Multi-Surface Simplex Spine Segmentation for Spine Surgery Simulation and Planning

Rabia Haq
Old Dominion University

Follow this and additional works at: https://digitalcommons.odu.edu/msve_etds

Part of the Bioimaging and Biomedical Optics Commons, Biomedical Commons, Computer Sciences Commons, and the Surgery Commons

Recommended Citation
https://digitalcommons.odu.edu/msve_etds/23

This Dissertation is brought to you for free and open access by the Modeling, Simulation & Visualization Engineering at ODU Digital Commons. It has been accepted for inclusion in Modeling, Simulation & Visualization Engineering Theses & Dissertations by an authorized administrator of ODU Digital Commons. For more information, please contact digitalcommons@odu.edu.
MULTI-SURFACE SIMPLEX SPINE SEGMENTATION
FOR SPINE SURGERY SIMULATION AND PLANNING

by

Rabia Haq
B.S. August 2004, Old Dominion University
M.S. December 2008, Old Dominion University

A Dissertation Submitted to the Faculty of
Old Dominion University in Partial Fulfillment of the
Requirements for the Degree of

DOCTOR OF PHILOSOPHY

MODELING AND SIMULATION

OLD DOMINION UNIVERSITY
December 2015

Approved by:

Michel A. Audette (Director)

Frederic D. McKenzie (Member)

Jiang Li (Member)

Stacie I. Ringleb (Member)

Jérôme Schmid (Member)
This research proposes to develop a knowledge-based multi-surface simplex deformable model for segmentation of healthy as well as pathological lumbar spine data. It aims to provide a more accurate and robust segmentation scheme for identification of intervertebral disc pathologies to assist with spine surgery planning. A robust technique that combines multi-surface and shape statistics-aware variants of the deformable simplex model is presented. Statistical shape variation within the dataset has been captured by application of principal component analysis and incorporated during the segmentation process to refine results. In the case where shape statistics hinder detection of the pathological region, user-assistance is allowed to disable the prior shape influence during deformation. Results have been validated against user-assisted expert segmentation.
Copyright, 2016, by Rabia Haq. All Rights Reserved.
My humble effort I dedicate to my extraordinary parents,

Inam-ul-Haq and Safia Inam.

whose unconditional love, encouragement and constant prayers brought me this far.
ACKNOWLEDGMENTS

This dissertation would not be possible without the guidance, encouragement and patience of my advisor, Dr. Michel Audette. I would like to express my gratitude to my committee members Dr. Frederic McKenzie, Dr. Stacie Ringleb, Dr. Jiang Li and Dr. Jérôme Schmid for their time and insightful feedback throughout the course of my dissertation.

I would like to acknowledge my friends and my colleagues for inspiring me to think outside the box.

I would like to thank my family for being a constant spring of hope and positivity. They have cheered me on when I was discouraged, have laughed at me when I was making a mountain out of a molehill, and have wiped my tears when research catastrophes struck. I am very grateful for their unyielding support and faith in me.
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT</td>
<td>Computed Tomography</td>
</tr>
<tr>
<td>FEM</td>
<td>Finite Element Model</td>
</tr>
<tr>
<td>GPA</td>
<td>General Procrustes Analysis</td>
</tr>
<tr>
<td>IID</td>
<td>Intervertebral Disc Degeneration</td>
</tr>
<tr>
<td>ICP</td>
<td>Iterative Closest Point</td>
</tr>
<tr>
<td>LOO</td>
<td>Leave-one-out</td>
</tr>
<tr>
<td>MDL</td>
<td>Minimum Description Length</td>
</tr>
<tr>
<td>MRI</td>
<td>Magnetic Resonance Imaging</td>
</tr>
<tr>
<td>PCA</td>
<td>Principal Component Analysis</td>
</tr>
<tr>
<td>PDM</td>
<td>Point Distribution Model</td>
</tr>
<tr>
<td>ROI</td>
<td>Region of Interest</td>
</tr>
<tr>
<td>SOFA</td>
<td>Simulation Open Framework Architecture</td>
</tr>
<tr>
<td>SSM</td>
<td>Statistical Shape Model</td>
</tr>
<tr>
<td>SVD</td>
<td>Singular Value Decomposition</td>
</tr>
</tbody>
</table>
# TABLE OF CONTENTS

| LIST OF TABLES | ix |
| LIST OF FIGURES | xiv |

## Chapter

1. INTRODUCTION ................................................................. 1
   1.1 Problem ................................................................. 2
   1.2 Proposed System .................................................... 3
   1.3 Contributions ....................................................... 5
   1.4 Dissertation Outline ............................................. 7

2. BACKGROUND ......................................................................... 9
   2.1 Spine Anatomy ...................................................... 9
   2.2 Disc Herniation .................................................... 11

3. MEDICAL IMAGE SEGMENTATION .................................. 13
   3.1 Voxel-based Segmentation ..................................... 13
   3.2 Surface-based Segmentation .................................. 19
   3.3 Spine Segmentation .............................................. 25

4. SIMPLEX MESHES ........................................................... 33
   4.1 Topological Operators ............................................ 33
   4.2 Geometric Representation ...................................... 36
   4.3 Simplex Evolution ................................................. 38

5. STATISTICAL SHAPE DEFORMABLE MODELS .................. 42
   5.1 Shape Model Construction .................................... 42
   5.2 Alignment ............................................................ 43
   5.3 Shape Decomposition ............................................ 45
   5.4 Correspondence .................................................... 47
   5.5 Statistical Sufficiency .......................................... 50

6. SEGMENTATION USING WEAK-SHAPE PRIORS .................. 52
   6.1 Testing Image Dataset ............................................ 52
   6.2 Data Preprocessing ............................................... 53
   6.3 Intervertebral Disc Segmentation ............................. 53
   6.4 Vertebrae Segmentation ........................................ 56

7. SHAPE STATISTICS-BASED SEGMENTATION ..................... 63
   7.1 Statistical Shape Model Construction ....................... 63
   7.2 Statistical Shape Model Evaluation Metrics ............... 69
Chapter | Page
---|---
8. RESULTS AND DISCUSSION | 71
  8.1 Segmentation Using Weak-Shape Priors | 71
  8.2 Segmentation using Strong-shape Priors | 79
  8.3 Healthy Intervertebral Disc Compression Simulation | 100
9. CONCLUSION | 105

BIBLIOGRAPHY | 108

VITA | 123
# LIST OF TABLES

<table>
<thead>
<tr>
<th>Table</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Comparison of voxel-based segmentation techniques</td>
<td>18</td>
</tr>
<tr>
<td>2. Various spine segmentation approaches</td>
<td>32</td>
</tr>
<tr>
<td>3. Average validation metrics comparing automatic segmentation results with corresponding semi-supervised segmentation of 16 healthy lumbar intervertebral discs</td>
<td>72</td>
</tr>
<tr>
<td>4. Average validation metrics comparing semi-supervised segmentation results with corresponding manual segmentation of 5 herniated lumbar intervertebral discs</td>
<td>74</td>
</tr>
<tr>
<td>5. Validation metrics comparing two sets of semi-supervised segmentations of a herniated intervertebral disc performed by the same anatomist and two different anatomists, demonstrating intra-rater and inter-rater variability respectively</td>
<td>78</td>
</tr>
<tr>
<td>6. Average validation metrics comparing 25 lumbar vertebrae automatic segmentation results, using weak shape priors, with corresponding minimally supervised segmentation of patients in MR images</td>
<td>78</td>
</tr>
<tr>
<td>7. Average validation metrics comparing automatic 16 lumbar disc segmentation results, using strong shape-based priors, with corresponding minimally supervised segmentation of patients in MR images</td>
<td>92</td>
</tr>
<tr>
<td>8. Average validation metrics comparing automatic 25 lumbar vertebrae segmentation results, using strong shape-based priors, with corresponding minimally supervised segmentation of patients in MR images</td>
<td>95</td>
</tr>
</tbody>
</table>
# LIST OF FIGURES

<table>
<thead>
<tr>
<th>Figure</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Comparison of normal and herniated lumbar discs in a T2-weighted MRI scan. The L4-L5 intervertebral disc is highlighted as herniated.</td>
<td>3</td>
</tr>
<tr>
<td>2. Multi-resolution segmentation refinement herniated disc model.</td>
<td>7</td>
</tr>
<tr>
<td>3. The human vertebral column regions. The lumbar region, vertebra L1-L5, are depicted in yellow. Reproduced from [17].</td>
<td>10</td>
</tr>
<tr>
<td>5. Comparison of a normal and herniated lumbar disc anatomy. The herniated disc is pinching the spinal nerve extending from the spinal cord, resulting in localized or radiating pressure and pain. Reproduced from [21].</td>
<td>12</td>
</tr>
<tr>
<td>6. Relevant Deformable Model Representations.</td>
<td>20</td>
</tr>
<tr>
<td>7. Topological operators for multi-resolution and duality between $k$-Triangulation and $k$-Simplex mesh. (a) Two topological operators of the Delingette simplex model [10]; (b) Two of several topological macro-operators introduced in the Gilles simplex model [11]. Reproduced from [11].</td>
<td>34</td>
</tr>
<tr>
<td>10. Simplex mesh local geometry. A vertex $P$ represented by its simplex parameters $\epsilon_1$, $\epsilon_2$ and $\phi$. Reproduced from [11].</td>
<td>37</td>
</tr>
<tr>
<td>11. A 2D example where a vertex and a medial point (in red) is tested towards a medial surface (blue). Gilles et al.’s [11] medial axis-based collision detection method detects 4 collisions.</td>
<td>40</td>
</tr>
<tr>
<td>Figure</td>
<td>Page</td>
</tr>
<tr>
<td>--------</td>
<td>------</td>
</tr>
<tr>
<td>12. Landmark placement on Simplex mesh and disc image boundary. (a) 6 corresponding landmarks placed on the simplex mesh template and disc image boundary. (b) 5 landmarks placed on the disc image boundary visible in the sagittal MR volume plane.</td>
<td>54</td>
</tr>
<tr>
<td>13. Input vertebra image volume.</td>
<td>58</td>
</tr>
<tr>
<td>14. Euclidean distance map $\lambda_1(x)$.</td>
<td>58</td>
</tr>
<tr>
<td>15. Normalized gradient of signed distance map $\lambda_2(x)$.</td>
<td>59</td>
</tr>
<tr>
<td>16. Outward Flux $\lambda_3(x)$.</td>
<td>59</td>
</tr>
<tr>
<td>17. Resulting $\lambda(x)$.</td>
<td>59</td>
</tr>
<tr>
<td>18. Triangulated medial axis-based template mesh.</td>
<td>60</td>
</tr>
<tr>
<td>19. Vertebra segmentation refinement using the multi-resolution scheme in Simplex deformable models.</td>
<td>61</td>
</tr>
<tr>
<td>20. Placement of landmarks on the vertebra template at high curvature points.</td>
<td>61</td>
</tr>
<tr>
<td>21. Vertebra template mesh initialization within MR image subvolume through affine registration using 9 homologous landmarks.</td>
<td>62</td>
</tr>
<tr>
<td>22. Comparison of an automatic L5-S1 healthy disc segmentation result against its corresponding semi-supervised segmentation (ground truth), with -1.16mm max. in, 2.45mm max. out error.</td>
<td>72</td>
</tr>
<tr>
<td>23. Spatial segmentation error of an L5-S1 herniated disc (a) Comparison of automatic segmentation using weak shape priors against manual segmentation, considered ground truth (-3.607mm max. in, 2.603mm max. out). (b) Comparison of semi-supervised segmentation against its corresponding manual segmentation (-3.467mm max. in, 1.872mm max. out).</td>
<td>75</td>
</tr>
<tr>
<td>24. Sagittal MRI slice of a herniated disc with corresponding segmentation and constraint points.</td>
<td>76</td>
</tr>
</tbody>
</table>
25. Maximum out (red) and maximum in (blue) segmentation error between two sets of herniated disc segmentations performed by (a) the same rater (0.905mm max. in, 1.214mm max. out) and (b) different raters (2.290mm max. in, 2.593mm max out). Over- and under-segmentation is present at the lateral margins and the pathology where constraint points were required to correct segmentation.

26. Comparison of an L3 vertebral segmentation using weak shape priors with minimally supervised segmentation (ground truth), with -3.56mm max. In, 4.37mm max Out. This is the worst encountered vertebra segmentation error.

27. Graphical representation of shape model variability (in mm) captured by the first three principal modes of the L1 vertebra SSM of 10 shapes, viewed from superior. Red corresponds to the maximum outward signed distance (mm) from the mean shape while blue corresponds to the maximum inward signed distance (mm) from the mean shape.

28. Graphical representation of shape model variability (in mm) captured by the first three principal modes of the combined L2 and L3 vertebra SSM of 20 shapes, viewed from inferior. Red corresponds to the maximum outward signed distance (mm) from the mean shape while blue corresponds to the maximum inward signed distance (mm) from the mean shape.

29. Graphical representation of shape model variability (in mm) captured by the first three principal modes of the combined L4 and L5 vertebra SSM of 20 shapes, viewed from superior. Red corresponds to the maximum outward signed distance (mm) from the mean shape while blue corresponds to the maximum inward signed distance (mm) from the mean shape.

30. Graphical representation of shape model variability (in mm) captured by the first three principal modes of the intervertebral disc SSM of 40 shapes, viewed from superior. Red corresponds to the maximum outward signed distance (mm) from the mean shape while blue corresponds to the maximum inward signed distance (mm) from the mean shape.
<table>
<thead>
<tr>
<th>Figure</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>31.</td>
<td>Compactness ability of (a) L1 vertebra (b) L2 and L3 vertebrae (c) L4 and L5 vertebrae and (d) Intervertebral disc shape models</td>
<td>86</td>
</tr>
<tr>
<td>32.</td>
<td>Generalization ability and Specificity of the L1 vertebra SSM (mm) (a) Generalization (Hausdorff) (b) Generalization (RMS) (c) Specificity (RMS)</td>
<td>87</td>
</tr>
<tr>
<td>33.</td>
<td>Generalization ability and Specificity of the combined L2 and L3 vertebrae SSM (mm) (a) Generalization (Hausdorff) (b) Generalization (RMS) (c) Specificity (RMS)</td>
<td>88</td>
</tr>
<tr>
<td>34.</td>
<td>Generalization ability and Specificity of the combined L4 and L5 vertebrae SSM (mm) (a) Generalization (Hausdorff) (b) Generalization (RMS) (c) Specificity (RMS)</td>
<td>89</td>
</tr>
<tr>
<td>35.</td>
<td>Generalization ability and Specificity of the Intervertebral Disc SSM (mm) (a) Generalization (Hausdorff) (b) Generalization (RMS) (c) Specificity (RMS)</td>
<td>90</td>
</tr>
<tr>
<td>36.</td>
<td>Segmentation of an L3-L4 intervertebral disc</td>
<td>93</td>
</tr>
<tr>
<td>37.</td>
<td>Segmentation evaluation of an L3-L4 intervertebral disc with minimally supervised segmentation, considered ground truth. The disc has a signed distance error of 1.08mm over-segmentation and 0.73mm under-segmentation</td>
<td>93</td>
</tr>
<tr>
<td>38.</td>
<td>Segmentation evaluation of an L4-L5 intervertebral disc with minimally supervised segmentation, considered ground truth. The disc has a signed distance error of 0.88mm over-segmentation and 0.412mm under-segmentation</td>
<td>94</td>
</tr>
</tbody>
</table>
39. Segmentation validation of an L3 vertebra with ground truth segmentation. Maximum over-segmentation error is 1.62mm, and maximum under-segmentation error is -0.84mm. ............................................ 96

40. Segmentation validation of an L2 vertebra with ground truth segmentation. Maximum over-segmentation error is 0.47mm, and maximum under-segmentation error is -1.01mm. .................................................. 96

41. Segmentation results of vertebrae and intervertebral discs of the lumbar spine. ............................................................................................................................... 97

42. Segmentation in axial view of the vertebrae and intervertebral discs. Contiguous structures segmented across a slice in the image volume, with a segmented L4-L5 intervertebral disc, the superior articular process of L5 vertebra (red), and interior articular processes of the L4 vertebra located above (blue). ................................................................. 98

43. Signed surface distance (a) between an L2-L3 disc and an L2 vertebra before collision handling; there is maximum inter-penetration of 0.47mm. (b) from L2 vertebra to L2-L3 disc after collision handling, (c) from L2 vertebra to L2-L3 disc after collision handling. .............................. 99

44. (a) Signed surface distance between an L4-L5 vertebra and an L4 vertebra before collision handling; there is maximum inter-penetration of 0.8mm. (b) Signed surface distance from L4 vertebra to L4-L5 disc after collision handling, reduced to 0.36. Area with surface distance below 0, identifying remaining mesh overlap, is highlighted. ............................ 101

45. 3D simulation of a healthy intervertebral disc under pressure. (a) Tetrahedral FEM. (b) Behavioral Model: The bottom nodes (red) are constrained to be fixed and the Neumann boundary condition is applied to the top surface (green) of the disc model. (c) Visual Model: Comparison of the disc model at rest (red) and deformed (green) configurations. 103
CHAPTER 1

INTRODUCTION

Lower back pain is the second most common neurological ailment in the United States after a headache. According to the American Association of Orthopedic Surgeons, approximately 80 percent of Americans will suffer from back pain at least once in their lifetime [1], spending approximately $50 billion dollars annually on acute or chronic back pain [2]. High incidence cases associated with back pain include intervertebral disc degeneration (IID), or disc herniation, in the spinal lumbar region, as well as sciatica, pain in the legs due to IID [3, 4]. Imaging studies indicate that 40% of patients suffering from chronic back pain showed symptoms of IID [5]. Primary treatment planning for lower back pain consists of non-surgical treatment. If non-surgical treatments are ineffective, a surgical procedure may be required to treat IID, known as spinal discectomy. Approximately 300,000 discectomy procedures, accounting for over 90% of all spinal surgical procedures [6], are performed each year, totaling $11.25 billion in costs per year. Other spinal surgeries include treatment for metastatic spinal tumors and spinal cord injury.

A patient-specific, high-fidelity spine anatomical model that faithfully represents any existing spine pathologies can be utilized

- as input to Finite Element Model (FEM) for biomechanical load and displacement modeling of a healthy and degenerated spine;
- in surgery planning and navigation, for use by expert surgeons;
- as an anatomical model for surgery simulation for training surgical residents;
to facilitate the fusion of several spine medical images into a probabilistic intensity atlas of the spine, which could provide intensity priors corresponding to various spine anatomical structures and thus support the identification of pathology in a minimally supervised manner.

This research proposes to develop a multi-surface spine segmentation model, which can serve as foundation of a simulation or treatment planning system for spine surgery.

1.1 Problem

The initial step towards determining the cause of lower back pain is acquiring and analyzing medical image scans of the patient. A Computed Tomography (CT) scan, based on X-ray imagery, of the lumbar spine assists the physician in determining any degeneration or fractures of the bony structures, namely vertebrae, in the spine. A Magnetic Resonance Imaging (MRI) scan is normally acquired to analyze the soft tissue structures and detect disc herniation in the spine. Figure 1 compares a healthy intervertebral disc with a pathological disc in T2-weighted MRI where the L4-L5 disc is herniated.

The standard procedure for detecting abnormalities in the spinal structures is through visual inspection of the medical images, which is subjective to the expertise of the radiologist in charge of the patient. Spine treatment planning requires a patient-specific 3D anatomical model of the spine capable of correctly representing the salient anatomical features, such as vertebrae, the inter-vertebral discs, the spinal cord and surrounding nerves. This requires identification of non-overlapping, homogeneous anatomical structures in medical images, a process referred to as image segmentation. The complexity of the anatomy of the spine due to several connected structures poses a segmentation problem. Low image resolution or noisy images hinder the detection of these complex structural boundaries,
affecting the accuracy of the constructed model.

Generally speaking, existing spine segmentation methods for identification of abnormalities provide an acceptable technique for detecting disc herniation or vertebra fracture in 2D image scans but are not sufficiently anatomically detailed to provide an accurate 3D reconstruction of the spine. Current methods \cite{7, 8, 9} detect vertebrae as simplified rectangular structures connected by inter-vertebral discs, which do not represent the anatomical shape of the vertebra, lacking the amount of anatomical information required to extract vertebrae, inter-vertebral discs, the spinal cord and surrounding nerves during spine treatment and surgery planning.

1.2 Proposed System

The thesis of this dissertation is: *Using statistical shape-based deformable*
models to segment 3D lumbar spine in T2-weighted MR images provides robust, accurate and minimally overlapping results.

This research proposes to develop a minimally supervised multi-surface spine segmentation method by incorporating statistical shape models (SSM) in discrete deformable models, namely multi-surface simplex meshes, to identify healthy vertebrae and inter-vertebral disc structures of the spine, as well as user-assisted disc pathological regions.

This research addressed the following aims

**Aim 1:** Construction of a statistical shape-based multi-surface spine deformable model.

**Aim 2:** Segmentation of healthy spine images through deformable model evolution.

**Aim 3:** User-assisted identification of pathological areas of the spine to assist with discectomy planning and simulation.

**Aim 4:** Patient specific, controlled-resolution and minimally overlapping segmentation of contiguous lumbar spine structures for instantiating a high fidelity FEM biomechanical model. This model simulates healthy disc compression under normal weight and gravitational loads.

This research proposes to combine the multi-surface simplex mesh [10] as proposed by Gilles [11] with the statistical shape model-based simplex mesh utilized by Schmid [12] and Tejos et al. [13] to segment lumber vertebrae and inter-vertebral discs. The deformable model utilized by Gilles et al. [14] provides a powerful scheme for multi-surface collision detection but was sensitive to image noise or low image resolution. Schmid et al. [15] incorporated prior shape and appearance knowledge of the anatomical structures to improve the segmentation process. This research inspires us to combine multi-surface collision detection with statistical shape knowledge to segment vertebrae and inter-vertebral discs to overcome
inherent shape complexity posed by the anatomy as well as low image resolution and low contrast.

A mean shape of the anatomical structures, along with the expected variations, has been extracted through statistical analysis of a set of healthy patient CT and MR image scans. Incorporation of statistical shape-based knowledge in deformable models mitigates the segmentation challenges introduced due to low resolution and image artifacts present in test MR images.

The proposed method enables segmentation of inter-vertebral disc herniation in MR images. In the case where the shape statistics-aware deformable model is unable to automatically and correctly identify the pathological region, the user is allowed to intervene to enable the strong shape influence to gracefully degrade while using minimal supervision to guide a robust and accurate segmentation.

1.3 Contributions

This research segments multiple anatomical spine surfaces by augmenting multi-surface deformable models with statistical shape models. The high prevalence of lower back pain and disc herniation motivates a segmentation framework to facilitate the development of a 3D patient-specific lumbar spine model for use in treatment planning, as well as simulation for surgical training.

1.3.1 Minimally Intersecting, Controlled Resolution Meshing of Lumbar Spine from T2-weighted MR Images

This research provides minimally intersecting, controlled resolution 3D segmentation results of vertebrae and intervertebral discs of the lumbar spine from T2-weighted MRI. Incorporation of strong shape priors within multi-surface Simplex deformable models for segmentation results in anatomically faithful meshes of
contiguous structures of the lumbar spine. These high fidelity meshes can be used as input anatomy for a surgery or biomechanical simulation. Figure 2 demonstrates segmentation of a herniated disc using the hierarchical resolution approach.

1.3.2 Average Spine Model Construction and Evaluation of Coupled Vertebrae and Intervertebral Discs

This research constructs and evaluates average statistical shape models of

- L1 vertebrae,
- coupled L2 and L3 vertebrae,
- coupled L4 and L5 vertebrae, and
- intervertebral discs of the lumbar spine

using evaluation metrics of compactness, generalization ability and specificity. Statistical shape model construction entails the analysis of a set of structures to determine an average shape and expected variations across a training population. This statistical inference requires that point-to-point correspondence between the dataset be analyzed, resulting in the same number of points representing co-registered shape surfaces. Correspondence is of utmost importance, as it ensures correct shape representation and parameterization. This research proposes to achieve and optimize correspondence between the training dataset through a particle energy minimizing scheme.

1.3.3 Segmentation of Healthy Spine using Strong Shape-based, Controlled-Resolution and Multi-Surface Deformable Models

This research combines simplex deformable models with statistical shape knowledge for segmentation of 3D lumbar vertebrae and intervertebral discs in MR
images. Simplex meshes are a unique discrete model that are topologically equivalent to triangulated meshes, with 3 constant-vertex connectivity. Topological operators introduced by Delingette [16] allow changes in mesh resolution that have been exploited in this research for multi-resolution segmentation that resulted in refined results that were able to faithfully capture anatomical details. A landmark-based vertebrae and disc localization scheme is adopted for initializing segmentation. These landmarks are placed on high curvature points of the structures, such as the transverse and spinous processes of the vertebrae and the lateral margins of the disc. A simplex template mesh is initialized within the image subvolume and allowed to deform to achieve a successful segmentation of spinal structures despite the presence of low resolution or ambiguous image boundaries.

1.3.4 Segmentation of 3D Spine Pathology in T2-weighted MR Images

In the case where the statistical shape model is unable to successfully segment the pathology, influence of the statistical-shape term in the region of pathology has been disabled. In this region, the Simplex model’s attraction to image features, assisted by user interaction, takes over, resulting in robust segmentation of herniated disc pathology. Moreover, limited research is devoted to using shape statistics in conjunction with local disabling of this prior information where pathology makes statistical shape modeling inapplicable. The proposed research addresses this limitation of such shape statistics-based surface models.
1.4 Dissertation Outline

The work contained in this dissertation is presented in nine chapters. Chapter 2 provides a brief anatomical overview of a healthy spine as well as lumbar disc herniation. Chapter 3 introduces a technical background on various voxel-based and surface-based segmentation approaches, and discusses several previous approaches for segmenting vertebrae and intervertebral discs in various imaging modalities. This is followed by an introduction to our segmentation scheme, Simplex deformable models, in Chapter 4. Details related to geometrical representation and topological operators enabling the multi-resolution scheme are presented. Chapter 5 provides an overview of statistical shape model construction and correspondence establishment. The methodology of segmentation of 5 MR images, comprising test data, using weak shape priors inherent in simplex meshes is presented in Chapter 6. Chapter 7 describes the methodology for development and incorporation of statistical shapes in simplex models for segmentation using strong shape-priors. Segmentation results using weak-shape priors as well as strong-shape priors are presented in Chapter 8. Evaluation results of the constructed statistical shape models are also presented. Chapter 9 concludes this dissertation and discusses limitations of our presented work.
CHAPTER 2

BACKGROUND

This chapter provides an introduction to the anatomy of the spine and disc herniation causes, detection and treatment for better understanding the challenges of the spine segmentation problem.

2.1 Spine Anatomy

The human spinal column is composed of bone and soft tissue. It protects the spinal cord, supports the weight of the head and provides stability to the general structure, shape, posture and movement of the entire body. Its main structures are the vertebral column, the inter-vertebral discs, the spinal cord and the spinal root nerves. The vertebral column, as depicted in Figure 3, consists of 33 vertebrae that are divided into 5 regions.

The region related to this research is the lumbar vertebral region, which is composed of 5 vertebrae (L1-L5) that support body weight and permit movement. Two adjacent vertebrae are joined by a soft tissue known as the inter-vertebral disc, which cushions the vertebrae to act as a shock-absorber between them. Figure 4(a) provides a lateral anatomical view of the lumbar spine with salient structures.

An individual lumbar vertebra has two main parts: the vertebral body and the vertebral arch, which is the posterior part of the vertebra. The arch consists of the transverse and spinous processes, which are the ridges protecting the spinal cord located within the vertebral foramen, which in turn is the opening in the vertebral bone as depicted in Figure 4(b). The inter-vertebral disc (Figure 5) is soft tissue between two adjacent vertebral bodies. It consists of a stronger outer layer
Fig. 3. The human vertebral column regions. The lumbar region, vertebra L1-L5, are depicted in yellow. Reproduced from [17].

Fig. 4. (a) Anatomy of the lumbar spine. Reproduced from [18] (b) Anatomy of a lumbar vertebra. Reproduced from [19].
of fibrous cartilage known as annulus fibrosus that surrounds the softer, jelly-like
nucleus pulposus and evenly distributes the pressure across the disc. It is the nu­
cleus pulposus that acts as a shock-absorber between the vertebrae and ensures
spinal flexibility.

2.2 Disc Herniation

Disc herniation, or prolapsed disc, is a medical condition caused when the
central portion, nucleus pulposus, of the inter-vertebral disc is forced out of the
stronger outer fibrous ring due to pressure or a tear in the annulus fibrosus. This
tear in the outer ring may cause considerable pain and possible nerve root com­
pression resulting in localized or radiating pain in the lower torso and legs. This
condition usually occurs in adults due to a trauma or injury to the spinal column
or due to wear and tear. It most often occurs in the lumbar spine as that region
supports most of the weight of the spine and back, with 95% cases located at the
L4-L5 disc or the L5-S1 disc [20]. Figure 5 depicts a normal and a herniated disc.

The treatment plan for disc herniation varies by the observed symptoms.
Depending on the level and location of pain and discomfort, the patient may be
recommended absolute rest and prescribed pain suppressants. If the problem per­
sists due to nerve compression, surgery may be required. The surgical procedure,
known as discectomy, entails removal of the disc material and the dislodged nu­
cleus pulposus to relieve spinal nerve pressure. During traditional disc surgery,
a surgeon makes a small incision at the location where the pathology is located,
then strips the muscles of the back away from the vertebrae in order to access the
area around the herniated disc. Once the bulging nucleus pulposus is removed, the
muscles are put back, and the incision is closed. An alternate, minimally invasive
technique known as microdiscectomy utilizes a special instrument to spread the
back muscles that reduces muscle damage. This procedure requires localization of
Fig. 5. Comparison of a normal and herniated lumbar disc anatomy. The herniated disc is pinching the spinal nerve extending from the spinal cord, resulting in localized or radiating pressure and pain. Reproduced from [21].

the inter-vertebral disc during surgery, which is subjective to the expertise of the surgeon and may be guided by medical images acquired during or before the procedure.
CHAPTER 3

MEDICAL IMAGE SEGMENTATION

Segmentation is a critical aspect of development of a computer-aided surgical navigation system. This identification process consists of partitioning of the original medical image dataset into a subset of points corresponding to distinct, compact anatomical structures.

Although various segmentation techniques have been developed for use in the medical imaging community, no general solution exists. This is due to inherent inhomogeneity present in anatomical structures, the multiplicity of imaging modalities as well as myriad clinical applications of these images, use of various image modalities and frequent occurrence of image artifacts captured during image acquisition that hinder segmentation. This section provides a brief overview of the current state of the art in segmentation techniques employed in the medical image community.

3.1 Voxel-based Segmentation

Voxel-based segmentation strives to assign a label to a voxel based on local intensity or measurements computed from local intensities centered at that voxel. Voxel-based techniques include thresholding, edge-based techniques, watershed algorithm and livewire.

3.1.1 Thresholding

The foreground of a medical image usually has a pixel or voxel intensity value that is different than the background intensity. This information can be exploited by setting a threshold of pixel or voxel value to divide the image into one
or more regions. A global threshold value can be set to partition an image into two regions: the foreground, representing the region of interest, and the background. This converts a greyscale image into a binary image. Any pixel or voxel intensity value that is equal to or greater than the global threshold value is assigned as foreground and any value lower than the threshold is assigned as background. In addition, an image can be mapped to more than one tissue by using two or more thresholds.

Thresholds can be selected manually based on a priori knowledge regarding the regions to be segmented or automatically by analyzing the image information. Automatic threshold detection can be further divided into histogram analysis and optimal thresholding groups [22].

The type of anatomical structures to be segmented in medical images is usually known, such as segmentation of a femur in a CT scan. This prior knowledge can be utilized to determine the corresponding Hounsfield unit range of the region to be segmented and subsequently used as a threshold value.

Threshold can be automatically selected by analyzing the peaks and valleys of the intensity histogram of the image to determine the appropriate intensity value corresponding to various regions. In the two-class problem of identifying tissue of interest and background, two intensity peaks are identified corresponding to image intensity foreground and background. The minimum of two peaks is set as the threshold for segmentation. Sezan [23] conduct histogram peak analysis by convolving a smoothing kernel with the image histogram to reduce noise sensitivity and a differencing kernel to determine sharp peaks. An objective function can be further applied to the regions segmented by histogram analysis for threshold selection. Otsu [24] minimize the within-class variance of a region’s histogram and calculate a global threshold between the means of the foreground and background intensity values. The iterative isodata method [25] similarly determines the local
threshold for each region. The Niblack thresholding method [26, 27] calculates the mean and standard deviation of each region to obtain a threshold. The Bayesian thresholding method, based on Bayesian decision theory [28], calculates the posterior probability of a voxel according to the Bayesian principle to estimate a threshold. The posterior probability $f(x)$ of observing a voxel belonging to a class is $p(f(x)|j)$, where $j \in \{0, 1\}$ is the unknown foreground of background class. Mardia and Hainsworth [29] utilize image spatial information to interpret voxel values at a given image location. Similar to the Bayesian thresholding method, their method assumes that the foreground and background regions follow Gaussian distributions with same variances. For a detailed review of various thresholding algorithms, the reader is directed towards surveys [30], [31] and [32].

Thresholding is the simplest and fastest segmentation technique if the regions of interest can be characterized by distinct intensity values that result in peaks and valleys during histogram analysis. In case the image background is distorted and introduces noise artifacts, the background consists of various ranges of intensity values that obstruct the thresholding method and cannot be partitioned with a single threshold value.

3.1.2 Edge Detection

Edge detection methods are based on the theory that region or tissue boundaries coincide with edges, which are characterized by sharp changes in image intensity values. Edges are detected and linked to identify enclosed regions that form a resulting binary image. Intensity value contrast is calculated by determining the presence of a strong image gradient, with the length of the edge representing its strength. Edge tracking techniques can be applied to determine image edges that are connected to form bounded segmented regions. The Canny edge detector
[33] performs an edge-enhancement step by applying a series of gradient smoothing filters and calculating the length and direction of the gradient orthogonal to the edge direction. The edges are then tracked by calculating the local maxima of the gradient length by selecting adjacent voxels that lie within a range of specified thresholds.

The watershed algorithm is a popular edge-based segmentation method for defining image segments. It is usually described using an analogy of water filling a landscape with basins, which are the local minima of the landscape [34]. It uses the gradient strength information of the intensity gradient to represent height of a basin, with the number of segments equal to the number of basins defined. Falling water in this landscape will initially be caught in the steepest basin. The algorithm sorts all image voxels in ascending order, with every voxel value describing the height. Starting from the lowest voxel value, the algorithm iterates through all voxels and assigns a label to all voxels according to their neighborhood information. At any level, if a voxel already has a neighbor, it is assigned to the same basin, hence the segment.

The watershed algorithm usually tends to over-segment an image because the underlying model for segment identification through local minima of the landscape does not capture the object boundary. Although it tends to provide an enclosed boundary, it does not provide a smooth segmentation result.

3.1.3 Live Wire

The live wire method is a user-interactive technique for edge-bounded segmentation. Every pixel in the image is converted into graph nodes that are connected by an edge if two pixels are within a defined four- or eight- neighborhood [35]. The user is required to select a starting point in the boundary. A number of
minimum cost paths, selected according to some optimality criterion, are calculated at each pixel node to all other points, and the user is asked to select the preferred end point amongst these options. This end point is further selected as the starting point of the next contour segment, and the image graph is iterated until the first point is reached, creating an enclosed contour. This method may provide an incorrect segment in the presence of image noise or a missing object boundary and is limited to 2D image segmentation.

3.1.4 Region-based Methods

Region-based segmentation methods can be classified as *region growing* and *region splitting and merging*.

The region growing segmentation technique exploits spatial information of the image to assign voxels to regions based on homogeneity criteria. It partitions the image into disjointed regions. This method can be categorized into seeded and non-seeded methods and used to evaluate image intensity. Seeded region growing methods require manual selection of a seed in the region of interest. Each seed represents a single region to be segmented.

Adam and Bischof [36] define the homogeneity criteria as the distance between a voxel value and the region mean to determine whether that voxel is included in the growing region. Revol et al. [37] proposed a non-connected region growing algorithm that allowed voxels to be removed as well as added to a region. Lin et al. [38] propose non-seeded region growing by assigning an arbitrary voxel as the region seed and use Adam and Bischofs [36] homogeneity criteria for region growing. If a voxel value lies outside a mean region value, it is assigned a new region.

Horowitz and Pavlidis [39] initially proposed region splitting and merging
TABLE 1 Comparison of voxel-based segmentation techniques

<table>
<thead>
<tr>
<th>Segmentation method</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thresholding</td>
<td>• Simple and fast method</td>
<td>• Assumes distinct change in voxel values between regions</td>
</tr>
<tr>
<td></td>
<td>• Effective approach for images with low noise and high contrast</td>
<td>• Segmented regions may not be contiguous without image spatial information</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Dependent on accuracy of threshold</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Sensitive to image artifacts that alter image intensity</td>
</tr>
<tr>
<td>Edge detection</td>
<td>• Isolates regions with sharp boundaries</td>
<td>• Challenging to produce enclosed region if too many edges detected</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Edges may be distorted if image noise interferes with edge intensity values</td>
</tr>
<tr>
<td>Watershed Transform</td>
<td>• Produces enclosed contours</td>
<td>• Tends to over-segment</td>
</tr>
<tr>
<td>Live Wire</td>
<td>• Fast and simple edge-detection method</td>
<td>• User-assisted</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Limited to 2D segmentation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• May follow incorrect segmentation with presence of noise or missing boundary</td>
</tr>
<tr>
<td>Region-based</td>
<td>• Good segmentation of regions with well-defined boundaries</td>
<td>• Requires manual interaction to select a seed</td>
</tr>
<tr>
<td></td>
<td>• Less sensitive than thresholding to image artifacts</td>
<td>• Over-segments regions with blurred image boundary</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Sub-optimal with partial volume effect in image</td>
</tr>
</tbody>
</table>

Techniques that over-segment the image and merge the partitions based on homogeneity criteria. This technique performs similarly to region growing without requiring manual seed selection. The image is arbitrarily split into four regions in a 2D image if it does not meet predefined criteria [40]. These regions are then recursively merged to fulfill region homogeneity requirements.

Region-based techniques may not produce optimal results in a single evaluation, as voxel values may need to be reassigned to new regions that may have been generated after the image was evaluated in the first algorithm pass. It is less sensitive to image artifacts such as background noise than the thresholding method but may produce segmentation bleeding if the region boundaries are blurred.

Table 1 summarizes the advantages and disadvantages of voxel-based segmentation techniques. Although used alone their segmentation results may be sub-
optimal, they are often utilized as one of the segmentation steps during image processing.

3.2 Surface-based Segmentation

Medical imaging analysis provides a detailed shape and organization of structural anatomical boundaries that can assist physicians in therapy and surgical planning, as well as simulation. Its role has expanded from providing visualization of anatomical structures to computer-aided diagnosis and treatment planning. Deformable models reconcile internal model behavior with fidelity to raw image information and are able to detect spatial as well as temporal anatomical changes.

Originally introduced in computer vision [41] and computer graphics [42] for modeling elastic bodies such as rubber and cloth, deformable models consist of geometry, physics and optimization approximation theory components: the geometry encapsulating the model shape with physics components that govern the external and internal forces that deform the shape over space and time [43]. Originally applied to 2D contour identification, and subsequently to identifying surfaces in 3D images, a deformable model is represented by an energy functional that balances two force terms, representing these internal and external forces respectively. This functional model reconciles continuity properties with fidelity to image gradient ensuring that calculated forces deform the model to fit tissue boundary. It is solved using optimization techniques to minimize model energy. A physical interpretation of the deformable model is an elastic contour or surface capable of deformation under applied forces and constraints, with inherent continuity properties. Montagnat et al. [44] categorize deformable models based on their geometric representation. Figure 6 provides an overview of these categories.

Deformable models can be categorized as continuous or discrete in representation. Continuous models are represented by a set of partial differential functions.
Explicit continuous models require parameterization to numerically compute the model energy function, limiting the number of degrees of freedom. For instance, explicit models based on a generalization of spherical harmonics can only encapsulate objects invariant to a sphere, and superquadrics can only represent symmetrical shapes. Explicit continuous models represent a shape through a variation of finite details, such as variation in the shape geometry. In contrast, implicit models are a function defined over the whole image domain whereby a contour or surface is determined implicitly in relation to function parameters. As opposed to continuous models, discrete deformable models are represented by a discrete set of data points. Continuous models represent model quantities, such as normals and curves, more faithfully due to their parameterization independence whereas discrete models are able to represent higher shape complexity.
3.2.1 Continuous Deformable Models

Snakes

Snakes, or "deformable contour models," were derived from the multi-dimensional deformable model theory represented by Terzopoulos [45, 46] and were primarily implemented for segmentation of medical images. Snakes represent 2D energy-minimizing deformable parametric contours to detect the object boundary shape and location based on the assumption that the boundary is piece-wise continuous or smooth. The following is the equation of a snake embedded in an image domain $I(x,y)$ that deforms towards $C[0,1] \rightarrow I(x,y)$

$$E(C) = \frac{\alpha}{2} \int_0^1 |C'(q)|^2 dq + \frac{\beta}{2} \int_0^1 |C''(q)|^2 dq + \gamma \int_0^1 |f(C(q))| dq \quad (1)$$

Model evolution is driven by two energies: an external energy that drives the model to capture the object or tissue boundary and an internal energy that applies smoothness constraints. The first two integrals of equation 1 try to limit the large variation of the first and second derivatives of the contour, and the third integral conforms the contour to the object boundary. Snakes represent 2D energy-minimizing deformable parametric contours to detect the object boundary based on the assumption that the boundary is piece-wise continuous. The snake is initialized close to the region of interest in an image and allowed to deform. This deformation is further improved through user interaction until the object is satisfactorily segmented. 2D snakes can be extended to segment 3D images by treating a volumetric image as a stack of 2D images. An image slice from the stack of image slices can be segmented using a snake contour. The result of the initial image segmentation can be used to initialize a contour in the next image and utilized to iteratively process all image slices. The resulting sequence of 2D snake contours can then be connected to form a continuous 3D active surface model representing the resulting segmentation [47, 48].
Snakes were inherently designed as interactive deformable model that require initialization close to the region of interest to be segmented and lead to bleeding effects and poor performance without proper initialization. Their internal energy constraints may limit geometrical flexibility and prevent a snake from deforming to a shape with higher variability. Moreover, due to its parametric properties, it is unable to undergo topological transformations, such as dividing or merging, during deformation without modifications. T-snakes, or topologically independent snakes [49] have been developed that allow the snake deformable model to represent shape with bifurcations and higher variability by dynamically sensing and changing its topology during segmentation.

**Level-sets**

Level-sets are non-parametric deformable models based on curve evolution theory [22]. Originally proposed by Osher and Sethian [50, 51] for tracking moving interfaces, level-sets are enclosed, non-intersecting hypersurfaces represented by an implicit function [52]. They are n-dimensional problems embedded in n + 1 spatial dimensions. The time aspect is also considered in simulation of curve propagation.

A curve propagating in a plane can be replaced by a time-varying two-dimensional surface propagating in three dimensions. A moving curve γ in R² can be regarded as a level curve of a function in a higher-dimension. Given an image I(x,y), and a moving contour γ, γ(0) corresponds to the user-initialized contour completely inside some boundary in I(x,y). The c-level γ of embedding function φ(x,y) represents the contour at all times during evolution. The embedding function is initialized as a signed distance map from γ(0) that is iteratively reinitialized at every time-step. The implicit function φ(x,y) of γ can thus be represented as
\{(x, y, z) \in \mathbb{R}^3 : z = \phi(x, y), (x, y) \in D(\phi)\}. \tag{2}

Likewise, this concept generalizes to higher dimensions whereby for a moving surface \( \sigma \) in \( \mathbb{R}^3 \) a function \( \phi(x, y, z) \) of three variables is the set
\[{(x, y, z, w) \in \mathbb{R}^4 : w = \phi(x, y, z), (x, y, z) \in D(\phi)}\]. \tag{3}

The \( c \)-level set \( \gamma \) is the intersection of the function with the plane \( z = c \), and similarly \( w = c \) for a surface, with the zero-level-set \( \gamma(0) \) corresponding to the actual position of the contour or surface where \( c = 0 \). The evolution of \( \gamma \) over time \( t \) is regarded as the \textit{Eulerian Formulation} and represented as
\[\phi_t = V| \nabla \phi|. \tag{4}\]

\( \phi_t \) propagates in the orthogonal direction with a speed \( V \), with \( \nabla \phi \) in the \( \pm \nabla \) direction, evolving in the positive direction inwards and in the negative direction outwards. Caselles et al. [53] and Malladi et al. [54] proposed the \textit{geometric active contour} model that combines the advantages of the snakes deformable model with the level-set method by introducing an additional multiplicative term to the evolution equation that slows down the curve evolution near the object boundary to improve edge detection. This contour combines the non-parametric properties of the level-set method to allow topological changes with improved edge detection. It is represented by the following equation:
\[\phi_t = u(x)(k + V_0)| \nabla \phi| \tag{5}\]

where \( u(x) \) is an additional force to stop the evolution based on the image gradient information, \( k \) is the curvature and \( V_0 \) is a constant force variable. This method requires the contour to be initialized enclosing the region of interest or completely inside the object boundary. In the case of a discontinued boundary with gaps, or
a blurry edge artifact, the curve evolution may fail to capture the object boundary and may continue to evolve beyond the boundary of interest. To propagate the curve back towards the boundary direction, Caselles at al. [55] and Yezzi et al. [56] suggested an additional term to the equation to pull back the evolution by attracting the curve to the boundary through an external force, similar to the external force applied in the snakes model and projecting it onto the normal direction of the object boundary. This \textit{geodesic active contour} can be represented by the equation

\[
\phi_t = u(x)(k + V_0)\nabla \phi| + \nabla u \cdot \nabla \phi
\] (6)

Level-set methods allow the speed function $V$ to be positive in some parts of the contour and to be negative in other parts of the contour, allowing the contour to evolve outward as well as inward to adapt to the gradient of the image to be segmented. Level-sets propagate at every pixel or voxel in the domain at every iteration, resulting in a time complexity of $O(n^d)$, where $d$ represents the dimensionality of $\phi$. To reduce computation time, the narrow-band level-set method [57] was introduced, which restricted most evolution to within a thin band of active region surrounding the object boundary, requiring careful initialization. Various implementations suggest voxel or pixel tracking methods in the active region to reduce the computation complexity. The Sparse field method [58], sparse block grid [59] and octree [60] propose tracking the linked active pixels/voxels during evolution through linked lists, grids and tree data structures respectively. The fast marching method [61] can be implemented in cases where model evolution only in the normal direction is sufficient, thus reducing computation complexity of the deformation.

Level-set methods allow for topological changes, such as splitting or merging, due to their embedded nature in $n + 1$ dimensions. They are vulnerable to bleeding effects because the model can spawn unwanted child contours, or surfaces, as a result of this topological flexibility. Parameterization independence allows for
accurate calculation of the model normals and curvature. However, it introduces computation complexity while solving the iterative optimization of the partial differential equations representing curve evolution. Addition of constraints to the model for faster implementations introduces more initialization parameters that increase the model complexity and algorithm sensitivity to initialization parameters, rendering it difficult for integration in clinical environments.

3.2.2 Discrete Deformable Models

Discrete models are explicit deformable models represented by a surface of discrete set of points. These models are expressed as a physically-based system, where point vertices are treated as point masses and edges model physical properties, such as a spring-like behavior, or object boundary smoothness. The most common discrete deformable model is a mesh representation, which is a set of points with connectivity information. A triangulated deformable surface is a set of vertices connected to produce a set of adjacent triangles with topological constraints. Discrete deformable models, namely triangulated meshes, are popular in computer graphics and simulation due to their topological adaptability and flexibility in application of topological and geometric constraints.

This research exploits simplex mesh deformable models. Initially defined by Delingette [16] and further optimized by Gilles [11], simplex surface vertices are modeled as dynamic particles with spring-like forces adhering to the Newtonian law of motion with internal and external energies. Further details regarding simplex models are provided in Section 4.

Audette et al. [62] have successfully represented controlled resolution of brain models for endoscopic pituitary surgery simulation using simplex meshes. Shi et al. [63] have employed a hierarchical scheme for segmentation of the vestibular system using a simplex deformation model.
3.3 Spine Segmentation

In this section, current research in spine segmentation is represented. Most methods have adopted a hierarchical segmentation approach that exploits prior knowledge by utilizing either shape and appearance-based statistical models or probabilistic models to identify the region of interest.

Aslan et al. [64, 7] propose a hierarchical 3D vertebra segmentation method incorporating graph cuts with statistical shape and appearance features to aid in analysis of vertebra osteoporosis and fracture analysis. A 3D shape model is constructed by extracting training shapes through manual segmentation of 3000 clinical CT images performed by an expert. The training images are aligned by rigid registration and binarized to form a shape volume composed of the vertebra object, the background and the allowed variability. Their method calculates variability within the dataset by calculating the marginal density of the object and background, denoted the distance probability model. The proposed framework is a two-step approach: identification of the vertebra region using the matched filtering method [65] and the segmentation of the region of interest using a graph cuts approach. The vertebral region in axial slices of a CT scan is automatically detected using the matched filter approach, typically utilized in pattern matching and face recognition, to maximize the cross-correlation between a reference and test image. This matched filter is the correlation filter of the complex conjugate of the 2D Fourier Transform of a reference image. The identified region is further segmented using the graph cuts method to find the optimal tissue boundary by converting the segmentation process into a graphical problem that finds the optimal path between user-initialized sink and source terminal vertices through energy minimization, which is conceptually similar to some of the active contour segmentation techniques. It optimizes region classification based on Markov random field models that represent region and boundary properties as well as shape constraints using
shape and appearance priors. Aslan et al. compared and contrasted the proposed framework and alternate approaches of b-spline and statistical level-set segmentation methods against expert segmentation of 11 clinical CT datasets. The proposed framework resulted in faster segmentation with the lowest mean error and standard deviation. Aslan et al. have mitigated user-intervention by identifying and detecting the region of interest using a matched filter. However, only 64.1% of the 117 datasets was successfully identified without any misclassification, with an average identification success rate of 85% that may have included parts of adjacent disc or vertebral structures. A quantitative estimate of the over-segmentation was not provided.

Gosh et al. [9] present an automatic, multi-step lumbar vertebra segmentation method in CT images to detect lumbar wedge compression fractures. They utilize a two-level probabilistic model to label the inter-vertebral discs in the sagittal plane of the CT based on image intensity as well as the disc location features. They further detect the vertebral skeleton in the sagittal CT images by performing thresholding and morphological operations using the prior knowledge that bone is typically 400 Houndsfield Units or higher. Individual vertebrae are segmented by applying the General Hough Transform on the gradient of the vertebral skeleton image and performing morphological and hole-filling operations. The General Hough transform [66] groups edge points into object candidates, such as a line or a curve, by performing an explicit voting procedure over a set of parameterized image objects, which correspond to the vertebral skeletons in this approach. The vertebra center line and left, right and center heights are subsequently calculated in order to detect any vertebrae with abnormal measurements due to fractures. This method can identify wedge compression fractures with a sensitivity of 91.7%. Gosh et al.'s segmentation framework provides good results without incorporating prior
statistical knowledge but is limited to a more simplistic segmentation representation in the shape of a rectangle and does not segment the sharp vertebra edges, such as the spinous process. Moreover, the method has a high over-segmentation rate, especially for the L5 vertebra, between 14% and 26%. This limitation may be attributed to the morphological operations used to smooth and refine the individual vertebra segmentation.

Khallaghi et al. [67] propose a volumetric registration framework of CT lumbar vertebral images to Ultrasound images to assist with spinal needle injections. They constructed a statistical shape model of 35 CT scans through semi-automatic segmentation and resampling to achieve shapes in correspondence. They apply a two-step registration approach for shape model construction as well as multi-modal registration by applying rigid registration using 6 random parameters and then multi-resolution b-spline deformable model [68] using 12 random parameters. Their framework was tested using 3D printed phantoms constructed from three actual CT scans against 5 corresponding landmarks placed by an expert in the CT and US images. Graphical Processing Unit (GPU) acceleration was applied to reduce the registration computation time from over 24 hours to under 20 minutes [69]. Results show about 80% success rate with less than 3.5mm acceptable registration accuracy, with least registration accuracy for the sagittal vertebrae images, which consists of sharp, distinct edges. This may be attributed to the size and resolution of the training dataset and the biased introduced by selecting a random training shape as a template for statistical shape model construction in the framework.

Rasoulian et al. [70] improve statistical shape model construction and vertebral registration by proposing a probabilistic surface-based group-wise registration method. They apply point-to-point correspondence for the training dataset using
the expectation-maximization (EM) method to solve a probability density estimation problem. This EM method assumes that voxel intensities on a shape are independent samples from a probability distribution class, which can be classified to a particular region by solving the likelihood function of the posterior probability of that voxel belonging to a region [22]. Given a set of allowed transformations within the mean shape, Rasoulian et al. determine the likelihood of a point located on the mean shape being mapped onto a point in each of the training shapes. The constructed SSM is rigidly registered to the extracted bone surface density in the ultrasound volumetric images.

Klinder et al. [71] propose an automatic 3D segmentation of the spinal column using statistical shape models coupled with an initialization of the region of interest based on the General Hough transform. They propose a two-step segmentation method that initially detects the global location and orientation of the spinal column shape by representing it as a collection of objects encapsulated by rigid transformations against a defined vertebra coordinate system (VCS). In the second step, non-rigid shape-constrained deformation of the individual triangulated mesh corresponding to each vertebra object is performed. Although the method promises 1mm accurate results, the results may be biased as the reference model is constructed using the same method with user guidance. Moreover, the VCS construction requires placement of landmarks by a domain expert that are necessary for mean model generation and achieving correspondence.

Ma et al. [72] present a hierarchical deformable surface-based thoracic vertebra segmentation method in CT images. 20 training samples comprising 12 thoracic vertebrae were manually segmented and their discrete triangulated mesh models were constructed using the Marching Cubes algorithm. A probabilistic edge detection method was used to sample 5 points along the normal direction for each triangle face of the mesh, where the intensity and gradient projection feature
vectors corresponding to each sample point were computed. These feature vectors were used to train the probabilistic model for detecting a vertebra edge. A coarse-to-fine template deformation mesh approach was adopted, where a vertebra was divided into 12 salient sub-regions whose edges were detected through deformation of a template. These sub-regions were subsequently optimally displaced to accurately capture the object boundary through piece-wise non-rigid registration, and then a mean shape was calculated from the resulting meshes. The presented method provided improved results over Klinder et al. with grouped vertebra segmentation of over 90% success rate. However, the coarse-to-fine approach is fairly insensitive to mesh resolution, and finding the optimal transformations using the learned edge detection technique for deformation is computationally expensive and dependent on the mesh resolution.

Howe et al. [73] propose a hierarchical segmentation scheme for 273 cervical and 262 lumbar x-ray images. They initially approximate vertebra location and orientation through the General Hough Transform edge detection method, and then subsequently utilize active appearance models (AAM) to deform a template towards the extracted edges in two stages. The first stage matches the intensity values to segment a vertebra and its two concurrent neighbors, and the second stage extracts a single vertebra by matching the weighted intensity values with the AAM template, giving priority to the vertebra edge where higher contrast is expected. Their 2D contour extraction is limited to areas of high gradient values and high-contrast x-ray images.

Benjelloun et al. [8] present a semi-automatic cervical vertebra segmentation method in x-ray images using active shape models. They require 2 landmark placements at the beginning and end of the cervical spinal column for model initialization and apply a Harris corner detector with additional filters to detect two corners of each cervical vertebra to localize the region of interest. A local vertebra
template is deformed to segment each vertebra in the region of interest. They also investigate the influence of the initialization of the statistical contour; the influence of number of landmarks placed on the vertebra boundary, with 20 landmarks used in their method; and training sample size, with 75 ideal shapes used. Their segmentation using the vertebra model resulted in a high success rate over 90% with a mean error of 0.6mm. The proposed technique provides good results, but they do not provide any statistical details of how the success rate was calculated, or any specific details for their ASM construction or corner detection scheme.

Zhao et al. [74] present a modified gradient vector flow deformable snake with additional external forces as a method for segmenting spine MRI images. The authors propose to segment vertebrae in the sagittal image plane and base their method on the observation that vertebra contours are similar to rectangles with concave edges in the 2D plane. Therefore, external forces, which can be modified through weighted coefficients, are augmented to the snake equation for utilization in segmentation, producing results that converge faster, with marginally improved results. However, this simplistic shape assumption cannot be translated towards volumetric image vertebrae segmentation. Table 2 summarizes the various image-based segmentation techniques employed by researchers to segment vertebra and inter-vertebral discs.

Our method supports the ability to successfully segment disc pathology, based on semi-supervised, spatially variable weighting of weak prior shape information. We also exploit controlled-resolution meshing conducive to a multi-resolution approach to segmentation, as well as producing anatomical models with low element count for interactive simulation.
<table>
<thead>
<tr>
<th>Reference</th>
<th>Modality</th>
<th>Structure</th>
<th>Techniques</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aslan et al. [7]</td>
<td>CT</td>
<td>Vertebrae</td>
<td>Graph cuts + prior shape matching, hierarchical, automatic, atlas-based</td>
</tr>
<tr>
<td>Khallaghi [67]</td>
<td>CT → US</td>
<td>Lumbar Vertebrae (L2-L4)</td>
<td>Parallel GPU processing Reg: rigid+b-spline deformable active contour+ volumetric SSM atlas (shape and appearance)</td>
</tr>
<tr>
<td>Rasoulian et al. [70]</td>
<td>CT → US</td>
<td>L1 and T12</td>
<td>Surface-based probabilistic SSM atlas (3D deformable model+ASM)</td>
</tr>
<tr>
<td>Howe et al. [73]</td>
<td>X-rays</td>
<td>Cervical and lumbar vertebrae</td>
<td>PDM, Hough transform edge detection, active appearance models (AAM), hierarchical approach</td>
</tr>
<tr>
<td>Gosh et al. [9]</td>
<td>CT</td>
<td>Lumbar vertebrae</td>
<td>3D Probabilistic model for labeling, Hough transform, morphological operations</td>
</tr>
<tr>
<td>Zhao et al. [74]</td>
<td>MRI, Sagittal plane</td>
<td>thoracic vertebrae</td>
<td>Snakes + external force constraints</td>
</tr>
<tr>
<td>Ma et al. [72]</td>
<td>CT</td>
<td>thoracic vertebrae</td>
<td>Discrete triangulated deformable model+ probabilistic edge detection using intensity and gradient features</td>
</tr>
<tr>
<td>Klinder et al. [71]</td>
<td>CT</td>
<td>Spinal column</td>
<td>Generalized Hough Transform to initialize ROI, global rigid registration + local 3D SSM triangulated mesh deformation</td>
</tr>
<tr>
<td>Benjelloun et al. [8]</td>
<td>X-rays</td>
<td>Cervical vertebrae</td>
<td>Edge detectors + ASM</td>
</tr>
</tbody>
</table>
CHAPTER 4

SIMPLEX MESHES

An efficient discrete deformable model representation is the simplex mesh introduced by Delingette [16] for 3D shape reconstruction and segmentation. A $k$-simplex mesh embedded in Euclidean $\mathbb{R}^d$ space, where $k < d$, is a $k$-manifold discrete mesh with exactly $k+1$ distinct neighbors. A simplex mesh has the property of constant vertex connectivity. Simplex meshes can represent various objects depending on the connectivity $k$, where a 1-simplex represents a curve, a 2-simplex represents a surface, and a 3-simplex represents a volume. Our research is focused on surface representation for image segmentation using 2-simplex meshes with constant 3-connectivity at each vertex, which is capable of representing arbitrary shapes of various values of genus and number of holes. This is especially relevant for this research, as the resulting intervertebral disc simplex mesh has genus = 0 while the vertebral simplex mesh has genus = 1.

The 2-simplex mesh is composed of vertices $V$, edges $E$ and faces $F$, which are linked together by the Euler relation

$$F - \frac{V}{2} = 2 * (1 - g)$$

$$E = \frac{3V}{2}$$

where $g$ is the genus of the arbitrary mesh [16].

4.1 Topological Operators

Delingette [16] introduced four topological operators to transform a simplex mesh (Figure 7.(a)). $TO_1$ and $TO_2$ operators allow addition or deletion of edges, leading to a multi-resolution scheme. $TO_3$ and $TO_4$ operators modify the
Fig. 7. Topological operators for multi-resolution and duality between $k$-Triangulation and $k$-Simplex mesh. (a) Two topological operators of the Delingette simplex model [10]; (b) Two of several topological macro-operators introduced in the Gilles simplex model [11]. Reproduced from [11].

topology of the simplex mesh allowing duality. Gilles [11] introduced macro-operators (Figure 7.(b)) to optimize the transformations and ensure higher mesh quality during topological changes, as well as a vertex preservation scheme during multi-resolution scheme.

4.1.1 Duality between $k$-Simplex Mesh and $k$-Triangulation Mesh

Simplex meshes are topologically equivalent to triangulated meshes: a spherical surface produced by a Simplex mesh leads to a spherical triangulated mesh while a Simplex toroid produces a triangulated toroid mesh. Delingette proposes operators to change the topology of a simplex surface mesh, as depicted in Figure 7.(a), by deleting or adding a simplex face, coinciding with $TO_1$ and $TO_2$ respectively. Gilles et al. [14] proposed an alternate tessellation approach by introducing new types of operators, illustrated in Figure 7.(b), that lead to higher quality faces and enforce a high geometric quality of the simplex mesh, as depicted
in Figure 7.(b).

This duality scheme modifies the topology of the mesh but does not guarantee geometrical duality between the \( k \)-simplex and \( k \)-triangulation meshes during topological conversion.

4.1.2 Multi-resolution Scheme

Simplex meshes can be utilized to modify the global mesh resolution in order to adapt to the complexity of the shape being segmented during coarse-to-fine segmentation. Thus, various simplex mesh resolutions of a shape can be generated through a multi-resolution scheme without. Delingette proposed a multi-resolution scheme that triples the number of vertices with a mesh resolution increase as demonstrated in Figure 9.(a). However, it does not preserve the vertices of the previous resolution resulting in loss of shape and feature information, especially at high curvature points. Gilles proposed an alternative multi-resolution tessellation scheme that increases the number of vertices four times with every resolution increase while preserving the vertices of the lower resolution resulting in a more regular multi-resolution adaptation as depicted in Figure 9.(b).
Fig. 9. Simplex mesh multi-resolution schemes. A 2-simplex mesh at resolution \(k\) (★ vertices and thick edges) yields a new 2-simplex mesh at resolution \(k + 1\) (• vertices and dotted edges). (a) Classic multi-resolution scheme of [16]. (b) Conservative multi-resolution scheme suggested by [11]. Reproduced from [12].

This research utilizes the optimized duality and multi-resolution scheme introduced by Gilles [11]. This research uses the following notation: Given a vectorized simplex mesh \(X^r\) at resolution \(r\) consisting of \(n^r\) vertices \(x_i^r\) where \(i \in (1, n^r)\), \(x_i^{r+1} \subseteq x_i^{r+1}\) such that the vertices of the lower resolutions are also contained within the higher resolution mesh. Similarly, the lower resolution mesh is a subset composed of the first \(t\) vertices \(\in (1, n^r)\) of the higher resolution mesh.

4.2 Geometric Representation

This research follows the 2-simplex model approach of Gilles [11] considered as a particle system, where each vertex is considered a dynamic particle with a position, velocity and acceleration. These dynamic particle positions are governed by internal and external forces regularized by damping. Collision detection during model evolution mitigates mesh inter-penetration to ensure the resulting contiguous mesh models do not overlap.

The constant connectivity of the 2-simplex mesh leads to three simplex
Fig. 10. Simplex mesh local geometry. A vertex $P$ represented by its simplex parameters $\varepsilon_1$, $\varepsilon_2$ and $\phi$. Reproduced from [11].

parameters corresponding to a vertex with a mass and its three neighboring vertices [10]. These independent simplex parameters can be utilized to represent the geometric constraints enforced upon a vertex with respect to its three neighbor vertices. Therefore, a vertex $P$ can be defined with respect to its neighbors $P_i$ with its simplex parameters $\varepsilon_1$, $\varepsilon_2$ and $\phi$.

Figure 10 represents the simplex surface local geometry for a vertex $P$ defined by its three neighbors $P_1$, $P_2$ and $P_3$ with its corresponding simplex parameters. $\varepsilon_i$ are the barycentric coordinates of the projection of vertex $P_\perp$ on the triangle $(P_1P_2P_3)$ such that $\varepsilon_1 + \varepsilon_2 + \varepsilon_3 = 1$. The orthogonal projection $P_\perp$ can be defined by the linear combination of the position of its neighbors $P_i$ with $\varepsilon_i$ along the normal direction. $\phi$ is the angle linked to the mean curvature on the mesh [16]. The neighborhood-based constraints of $P$ are thus uniquely governed by the equation

$$P(\varepsilon_1, \varepsilon_2, \phi) = \varepsilon_1 P_1 + \varepsilon_2 P_2 + (1 - \varepsilon_1 - \varepsilon_2) P_3 + h(\phi)n$$  \hspace{1cm} (8)$$

where $n$ is the normal

$$n = \frac{P_1P_3 \wedge P_1P_2}{\|P_1P_3 \wedge P_1P_2\|}$$  \hspace{1cm} (9)$$
Gilles [14] demonstrated that equation 8 uniquely defines $P$ only when vertex $P$ is projected within the circumscribed circle of its neighbors $P_i$. A proposed alternative is the utilization of the elevation parameter $h_n = h.S^t^{-1/3}$ where $St$ is the area of the triangle $(P_1P_2P_3)$ formed by the neighbors and $\beta$ controls the scale invariant aspect of the vertex. This scaled elevation replaces the simplex angle as the third simplex parameter. The vertex definition is similitude invariant with $\beta = 2$ and invariant only through rigid transformation with $\beta = \infty$. Gilles set $\beta = 4$ to define shape memory forces of $P$ as

$$P(\epsilon_1, \epsilon_2, \phi) = \epsilon_1 P_1 + \epsilon_2 P_2 + (1 - \epsilon_1 - \epsilon_2)P_3 + h_n S_n^{t^{-1/3}}$$

(10)

### 4.3 Simplex Evolution

The deformation of simplex meshes is governed by the position of a vertex with respect to its three neighbors. The dynamics of each vertex $P$ is governed by a Newtonian law of motion represented by the equation

$$m \frac{d^2 P_i}{dt^2} = -\gamma \frac{dP_i}{dt} + \alpha F_{int} + \beta F_{ext}$$

(11)

where $m$ is the vertex mass, $\gamma$ is the damping force and $\alpha$ and $\beta$ are the weight factors of the internal and external forces respectively. $F_{int}$ is the sum of internal forces represented by an elastic force that enforces smoothness constraints and $F_{ext}$ is the sum of external forces. This physically-based deformable model is governed by forces to maintain internal regularization through $F_{int}$ and global volume conservation through volume constraints.

Let vertex $P_i$ have the $P_\perp$ associated orthogonal projection. The evolution of simplex mesh under the law of motion is the discrete displacement of vertex $P^t_i$ to $P^{t+1}_i$ at time $t$ and can be computed as

$$P^{t+1} = P^t + (1 - \gamma)(P^t - P^{t-1}) + \alpha F_{int} + \beta F_{ext}$$

(12)
These total vertex forces are enforced during evolution as

\[ F = \alpha P_\perp P'_\perp \]  

(13)

with \( P' \) as the displaced vertex. \( P'_\perp \) and \( P_\perp \) are the associated orthogonal projections with target vertex \( P' \) and current vertex \( P \) respectively. These Newtonian energies are stabilized using an implicit Euler scheme resulting in regularized and smooth deformation.

4.3.1 Internal Forces

\( F_{int} \) is the sum of internal forces represented by an elastic force that enforces smoothness and weak shape-based constraints. This physically-based deformable model is governed by forces to maintain internal stabilization through \( F_{int} \).

\[ F_{int} = F_{Tangent} + F_{Normal} \]  

(14)

The tangent force \( F_{Tangent} \) enforces mesh regularization constraints during simplex evolution by controlling the position of vertex \( P_i \) with respect to its three neighbors in the tangent plane. \( F_{Tangent} \) is thus the spring force between the two vertices such that

\[ F_{Tangent} = P'_\perp - P_\perp \]  

(15)

where \( P'_\perp \) is orthogonal projection associated with \( P' \) that vertex \( P \) is trying to reach during displacement.

Weak shape memory is enforced by constraining the \( F_{Normal} \) internal force along the normal direction of vertex \( P \). This is implemented by constraining the mean curvature at vertex \( P \) governed by the simplex angle \( \phi \) by setting \( \phi = \phi_c \), where \( \phi_c \) is a constant \([10]\). The associated barycentric coordinates and simplex angle (equation 10) are calculated \textit{apriori} and thus enforce a shape constraint on the
4.3.2 External forces

$\vec{F}_{ext}$ is the sum of external forces comprised of image information and non-overlap constraints. Image information, such as image edge and gradient intensity values, comprises of the similarity criteria to be maximized during simplex evolution along the normal direction.

4.3.3 Collision Detection

During multi-region segmentation, collision handling ensures that object boundaries do not overlap or self-penetrate. Gilles [11] applied collision detection as an additional step after bone segmentation by the distance field method where the faces of the medial axis surface boundaries are stored into a bounding volume hierarchy in a pre-processing step. As bounding volumes are inflated, colliding regions result in overlapping bounding volumes. Figure 11 provides a 2D example of the medial-axis based collision detection method. A collision vector $P_c$ between

Fig. 11. A 2D example where a vertex and a medial point (in red) is tested towards a medial surface (blue). Gilles et al.'s [11] medial axis-based collision detection method detects 4 collisions.
a colliding vertex $P$ and mesh face composed of $P_t$ vertices is defined as the linear combination $P_c = \sum_i w_i P_t - P$. Expected collisions are pre-detected by storing the indices and weights of the collision vector $P_c$ during initialization. This $P_c$ vector is updated during deformation as a collision response. In order to enforce smooth vertex changes during collision handling, collision velocities in the normal direction of the colliding region are gradually altered such that $\Delta V_c = -V_c - P_c/dt$. 
CHAPTER 5

STATISTICAL SHAPE DEFORMABLE MODELS

The shape of an object is the geometrical information that remains after effects of translation, rotation and scaling have been filtered [75]. Although medical images consist of considerable variability by default, appearance and shape of the anatomical structure of interest to be identified are consistent across individuals. This information can be exploited by integrating statistical analysis in deformable models to optimize the segmentation process. Information to be utilized may be shape-based, such as points on a discrete mesh or curves in a continuous model. They may be appearance-based, such as global patterns of image intensity or gradient occurring regularly within a sample of images taken from a subject population.

Salient points constructing a shape are known as landmarks. Anatomical landmarks are points of correspondence on each shape that match between and within populations [76]. Cootes et al. [77] utilized landmarks in statistical shape models to create Point Distribution Models. This section provides an overview of a statistical model construction based on shape features and can be similarly extended to appearance-based features. Organization of the following section is influenced by a review by Heimann and Meinzer [78], Schmid [12], Stegmann [79] and Dryden [76].

5.1 Shape Model Construction

Shape model construction consists of

• aligning a training dataset,
• applying principal component analysis,
• extracting principal modes of variation, and
• calculating an average shape model with expected shape variability

The calculated average shape and expected variations can be utilized to constraint the model deformation process. The training dataset used for model construction should be in point correspondence, which can be achieved by various methods discussed in section 5.4.

5.2 Alignment

A shape is invariant under similarity transformations of rotation, translation and scaling in 2D space. Alignment is the process of calculating the optimal $m \times m$ rotation matrix $\Gamma$, $m \times 1$ translation vector $T$ and scale parameter $\beta$ to align all training shapes within a common coordinate space. Given a shape $X$ in $m$ dimensions (e.g. $m = 2$) with $n$ points, vectorization of $X$ would be as follows:

$$X = [x_1, x_2, \ldots, x_n, y_1, y_2, \ldots, y_n]^T$$

(16)

The most popular data alignment method is the Procrustes analysis that minimizes the Euclidean mean squared distance between shapes, known as the Procrustes shape distance. The full Procrustes ordinary sum of squares (OSS) distance between two shapes is calculated as

$$OSS(X_1, X_2) = \|X_2 - \beta X_1 \Gamma - 1_k T^T\|^2$$

(17)

Procrustes alignment is the minimization of $OSS(X_1, X_2)$ by removing scaling, translation and rotation effects in the training dataset. To remove the scale $\beta$ between shapes, the centroid size for each shape is calculated as

$$S(X) = \sum_{i=1}^{n} \sqrt{(x_i - \bar{x})^2 + (y_i - \bar{y})^2}$$

(18)
where
\[(\bar{x}, \bar{y}) = \left( \frac{1}{n} \sum_{i=1}^{n} x_i, \frac{1}{n} \sum_{i=1}^{n} y_i \right)\]  \quad (19)

Translation between two shapes can be removed by translating the centroid of one shape onto another. The \(m \times m\) rotation matrix \(\Gamma\) can be represented as
\[\Gamma = UV^T\]  \quad (20)

U and V orthogonal matrices can be obtained by Singular Value Decomposition (SVD) \(^1\) of the matrix
\[X_2^T X_1 = \|X_1\| \|X_2\| V \Lambda U^T\]  \quad (21)

where U and V are rotation matrices that superimpose \(X_2\) onto \(X_1\) and \(\Lambda\) is a diagonal matrix of positive values capturing the correlation between the two shapes. Rotation matrix \(\Gamma\) can then be decomposed as
\[\Gamma = UV^T = \begin{bmatrix} \cos(\theta) & -\sin(\theta) \\ \sin(\theta) & \cos(\theta) \end{bmatrix}\]  \quad (22)

The optimal scaling factor \(\beta\) can be calculated as
\[\beta = \frac{\text{trace}(X_1^T X_2 \Gamma)}{\text{trace}(X_1^T X_1)}\]  \quad (23)

Generalized Procrustes analysis (GPA), developed by Gower [80] iteratively minimizes the generalized sum of squared norms of pairwise differences for two or more training shapes represented by the equation
\[G(X_1, X_2, \cdots, X_n) = \frac{1}{n} \sum_{i=1}^{n} \sum_{j=i+1}^{n} \|X_i - X_j\|^2\]  \quad (24)

where the average centroid size of all shapes is scaled to 1. Each shape \(X_i\) has the Procrustes coordinates
\[X_i^p = \hat{\beta}_i X_i \hat{\Gamma}_i + 1 \hat{T}_i^T, \quad i = 1, \cdots, n\]  \quad (25)

---

\(^1\)SVD of \(V \Lambda U^T\) where columns of \(V\) are eigenvectors of \(A A^T\), columns of \(U\) are eigenvectors of \(A^T A\) and \(\Lambda\) is the diagonal matrix of positive elements corresponding to the eigenvalues of covariance between shapes \(X_1\) and \(X_2\). \(A\) is an \(m \times n\) matrix of \(\mathbb{R}\) or complex numbers. SVD identifies and orders the dimensions along which the shape points have maximum variability.
represented by the minimizing parameters $\hat{\Gamma}_i$ as the rotation matrix, $\hat{\beta}_i$ as the scaling factor and $\hat{T}_i^T$ as the translation vector for shape $i$ calculated using the method described above. Thus, the generalized mean shape can be calculated as

$$\bar{X} = \frac{1}{n} \sum_{i=1}^{n} X_i^P$$

(26)

The GPA algorithm is as follows:

1. Set an arbitrary shape within a population of shapes as the mean shape $\bar{X}$.

2. Calculate the Procrustes coordinates $X_i^P$, where $i = 1 \cdots n - 1$ for remaining shapes w.r.t $\bar{X}$.

3. Set $\bar{X}$ as the Procrustes mean shape according to equation 26.

4. Repeat steps 2 and 3 until sum of squares according to equation 24 cannot be further minimized.

5.3 Shape Decomposition

Variations of shape within a training population can be modeled using Principal Component Analysis (PCA), also known as Karhunen-Loève expansion. Assuming that the training dataset covers a set of closely related shapes, correlation between shape points exists that can be represented by a multivariate Gaussian distribution. As a very large number of shape points need to be analyzed for statistical analysis, PCA is utilized to extract the principal modes, which represent data correlation along principal directions within the dataset, to reduce problem dimensionality. PCA is the process of determining the set of modes that captures the expected geometric variability within the training set. A shape can be mapped onto another shape in a correlated dataset by a linear transformation. Given $N$ number of shapes represented by shape $X$ according to equation 16 with mean represented
by the equation 19, a linear transformation $Y$ of $X$ can be represented as

$$Y = MX$$  \hspace{1cm} (27)$$

where $M$ is an orthogonal transformation matrix \footnote{$M^{-1} = M^T$}, and the shape covariance matrix of $X$ can be represented as

$$\Sigma_X = \frac{1}{N} \sum_{i=1}^{N} (X_i - \bar{X}) (X_i - \bar{X})^T$$ \hspace{1cm} (28)$$

Therefore, the mean of $Y$ can be represented as

$$\bar{Y} = \frac{1}{N} \sum_{i=1}^{N} (Y_i) = \frac{1}{N} \sum_{i=1}^{N} MX_i = M\bar{X}$$ \hspace{1cm} (29)$$

and the covariance of $Y$ can be calculated as

$$\Sigma_Y = \frac{1}{N} \sum_{i=1}^{N} (Y_i - \bar{Y})(Y_i - \bar{Y})^T = M\Sigma_Y M^T$$ \hspace{1cm} (30)$$

substituting transformation matrix $M$ with eigenvectors $\Phi$ \footnote{A scalar $\lambda$ is called an eigenvalue of the matrix $M$ if there is a nontrivial solution $X = 0$ of $MX = \lambda X$. Such an $X$ is called an eigenvector corresponding to the eigenvalue $\lambda$. If $MX = \lambda X$ then transformation of $X = \lambda X$.} and rearranging

$$M^T\Sigma_Y = \Sigma_X M^T$$ \hspace{1cm} (31)$$

$$\Sigma_X \Phi = \Phi \Sigma_Y$$ \hspace{1cm} (32)$$

Therefore, since the covariance matrix of the training shapes $\Sigma_X$ is symmetric, if $\Phi$ represents the eigenvectors of $\Sigma_X$, then covariance of the transformed shapes $\Sigma_Y$ represents the diagonal matrix of eigenvalues $\lambda_i$ belonging to the dataset.

Each eigenvector $\phi_i$ represents the modes of variation within the training dataset, and the corresponding eigenvalue $\lambda_i$ captures the amplitude of variation along the corresponding eigenvector direction, with the largest $\lambda$ corresponding to the largest deformation in corresponding modes. The eigenvalues of $\Phi$ are sorted in descending order such that $\lambda_i > \lambda_{i+1}$ and the largest $t$ eigenvalues and corresponding eigenvectors are kept so that

$$\Phi_t = (\phi_1, \phi_2 \ldots \phi_t)$$ \hspace{1cm} (33)$$
A sample shape $X$ can be approximated as a linear combination of the mean shape and first $t$ modes of variation represented by

$$X = \bar{X} + b_t \Phi_t$$  \hspace{1cm} (34)

where $b_t$ is a $t$-dimensional vector representing modes of variation. Assuming the mean shape $\bar{x}$ is located at the origin, 3 standard deviation of $\lambda_t$ usually captures expected shape variability with a 99.7% confidence interval.

The statistical-shape energy functional can be defined as

$$E_{\text{shape}}(S) = \frac{1}{2}(S - \bar{S})^T \Sigma_{\lambda}^{-1} (S - \bar{S})$$  \hspace{1cm} (35)

where $S$ is the Simplex model, $\bar{S}$ is the mean Simplex shape and $\Sigma_{\lambda}^{-1}$ is the inverse of the regularized covariance matrix.

Statistical shape modeling determines a mean shape and allowed variability within the model as well as construction of new shapes through a combination of the principal modes of variation within the expected shape. This SSM property can be combined with deformable models to constrain a deformation towards an expected shape during the segmentation process in the presence of image noise or artifacts that otherwise hinder object boundary detection. Tejos et al. [13] have combined statistical knowledge with simplex meshes and snakes evolution to segment knee structures. Schmid et al. [15] augment simplex meshes with shape and appearance knowledge for segmentation of MRI musculoskeletal structures with limited field of view or presence of image artifacts. Although shape models can provide robust segmentation with presence of image artifacts and low contrast, their performance is dependent on initialization. Moreover, they only allow deformation already captured within the modes of variation during model construction and do not consider any image information outside the scope of the estimated model shape during deformation.
5.4 Correspondence

Statistical shape model construction through principal component analysis requires point-to-point correspondence between a dataset. It is the process for finding a set of points on one image or shape that can be mapped as the same set of points on another image. Correspondence ensures that each structural boundary consists of identical number of co-registered points. Anatomically meaningful and correct correspondence is of utmost importance, as it ensures correct shape parametrization and shape representation. This can be achieved by co-registering manual landmarks onto the shape boundary in 2D shape space but is challenging in 3D space as it is difficult to identify identical points on 3D surfaces. Manual landmarking is also time consuming and subjective making the process more error-prone.

Correspondence can alternatively be achieved by performing automatic registration between the shapes of the training dataset. The following sections provide an overview of various registration methods utilized for computing correspondence within a training dataset.

5.4.1 Model-to-Model Registration

This registration approach registers two mesh models in a training dataset to achieve one-to-one landmark or point correspondence. One of the best-known algorithms for achieving point-to-point correspondence is the Iterative Closest Point algorithm [81], which is used to minimize the difference between two clouds of points. It iteratively calculates the optimal linear transformations required to minimize the distance between two point datasets. These points may correspond to the vertices in a mesh. This algorithm can be used to achieve correspondence on a set of training shapes by calculating the transformations required to register a reference mesh with the rest of the meshes in the dataset. These transformations
can be applied to map the reference mesh vertices onto the rest of the meshes, resulting in same number of vertices across all meshes. The drawback to this method is the bias introduced by the selection of the reference mesh, despite the use of an average shape for co-registration. In case large variation exists within the shapes, the registration of spatially close points may not produce robust results. Non-rigid registration using as B-Splines [82] for achieving correspondence has been proposed as an alternative to capture large variability in the training dataset.

5.4.2 Model-to-Image Registration

In this registration method, a template mesh is deformed directly to a segmented image volume. This method eliminates the need for pre-segmentation of the shapes for creation of a parameterized mesh but is limited to images that may be reliably segmented using templates, such as images without too much boundary variability. The number of points within each resulting shape would be identical and related to the resolution of the template deformed to the image volume. This method is dependent on the deformable surface model used for template matching.

5.4.3 Image-to-Image Registration

This registration method consists of deformation of a volumetric atlas to the training images. A deformation field is calculated to place landmarks on a mesh extracted from the atlas template. These landmarks are propagated to all training images and utilized for calculating the correspondence between images. Training shapes with high similarity or salient anatomical features would inherently result in better registration resulting in more accurate shape model construction.
5.4.4 Parameterization-to-Parameterization Registration

This registration method aims to achieve point-to-point correspondence by performing a one-to-one mapping of all training shapes onto a common base domain. Landmarks can be placed onto the extracted base domain, which are transferred onto the shapes by performing bijective mapping. As parameterization of 3D shapes is more complex, this method is preferable for 2D shapes without holes that can be represented by a common base domain, such as a sphere. Kelemen et al. [83] propose spherical harmonics (SPHARM) mapping for each training shape to align training shapes to a base domain of a sphere. Accuracy of this method is dependent on the utilization of the base domain.

5.4.5 Population-based Optimization

This registration method is based on the use of optimization approaches to update shape parameterizations based on an optimization criteria. Similar to the parameterization-to-parameterization correspondence approach, all training shapes are abstracted to a basic domain through bijective mapping, which is used to place landmarks onto the training shapes. This method focuses on achieving a robust statistical shape model by targeting a desired sparse set of eigenmodes. This is achieved by minimizing a mapping function based on the determinant of the covariance matrix (DetCov) to optimize the placement of the landmarks on the base domain and consequently modifying the shape correspondence. Davies et al. [84] proposed an improved objective function based on minimum description length (MDL) of the SSM. It provides robust results for shapes with closed surfaces similar to spherical domain but suffers from a complex cost function that is computationally expensive. Interested readers are directed to [78] for further details.
5.5 Statistical Sufficiency

Sufficient data is required to obtain a statistically significant average model with variations of a shape through PCA. The minimum number of training shapes required to stabilize the average shape is dependent on the variation contained within the shape. An evaluation of correspondence methods yields that statistical shape models with good correspondence result in good compactness, good generalization and good model specificity [85].

The quality of shape training determines the final results of segmentation or of predicting a new shape in the statistical population. Jeong et al. [86] propose a correlation measure, goodness of prediction, to evaluate the predictive power of the statistical shape as a function of the training sample size. They perform multivariate linear regression analysis by calculating the ratio of covariance between the test dataset and the training dataset to determine the accuracy with which the statistical shape model (SSM) can predict a new shape. Such goodness of prediction tests can be performed alongside PCA to determine the sufficient number of training shapes required to adequately capture shape variability.

Mei et al. [87] propose selection of principal modes that capture the most structural variance of the training dataset rather than a percentage of the variation. They propose a stability analysis method based on mode directions for an efficient shape dimension selection during PCA and to determine sufficient sample size. Their validation tests conclude that there is no universal sample size guideline for shape model construction due to the inherent variability within anatomical structures.
CHAPTER 6

SEGMENTATION USING WEAK-SHAPE PRIORS

Weak shape priors in Simplex mesh deformable models are exploited to deform an ellipsoidal template mesh for segmentation of an intervertebral disc. In the event that the simplex fails to accurately capture a herniated disc boundary, the user is allowed to manually facilitate the segmentation process by placing constraint points in the image volume. Similarly, ground truth for healthy intervertebral discs and vertebrae has also been generated by implementing this semi-supervised technique, where the user is allowed to manually assist the deformation to correct existing segmentation errors.

The remainder of this chapter discusses the image dataset and image preprocessing steps, followed by the automatic Simplex mesh deformation and optional user-guidance through constraint points in the presence of disc pathology. The data validation technique is presented to quantify the proposed framework’s performance in Section 8.1.

6.1 Testing Image Dataset

Our test and validation dataset consists of MR images of the lumbar spine pertaining to 5 patients with various pathologies, such as herniated discs. 4 intervertebral discs have been identified as degenerated due to vertebral fractures and disc compression and have been discarded from the dataset. Herniated discs are mostly located in the L4-L5 and L5-S1 lumbar region and have been identified in the dataset under expert supervision. T2-weighted MRI scans, acquired on a 1.5T device using spin-echo scanning sequence with repetition time (TR) = 1500 ms, echo time (TE) = 147 ms, flip angle = 150 and number of averages = 2, having a
resolution of $0.5 \times 0.5 \times 0.9\text{mm}^3$ have been utilized for testing and validating the segmentation approach.

Five herniated discs have been manually segmented under expert supervision to be used for quantitative evaluation of the proposed semi-supervised automatic segmentation framework, with results discussed in the Section 8.1.1.

6.2 Data Preprocessing

An anisotropic diffusion [89] filter (conductance = 0.8, timestep = 0.5, iterations = 50) has been applied to the volumetric images to reduce image noise within the structures while preserving image boundaries. The filter mitigates image intensity inhomogeneity located around the disc due to overlapping image intensities around the herniated disc boundary and the surrounding posterior ligament. The Insight Segmentation and Registration Toolkit (ITK) [90] has been utilized for applying image preprocessing filters.

6.3 Intervertebral Disc Segmentation

This section describes the initialization method for segmentation of healthy and pathological lumbar discs in T2-weighted MR images and the segmentation of disc pathology in the proposed research.

6.3.1 Template Initialization through Landmark-based Affine Registration

An ellipsoidal template mesh is initialized within the herniated disc image volume for simplex mesh deformation. Arbitrary translation, rotation and scaling effects need to be captured between the template mesh and MRI image. Six landmarks are manually placed on the ellipsoidal template mesh corresponding to landmarks within the herniated disc image boundary to initialize the template
Fig. 12. Landmark placement on Simplex mesh and disc image boundary. (a) 6 corresponding landmarks placed on the simplex mesh template and disc image boundary. (b) 5 landmarks placed on the disc image boundary visible in the sagittal MR volume plane.

within the herniated disc image through affine registration. These landmarks are placed at the center, as well as the superior, inferior, anterior and posterior points of the disc, as well as one at the center of the superior disc surface to characterize rotation. Figure 12 depicts landmark placement, with 5 landmarks visible in the sagittal plane of an MRI volume in Figure 12.(b).

The global mesh resolution is adapted to the complexity of the anatomical shape being segmented in a coarse-to-fine segmentation approach. Thus, various
simplex mesh resolutions of the template have been generated through a multi-resolution scheme without loss of vertex connectivity for segmentation refinement, as demonstrated in Figure 2.

Template mesh deformation is guided by the presence of MR image gradient forces, resulting in 1-2 minutes of segmentation time per disc or vertebra. The resulting simplex mesh is converted to a dual triangulated surface mesh with resolution control, which in turn is directly input to a tetrahedralization of similar resolution for simulation, as discussed in Section 8.3.

The initialized template mesh is then allowed to automatically deform using a multi-resolution surface model, as described in Chapter 4.

6.3.2 Detection of Pathology

In the event that the internal simplex shape memory influence hinders detection of pathology, as detected via visual inspection, user input is allowed to locally turn off the shape feature and assist model deformation. This assistance is implemented by placing internal and external constraint points on the volumetric image that gracefully constrain the deformation to correct under- and over-segmentation. Constraint point forces are enforced as an addition to the total external force. The number of constraint points applied to the images typically range between 37-60, while requiring 5-7 minutes, depending on the shape of the pathology that the automatic Simplex model deformation may fail to capture. Results of weak shape-prior intervertebral segmentation are discussed in Section 8.1.1.

This semi-supervised segmentation method has also been utilized for manual correction of healthy intervertebral disc segmentation, which serves as ground truth for validation of our healthy disc segmentation results. Similar segmentation evaluation techniques have been employed in literature using manually corrected active shape models for segmentation of anatomical structures [13], [71]. Manual
segmentation is a labor intensive process; each MRI volume consists of about 85-90 image slices in the sagittal plane, with an average segmentation time of approximately 7 hours of manual segmentation time per disc. An anatomist performed manual and semi-supervised segmentation for generation of ground truth verified by a neuroradiologist.

6.4 Vertebrae Segmentation

L1 to L5 vertebrae of 5 patients were segmented in T2-weighted MR images using inherent weak shape-priors in Simplex deformable models. Since the vertebral body resembles a deformed toroidal shape with genus 1, a Simplex template mesh was constructed from the medial axis of the vertebra to accurately represent the anatomical shape of the vertebral structure. This template mesh is then allowed to deform according to external image gradient descent along the normal direction to capture the vertebra MR image boundary.

6.4.1 Medial-axis based Template Construction and Initialization

Medial-axis extraction is the process of reducing dimensionality of the structure without loss of topology. Traditional 3D skeletonization methods, such as binary thinning [91] or level-set based centerline extraction [92] do not guarantee a connected component. This research modifies and augments the skeletonization approach of Hassouna et al. [93] for generating a topologically consistent and connected vertebral 3D medial axis from a binary image, which is subsequently converted into a triangulated and a simplex template mesh.

Hassouna et al. propose the minimum cost path between two medial points as

\[ F(x) = e^{\alpha\lambda(x)}, \alpha \geq 0 \]  

(36)
\[ \lambda(x) = \lambda_1(x) + \lambda_2(x) + \lambda_3(x) \] (37)

\[ \lambda(x) = D(x) + \omega \left( \frac{1.0}{1.0 + \| \nabla \|} + | \nabla \cdot \nabla D(x) | \right) \] (38)

where \( \lambda(x) \) is a medial descriptor function controlling the propagation front of the fast marching method, \( \omega \) is a weight \( < 1 \), and \( \nabla \) is the gradient operator. \( \lambda_1(x) \) is the distance map of the 3D image, describing the minimum distance from the structure boundary and provides a smooth transition during fast marching. \( \lambda_2(x) \) is the medial descriptor function describing the signed, inverted gradient of the distance map. The gradient of the distance map is zero at local maximum, which is the maximum distance from the image boundary describing the medial points of the image. \( \lambda_2(x) \) function is successfully able to identify strong medial points with small gradient values. \( \lambda_3(x) \) is the outward flux medial descriptor function defining the gradient of the distance field. The centerline points of the image are the local image maximum, located inwards towards the center of the image. This image traversal can be described as a fluid mechanics problem, with medial axis points having strong negative divergence and boundary points having strong positive divergence. This research employs Siddiqui et al.'s [94] modification of divergence theorem as an outward flux from the image boundary to a medial point in the image volume center, making \( \nabla \) differentiable.

Using a vertebral image (Figure 13) as input, the distance map \( \lambda_1(x) \) (Figure 14), the gradient of the signed \( D(x) \lambda_2(x) \) (Figure 15), and outward flux \( \lambda_3(x) \) (Figure 16) are calculated respectively. The image is normalized from 0.0 to 1.0 after every medial descriptor function.

Using \( \omega=0.2 \) in equation 6.4.1, the resulting, combined medial descriptor \( \lambda(x) \) of the image is depicted in Figure 17. This signed distance map is then thresholded (threshold = 60) to extract the medial axis subvolume represented by the maximum intensity values in the image. This subvolume is smoothed, and a
Fig. 13. Input vertebra image volume.

Fig. 14. Euclidean distance map $\lambda_1(x)$. 
Fig. 15. Normalized gradient of signed distance map $\lambda_2(x)$.

Fig. 16. Outward Flux $\lambda_3(x)$.

Fig. 17. Resulting $\lambda(x)$. 
The constructed medial axis-based template mesh is initialized within the vertebra MR image volume by placing 9 homologous landmark points on the mesh surface as well as the MR image region of interest. These landmarks are placed on the high curvature points of the vertebra, which are the right and left transverse processes, the spinous process, the superior and anterior articular processes, and on the vertebral body itself. The template mesh is placed within the image volume through affine registration and allowed to deform according to simplex internal and external forces using a multi-resolution scheme, as depicted in Figure 19. Results of the vertebral segmentation using weak-shape priors are discussed in
Fig. 19. Vertebra segmentation refinement using the multi-resolution scheme in Simplex deformable models.

Fig. 20. Placement of landmarks on the vertebra template at high curvature points.

Similarly, an SSM-based average vertebra shape template is placed through affine registration within the vertebra image boundary to initialize segmentation using strong shape-based priors, as depicted in Figure 21. Figure 20 displays the placement of 9 landmarks on the high curvature points of the vertebral template surface, with 8 landmarks visible in the image. This average vertebral template is again allowed to deform according to the simplex and image gradient forces, with an increase in mesh resolution and relaxation of shape priors leading to a refined
Fig. 21. Vertebra template mesh initialization within MR image subvolume through affine registration using 9 homologous landmarks.

segmentation result. Vertebrae segmentation results using strong shape-priors are discussed in Section 8.2.3.
CHAPTER 7

SHAPE STATISTICS-BASED SEGMENTATION

Discectomy procedure simulation requires patient-specific and robust 3D representation of vertebral and intervertebral disc structures, as well as existing pathology, of the lumbar spine. Although lumbar vertebral structures have high variability, the prominent features of the bone are consistent within a sample population. This facilitates the incorporation of a statistical shape model with expected variations into a volumetric image segmentation framework. Low image resolution and image artifacts, such as image noise, make biomedical volumetric image segmentation a challenge. Ambiguous image intensity results in incorrect, or even disconnected, boundary detection of the structure of interest. Prior knowledge, such as expected shape and variance within a sample population, can be incorporated through statistical shape models to optimize the image segmentation process.

7.1 Statistical Shape Model Construction

This section describes a framework for the construction of statistical shape models (SSMs) of lumbar vertebrae and intervertebral discs from CT and MR images respectively of healthy subjects. The generated SSMs are utilized as a reference for knowledge-based priors to optimize segmentation of vertebrae and intervertebral discs in volumetric MR images. These shape models can be incorporated into a controlled-resolution deformable segmentation model of the lumbar spine. Incorporation of strong shape priors would facilitate quantification and analysis of shape variations across healthy subjects. It is aimed as a tool for improving spine segmentation results that can be utilized as part of an anatomical input to an interactive spine surgery training simulator, especially a discectomy procedure. [95].
Statistical shape models from 9 L1 vertebrae, 20 L2-L3 and 20 L4-L5 vertebrae as well as 40 L1 to L5 intervertebral discs have been generated to be utilized as shape priors during spine segmentation from volumetric MR images. Correspondence between instances within each model has been established using entropy-based point placement on the image surfaces [96, 97], which is independent of any reference bias or surface parameterization techniques.

7.1.1 Image Dataset and Preprocessing for SSM Construction

Datasets provided by the SpineWeb Initiative have been utilized for generating shape models of an L1 vertebra and an L1-L2 intervertebral disc. Volumetric CT scans of healthy subjects, along with binary masks, of 10 anonymized patients [98] were used for model construction of L1, coupled L2-L3 and L4-L5 vertebrae. The CT scans and binary masks had a resolution of 0.2 × 0.3 × 1mm³. In addition, 40 expert intervertebral disc segmentations of 8 anonymized patients, with 2.0 × 1.25 × 1.25mm³ resolution [99], were preprocessed as input to the correspondence and shape model construction method.

These binary images were initially aligned along the first principal mode, and any aliasing artifacts were removed during image preprocessing. The fast marching method was applied to generate distance maps of the binary images, which were used for 3D surface reconstruction and establish correspondence between instances of both vertebra and disc shape models.

7.1.2 Correspondence Establishment

Correspondence establishment is the process of finding a set of points on one 2D contour or 3D surface that can be mapped to the same set of points in
another image. Anatomically meaningful and correct correspondences are of utmost importance, as they ensure correct shape parametrization and shape representation. This can be achieved by co-registering manual landmarks onto the shape boundary in 2D shape space but is challenging in 3D space. Anatomical landmarks are points of correspondence on each shape that match within a sample population [76], which may be manually or automatically placed. Correspondence landmarking may entail identifying matching parts between 3D anatomical structures, which is challenging due to inherent variability within geometry or shape of the anatomical structure across a population. [85]. Therefore, landmark placement to establish correspondence for robust statistical analysis is a significant task.

According to Heimann et al. [78], a number of methods for correspondence establishment are feasible, where a generic template mesh is registered onto a set of instances through model-to-model or model-to-image registration to achieve a set of instances with automatic point-to-point correspondences through distance [100]. However, this method introduces a bias through selection of a reference topology [72, 101]. To mitigate the reference bias, Rasoulian et al. [70, 102] utilized forward group-wise registration to establish probabilistic point-to-point correspondences to generate 3D training shapes of L2 vertebrae. Similarly, Mutsvangwa et al. [103] employed rigid and non-rigid registration of pointsets and implemented a probabilistic PCA to mitigate outlier effects of a 3D scapula model. Vrtovec et al. [104] established correspondences through a hierarchical elastic mesh-to-image registration of an extracted reference across 25 lumbar vertebral image volumes. Kaus et al. [105] rigidly aligned a reference triangular mesh to training shapes and then utilized discrete deformable models to locally adapt the reference mesh to segmented volumes, thus propagating the reference pointset across 32 vertebral images. Lorenz et al. [106] performed curvature-adaptive landmark-guided warping and mesh relaxation of a reference mesh across a set of 31 lumbar vertebral image
volumes for 3D statistical model construction. Becker et al. [107] parameterized 14 lumbar vertebral shapes to a rectangle by utilizing a graph embedding method and reduced mesh distortion using energy minimization-based adaptive resampling. Heitz et al. [108] also implemented non-rigid b-spline based warping to construct models of C6 and C7 cervical vertebrae. This list is a reference of 3D vertebral and intervertebral disc statistical shape models and is by no means exhaustive. In contrast, 3D shape variability of intervertebral discs is less explored in the literature. Peloquin et al. [109] constructed a statistical shape model of 12 L3-L4 intervertebral discs from signed distance maps of manually segmented binary images.

This research focuses on the refinement of a correspondence technique introduced by Cates et al. [110, 96] that is independent of structure parameterization or a reference bias. The utilized technique employs a two-stage framework, with soft correspondence establishment in the first stage and correspondence optimization across all instances of the shape space in the second stage. Soft correspondence is established by automatically placing homologous points on the shape surface through an iterative, hierarchical splitting strategy of particles, beginning with a single particle. A 3D surface can be sampled using a discrete set of $N$ points that are considered random variables $Z = (X_1, \ldots, X_N)$ drawn from a probability density function (PDF) $p(X)$. Denoting a specific shape realization of this PDF as $z = (x_1, x_2, \ldots, x_N)$, the amount of information contained in each point is the differential entropy of the PDF function $p(x)$, which is estimated as the logarithm of its expectation $log\{E(p(x))\}$, $E(\cdot)$ estimated by Parzen Windowing. The cost function $C$ becomes
\[ C\{x_1, \ldots, x_N\} = -H(P^i) \]
\[ = \sum_j \log \frac{1}{N(N-1)} \sum_{k \neq j} p(x_j) \]
\[ = \sum_j \log \frac{1}{N(N-1)} \sum_{l \neq j} G(x_j - x_l, \sigma_j) \] (39)

where \( G \) is an isotropic Gaussian kernel with standard deviation \( \sigma_j \). These dynamic particles have repulsive forces that interact within their circle of influence limited through the Gaussian kernel until a steady state is achieved and are constrained to lie on shape surface through gradient descent in the tangent plane.

These correspondences are further optimized by entropy-based energy minimization of particle distribution along gradient descent by balancing the negative entropy of a shape instance with the positive entropy of the entire shape space encompassing all instances (known as an ensemble) [111]. Consider an ensemble \( \epsilon \) consisting of \( M \) surfaces, such as \( \epsilon = (z_1, z_2, \ldots, z_M) \), where points are ordered according to correspondences between these surface pointsets. A surface \( z_k \) can be modeled as an instance of a random variable \( Z \), where the following cost function is minimized:

\[ Q = H(Z) - \sum_k H(P_k) \] (40)

The cost function \( Q \) favors a compact representation of the ensemble and assumes a normal distribution of particles along the shape surface. Hence, \( p(z) \) is modeled parametrically with a Gaussian distribution with covariance \( \Sigma \). This ensemble entropy term can be represented as

\[ H(z) \approx \frac{1}{2} log \| \Sigma \| = \frac{1}{2} \sum_k \lambda_k \] (41)

where \( \lambda_k \) are ensemble covariance eigenvalues. This process optimally repositions
the particles of the shapes within the ensemble to generate robust shape representations with uniformly-distributed particles.

ShapeWorks [112] was used to establish dense correspondences of 16,384 homologous points on 49 lumbar vertebral instances and 4,038 points on 40 L1-L5 intervertebral disc instances. The ensemble shapes were respectively normalized according to centroid-referred coordinates and were further aligned during the correspondence optimization process through iterative Procrustes analysis [80]. Statistical shape models were respectively generated for vertebrae and discs using these point clouds in the manner summarized in Section 5.1.

7.1.3 Statistical Shape-based Simplex Mesh Evolution

Three SSMs of vertebrae were generated as follows:

- an L1 vertebra SSM comprising of 9 vertebral shapes,
- a coupled L2-L3 vertebrae SSM comprising of 20 training shapes, and
- a coupled L4-L5 vertebrae SSM comprising of 20 training shapes.

An intervertebral disc SSM representing shape variations of all five lumbar discs was constructed using 40 disc training shapes. These shape models are further evaluated to determine their statistical sufficiency, and ensure that allowable shape variations within the dataset are efficiently represented. PCA-based forces (Section 5.1 were included as an additional external force in the simplex deformable model, as described in Section 5.3.

A mean shape is initialized within the structure of interest through landmark-based affine registration. A shape closest to the structure boundary is determined by iteratively calculating the optimal transformation and shape variations. Simplex deformation is constrained by allowable variations within the PCA
in the lower resolutions during the initial segmentation stage, leading to a more rigid deformation. This PCA-based shape influence is relaxed in the higher resolution, where the simplex mesh is closer to the image boundary, where the deformation is more influenced by the presence of image-based external forces. This results in robust segmentation of global and local variations within the population, leading to a more refined result capturing structural details present within the MR images.

7.2 Statistical Shape Model Evaluation Metrics

Shape model correspondences and the constructed statistical models may be evaluated through established metrics, such as model compactness, generalization ability, and specificity [85]. A robust statistical model should have low generalization ability, low specificity and high compactness for the same number of modes.

Compactness is the ability of the model to use a minimum number of parameters to faithfully capture shape variance within the dataset. This may be calculated as the cumulative variance captured by the first \( m \) number of modes

\[
C(m) = \sum_{i=1}^{m} \lambda_i
\]

where \( \lambda_i \) is the largest eigenvalue of the \( ith \) mode.

The generalized ability of the statistical model to represent new, unseen instances of a new shape that are not present in the training dataset was evaluated by performing leave-one-out experiments. Vertebra and disc statistical shape models were generated using all training samples except one, which was considered the test sample. This test sample was then reconstructed using the statistical shape model, and the root-mean-square (RMS) distance and Hausdorff distance errors were calculated between the reconstructed sample and the original test sample after rigid registration. This method was repeated over the entire vertebra and disc datasets respectively, to calculate an average and worst measure of error for both
statistical models. Generalization ability \( G(m) \) and its associated standard error \( \sigma_{G(m)} \) can be mathematically represented as

\[
G(m) = \frac{1}{n} \sum_{i=1}^{n} D_i(m) \tag{43}
\]

\[
\sigma_{G(m)} = \frac{\sigma}{\sqrt{n - 1}} \tag{44}
\]

where \( D_i(m) \) is the RMS or Hausdorff distance error between the test sample and the instantiated shape, \( n \) is the number of shapes and \( \sigma \) is the standard deviation of \( G(m) \).

Model specificity is the measure of a model to only instantiate instances that are valid and similar to those in the training dataset. To measure our statistical models’ specificity, \((n - 1)\) instances were randomly generated within \([-3\lambda, +3\lambda]\) using our statistical models and compared to the closest shape in the training dataset. Specificity \( S(m) \) and its standard error have been calculated as

\[
S(m) = \frac{1}{n} \sum_{j=1}^{n} D_j(m) \tag{45}
\]

\[
\sigma_{S(m)} = \frac{\sigma}{\sqrt{n - 1}} \tag{46}
\]

where \( n \) is the number of samples, \( D_i(m) \) is the RMS distance error between a randomly generated instance and its nearest shape within the training dataset. \( \sigma \) is the standard deviation of \( S(m) \).

Evaluation results of the three constructed vertebrae SSMs and intervertebral disc SSM are presented in Section 8.2.1.
CHAPTER 8

RESULTS AND DISCUSSION

Lumbar intervertebral disc and vertebral segmentation results using inherent weak-shape priors and, consequently, strong-shape priors are presented. MeshValmet [113] has been utilized for calculation of quantitative validation metrics. The mean absolute shape distance, MASD, (in mm) and absolute standard deviation of all errors (in mm), absolute mean square distance MSD (in mm), the Hausdorff distance (in mm) and DICE similarity coefficient comparison metrics have been calculated to compare the quality of our segmentation approach with ground truth. The Hausdorff distance is the maximum surface distance between two surface meshes and quantitatively represents a measure of the worst segmentation error. The DICE similarity coefficient compares the similarity between the resulting segmentation and ground truth and has been calculated as 
\[ s = \frac{2|X \cap Y|}{|X| + |Y|} \].

8.1 Segmentation Using Weak-Shape Priors

This section discussed the segmentation results of lumbar vertebrae as well as intervertebral discs using inherent weak-shape priors in Simplex deformable models.

8.1.1 Intervertebral Disc Segmentation

Statistical comparison of 16 automatic segmentations of healthy lumbar intervertebral discs with minimally supervised segmentation results, considered ground truth, is represented in Figure 3. The average absolute mean error of
TABLE 3 Average validation metrics comparing automatic segmentation results with corresponding semi-supervised segmentation of 16 healthy lumbar intervertebral discs

<table>
<thead>
<tr>
<th>Validation Metric</th>
<th>Healthy disc</th>
</tr>
</thead>
<tbody>
<tr>
<td>MASD (mm)</td>
<td>0.321</td>
</tr>
<tr>
<td>Absolute Std. dev. (mm)</td>
<td>0.455</td>
</tr>
<tr>
<td>MSD (mm)</td>
<td>0.342</td>
</tr>
<tr>
<td>Average Hausdorff distance (mm)</td>
<td>3.261</td>
</tr>
<tr>
<td>DICE coefficient</td>
<td>0.954</td>
</tr>
</tbody>
</table>

Fig. 22. Comparison of an automatic L5-S1 healthy disc segmentation result against its corresponding semi-supervised segmentation (ground truth), with -1.16mm max. in, 2.45mm max. out error.
healthy disc segmentation approach is 0.323 mm±0.455mm, with an average Hausdorff distance of 3.26 mm and average DICE score of 0.954. The maximum surface error was generally located at the lateral margins of the intervertebral disc, where the automatic segmentation approach failed to faithfully capture the image boundary due to image intensity ambiguity caused by surrounding spine tissues and ligaments. Figure 22 compares automatic segmentation of a healthy L5-S1 disc with the semi-supervised segmentation result, considered as ground truth. Maximum In error corresponds with maximum under-segmentation error and maximum Out error represents the over-segmentation error. Our automatic weak-shape prior segmentation approach under-segmented the lateral margins with a maximum In error of -2.45 mm and a mean absolute segmentation error of 0.19mm±0.29mm. This result is improved to 0.079mm ± 0.14mm using strong shape-priors for healthy disc segmentation, as discussed in Section 8.2.2.

Herniated Disc Segmentation

Average results of 5 herniated discs comparing semi-supervised segmentation results against manual segmentation have been calculated. Evaluation results have been obtained by calculating the surface to mesh difference between the manual segmentation, considered ground truth, and the simplex model result from our approach of the corresponding intervertebral disc. Our approach demonstrates mean absolute shape distance of 0.61 mm± 0.52 mm of segmentation of 5 herniated intervertebral discs (Table 4). Our results are favorable in comparison with competing 2D segmentation methods of herniated discs and 3D segmentation methods of healthy discs respectively. Michopoulou et al. [114] reported a 2D mean absolute distance of 0.61mm whereas Neubert et al. [115] achieved a 3D segmented Hausdorff distance of 3.55mm for healthy discs in high-resolution 0.34 x 0.34 x 1-1.2 mm³ MR images; in our case, the average Hausdorff distance is
TABLE 4 Average validation metrics comparing semi-supervised segmentation results with corresponding manual segmentation of 5 herniated lumbar intervertebral discs

<table>
<thead>
<tr>
<th>Validation Metric</th>
<th>Herniated disc</th>
</tr>
</thead>
<tbody>
<tr>
<td>MASD (mm)</td>
<td>0.608</td>
</tr>
<tr>
<td>Absolute Std. dev. (mm)</td>
<td>0.518</td>
</tr>
<tr>
<td>MSD (mm)</td>
<td>0.638</td>
</tr>
<tr>
<td>Average Hausdorff distance (mm)</td>
<td>3.485</td>
</tr>
<tr>
<td>DICE coefficient</td>
<td>0.917</td>
</tr>
</tbody>
</table>

3.261mm using weak shape-priors.

Figure 23 shows the spatial distribution of error between initial automatic segmentation using weak shape priors, semi-supervised segmentation result after constraining model deformation and the corresponding manual segmentation of the herniated disc results. Weak shape priors are successfully able to segment the disc with a maximum in error of -3.607mm near the disc pathology, resulting in under-segmentation at the area of disc pathology. This error is reduced to -3.467mm through semi-supervised segmentation of pathology. Figure 24 displays disc pathology with its corresponding segmentation using constraint points in a sagittal MRI slice. As herniated disc anatomy cannot be faithfully captured by prior shape or intensity features, weak shape prior influence is turned off locally and graceful degradation from these priors is allowed in a user-controlled manner, refining the segmentation result. It can be observed that maximum error in our semi-supervised segmentation result is located at the lateral portion of the intervertebral disc. This is likely due to ambiguity in determining the intervertebral disc boundary at the lateral margins of the anatomy during manual segmentation.
Fig. 23. Spatial segmentation error of an L5-S1 herniated disc (a) Comparison of automatic segmentation using weak shape priors against manual segmentation, considered ground truth (-3.607mm max. in, 2.603mm max. out). (b) Comparison of semi-supervised segmentation against its corresponding manual segmentation (-3.467mm max. in, 1.872mm max. out).
Fig. 24. Sagittal MRI slice of a herniated disc with corresponding segmentation and constraint points.

**Inter- and Intra-rater Variability**

Robustness to variability in user supervision and landmark-placed template mesh initialization is demonstrated in a series of experiments where the same anatomist’s results are compared over several initializations, and where two anatomist results are also compared.

Table 5 displays the intra-rater and inter-rater user variability during semi-supervised segmentation of an L5-S1 herniated disc. As demonstrated in Figure 25, intra-rater variability is present at the disc pathology where constraint points were required to correctly segment the herniated part of the anatomy. More variability exists between different anatomists, with a larger mean segmentation error of 0.254mm, present at the lateral margins of the disc as well as the disc pathology, where manual interaction was required.

8.1.2 Vertebrae Segmentation

Table 6 summarizes the segmentation results of L1 to L5 vertebral discs of
(a) Intra-rater herniated disc error

(b) Inter-rater herniated disc error

Fig. 25. Maximum out (red) and maximum in (blue) segmentation error between two sets of herniated disc segmentations performed by (a) the same rater (0.905mm max. in, 1.214mm max. out) and (b) different raters (2.290mm max. in, 2.593mm max out). Over- and under-segmentation is present at the lateral margins and the pathology where constraint points were required to correct segmentation.
TABLE 5 Validation metrics comparing two sets of semi-supervised segmentations of a herniated intervertebral disc performed by the same anatomist and two different anatomists, demonstrating intra-rater and inter-rater variability respectively

<table>
<thead>
<tr>
<th>Validation Metric</th>
<th>Intra-rater</th>
<th>Inter-rater</th>
</tr>
</thead>
<tbody>
<tr>
<td>MASD (mm)</td>
<td>0.050</td>
<td>0.254</td>
</tr>
<tr>
<td>Absolute Std. dev. (mm)</td>
<td>0.062</td>
<td>0.323</td>
</tr>
<tr>
<td>Maximum out error (mm)</td>
<td>-1.214</td>
<td>-2.593</td>
</tr>
<tr>
<td>Maximum in error (mm)</td>
<td>0.905</td>
<td>2.290</td>
</tr>
<tr>
<td>Hausdorff distance (mm)</td>
<td>1.214</td>
<td>2.593</td>
</tr>
</tbody>
</table>

TABLE 6 Average validation metrics comparing 25 lumbar vertebrae automatic segmentation results, using weak shape priors, with corresponding minimally supervised segmentation of patients in MR images

<table>
<thead>
<tr>
<th>Validation Metric</th>
<th>Lumbar Vertebrae</th>
</tr>
</thead>
<tbody>
<tr>
<td>MASD (mm)</td>
<td>0.417</td>
</tr>
<tr>
<td>Absolute Std. dev. (mm)</td>
<td>0.313</td>
</tr>
<tr>
<td>MSD (mm)</td>
<td>0.375</td>
</tr>
<tr>
<td>Avg. Hausdorff distance (mm)</td>
<td>2.863</td>
</tr>
<tr>
<td>DICE coefficient</td>
<td>0.932</td>
</tr>
</tbody>
</table>

the lumbar spine using inherent weak shape priors during segmentation pertaining to 5 patients. The absolute mean standard error is 0.417mm, with an average Hausdorff distance, representing average worst error, is 2.863mm. The average maximum and minimum segmentation errors observed for the remaining 24 vertebral segmentations were -3.22mm to 2.34mm respectively, with an average DICE coefficient of 0.93. This maximum segmentation error was mostly located at the superior or interior processes, or the spinous processes where contiguous vertebral
structure boundaries were present in the image volume. Presence of low image-to-noise ratio and low image contrast of the bones in T-2 weighted MR images likely caused image boundary ambiguity, resulting in over- or under-segmentation of these bone sub-structures.

Figure 26 depicts the worst vertebrae segmentation error encountered during an L3 segmentation, demonstrating the need for strong-shape priors to guide the segmentation result. It can be observed that the maximum In. error, corresponding to under-segmentation, is located at the spinous processes. This is likely due to the ambiguity in vertebral boundary at that image sub-volume, where the spinous process of an L3 vertebra is close to the spinous process of the L2 vertebra located above, with ligaments in between. The model was also unable to capture the lateral margins of the vertebral body, resulting in under-segmentation. The superior articulate process and the lamina were over-segmented, resulting in over-segmentation of maximum Out. error of 4.37mm.

Segmentation of vertebral structures is a challenging task in MR images due to the low image contrast associated with bone in the image modality. Moreover, the thin ligaments surrounding the complex shape of the vertebral body, especially between the processes of the vertebrae, provide low image intensity and gradient change, resulting in image boundary ambiguity. Therefore, strong prior knowledge of the average vertebral shape, with allowed variations, have been incorporated within simplex models to guide and improve the segmentation of these complex structures. Vertebrae results using PCA-based segmentation are described in Section 8.2.3.

8.2 Segmentation using Strong-shape Priors

Statistical Shape models have been incorporated into Simplex deformable models for segmentation refinement. This chapter discusses the evaluation results
Fig. 26. Comparison of an L3 vertebral segmentation using weak shape priors with minimally supervised segmentation (ground truth), with -3.56mm max. In, 4.37mm max Out. This is the worst encountered vertebra segmentation error.

of the three vertebral SSMs and intervertebral disc SSM. Then the segmentation results of the strong shape-based simplex deformable models are presented. A proof of concept of a healthy disc compression is presented to demonstrate application of the multi-resolution segmentation results within a Finite Element Model (FEM) simulation.

8.2.1 Statistical Shape Model Evaluation

This section evaluates the 3 vertebrae statistical shape models and one intervertebral disc SSM incorporated within the segmentation framework by calculating model compactness, generalization ability and specificity validation metrics as described in Section 7.2. Figure 27 illustrates the changes in the shapes along the first three principal modes of variation by $3\sigma$ for the constructed L1 vertebra SSM. The first mode of the shape model mainly captures scaling across the population. The maximum vertebral variability (16mm) is observed at the inferior and superior articular processes and the spinous process. The second and third modes in
Fig. 27. Graphical representation of shape model variability (in mm) captured by the first three principal modes of the L1 vertebra SSM of 10 shapes, viewed from superior. Red corresponds to the maximum outward signed distance (mm) from the mean shape while blue corresponds to the maximum inward signed distance (mm) from the mean shape.

In contrast, the first mode of the intervertebral disc model varies maximally by 7mm. The second principal mode captured stretching in the lateral parts of the disc and the third mode captured rotational effects in the lateral part of the disc respectively.

Figure 28 illustrates the changes in the shapes along the first three principal modes of variation by $3\sigma$ for the combined L2 and L3 vertebra SSM. The
first mode of the model mainly captures scaling of the vertebral body across the L2 and L3 vertebrae training shapes. The maximum vertebral variability (7mm) is observed at the shape and size of the vertebral body, as well as the articular processes. Similar to the L1 vertebra SSM, the second and third modes in the vertebral model capture variation and scaling in the transverse processes and foramen size respectively. Statistical shape models combining two neighboring vertebrae were constructed to exploit the similarity in shape between consecutive vertebrae, as well as to increase the training size.

Fig. 28. Graphical representation of shape model variability (in mm) captured by the first three principal modes of the combined L2 and L3 vertebra SSM of 20 shapes, viewed from inferior. Red corresponds to the maximum outward signed distance (mm) from the mean shape while blue corresponds to the maximum inward signed distance (mm) from the mean shape.

Variation across the first three modes of variation in the combined L4 and
L5 vertebral SSM is depicted in Figure 29. The mean shape represents an average combined shape of the L4 and L5 vertebrae, with variation in the overall thickness and size of the vertebra captured by the first principal mode. The second mode captures variation in size while the third mode captures the thickness of the vertebral processes.

![Graphical representation of shape model variability](image)

**Fig. 29.** Graphical representation of shape model variability (in mm) captured by the first three principal modes of the combined L4 and L5 vertebra SSM of 20 shapes, viewed from superior. Red corresponds to the maximum outward signed distance (mm) from the mean shape while blue corresponds to the maximum inward signed distance (mm) from the mean shape.

The fourth constructed SSM capturing expected mean and variation in all five intervertebral discs of the spine from 40 shapes is depicted in Figure 30. As expected, the first mode captures variation in disc size, specifically in the posterior
shape. The second mode captures size variation and shape change along the ante-
rior portion of the disc. The third mode captures changes in curvature of the disc.

![Graphical representation of shape model variability](image)

Fig. 30. Graphical representation of shape model variability (in mm) captured
by the first three principal modes of the intervertebral disc SSM of 40 shapes,
viewed from superior. Red corresponds to the maximum outward signed distance
(mm) from the mean shape while blue corresponds to the maximum inward signed
distance (mm) from the mean shape.

Figure 31 graphically illustrates the compactness of the four statistical mod-
els as a function of the number of modes required to capture 100% of the variation
across the population. Each principal mode represents a distinct shape variation
amongst the shape population. The L1 vertebra shape model was able to capture
variance within the first 7 principal modes, with 39.45% variance of the captured
by the first principal mode. The combined shape models showed some improve-
ment in compactness, due to the increase in training dataset size. Both combined
vertebrae SSMs were able to capture 95% variability within the first 12 modes. In
contrast, the disc SSM performed much better due to a larger training dataset and captured 95% variability within the first 11 modes, with 42% variation captured by the first mode.

Figures 32, 33, 34 and 35 depict the generalization ability and the specificity of the L1 vertebra, combined L2 and L3 vertebrae, combined L4 and L5 vertebrae, and the intervertebral disc shape models respectively. The generalization ability is the ability of the model to represent unseen shapes, while specificity describes the robustness of the shape model in representing seen instances, such as from within the dataset. Results presented were calculated by performing Leave-one-out analysis using their respective training datasets.

Results of the generalization ability of the constructed models are compared. For the first mode of variation, the average reconstruction error for an unseen instance is for the L1 vertebra model is 0.47mm with a confidence interval of 0.03mm, with an initial Hausdorff distance of 8.2mm. This error converges to 0.4mm with worst mean error of 7.6mm. Our L1 vertebra models cumulative specificity error is 1.43mm in 7 principal modes with negligible standard error. The Hausdorff error for generalization ability of the L2 and L3 model using only the first mode of variation is 0.9mm, which is reduced to 0.58mm after 17 total modes. Similarly, the average Hausdorff distance for representing unseen shapes for the L4 and L5 vertebrae model is initially 8.2mm, reducing to 6.7mm over 17 modes of variation. It can also be noted that although the Generalization ability RMS error for the combined shape models is lower than that of the L1 vertebral model, the combined models are less compact due to higher variability within the training dataset, introduced not only due to larger dataset size but also because it represents variations between the two consecutive vertebrae as well.

Our vertebra model results are similar to those in the literature. Vrtovec et
Fig. 31. Compactness ability of (a) L1 vertebra (b) L2 and L3 vertebrae (c) L4 and L5 vertebrae and (d) Intervertebral disc shape models.
Fig. 32. Generalization ability and Specificity of the L1 vertebra SSM (mm) (a) Generalization (Hausdorff) (b) Generalization (RMS) (c) Specificity (RMS).
Fig. 33. Generalization ability and Specificity of the combined L2 and L3 vertebrae SSM (mm) (a) Generalization (Hausdorff) (b) Generalization (RMS) (c) Specificity (RMS).
Fig. 34. Generalization ability and Specificity of the combined L4 and L5 vertebrae SSM (mm) (a) Generalization (Hausdorff) (b) Generalization (RMS) (c) Specificity (RMS).
Fig. 35. Generalization ability and Specificity of the Intervertebral Disc SSM (mm)
(a) Generalization (Hausdorff) (b) Generalization (RMS) (c) Specificity (RMS).
al. [104] model is more compact, capturing 52% variability within the 1st principal mode. Rasoulian et al. [70] capture $G(m)$ RMS error of 0.95$mm$, with Hausdorff error 9$mm$ within the 1st principal mode, which is decreased to 0.8$mm$ RMS and 7.5$mm$ after 7 modes. Their model is worse in generalization and specificity but outperforms in model compactness (capturing 60% in 1st mode). Kaus et al. [105] reported 1.66$mm$ mean error after 20 modes, with 30% 1st mode compactness, constructed with 32 (L1-L4) vertebral training shapes.

Our intervertebral disc model is able to represent unseen instances with an initial RMS error of 1.4$mm$ and Hausdorff distance of 4.08$mm$, which converges to 0.18$mm$ RMS error and 1.5$mm$ worst error after 35 principal modes.

Overall, the compact model transitions coherently, with a tradeoff between compactness and the ability to faithfully represent new training shapes. Some outliers in the first principal mode can be noted in the variant vertebral shapes. These outliers may be reduced by increasing the size of the population dataset, as well as exploring probabilistic PCA instead of simple PCA, which may better account for any outliers in the model. Moreover, large variability exists between the vertebrae instances, leading to large variability in the shape models itself. An increase in the training dataset would lead to more robust and faithful vertebral shape models better able to represent variability within a population.

8.2.2 Intervertebral Disc Segmentation using SSM

Table 7 shows the validation metrics comparing automatic strong shape-based segmentation results with minimally supervised ground truth of 16 healthy intervertebral discs of the lumbar spine. The average DICE coefficient achieved is 0.979, which is an improvement over 0.95 achieved without SSM incorporation. The absolute mean distance has reduced to 0.79$mm \pm 0.19mm$, with average Hausdorff distance reduced to less than 1 mm.
TABLE 7 Average validation metrics comparing automatic 16 lumbar disc segmentation results, using strong shape-based priors, with corresponding minimally supervised segmentation of patients in MR images

<table>
<thead>
<tr>
<th>Validation Metric</th>
<th>L1-L2</th>
<th>L2-L3</th>
<th>L3-L4</th>
<th>L4-L5</th>
<th>L5-S1</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>M ASD (mm)</td>
<td>1.44</td>
<td>0.44</td>
<td>0.93</td>
<td>0.51</td>
<td>0.64</td>
<td>0.79</td>
</tr>
<tr>
<td>Absolute Std. dev. (mm)</td>
<td>0.229</td>
<td>0.210</td>
<td>0.159</td>
<td>0.087</td>
<td>0.25</td>
<td>0.187</td>
</tr>
<tr>
<td>MSD (mm)</td>
<td>0.53</td>
<td>0.149</td>
<td>0.25</td>
<td>0.76</td>
<td>0.67</td>
<td>0.74</td>
</tr>
<tr>
<td>Avg. Hausdorff distance (mm)</td>
<td>1.63</td>
<td>1.12</td>
<td>1.09</td>
<td>0.984</td>
<td>0.982</td>
<td>0.979</td>
</tr>
<tr>
<td>DICE coefficient</td>
<td>0.77</td>
<td>0.981</td>
<td>0.971</td>
<td>0.984</td>
<td>0.982</td>
<td>0.979</td>
</tr>
</tbody>
</table>

Figure 36 displays the segmentation result of an L3-L4 intervertebral disc within the image volume in sagittal, coronal and axial view respectively. The resulting segmentation is evaluated with the minimally supervised segmentation, which is the manually corrected segmentation considered as ground truth. These segmentation results are depicted in Figure 37, which displays the signed maximum and minimum distance error. The error is located at the lateral margins of the disc with maximum over-segmentation error as 1.08mm, and maximum under-segmentation (maximum In. error) as -0.734mm. PCA-based shape forces are relaxed very close to the image boundary using a high-resolution mesh for segmentation, and image gradient descent is allowed to guide the deformation along the normal direction, so that local shape variation and details of the structure can be accurately captured. Image boundary ambiguity at the lateral margins of the disc may result in over or under estimation of the structure boundary.

Figure 38 displays the segmentation result of an L4-L5 intervertebral disc with maximum over-segmentation as 0.88mm, and maximum under-segmentation of -0.412mm. The maximum Out error can be observed at the anterior margins of
Fig. 36. Segmentation of an L3-L4 intervertebral disc.

Fig. 37. Segmentation evaluation of an L3-L4 intervertebral disc with minimally supervised segmentation, considered ground truth. The disc has a signed distance error of 1.08mm over-segmentation and 0.73mm under-segmentation.

The statistical shape-based segmentation results show significant improvement of results, with reduced error observed at the lateral margins of the disc as compared to results of weak-shape prior segmentation. Our results are comparable with the state of the art, with Mean absolute error as 0.79mm.
Fig. 38. Segmentation evaluation of an L4-L5 intervertebral disc with minimally supervised segmentation, considered ground truth. The disc has a signed distance error of 0.88mm over-segmentation and 0.412mm under-segmentation.

8.2.3 Vertebrae Segmentation using SSM

Strong shape-based segmentation results of lumbar vertebrae of 5 MR images are presented in Table 8. Automatic segmentation results of 25 L1 to L5 vertebrae have been validated against minimally supervised segmentation, considered as ground truth. Our proposed method performs very well, with overall average DICE coefficient of 0.981, with average absolute mean error as 0.685mm ± 0.147mm. The average Hausdorff distance was observed to be 1.18mm. Although the Mean Absolute Shape Distance (MASD) has increased from 0.42mm with SSM incorporation, the overall results demonstrate consistent improvement over results obtained from segmentation using weak-shape priors. The average Hausdorff distance, a measure of the worst error, has reduced from 2.86mm to 1.18mm, with an expected decrease in Mean Square Distance (MSD) error from 0.375mm to 0.297mm.
TABLE 8 Average validation metrics comparing automatic 25 lumbar vertebrae segmentation results, using strong shape-based priors, with corresponding minimally supervised segmentation of patients in MR images

<table>
<thead>
<tr>
<th>Validation Metric</th>
<th>L1</th>
<th>L2</th>
<th>L3</th>
<th>L4</th>
<th>L5</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>MASD (mm)</td>
<td>0.176</td>
<td>1.182</td>
<td>0.72</td>
<td>0.491</td>
<td>0.22</td>
<td>0.685</td>
</tr>
<tr>
<td>Absolute Std. dev. (mm)</td>
<td>0.148</td>
<td>0.054</td>
<td>0.133</td>
<td>0.147</td>
<td>0.254</td>
<td>0.147</td>
</tr>
<tr>
<td>MSD (mm)</td>
<td>0.288</td>
<td>0.486</td>
<td>0.20</td>
<td>0.316</td>
<td>0.19</td>
<td>0.297</td>
</tr>
<tr>
<td>Avg. Hausdorff distance (mm)</td>
<td>1.068</td>
<td>1.162</td>
<td>1.629</td>
<td>1.189</td>
<td>0.863</td>
<td>1.182</td>
</tr>
<tr>
<td>DICE coefficient</td>
<td>0.984</td>
<td>0.989</td>
<td>0.978</td>
<td>0.976</td>
<td>0.981</td>
<td>0.982</td>
</tr>
</tbody>
</table>

Figure 39 displays the segmentation result of an L3 vertebra. The maximum over-segmentation error (1.62mm) can be observed at the superior articular process, with some over segmentation of the spinous process. Our method under-segmented the vertebra spine by 0.843mm. Figure 40 displays the segmentation result of an L2 vertebra. It can be observed that our model slightly over-segmented the structure, with maximum Out error (0.48mm) and maximum In error (-1.01mm) observed at the superior and interior articular processes. Similar to the observation of the weak prior shape-based segmentation results, most error lies at the articular and spinous processes of the vertebrae, where there may be image intensity ambiguity due to low image contrast between contiguous anatomical structures or ligaments surrounding the vertebral body.

Contiguous vertebrae and disc structures were segmented with collision detection to mitigate any resulting mesh overlap. Figure 41 displays the segmentation of the lumbar vertebral and intervertebral structures of one of the testing MR datasets. Figure 42 displays segmentation in axial view of the vertebrae and intervertebral discs of the lumbar spine. It displays the segmentation of contiguous
Fig. 39. Segmentation validation of an L3 vertebra with ground truth segmentation. Maximum over-segmentation error is 1.62mm, and maximum under-segmentation error is -0.84mm.

Fig. 40. Segmentation validation of an L2 vertebra with ground truth segmentation. Maximum over-segmentation error is 0.47mm, and maximum under-segmentation error is -1.01mm.
Fig. 41. Segmentation results of vertebrae and intervertebral discs of the lumbar spine.

structures across a slice in the image volume, with a segmented L4-L5 intervertebral disc, the superior articular process of L5 vertebra (red), and interior articular processes of the L4 vertebra located above (in blue).

The segmented intervertebral disc surfaces were treated as hard bodies during vertebrae segmentation, such that the surface points of the intervertebral discs were considered as a repelling external force for the deforming vertebral simplex mesh. Collision handling forces were activated during the high resolution segmentation scheme when the deforming vertebral mesh was close enough to the vertebral image boundary and the contiguous intervertebral disc boundaries. Figure 43
Fig. 42. Segmentation in axial view of the vertebrae and intervertebral discs. Contiguous structures segmented across a slice in the image volume, with a segmented L4-L5 intervertebral disc, the superior articular process of L5 vertebra (red), and interior articular processes of the L4 vertebra located above (blue).

displays the signed surface distance between an L2-L3 vertebra and an L2 vertebra without collision handling forces activated during segmentation, and with collision detection. Meshes are considered to be contiguous and non-overlapping at distance 0.0mm. There was surface inter-penetration, indicating over-segmentation, of 0.47mm, which was reduced to $0.2 \times 10^{-4}$, resulting in non-overlapping surface meshes.
Fig. 43. Signed surface distance (a) between an L2-L3 disc and an L2 vertebra before collision handling; there is maximum inter-penetration of 0.47mm. (b) from L2 vertebra to L2-L3 disc after collision handling, (c) from L2 vertebra to L2-L3 disc
Most vertebrae results without collision handling resulted in over-segmentation between 0.1mm to 0.5mm, with few under-segmented results. However, in case the surface overlap was over 0.5mm, collision detection at high resolution was less efficient. Figure 44 shows signed surface distance between an L4-L5 intervertebral disc and an L4 vertebra, with the vertebral mesh segmented with and without collision handling. The vertebra is over-segmented by 0.8mm, which is reduced to 0.36mm after segmentation with collision detection. The location of the remaining surface overlap is indicated on the L4-L5 intervertebral disc surface in Figure 44.(b) by identifying surface area where the signed distance map is below 0.0mm.

Incorporation of strong shape-based priors in Simplex deformable models provided much accurate results, reducing the average Hausdorff distance error, which is a measure of the maximum error, to less than 1.5 mm for both vertebrae as well as intervertebral disc segmentation. A significant improvement in performance accuracy was achieved by utilizing Statistical Shape Models for vertebrae segmentation, where the DICE coefficient increased from 0.93 to 0.98. This is an improvement to current segmentation techniques, where the lowest obtained DICE coefficient value of 0.935 is presented by Vrtovec et al. [116]. However, segmentation results of the proposed method cannot be directly compared with current literature as they were validated on different training and testing datasets.

### 8.3 Healthy Intervertebral Disc Compression Simulation

Simulation Open Framework Architecture (SOFA) [117] is an open-source object-oriented software toolkit that is targeted towards real-time interactive medical simulations. Several components of a model can be combined in hierarchies through an easy-to-use scene file format to represent various model parameters.
Fig. 44. (a) Signed surface distance between an L4-L5 vertebra and an L4 vertebra before collision handling; there is maximum inter-penetration of 0.8mm. (b) Signed surface distance from L4 vertebra to L4-L5 disc after collision handling, reduced to 0.36. Area with surface distance below 0, identifying remaining mesh overlap, is highlighted.
such as material properties, deformable behavior, constraints and boundary conditions, which makes SOFA a very powerful and efficient prototyping tool. The following section describes a SOFA-based deformation application using the disc surface mesh based on an FEM model.

A healthy lumbar intervertebral disc has been modeled using SOFA to simulate the biomechanical and physiological changes of the disc under compression. The tetrahedral mesh of the healthy L2-L3 disc has been generated from the segmented surface mesh using the isosurface stuffing method [118]. This volumetric mesh has been used to define the tetrahedral corotational finite element model of the disc, depicted in Figure 45.(a), which corresponds to the Behavior Model¹ of the deformable object. The boundary conditions and external compression forces have been defined through the segmented surface mesh, which is linked to the underlying Behavior Model of the deformable object (Figure 45.(b)). Following the actual anatomy of the simulated intervertebral disc, the bottom nodes that are in direct contact with the below rigid vertebral body have been constrained to be fixed to their initial locations, and a prescribed vertical pressure of $100\,N/cm^2$ has been applied to the top surface of the disc using SOFA's TrianglePressureForceField² component.

In the simulation phase, we have assumed a uniform isotropic material model for representing the intervertebral disc. Our intervertebral disc biomechanical properties are consistent with values published by Malandrino et al. [119] and Spilker [120]. Using these studies, we have chosen Poisson's ratio to be 0.4 and Young's modulus to be $15800\,Pa$, representing the ratio of disc model expansion versus compression and the stiffness of the elastic model respectively. The effect of the compression force on the disc has been captured in terms of the relative displacement of the surfaces of the original and deformed configurations (Figure

²http://www.sofa-framework.org/classes?show=Triangle-PressureForceField
Fig. 45. 3D simulation of a healthy intervertebral disc under pressure. (a) Tetrahedral FEM. (b) *Behavioral Model*: The bottom nodes (red) are constrained to be fixed and the Neumann boundary condition is applied to the top surface (green) of the disc model. (c) *Visual Model*: Comparison of the disc model at rest (red) and deformed (green) configurations.
45.(c)), where the uncompressed disc is depicted in red and the compressed configuration in green. The simulation results in a slightly bulging disc.

This implementation is intended as a proof of concept to demonstrate use of segmentation results to initiate a patient-specific simulation in SOFA, such that an interactive response is feasible. Meanwhile, competing spine modeling methods emphasize dense tetrahedral decomposition and onerous finite element computations that preclude an interactive response. In particular, our controlled-resolution modeling technique can produce a coarse triangular surface for constraining a coarse tetrahedralization for a *Behavior Model*, a medium-resolution surface mesh for a *Collision Model*, and a fine-resolution surface mesh for a *Visual Model*, all running on SOFA and mapped to each other.
CHAPTER 9

CONCLUSION

Surgery and biomechanical simulations require patient-specific, high fidelity and robust 3D segmentation of vertebral and intervertebral disc structures, and existing pathology, of the lumbar spine. This thesis describes a framework for segmentation of lumbar vertebrae and discs from T2-weighted MR images of the spine. Our segmentation approach is based on Simplex discrete deformable models.

This research initially exploits weak shape priors inherent in simplex deformable models for segmentation. An ellipsoid template mesh and a medial-axis based template is initialized within the disc and vertebra volume image respectively using landmark-based affine registration. This template is allowed to deform according to Simplex internal and external forces. In case the Simplex mesh fails to capture image boundary in existence of disc pathology, weak shape priors are degraded gracefully and the user is allowed to guide mesh deformation by placing constraint points on the image volume. This minimally supervised segmentation method has also utilized for generating ground truth used for validation of our test results. Segmentation results using weak shape priors pertaining to 5 patients yield DICE coefficients of 0.93 for vertebrae and 0.95 for intervertebral discs. Our method demonstrates the ability to successfully segment disc pathology, based on minimally supervised, spatially variable weighting of shape prior information. Vertebral segmentation in MR images posed a challenge due to low image contrast for bone in MR images, as well as presence of image artifacts, thus requiring incorporation of strong shape priors in Simplex models.

Statistical shape models of vertebrae and disc were generated using training data of 10 and 8 patient datasets receptively. Three SSMs of vertebrae: an L1
vertebral SSM, a coupled L2 and L3 vertebral SSM, and a coupled L4 and L5 vertebral SSM were constructed. An intervertebral disc SSM was generated using 40 training shapes. These vertebrae and disc SSMs were shown to faithfully capture variance within a population with few particle outliers, capturing 95% of variability within the first 12 modes of variation.

Strong shape priors incorporated in our deformable model have been utilized for resegmentation of MR image testing dataset. PCA-based average shapes were initialized within the structure volume boundary through landmark-based affine registration using a multi-resolution scheme. The shape model was set as a template mesh that was allowed to deform and capture the image boundary while constraining the mesh according to expected variation. The PCA shape influence was relaxed with increase in mesh resolution for result refinement. The proposed strong shape-based deformation method results in robust segmentation with DICE coefficient of 0.979 for intervertebral discs and 0.981 for vertebrae. We also exploit controlled-resolution meshing conducive to a multi-resolution approach to segmentation as well as producing anatomical models with low element count for interactive simulation.

Evaluation of the proposed framework can be improved by increasing the size of the training dataset utilized for generation of vertebral and intervertebral SSMs. Images of diseased or degenerated vertebrae, such as compressed vertebrae or vertebral fractures that may occur due to osteoporosis, may be included during SSM construction to increase captured variation within the population. Incorporation of intensity based features, such as statistical appearance models along with statistical shape models to classify intensity variation between a healthy and herniated disc image may assist with identification of disc pathology.

This research performs localization of the vertebrae and intervertebral discs
within the volume image through landmark-based affine registration. This localization is limited by, and dependent on, manual input from the user through placement of landmarks on the initialized template, as well as the volume image. This user interaction can be eliminated by introducing an automated disc and vertebrae localization scheme that identifies the position of the vertebrae and intervertebral discs, which can be further used to initialize segmentation. Moreover, the proposed framework is limited by manual interaction for segmentation refinement in case disc pathology cannot be faithfully captured.

An alternate approach to generation of statistical shape models could be a hierarchical shape model approach, where one SSM of all lumbar vertebrae, as presented by Rasoulian et al. [121], can be utilized to capture vertebral global pose and shape of the entire spine during low-resolution segmentation, and individual SSMs corresponding to each vertebrae can be used at higher resolutions to capture local shape variation. However, a large training dataset is required for such implementation that was not available at the time of the proposed framework.

While there are similarities between our work and related research, our work features innovations essential to the development of an interactive spine surgery simulator, as well as a biomechanical FEM model. First, the proposed anatomical modeling enables a trade-off between shape priors and limited user supervision near the pathology of interest to the simulation. Second, our approach specifically emphasizes resolution control with the final simplex surface mesh, which leads to a controlled-resolution triangulated mesh by duality; moreover the latter controlled-resolution triangulated mesh in turn leads to a like-resolution tetrahedral mesh bounded by it. Both aspects of the meshing are essential to the low element count needed for an interactive virtual tissue response.
BIBLIOGRAPHY


    http://www.fizyoterapistim.net/icerik/lumbar-bolge.


    tourism/procedures/spine-surgery/slipped-herniated-disc-surgery/.

    Segmentation Techniques*, Biomedical Engineering. 2009.

[23] M. I. Sezan. A peak detection algorithm and its application to histogram-
    based image data reduction. *Computer Vision, Graphics, and Image Processing*,


    1978.

[27] Oivind Due Trier and Torfinn Taxt. Evaluation of binarization methods for


[29] K. V. Mardia and T. J. Hainsworth. A spatial thresholding method for im-


[31] Oliver Wirjadi. Survey of 3d image segmentation techniques. Technical Re-

and quantitative performance evaluation. *Journal of Electronic Imaging*,


[35] Klaus D. Yoennies. *Guide to Medical Image Analysis: Methods and Algo-


[113] Meshvalnet: Validation metric for meshes.


VITA

Rabia Haq
Department of Modeling and Simulation
Old Dominion University
Norfolk, VA 23529

Educational Background
M.S. December 2008, Old Dominion University, Norfolk, VA
Major: Computer Science

Publications


Typeset using \LaTeX.