents the decrease in the rate of air flow caused by the decrease in the trans-pulmonary pressure range. The subsequent decrease in the time taken for the inhalation and exhalation are given by replacing \( dV \) by \( d\dot{V} \) in equations (8.3), (8.4) and (8.5). The change in 3D lung shape is obtained as explained for closed pneumothorax. We now introduce \( \dot{dV}_{sum} \) which represents the volume of air in the pleural cavity. After a few breathing cycles \( \dot{dV}_{sum} \)
reaches a volume $V_{\text{max}}^1$ after which the affect lung cannot inhale or exhale. Now, for any amount of air directly entering the pleural cavity, the collapsed lung now applies pressure on the ventricle of the heart and the superior vena cava forcing them to collapse. Thus the overall blood circulation is stalled. Thus the unaffected lung undergoes a hyper-expansion whereby it reaches a maximum volume $V_{\text{max}}^2$, above which it cannot expand. So both lungs reach a state of arrest.[10] In order to model the lateral movement of the affected lung we introduce the parameter $q_i^1$, which represents the percentage volume of the bounding box of the left ($i=1$) and right ($i=2$) lungs which is inside the respective lungs. Let $b_{x_i}^1$, $b_{y_i}^1$ and $b_{z_i}^1$ be the dimensions of the bounding box of the $i^{th}$ lung in X,Y and Z at the end of the $t^{th}$ inhalation, respectively. We can now represent $q_i^1$ as

$$q_i^1 = \frac{V_i^1}{b_{x_i}^1 \times b_{y_i}^1 \times b_{z_i}^1}.$$  

(8.11)

The magnitude of the global displacement in volume is equal to the volume of air directly entering the pleural cavity and is computed as follows. The displacement of the bounding box of the affected lung ($i=1$) towards the mediastinum (along the X-axis), denoted by $db_{X_i}^1$ is given by the relation,

$$dV_i^t = db_{X_i}^1 \times b_{y_i}^1 \times b_{z_i}^1.$$  

(8.12)

The displacement of the lung towards the mediastinum can now be represented by replacing $db_{X_i}^1$ with $q_i^1 \times dX_i^1$ in the above equation and simplified as,

$$dX_i^1 = \frac{dV_i^t}{q_i^1 \times b_{y_i}^1 \times b_{z_i}^1}.$$  

(8.13)
Let $\beta$ denote a cardiovascular factor that represents the global displacement by the lung in the state of arrest at which the superior vena cava closes. The closing of vena cava leads to the collection of blood in lungs and its hyper-expansion until its volume $V_2$ reaches $V_{2\max}$, after which it attains the state of arrest. The value of $\beta$ is set to be equal to the average diameter of the vena cava (i.e. 18 mm) for simulation purposes. An illustration of hyper expansion during tension pneumothorax is shown in Figure 8.3. In this case the patient’s left lung is at $V_{\min}$ and the right lung is at a volume of $V_{\max}$. The lungs have reached a state of arrest.

8.2 Tumor-influenced Lung Dynamics

The focus of this section is on simulating and visualizing the patient-specific tumor-influenced lung dynamics. The end result of such an effort will provide visualization for clinicians to more accurately track and treat tumor areas as they change over time. The method presented allows us to visualize tumor-influenced 3D lung dynamics by first estimating the deformation parameters from patient-specific high-resolution 3D lung models and then re-
simulating the 3D lung dynamics under different breathing conditions modeled by the PV relation. The details of the method and the results were discussed in [26].

Figures 8.4a and 8.4b represent the 3D lung shape of tumor-influenced lungs at the start and end of the inhalation. We now discuss a mathematical approach to solve for the transfer function that is specific to the tumor-influenced lungs. The general form of the Green’s transfer function row is described in two different representations. The first one is given as

$$K(J, I) = P_J \cos z(J, I) + Q_J \sin z(J, I),$$  \hspace{1cm} (8.14)

where $z(J, I)$ is a function that returns a value in the range of zero to $2\pi$. $P_J$ and $Q_J$ are arbitrary constants that take values between zero to 1. [51] Such a representation of the kernel (transfer function) row is also referred to as a discrete spectral representation. The values of $P_J$ and $Q_J$ can be arbitrarily varied in order to simulate variations in the breathing conditions. With respect to
the lung dynamics, the steerable constants of the discrete spectral representation can be used to model variations induced by diaphragm and abdominal movements. The above equation represents the kernel (transfer function) as a continuous trigonometric function discretized by the values of \( z(J,I) \). We introduce a further mathematical simplification of equation (8.14) as

\[
K(J,I) = C_I \cos z'(J,I), \quad z'(J,I) = z(J,I) + \phi_I, \quad (8.15)
\]

where \( C_I \) is an arbitrary constant and \( z'(J,I) \) is a function that returns a value in the range of 0 to \( \pi/2 \). Equation (8.15) represents a row of the kernel (transfer function) matrix as a cosine function. The second general form of the kernel (transfer function) row is described as a proportionality function of the piecewise Euclidean distance \( d(J,I) \) between \( I \) and \( J \).[104] It can thus be written as

\[
K(J,I) = \frac{D_I}{4\pi d(J,I)}, \quad (8.16)
\]

where \( D_I \) is a proportionality constant, which depends on the deformation mechanics of the lungs. Equation (8.16) was proposed as a mathematical solution to the Green’s function.[104] This solution has been used for modeling unique cases pertaining to the mechanics. These unique cases discussed by Stakgold presents the different values of the proportionality constant.[51] In the case of lungs, the proportionality constant \( D_I \) remains unknown. We now merge the two definitions of the kernel (transfer function) in order to solve for \( z'(J,I) \). Since both \( C_I \) and \( D_I \) of equation (7.15) and (7.16) act as proportionality constants, the values of \( \cos(z'(J,I)) \) and

\[
\frac{1}{4\pi d(J,I)}
\]

can be equated. \( z'(J,I) \) can now be written as

\[
z'(J,I) = \left[ \cos^{-1}\left( \frac{1}{4\pi d(J,I)} \right) \right], \quad (8.17)
\]
It can be seen that for higher values of the Euclidean distance between $J$ and $I$, the value of $K(J,I)$ tends to zero. Additionally, the values of $z'(J,I)$ and $d(J,I)$ are proportional. However, in the case of lungs we consider a heterogeneous elastic representation in order to account for the regional variations in the alveolar expansion. Thus equation (8.17) is modified as

$$z'(J,I) = \cos^{-1}\left(\frac{1}{4\pi d'(J,I)}\right),$$  

(8.18)

where $d'(J,I)$ is a function that takes into account both the distance and the local elastic properties. For higher values of $d'(J,I)$ the value of $K(J,I)$ tends to zero. An initial representation for $d'(J,I)$ is given as a linear combination of the distance and the elastic interaction.

$$d'(J,I) = A_I d(J,I) + B_I e(J,I),$$  

(8.19)

where $A_I$ and $B_I$ are arbitrary constants. These constants are also referred to as structural constants in the paper, since they both compute the function $d'$. The function $e(J,I)$, which represents the elastic interaction between nodes $J$ and $I$, is given as a difference in the alveolar expansion of the region surrounding nodes $J$ and $I$. Such a representation is based on the fact that the air flows to the region of least resistance, which in our case is the region of higher alveolar expandability. The regional alveolar expandability is thus an indirect indicator of the Young’s modulus. The regional alveolar expandability has been previously discussed in [58], [105], and [56]. The function $e$ is thus defined as

$$e(J, I) = a(J) - a(I),$$  

(8.20)

where $a(J)$ is a function representing an estimated alveolar expandability in the region surrounding node $J$. The definition of the function in terms of the alveolar expansion is an essential factor in estimating the kernel (transfer function) for the 3D lungs. It can be seen that the inverse lung deformation problem mathematically relates to computing the values of $A_I$, $B_I$, ...
and \( C_I \) for each node \( I \). We now continue our discussion on (i) estimating the values of \( A_I, B_I, \) and \( C_I \) for each node \( I \), and (ii) estimating the values of \( P_I, Q_I \) and the function \( Z'(J,I) \).

A method to estimate the values of \( A_I \) and \( B_I \) using simultaneous equation based representation of equation (8.17) coupled with approximated kernels, discussed in chapter 5, is as follows. For the 3D lung model extracted from the patient-data, two different estimates of the deformation kernel (transfer function) are first computed. Each deformation kernel (transfer function) is estimated, using only the structural parameters (piecewise Euclidean distance, and regional alveolar expandability). The second kernel (transfer function) is computed with the distance between any two nodes to be twice that of the distance used in the estimation of the first kernel (transfer function). Now using equation (8.17) we form two simultaneous equations for each node \( I \), with the unknown being \( A_I \) and \( B_I \). One may also note that \( D_I \) is eliminated in these equations.

The values for the structural constants for each node are thus solved. The value of \( C_I \) can be computed using equation (8.15) as

\[
C_I = \frac{D[I]}{\sum_{J=0}^{N} f[J] \times \cos(z'(J,I))}.
\]

(8.21)

The values of \( C_I \) for the tumor-influenced left and right lung models are plotted in Figure 8.5a and 8.5b respectively. For comparison purposes, we show the values of \( C_I \) for normal left and right lung models in Figure 8.5c and 8.5d. It can be seen that changes in both the left and right lungs can be seen in tumor-influenced lung dynamics when compared to normal lungs. Such changes are attributed to the effects caused by the tumor.
Now the values of $P_i$ and $Q_i$ can be written as

$$P_i = C_i \cos \phi_i \quad \text{and} \quad Q_i = C_i \sin \phi_i,$$

(8.22)

where $\phi_i$ is an arbitrary parameter that takes value between $0$ to $2\pi$. The variations in lung deformations induced by varying the values of $\phi_i$ are discussed in section 4. The proposed framework takes into account the changes in deformation constraints imposed by the tumor (through the PV curve) on the lung’s air-volume. The deformation operator is represented using the discrete spectral representation of the GF, which facilitates obtaining physically-realistic variations of 3D lung deformation caused by variations in the rib-cage and diaphragm movements. The feasibility of simulating such variations is demonstrated in Figure 8.6a and 8.6b and visually validated by clinical experts. In Figure 8.6a the value of $\phi_i$ was set to the normalized distance from the supporting surface (posterior side of lungs). In Figure 8.6b the value of $\phi_i$ was set to the square of the normalized distance from the supporting surface. The accuracy of such variations needs to further verified and will be discussed in our future investigations.
Figure 8.5 The values of constants $C_I$ are plotted against the normalized $Z$ values of the vertexes for the tumor-influenced left and right lung ((a) and (b)) and normal left and right lung ((c) and (d)).
Figure 8.6 3D deformed point-cloud models (red color) of tumor influenced lungs superimposed over 3D point-cloud models (white color) at the start of inhalation. Variations induced in the deformation is simulated by (a) setting the value of $\phi_I$ for each node $I$ to the normalized distance from the supporting surface (posterior side of lungs), and (b) setting the value of $\phi_I$ for each node $I$ to the square of the normalized distance from the supporting surface.

### 8.3 Distributed Lung Simulation

In this section we discuss an extension to the lung dynamics framework that allows us to visualize and interact with the lung dynamics from a remote location. Specifically, a data distribution capability is added to the framework, which synchronizes a group of the lung dynamics framework instantiations running on different computers connected through the network. Such a data-distribution can substantially facilitate geographically separated experts to collaborate and make effective decisions for remotely located patients requiring emergency
clinical intervention. Also, the remotely located experts will be able to train clinical students on various clinical maneuvers. The details of this method and the results were published in [27, 28].

To control the 3D lung dynamics remotely, we decided to use a bandwidth-conserving method, i.e., we aim at reducing the number of packets sent between nodes, by sending the deformation parameters as a single packet at the start of every breathing cycle. Data is distributed in the form of custom defined data-packages denoted as Control Packet Objects (CPOs). Each packet contains the boundary values of the pressure and volume, control constants, force coefficients and elasticity coefficients. The boundary values for volume are the lung Functional Residual Capacity (FRC) and the lungs Tidal Volume (TV). “PR” denotes the maximum pressure value while “V” denotes the breathing rate. The control constants \((CP_0, ..., CP_N)\) represent the PV relationship required for modeling patient’s breathing condition as discussed in the first stage of 3D lung dynamics [106], and “N” denotes the number of control constants. The force coefficients \((F_0 - F_M)\) are the SH coefficients that describe the force applied on every node of the 3D model. The number of force coefficients is denoted by “M”. The deformation of the 3D model at any remote location is computed as the product between the force and the elasticity coefficients.

To compensate for the communication latency, we combined the distributed application with an adaptive delay measurement algorithm which estimates the delay between each pair of users that interact and predicts the next CPO values. We optimized the data distribution by reducing the number of packets, i.e., for each change in the lung dynamic parameters, a CPO packet was sent. Once the packet is received, each node knows how to drive its own lung deformation simulation.
We have deployed the framework using inexpensive Linux based PC’s with NVidia™ GeForce4 graphical processing units on our 100 Mbps local area network using a typical client-server architecture (i.e., the PC connected to the HMD was acting as the server, while other PCs, the clients, on the same network could visualize the 3D model of the Lung remotely). Instead of a real patient we used a HPS from Medical Educational Technologies.

We superimposed the deformable model on the HPS using a Polaris™ infrared optical tracking system. The update cycle was combined with the deformation rendering cycle to obtain an average frame rate of 66 frames per second. We ran the framework for fifteen minutes and recorded the normalized breathing volume for each breathing cycle. The frequent update method deployed on the 1ms network infrastructure delayed the deformation of the lungs at the client side with respect to the deformation seen at the server side for every breathing cycle as illustrated in Figure 7.7a.

The CPO updates method reduced the number of packets flowing in the network by two orders of magnitude and produced a smoother rendering as compared to the frequent updates method. The simulation was improved because after the parameters were received, rendering proceeded independently at each site and was not affected by the network latency. Still without latency compensation, the deformation of the lungs at the client side fell behind the deformation seen at the server side at every breathing cycle, as illustrated in Figure 8.7b.
Figure 8.7 3D lung model volume as seen at the client and server during one breathing cycle with
(a) frequent update, and (b) per-breathing update.

We now combine the per-breathing update approach with network delay compensation. In this case, the normalized breathing volume reached the same values over time simultaneously at each node, as shown in Figure 8.8. Since the lungs deformation is driven by the values of the volume, we objectively assessed the consistency of the distributed environment and proved that a distributed lung dynamics and its visualization can be achieved with minimal error in synchronicity.
To investigate the scalability of the approach, we have increased the number of participants consecutively to two and three. To quantify the scalability of the adaptive synchronization algorithm regarding the number of participants we define a metric analyzing the relationship between the number of participants in the system and the drift values among their views.

Figure 8.8 3D lung model volume as seen at the client and server during one breathing cycle with per-breathing update and network delay compensation.

Figure 8.9 3D lung model volume as seen by three participants during one breathing cycle.
The average normalized breathing volume drift per breathing cycle was in this case 0.01% as shown in Figure 8.8, which is negligible. The shared state consistency ultimately depends on the network infrastructure as well as on the hardware systems complexity. The PC’s hardware attributes involved in the three participants setup are described in Table 8.1.

<table>
<thead>
<tr>
<th>Node no.</th>
<th>CPU (GHz)</th>
<th>RAM (GB)</th>
<th>GPU (GeForce)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1(server)</td>
<td>2.8 AMD</td>
<td>0.5</td>
<td>Ti4200</td>
</tr>
<tr>
<td>2(client)</td>
<td>2.4 Intel</td>
<td>1</td>
<td>Ti4800</td>
</tr>
<tr>
<td>3(client)</td>
<td>1.5 AMD</td>
<td>0.5</td>
<td>Ti4200</td>
</tr>
</tbody>
</table>
CHAPTER NINE : CONCLUSION

We have presented a survey of the deformation methods previously used for modeling 3D lung dynamics. We have proposed a novel framework for modeling the 3D lung deformations in real-time in order to cater the needs of advanced visualization systems. Such a framework will allow users to visualize the normal and pathophysiological 3D lung dynamics under different breathing conditions.

The Pressure-Volume relationships presented in this study (chapter 5) act as a driver for modeling the 3D lung dynamics. The method was validated with published human and sheep data and results of pressure-volume recordings made in human subjects. The method is adaptive and prognostic to any change in physical conditions by varying the steerable control constants. The applicability of this method for modeling pathological lung states provides an area of future investigation. Future work in this model involves modeling PV curves using subject data that explicitly represents the muscle movements and the motor drive of breathing.

We demonstrated in chapter 6 the pre-computation of physically based lung deformations and the deformation of a high-resolution lung model. The deformation being independent of the absolute assignment of the initial Young modulus of each node facilitates easier creation of physically based deformation. The pre-computation approach also provides real-time deformations, which are highly suitable for AR environments. The proposed method was validated by (i) re-simulating the lung deformation and comparing it with the actual patient data, (ii) comparing the 3D positions of the landmarks on the 3D lung surface which were
selected by a medical expert, and (iii) analyzing the extracted applied force from the 4D HRCT data. The deformation method and the validation is also discussed in [22]. For additional validation future work involves investigating more patient data using invasive methods and comparing the observations with simulated lung dynamics.

In chapter 7 we have discussed a method to compute 3D lung deformations in a GPU for an AR environment that accounts for changes in the deformations for changes in the orientation of the patient or HPS. Such visualization may play a significant role in assessing clinical interventions for a patient. The usage of high-resolution models in the visualization supports meticulous modeling of tissue-degenerations. The method is also detailed in [107]. Future work involves validating the number of SH coefficients used and applying the proposed framework for visualization of patho-physical lung morphology.

Chapter 8 focused on investigating the utility of the framework in modeling different diseased lungs and the possibility of extending the framework for distributed lung simulations. The disease states we considered were (i) pneumothorax and (ii) lung tumors. In the case of pneumothorax, where death can be as quick as 30 minutes, we showed the possibility for clinical technicians to visualize the deformation changes in order to decide the appropriate clinical intervention. This modeling effort is also discussed in [25]. In the case of lung tumors, we have modeled a subject-specific lung breathing in order to visualize the patient’s breathing under different breathing conditions. This modeling effort is also discussed in [26]. Future work on these two disease states will involve validating the lung deformations using subject-data collected at different breathing conditions.
A distributed visualization of 3D lung dynamics was presented in chapter 8 as an extension to the proposed framework. In this extension, 3D lung simulations instantiated in different geographical locations were connected using a data network and synchronized. Such a framework allows experts in different locations to interact and decide on the required clinical maneuvers for a given patient. The method and the results are detailed in [27].

From the clinical usage perspective, the framework can be considered for training and planning under three conditions: (i) without any invasive intervention, (ii) with minimal invasive intervention, and (iii) with thorough invasive intervention.

(i) Without any invasive intervention: Such clinical scenarios would include investigating a patient’s general breathing patterns and discomfort (e.g. dyspnea). For this case, the framework allows the user to view subject-specific breathing under different physical conditions and orientations of the patient.

(ii) With minimal invasive intervention: Such interventions would include procedures such as intubation, endoscope and needle insertion etc. During such interventions, the proposed framework would be an effective tool since it can show the position of the minimally invasive tools as well as the breathing changes that are caused by the subjective discomfort and the effect of the clinical intervention.

(iii) With thorough invasive intervention: Such interventions would include pre-planned procedures such as lung transplants and lung volume reduction. Under such interventions, AR would be an effective tool for visualizing pre-operative conditions and post-operative prognosis for the patient. For instance, in the case of lung transplants, care needs to be taken regarding the
changes in the subject’s breathing pattern caused by (i) Pleural space complications such as Pneumothorax, (ii) Parenchymal space complications such as Empyema (pulmonary infection) and (iii) Opportunistic infections such as Pneumonitis. Such complications may be avoided by visualizing the patient’s breathing morphology in an AR based environment. Emergency events, which occur along with lung transplants and volume reduction surgery were discussed in [108]. Simulating intra-operative conditions would heavily rely on the bio-mathematical interactive 3D models that can accurately account for user-induced variations in the subject’s anatomy. For a subject-specific lung, developing such 3D models is currently an open research problem.

The key technical issue that pertains to the applicability of such a framework deals with the choice of equipments and the smoothness in the simulations. One may note that different tracking systems may be employed as part of the AR framework. Of particular importance is the electromagnetic tracking, which is widely used for AR applications. However, care needs to be taken on its usage since the interference between the tracking system and the surgical (metal & carbon fibre) tools present in the room can induce errors in the tracking process. While the large scale tracking of either the patient or the trainer has been broadly used in the VR environment using magnetic trackers, their success in an AR environment, where both real and virtual objects must come-in-register, is debatable. Recently, micro-trackers (approx. 1 mm diameter) have opened the use of magnetic trackers in the surgical room.

From a simulation and visualization perspective, non-smooth simulations can be addressed under the following three different conditions:
(i) Without patient’s motion and breathing changes: In Chapters 4-7 we have presented a detailed account of the respiratory motion and the generation of real-time physically-based 3D deformable lung models. A key aspect of the 3D lung deformations is their ability to satisfy real-time constraints. Using state-of-art graphics processing units, we display the lung deformation at a rate of 75 frames per second (without tracking), which eliminates any occurrence of any discontinuity in the lung dynamics for the viewer through the HMD.

(ii) With patient’s breathing variations: On some of our recent work, we have accounted for the changes in the lung dynamics caused by the changes in the physiological (caused by lung tissue degenerations) and behavioral conditions (caused by subjective perception of discomfort) of the patient. The tissue degenerations were accounted by modifying the deformation kernel (transfer function), and the subjective perception of the discomfort was simulated by modifying the PV curve. Such modifications had no significant effect on the simulation frame rate.

(iii) With patient’s motion and breathing variations: One may note that the task of simulating respiratory motion with patient’s motion compensation is a complex task. In our approach we have compensated for the patient’s motion by modifying the SH coefficients of the applied force by interpolating among a set of pre-computed applied forces for each orientation of the subject. The interpolation did not induce any computational delay and did not affect the real-time nature of the simulation.

We are currently in collaboration with the Department of Radiation Oncology at M.D. Anderson Cancer Center for optimizing the framework for tracking tumor motion and morphological
changes during high-precision radiation therapy and the Pulmonary Critical Care at Ocala Regional Health Care for modeling pneumothorax related emergency events. We are currently in discussions with the Department of Public Health and Affairs at the University of Central Florida for extending the framework to a prognostic system that helps in the detection of asthma and throat cancer by combining the upper and lower airway visualization.
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