

SHAPE DEFORMATION STATISTICS AND REGIONAL TEXTURE-BASED  
APPEARANCE MODELS FOR SEGMENTATION

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## **ABSTRACT**

**JARED VICORY: Shape Deformation Statistics and Regional Texture-Based Appearance Models for Segmentation.**

(Under the direction of Stephen M. Pizer)

Transferring identified regions of interest (ROIs) from planning-time MRI images to the trans-rectal ultrasound (TRUS) images used to guide prostate biopsy is difficult because of the large difference in appearance between the two modalities as well as the deformation of the prostate's shape caused by the TRUS transducer. This dissertation describes methods for addressing these difficulties by both estimating a patient's prostate shape after the transducer is applied and then locating it in the TRUS image using skeletal models (s-reps) of prostate shapes.

First, I introduce a geometrically-based method for interpolating discretely sampled s-reps into continuous objects. This interpolation is important for many tasks involving s-reps, including fitting them to new objects as well as the later applications described in this dissertation. This method is shown to be accurate for ellipsoids where an analytical solution is known.

Next, I create a method for estimating a probability distribution on the difference between two shapes. Because s-reps live in a high-dimensional curved space, I use Principal Nested Spheres (PNS) to transform these representations to instead live in a flat space where standard techniques can be applied. This method is shown effective both on synthetic data as well as for modeling the deformation caused by the TRUS transducer to the prostate.

In cases where appearance is described via a large number of parameters, such as intensity combined with multiple texture features, it is computationally beneficial to be able to turn these large tuples of descriptors into a scalar value. Using the inherent localization properties of s-reps, I develop a method for using regionally-trained classifiers to turn appearance tuples into the probability that the appearance tuple in question came from inside the prostate boundary. This

method is shown to be able to accurately discern inside appearances from outside appearances over a large majority of the prostate boundary.

Finally, I combine these techniques into a deformable model-based segmentation framework to segment the prostate in TRUS. By applying the learned mean deformation to a patient's prostate and then deforming it so that voxels with high probability of coming from the prostate's interior are also in the model's interior, I am able to generate prostate segmentations which are comparable to state of the art methods.

*To my friends and family.*

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## LIST OF ABBREVIATIONS

<b>CPNS</b>	Composite Principal Nested Spheres
<b>DSC</b>	Dice Similarity Coefficient
<b>DWD</b>	Distance-weighted Discrimination
<b>GPCA</b>	Geodesic Principal Component Analysis
<b>LDDMM</b>	Large Deformation Diffeomorphic Metric Mapping
<b>MAD</b>	Mean Absolute Distance
<b>MRI</b>	Magnetic Resonance Imaging
<b>MSE</b>	Mean Squared Error
<b>PCA</b>	Principal Component Analysis
<b>PDM</b>	Point Distribution Model
<b>PGA</b>	Principal Geodesic Analysis
<b>PNS</b>	Principal Nested Spheres
<b>ROI</b>	Region of Interest
<b>S-rep</b>	Skeletal Representation
<b>SVM</b>	Support Vector Machine
<b>TPS</b>	Thin Plate Spline
<b>TRUS</b>	Trans-rectal Ultrasound

# 1 INTRODUCTION

The driving problem for the work in this dissertation is segmentation of the prostate in 3D trans-rectal ultrasound (TRUS) during an image-guided biopsy procedure. The main task is to identify the prostate and certain regions of interest (ROIs) identified during pre-biopsy planning. This problem presents several challenges, including

1. Low contrast between the prostate and surrounding tissue
2. High noise and noise-like (speckle) artifacts present in ultrasound
3. Highly varying appearance around the prostate boundary
4. Deformation of the prostate caused by the TRUS transducer

The first three items combine to make segmentation of the prostate challenging using standard techniques which may work well in other imaging modalities. The fourth makes using prior knowledge of the shape of a particular patient's prostate gained during planning difficult as well as locating corresponding regions of the prostate post-deformation.

I argue that a method designed to solve this driving problem needs

1. A model of shape that supports
  - identification of corresponding local regions across multiple cases
  - continuous representation of both the boundary and interior of the prostate
2. An appearance model that
  - is defined locally rather than globally

- uses features suitable for analysis of ultrasound appearance, especially texture

### 3. Statistical analysis of the differences between pairs of shapes

This dissertation describes novel methodological contributions in each of these areas. The following sections further develop the driving problem and the intuition behind each of the items listed above.

## **1.1 Image-guided Prostate Biopsy**

Prostate cancer is the most commonly diagnosed cancer among adult men (excluding basal cell carcinoma) and is the second leading cause of cancer death among men in the United States [1]. Early diagnosis is important for improving survivability of prostate cancer. The standard method for obtaining this diagnosis is through a TRUS-guided biopsy of the suspected cancer.

Often, the ROIs for the biopsy procedure are identified on an MRI of the pelvis. On MRI there is typically good contrast in the soft tissue and relatively easy detection of ROIs. During the biopsy procedure the available TRUS images are of very different appearance and quality than the planning MRIs, making accurate identification of the ROIs difficult. Compounding this problem is the fact that the TRUS transducer puts pressure on and deforms the prostate, causing it to have a different shape compared to planning-time. These factors make TRUS-guided biopsy error-prone and can lead to missing a significant fraction of cancers. In order to improve the accuracy of the biopsy procedure, it is important to be able to accurately identify not only the prostate boundary in TRUS but also regions of the prostate which correspond with MRI-identified ROIs.

A team led by Dr. Aaron Fenster at the Robarts Research Institute at Western University has developed a system which allows for segmentation of the prostate from TRUS and registration with a planning MR image to identify biopsy targets. They have shown that, when done correctly, this approach can reduce the number of needle insertions needed to accurately diagnose prostate cancer by up to half [2].

## 1.2 Segmentation of the Prostate from TRUS

Segmentation of the prostate in TRUS is most effectively done by analyzing the texture of the image, whether on a global or local scale. Many of these methods also include some type of shape prior in order to keep the segmented shape regular. Point distribution models (PDMs) [3] are commonly used in shape-informed segmentation methods for the prostate as well as many other organs throughout the body. These methods will often learn statistics on a population of PDMs using principal component analysis (PCA) and restrict the set of candidate shapes to the space of shapes spanned by some number of eigenmodes of this learned distribution.

PDMs have several useful properties, including ease of model creation, simplicity of representation, and straightforwardness of various computations involving their representation. The geometry captured by PDMs, however, is somewhat limited, particularly when restricted to boundary points only (as is often the case). Boundary PDMs capture only  $0^{th}$ -order information about the object’s surface explicitly and thus lack higher-order information such as boundary normal directions or surface curvatures. These can be estimated if the surface has connectivity information, but the accuracy will be limited by the sample density. Boundary PDMs also do not explicitly model the object interior, which is important for applications needing corresponding locations in the object’s interior.

## 1.3 Skeletal Representations

Skeletal representations model an object via a skeletal locus running through the interior of an object and a non-crossing vector field defined on this skeleton and pointing to the object’s boundary. Discrete skeletal representations, called *s-reps*, consist of samples of the interior skeleton, either two (interior samples) or three (exterior samples) vectors called *spokes* anchored at the skeleton and pointing towards the boundary, and corresponding spoke lengths giving the distance from the skeleton to the object boundary along each spoke [4]. Compared to boundary PDMs, this representation offers several advantages. Most importantly, s-reps model the entire object interior as opposed to just the boundary and include directional ( $1^{st}$  order) information in addition to purely

position information about the object’s surface. This representation has been shown to be superior to boundary PDMs for uses such as classification [5] and estimating object correspondences. [6].

Due to the non-Euclidean nature of most of an s-rep’s features, standard Euclidean statistical methods such as PCA are not directly applicable to s-reps. Instead, an alternative approach called *Euclideanization* is used to turn these non-Euclidean features into Euclidean ones to which standard methods can then be applied. This Euclideanization of the sphere-resident features is done via principal nested spheres (PNS), which analyzes the s-rep features on the abstract spheres they naturally live on. Performing PCA on these Euclideanized features yields an s-rep shape space which can be used for segmentation as described previously.

#### **1.4 Statistics on Shape Differences**

As mentioned previously, the TRUS transducer causes the shape of the prostate to deform from what is observed on the planning MRI. In segmenting the prostate from TRUS, I wish to leverage information learned from a patient’s MRI. For this, it is not enough to simply learn a distribution of shapes of the prostate post deformation; we must also learn how the transducer causes the prostate to deform.

Given an MRI/TRUS image pair for a specific patient and manual segmentations of the prostate, I can learn the transducer-induced deformation by fitting consistent s-reps to both segmentations and computing a deformation from the MRI to the TRUS models. Given a population of such pairs, a probability distribution of these shape changes can be learned. To do this in a meaningful way, both the deformations and the probability distribution must be computed while keeping the non-Euclidean nature of s-reps in mind.

In Euclidean space, differences between two points are easily computed by simple subtraction, and probability distributions of these differences can again be estimated via PCA after translation to the origin. For objects which live on a curved manifold, this procedure becomes less well-defined. The difference between two points on a manifold is generally computed as a geodesic along the surface between these two points, but depending on the manifold these geodesics can be

difficult and expensive to compute. Moreover, given a population of geodesics on the manifold, they must first be transported to a common starting point before they can be compared, a far from trivial task except in spaces where a closed-form solution is known.

Instead, because the exact structure of the manifold s-reps live on is known and there are statistical methods capable of analyzing them directly on this manifold, I again apply the Euclideanization idea to computing the difference between two s-reps. Taking the pooled group of MRI and TRUS prostate models, I compute PNS and thus a common polar system for Euclideanization. Then, the Euclideanized s-reps can be directly analyzed in Euclidean space as described previously, yielding a mean deformation and modes of deformation variation.

Given a new patient’s manually segmented MRI, I can apply this mean deformation to yield a patient-specific initialization for the prostate’s shape in the TRUS image and deform it over these modes of deformation variation to better match the image using some model of the prostate’s appearance in TRUS.

### **1.5 Appearance via Regional Texture Classifiers**

Analyzing the appearance of an organ in ultrasound imaging is a difficult task. Relying on intensity information alone is unsatisfying because of issues of low contrast between neighboring organs as well as the noise-like speckle artifacts found in ultrasound images. Instead, texture features are often used to model the appearance of the prostate in TRUS images. Gabor filters, either 2D or 3D, are a common choice for this task. I compute texture using 48 oriented Gabor features which, together with the smoothed image intensity, yields a 49-tuple of appearance information at each image voxel.

However, this texture cannot be learned globally, as the texture of the areas surrounding the prostate boundary vary widely around the object. Instead, I learn texture on a local scale. The s-rep provides a natural method of defining local regions around the boundary of an object using the spoke ends as landmarks, as the s-rep fitting process ensures reasonable correspondence over a population of objects. By learning separate texture profiles on each s-rep spoke, I can be more



robust to the changes in TRUS appearance around the prostate than methods which model texture globally or using large regions of the image.

I learn these local texture profiles by, about each spoke, pooling texture features from just inside and just outside the prostate boundary into two classes and training a classifier to distinguish between them. For a new case to be segmented, we apply these classifiers to the voxels near the boundary of a candidate object and optimize the model so that more likely inside voxels are inside the boundary and vice versa.

## **1.6 Interpolation of Discrete S-reps**

For many applications, including the segmentation problem here, it is desirable to have a more finely sampled s-rep than the base model. This is desirable for fitting an s-rep to an object. It is also used for representing an object in terms of object-relative coordinates, which is an important component for producing regional appearance models for segmentation. These objectives require the development of a method for continuously interpolating a discrete s-rep. Building on the calculus of skeletal models, I develop a geometry-based method for interpolating an s-rep into a continuous object while maintaining its useful geometric properties.

## **1.7 Thesis & Contributions**

*Thesis: Segmentation of an object deformed from a base state in a systematic way with appearance that varies around its boundary benefits from combining the following two approaches:*

- 1. Statistical analysis of the object deformation by a method suited for analysis in curved spaces*
- 2. Regionally trained appearance models to distinguish voxels inside and outside of the object's boundary.*

*Instead of the more typical boundary-based approach, continuously interpolated skeletal models form a strong basis for the training of statistics of object deformation as well as the creation of object-relative regions on which to train appearance models.*

The major methodological contributions of this dissertation are as follows:

1. A geometric interpolation method for computing continuous skeletal models from discrete s-rep models.
2. A method for computing a probability distribution of differences between pairs of shapes which leverages the non-Euclidean nature of shape and shape representations.
3. A novel appearance model which leverages the ability of the s-rep to produce corresponding local regions around an object to define local classifiers of image texture.
4. The application of the aforementioned techniques in a deformable model-based segmentation method for segmenting the prostate from TRUS.

In addition to these, I have also accomplished the following engineering contributions:

1. Implementation in Pablo, the main piece of software used to fit and visualize s-reps, of code allowing optimization over a shape space defined by CPNS
2. Implementation in Pablo of spoke interpolation in both the display and fitting of s-reps
3. Implementation of code to compute and optimize over spaces of shape differences
4. Implementation to compute regional classifiers of inside/outside boundary appearance features and computation of images of probability of being inside and object
5. Implementation in Pablo of code allowing optimization of a model to best fit a probability image, including both optimization over a global shape space and local refinements
6. Numerous bug fixes and improvements to Pablo

The rest of this dissertation is laid out as follows. Chapter 2 gives background information necessary to fully understand the following chapters, chapter 3 details and evaluates the s-rep spoke interpolation method, chapter 4 describes and evaluates the method by which I compute probability distributions of shape differences, chapter 5 describes and evaluates the s-rep-based regional

appearance model, chapter 6 describes the segmentation framework as applied to TRUS prostate segmentation with an evaluation that emphasizes the statistical frameworks developed in the earlier chapters, and chapter 7 contains concluding thoughts and discussion.

## 2 BACKGROUND

This section covers information which is common background information for each of the following chapters. Background information specific to only one chapter can be found there.

### 2.1 Object Representations

#### 2.1.1 Point Distribution Models

Point distribution models (PDMs) are shape models which are a collection of points which are in corresponding locations on each object of a population. Though they are often formed using only boundary points, they are not restricted to be so. There are several methods for producing PDMs from a set of objects, including manual placement of landmarks, automatic generation of corresponding points such as SPHARM-PDM [7], and methods for optimizing the correspondence of existing models such as the entropy-based method of Cates [8].

#### 2.1.2 Skeletal Representations

The s-rep is a quasi-medial skeletal model that models not only an objects boundary but its interior as well. The s-rep is a collection of points sampled from a skeleton of an object which have associated non-crossing vectors called spokes pointing from the skeleton to the objects boundary. S-reps attempt to be as close to medial as possible while remaining non-branching and require the spokes to touch the object boundary and be nearly orthogonal to it. These samples can then be interpolated via the method described in chapter 3 to produce a continuous representation of an objects boundary and interior. This provides an object-relative coordinate system  $(u, v, \tau)$  for the objects volume, where  $(u, v)$  parameterizes the skeleton and  $\tau$  moves from the skeleton ( $\tau = 0$ ) to the boundary ( $\tau = 1$ ).

S-reps are fit to an object via an optimization which tries to match the s-rep's implied boundary to an object while remaining as medial as possible. Current s-rep fitting is initialized via warping

a template model into an individual case via a thin plate spline (TPS) interpolation of the boundary correspondences of the template object and the target object followed by an optimization which more closely matches the spokes to the object's boundary. For producing these correspondences, I use the thin shell demons [9] method to register a reference PDM to a target PDM and use the implied correspondences to fuel the TPS warping.

In the past several years, s-reps have been shown to be powerful and in most cases superior to PDMs for a variety of statistical tasks, including hypothesis testing [10], classification [5], and producing corresponding objects [6].

## 2.2 Statistical Methods

### 2.2.1 Principal Component Analysis

Principal component analysis (PCA) is an important statistical procedure designed to be used for probability distribution estimation and dimensionality reduction of Euclidean data. The result of PCA on data of dimension  $d$  can be understood as the fitting of a  $d$ -dimensional Gaussian distribution to the data.

PCA can operate in either a forward or backward manner, the results of which are equivalent for Euclidean data. In the typical forward approach, the first step is to compute the mean of the data, which is the best fitting linear subspace of dimension 0. The line through the mean which minimizes the sum of the squared projections of each data point to the line, the best-fitting subspace of dimension 1, is called the first principal component. Next, the plane containing the first principal component which minimizes the projection error is computed. The vector contained by this plane which is orthogonal to the first principal component is the second principal component. This procedure of fitting the best-fitting linear subspace of successively increasing dimension is repeated  $d$  times.

Instead of this approach which builds a set of best-fitting subspaces of increasing dimension, an alternative method [11] is to start by fitting the best-fitting  $d - 1$  dimensional subspace (with the direction orthogonal to it being the  $d$ th principal component), project the data onto it, and repeat

until  $d - 1 = 0$ , yielding a mean. In this approach, PCA can be thought of as a successive addition of constraints to the original data rather than a construction of best-fitting lines as in the forward approach. In a Euclidean space both approaches yield the same result, but this property does not hold in general.

PCA can be computed by an eigendecomposition of the data covariance matrix. When sorted from largest to smallest eigenvalue, the corresponding eigenvectors represent the principal components in decreasing order, while the eigenvalues represent the variances of the 1-dimensional Gaussians in orthogonal spaces which compose the overall distribution.

One of the most important characteristics of a PCA-generated probability distribution is having as few large eigenvalues as possible given the data being analyzed. This typically indicates that the data are well represented by a small number of linear subspaces, yielding strong dimensionality reduction with low loss of information.

### 2.2.2 Non-linear Statistical Methods

PCA is a powerful analysis technique, but it assumes that the underlying data are samples from some distribution on a flat space. However, if the data are instead samples from some curved manifold, this assumption often causes PCA to produce distributions with many significant eigenvalues, meaning that many dimensions are needed to keep information loss adequately low. Modeling manifold data using linear subspaces also yields data points outside of the original manifold. Figure 2.1 shows a simple example of computing the mean of two data points sampled from an arc of a circle. In this case, the mean computed via a metric which knows about the manifold's structure is more appropriate than the traditional Euclidean mean.

In the area of statistical shape analysis, most of the data encountered live on curved manifolds. While PCA is widely used in the analysis of PDMs, this approach is not ideal because it does not take the structure of the underlying manifold into consideration and can yield ineffective analysis. The use of more complex and powerful models such as s-reps only increases the deficiencies inherent in this approach because of the increased complexity of the underlying manifold structure.

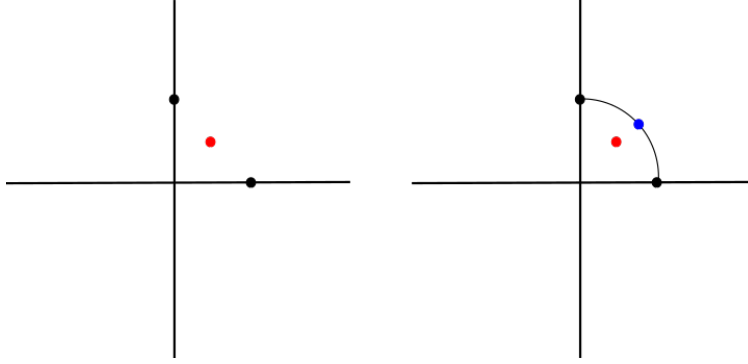


Figure 2.1: On the left, without knowledge of the data’s original manifold, the Euclidean mean (red point) is a good approximation. On the right, knowing the data are samples from an arc, the mean using the manifold’s metric (blue point) is more reasonable.

Because of this, methods which can analyze data directly on their manifold are desired.

A popular method for analyzing data on a curved manifold is principal geodesic analysis (PGA) [12]. In its most common form, PGA computes a mean of the data on the manifold. Then, all of the data is mapped onto the tangent plane at the mean and PCA is computed on this projected data.

Geodesic PCA (GPCA) [13] is a method which works similarly to PGA, but instead of using PCA in the tangent space it instead minimizes projection error to geodesics on the manifold itself. This method has the drawback that it needs explicit formulas for manifold geodesics, which are often not available.

PGA and related methods work on data which live on some manifold which may not be easy to work with directly. In cases where the underlying manifold is known, however, approaches which can use this knowledge directly can produce more accurate and efficient results. Many shape representations either are or are composed of data which live on abstract spheres, such as PDMs [14] and s-reps [4].

Kendall [14] notes that PDMs comprised of  $n$  points, when translated to have center of mass at the origin and scaled to unit length, are points on  $\mathbb{S}^{3n-4}$  (3 degrees of freedom removed for translation, 1 for scaling). In s-reps, the PDM which makes up the collection of skeletal samples is a spherical entity, as well as the collection of unit spoke directions, each of which live on  $\mathbb{S}^2$ .

Because so many of these features are spherical, a method tailored to analyzing spherical data is desirable.

### 2.2.3 Principal Nested Spheres

Principal nested spheres (PNS) [15] is a method that operates in a PCA-like backwards fashion on spherical data. Starting from  $\mathbb{S}^d$ , the best-fitting subsphere  $\mathbb{S}^{d-1}$  is computed and represented as a pole  $w$  and angle  $\psi$ . Each point  $p_i$  is projected onto the subsphere, and the process is repeated on each subsphere until a single point, the backwards mean, is reached. At each projection step, the signed geodesic distance  $Z_{d,1}$  from each point to the fit subspace is recorded, yielding  $d$  residuals for each data point. These residuals are called the *Euclideanized* form of the data, while the collection of poles and angles defining the subspheres form a *polar system* which can be used to Euclideanize a new shape via this repeated projection. A Euclideanized shape can be returned to its original ambient space by undoing these projections to recover the original representation. Figure 2.2 shows an example PNS step.

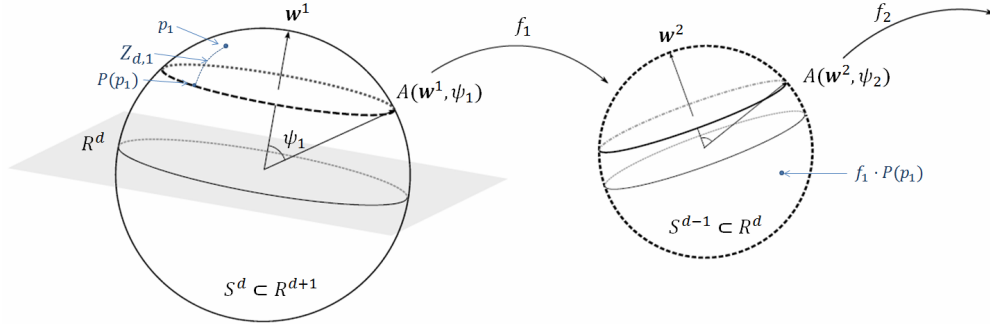


Figure 2.2: An example projection step from a PNS analysis. The point  $p_1$  is projected onto the subsphere defined by the polar system  $A(w^1, \psi_1)$ . The projection distance  $Z_{d,1}$  is a Euclideanized feature.

### 2.2.4 Composite Principal Nested Spheres

Because PNS transforms spherical data into Euclidean data, we can analyze its results using standard Euclidean techniques such as PCA. S-reps are represented as a collection of hub points which can be represented as a PDM along with many spokes, each of which has a length and direction. There are several different PNS analyses which must be done for s-reps: one to Euclideanize



the hub PDM and one for each s-rep spoke direction. For each s-rep, the resulting Euclideanized values are combined with the log-transformed spoke lengths into a single vector  $Z$  in a step called compositing. The collection of  $Z$  vectors for a population of s-reps can then be analyzed using PCA. This technique is known as composite principal nested spheres (CPNS).

Experimentally, it has been shown that s-rep features, particularly spoke directions, tend to lie on or near subspheres and are thus well modeled via PNS. CPNS has been shown to produce more efficient representations and statistics for both PDMs and s-reps than either PCA or PGA, leading to improved performance in tasks such as hypothesis testing [10] and classification [5]. These results indicate that CPNS-based Euclideanization is a powerful technique for the analysis of s-reps.

#### 2.2.5 Appearance Models and Segmentation

In this section, I discuss previous work on how to model image appearance for segmentation, focusing on methods used for ultrasound prostate segmentation. I divide the methods into two broad categories: those that attempt to segment an object via appearance directly, and those that combine image information with some type of deformable model to perform segmentations. Full surveys of prostate segmentation methods can be found in [16] and [17].

#### 2.2.6 Appearance-based Segmentation

While the simplest method for modeling image appearance is by using the raw image intensity values directly, it is rarely used due to the statistical variation of intensity features typical of medical image acquisition, a problem which is particularly bad for ultrasound. The most straightforward method of appearance modeling used in practice is to localize edges in an image using intensity gradients and use these derived edges to directly segment the object of interest. These methods fail in situations where there is low contrast or large amounts of noise or other artifacts, such as speckle in ultrasound. There are several techniques which can be used to address these problems. Aarnink et al. [18] used local standard deviations of intensity at multiple scales to identify homogeneous regions in an image. Pathak et al. [19] used a stick filter to reduce speckle and enhance contrast

in the ultrasound image by using the fact that speckle is correlated over large distances. Mahdavi et al. [20] use measures of edge strength in vibro-elastography (VE) ultrasound images rather than typical B-mode images to perform segmentation. A common approach in all imaging modalities to smooth image intensity while preserving edges is to use an anisotropic diffusion filter. In my work on modeling ultrasound appearance in chapter 5, I use the speckle-reducing anisotropic diffusion method of Yu et al.[21] to get smoothed ultrasound images.

Graph-based segmentation algorithms model image voxels or groups of voxels as nodes in a graph. The edges linking a voxel to its neighbors have an associated cost, typically related to the gradient of the image. The image is segmented by trying to cut the graph into different pieces while minimizing the cost of these cuts. Zouqi et al. [22] used graph partitioning to segment the prostate with the user defining seed points which act as the sink and source nodes for a max flow optimization. Qiu et al. [23] segment the prostate using a coherent continuous max-flow model which enforces geometric consistency across multiple 2D slices to segment the prostate in 3D.

Classification of image voxels can be used to segment objects. These methods use supervised machine learning techniques to train classifiers to distinguish between different classes of voxels. Each voxel typically has associated with it a vector of features (including image intensity, texture, physical features, etc.) with the hope of learning which features distinguish different groups of voxels. Zaim et al. [24] used spatial locality and image texture in a self-organizing map to segment the prostate from ultrasound. Zaim et al. [25] also used entropy and wavelet transform coefficients to segment the prostate using an SVM. Mohammed et al. [26] used multi-resolution Gabor features to identify ROIs and classify the ROIs based on various spectral features to obtain a segmentation.

Clustering-based methods have also been used for segmentation. Like the classification-based methods, they also use feature vectors to represent voxels. Instead of attempting to determine if a single voxel is from one class or another, they attempt to group voxels into different groups based on these features with the goal of collecting all voxels from the particular object of interest into one group. Richard et al. [27] use mean-shift on four texture features to perform segmentations by

determining the mean and covariance for each of a set of clusters and assigning a probability to each voxel for each cluster. The object boundary was then refined using spatial information, with spatially close voxels being more likely to have come from the same cluster.

### 2.2.7 Model-based Segmentation

The class of methods described in section 2.2.6 attempt to capture the boundary of an object purely by considering its appearance and attempting to separate it from surrounding tissue. While they have been successful in many applications, methods of this class can result in segmentations which are non-smooth or possibly not even continuous, especially if they are working on a voxel-by-voxel basis rather than considering spatial locality. To combat this problem, these methods can be supplemented by models which can deform to match a boundary located by analyzing an image's appearance. Regularity constraints can be used in order to ensure that the resulting boundaries are smooth and continuous while still closely matching the object of interest.

A common class of model-based methods are active contour models (ACMs). Initially developed by Kass et al. [28], ACMs or snakes can be represented as sequential sets of control points connected by curves and can leverage many of the appearance analysis techniques described in section 2.2.6 in order to locate an object's boundary. They proceed by moving an initial contour (via moving the control points) closer to the object rather than attempting to capture its edge directly such as the purely edge-detecting methods which, along with a regularization, guarantees a smooth and continuous boundary for the object. Jendoubi et al. [29] used a gradient vector flow model computed via a combination of Laplacian of Gaussian and Sobel operators to move the ACM towards the prostate boundary and improve its capture range, lessening its reliance on accurate initialization. ACMs can also work with more complex methods of modeling of image appearance. Knoll et al. [30] used the dyadic wavelet transform to determine prostate edges and deform an ACM to match the prostate boundary. Zaim et al. [31] used differences of Gaussians to detect dot-pattern features consistent with prostate tissue texture while using a priori knowledge of mean prostate shape. Garnier et al. [32] use discrete dynamic contours [33] to initialize an Optimal

Surface Detection [34] segmentation. Ladak et al. [35] and Ding et al. [36] improve on the initial ACM by using more sophisticated spline-based techniques for connecting the control points and thus improving the smoothness of the boundary.

Active shape models (ASM) [3] were proposed to counter the weakness of other model-based methods that the resulting boundaries can often be atypical of the shape of the object being segmented. ASMs work by performing statistical analysis (most commonly PCA) of PDMs of corresponding landmarks across a population of shapes. The modes of variation resulting from PCA form a shape space over which the mean PDM can be deformed to better match image data while still remaining consistent with the shape of the object in question. This prior shape information makes the resulting segmentations more robust to noise and artifacts. Shen et al. [37] used rotation-invariant Gabor features to both smooth and detect prostate edges. They then segmented the prostate using an ASM by refining it at multiple scales. Betrouni et al. [38] enhanced the prostate edge using prior knowledge of the noise distribution of TRUS images. Zhan et al.[39] use classifiers trained on Gabor filter-derived features to divide texture space into prostate and non-prostate regions to drive a deformable segmentation of the prostate. In later work, Zhan et al.[40] use locally-trained classifiers learned on Gabor texture features to classify regions of the image as prostate or not to guide an ASM. Cosio et al. [41] used a Gaussian mixture model to cluster prostate and non-prostate tissues and used a Bayesian classifier to identify prostate voxels followed by an ASM-based segmentation.

Active appearance models (AAM) [42] are models which statistically model not only an object's shape but its appearance as well in a joint fashion. Medina et al. [43] used AAM segment the prostate. Ghose et al. [44] used approximations via Haar wavelets to reduce speckle and contrast-invariant texture features to improve AAM segmentation accuracy.

Tutar et al. [45] use statistics computed on spherical harmonic coefficients together with derived edge maps to segment the prostate.

Another class of deformable model-based segmentation methods are atlas-based methods.

These methods work by constructing an atlas from a set of manual segmentations. Segmentation is performed by deforming the atlas image to better match a target image. In this way, atlas-based segmentation can be treated as a registration problem. Yang et al.[46] computed Gabor filters in three orthogonal planes and classifiers were trained on six image subvolumes. Segmentations were then performed by warping atlas images to the target image and applying subvolume classifiers to enhance the segmentation. Atlas-based segmentation of the prostate must often be refined via a separate deformable model to improve accuracy, such as in the method of Martin et al.[47].

While the segmentation method presented in this dissertation is similar in some ways to many of these methods, it has several important properties which are not combined fully into any of the other approaches. Most importantly for modeling ultrasound appearance, it trains classifiers locally rather than globally, and on a much finer scale than other methods are able to do, allowing for much finer tuning of the classifier to the specific appearance of that particular region. I am able to accomplish this by leveraging the inherent correspondence gained by using s-reps as the underlying shape model, which have been shown to produce better correspondence than PDMs even when not optimized to do so [6]. A second important characteristic is the use of patient-specific initial shape models rather than an overall population mean as is typical of other deformable-model based approaches, allowing for a good initialization which can help avoid local minima of the objective function which may be far from the optimal solution. This use of a patient-specific shape model is contrasted with methods that use patient-specific appearance information. An example is the work of Gao et al. [48] which uses patient-specific information to refine a pre-trained appearance classifier to focus on training data which are similar in appearance to the current patient to segment the prostate in CT.

### 3 CONTINUOUS INTERPOLATION OF SKELETAL REPRESENTATIONS

#### 3.1 Introduction

Discrete s-reps have been shown to be powerful shape representations for a variety of tasks. Tasks involving statistical analysis often analyze the s-rep’s sampled representation directly. However, other applications such as s-rep fitting and s-rep-based segmentation benefit from having a continuous model rather than operating from these samples alone.

Consider the fitting case in figure 3.1, where an s-rep is being fit to an object boundary (black). If fitting is done considering only how well the s-rep matches the object at the base s-rep spokes, the resulting s-rep implied boundary (blue) will miss the bump in the object surface. If, however, the fit is done using interpolated spokes (red), the optimization will have to shift the base spokes to better model this bump, thus increasing accuracy of the fit. Similarly, segmentation benefits from considering a dense object rather than a set of samples. An alternative approach would be to use very densely sampled base s-reps, but this would greatly increase computation time and model complexity with little benefit over an interpolation approach.

S-rep interpolation also allows for the computation of a continuous object-relative coordinate

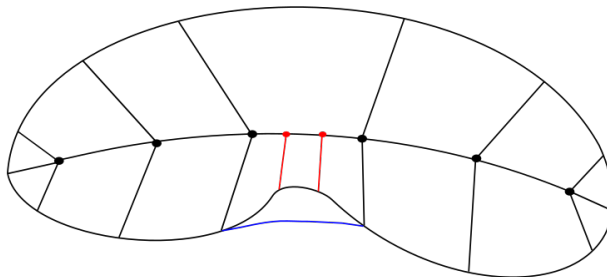


Figure 3.1: An s-rep whose base spokes miss the bump in the object boundary. Fitting via the interpolated spokes (red) can detect and help correct this problem.

system, giving every point on the interior (and exterior) of an s-rep a unique coordinate in  $(u, v, \tau)$  space. This is important for several applications, including the transfer of labels from one s-rep to another corresponding s-rep based on their object-relative coordinates, and the creation of s-rep-relative patches such as those used in the appearance model described in chapter 5.

Previous attempts for producing interpolated s-reps (or m-reps, their predecessor) include the use of purely boundary-based interpolation as well as attempts to leverage the geometric properties of medial or skeletal models to varying degrees of success.

Any method which can interpolate a tile mesh into a continuous surface can be applied to the mesh formed from s-rep boundary points. While these methods will often produce smooth boundary surfaces, the lack of consideration of the underlying skeletal structure is a major weakness. Because they produce a boundary without producing a corresponding interpolation of the object's interior, these methods are unsuitable for use when having an object-relative coordinate system is desirable, such as the creation of the s-rep-based appearance model discussed in chapter 5.

Crouch [49] extended the use of purely boundary-based interpolation to include the skeleton by using cubic b-splines to separately interpolate the medial sheet and boundary for m-rep models. Medial positions were then connected to boundary positions of the same parameter value to produce m-rep spokes. Because these interpolations are done without consideration of the explicit relationship between changes of a medial surface and their effects on the m-rep's implied boundary, this method does not guarantee legal m-rep or s-rep spokes.

Han [50] developed a method for interpolating m-reps by leveraging the mathematics of medial structures developed by Damon [51]. He first interpolates the medial sheet via cubic Hermite patches. Then, he estimates spoke derivatives via finite differences and interpolates the matrix representing the radial shape operator  $S_{rad}$  by separately interpolating its eigenvectors and eigenvalues. By continuously interpolating these derivatives, a numerical integration is used to compute interpolated spokes via moving along a path between a base spoke and the desired position. While

mathematically sound for purely medial models, the direct implementation of this method has several challenges. First, because the spoke derivatives are estimated numerically, the  $S_{rad}$  matrix is not guaranteed to have real eigenvalues. The case where the eigenvectors switch ordering is also not addressed. Finally, the mathematics of this method are applicable only to purely medial models and not generalized skeletal structures such as s-reps.

The interpolation method presented in this chapter begins from a similar approach as that of Han but has several important improvements. First, instead of being based purely on medial mathematics, the mathematics are based on that of non-medial skeletal structures, allowing for the direct application of this method to s-reps. Second, to avoid the problems associated with estimating spoke derivatives via interpolation of the  $S_{rad}$ , quaternion splines are fit to the unit spoke directions so that their derivatives can be computed analytically anywhere. Finally, the interpolation method is extended to also apply around the crest of the s-rep instead of only on the top or bottom, allowing for consistent interpolation of an entire object.

### 3.2 Mathematics of Skeletal Representations

A 3D, continuous s-rep describes an object interior via two functions:

- $\mathbf{p}(u_1, u_2)$ : a 2D, non-branching skeletal surface inside and approximately in the middle of the object
- $\mathbf{S}(u_1, u_2)$ : a field of non-crossing vectors pointing from the skeletal surface to the object boundary.

$\mathbf{S}$  can be further decomposed into a product of two functions:  $\mathbf{U}(u_1, u_2)$ , a unit vector field pointing in the direction of  $\mathbf{S}(u_1, u_2)$  and  $r(u_1, u_2)$ , a scalar function representing distance from the skeletal sheet to the object boundary along the direction  $\mathbf{U}(u_1, u_2)$ .

In this formulation, a point on the object's boundary is represented as  $\mathbf{B}(u_1, u_2) = \mathbf{p}(u_1, u_2) + r\mathbf{U}(u_1, u_2)$ , meaning that every point on the boundary corresponds to a unique point on the object's skeleton. The addition of a third parameter,  $\tau$ , representing distance as a fraction of  $r$  along  $\mathbf{U}$ ,



gives every point in the interior of the object a unique coordinate inside the s-rep  $\mathbf{M}$ :

$$\mathbf{M}(u_1, u_2, \tau) = \mathbf{p}(u_1, u_2) + \tau r(u_1, u_2) \mathbf{U}(u_1, u_2). \quad (3.1)$$

We call this the *object-relative coordinate system* of the s-rep, where  $\tau = 1$  gives points on the object boundary and  $\tau = 0$  gives points on the object skeleton.

As the parameter  $\tau$  decreases from 1 to 0, the s-rep can be thought of as deflating from the boundary toward the skeleton. At  $\tau = 0$ , the s-rep is a flat 2D surface but still retains its spherical topology much like a deflated ball.

A discrete s-rep is a sampling of this continuous skeletal model. It consists of an  $m \times n$  grid of samples, called *hubs*, from the skeletal surface with either two (on the interior) or three (along the crest) vectors called *spokes* pointing from the skeleton to the boundary. These crest spokes are an approximation of the actual configuration in continuous models. In the continuous case there is one spoke emanating from every position on the deflated ball mentioned above. This means that there are two spokes for every non-fold skeletal position and one spoke along the fold curve. As you move along the skeleton the last  $\epsilon$  distance to the fold region, the spokes begin to swing with infinite velocity as you move around the fold and onto the other side. The triple-spoked hub for discrete s-reps allow represent this by extending the length of the fold spoke back  $\epsilon$  distance to a hub before the swing begins, restricting that last  $\epsilon$  length step to be straight.

Figure 3.2 shows an example s-rep and the surface implied by varying  $\tau$  values. The grid structure on the skeleton forms a collection of quadrilaterals with a hub at each corner. It is this discrete representation which must be interpolated back into a continuous model.

The grid structure of the discrete s-rep parameterization lends itself naturally to interpolating in a patchwise fashion. Because of the desire for a smooth interpolated object, the method described in this chapter was designed to ensure the resulting object is not only continuous, but continuously differentiable as well.

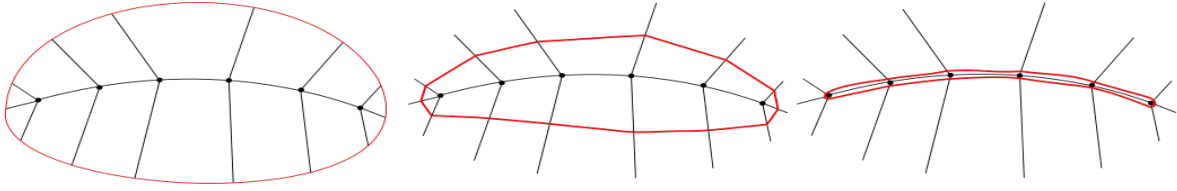


Figure 3.2: A 2D s-rep model showing the surface given at  $\tau$  values of 1 (left), 0.5 (middle), and 0 (right). The two sides of the surface for  $\tau = 0$  occupy the same region of space but retain spherical topology. Note that the first and last hubs have 3 spokes, the third being the additional crest spoke which transitions from the top side to the bottom.

### 3.3 Skeleton Interpolation

As in [50], interpolation of the hubs into a continuous skeleton is done by fitting cubic Hermite patches to the quads of discrete samples which form the surface. This interpolation requires 16 control values: the 4 corner points  $\mathbf{p}(u_1^0, u_2^0)$ ,  $\mathbf{p}(u_1^1, u_2^0)$ ,  $\mathbf{p}(u_1^0, u_2^1)$ ,  $\mathbf{p}(u_1^1, u_2^1)$ , the 8 first derivatives of each corner point in both parameter directions which are computed via finite difference approximation, and the 4 second order mixed partial derivatives of each corner point, which are set to 0. The matrix  $H_c$  containing these control values which will be used to interpolate the skeleton is

$$H_c = \begin{pmatrix} \mathbf{p}(u_1^0, u_2^0) & \mathbf{p}(u_1^1, u_2^0) & \mathbf{p}_{u_2}(u_1^0, u_2^0) & \mathbf{p}_{u_2}(u_1^1, u_2^0) \\ \mathbf{p}(u_1^0, u_2^1) & \mathbf{p}(u_1^1, u_2^1) & \mathbf{p}_{u_2}(u_1^0, u_2^1) & \mathbf{p}_{u_2}(u_1^1, u_2^1) \\ \mathbf{p}_{u_1}(u_1^0, u_2^0) & \mathbf{p}_{u_1}(u_1^1, u_2^0) & 0 & 0 \\ \mathbf{p}_{u_1}(u_1^0, u_2^1) & \mathbf{p}_{u_1}(u_1^1, u_2^1) & 0 & 0 \end{pmatrix}$$

Let  $\mathbf{H}(x) = (H_1(x), H_2(x), H_3(x), H_4(x))$  and  $\mathbf{H}'(x) = (H'_1(x), H'_2(x), H'_3(x), H'_4(x))$  where  $H_i$  are the cubic Hermite spline basis functions:

$$H_1(x) = 2x^3 - 3x^2 + 1$$

$$H_2(x) = -2x^3 + 3x^2$$

$$H_3(x) = x^3 - 2x^2 + x$$

$$H_4(x) = x^3 - x^2$$

and  $H'_i$  are their derivatives. Computation at a point  $(u_1^*, u_2^*)$  inside a quad is given by

$$\mathbf{p}(u_1^*, u_2^*) = \mathbf{H}(\delta u_1) \cdot H_c \cdot \mathbf{H}(\delta u_2)^\top.$$

Derivatives of the skeletal surface can be computed by replacing the appropriate set of basis functions by their derivatives:

$$\mathbf{p}_{u_1}(u_1^*, u_2^*) = \mathbf{H}'(\delta u_1) \cdot H_c \cdot \mathbf{H}(\delta u_2)^\top; \quad \mathbf{p}_{u_2}(u_1^*, u_2^*) = \mathbf{H}(\delta u_1) \cdot H_c \cdot \mathbf{H}'(\delta u_2)^\top \quad (3.2)$$

Figure 3.3 shows the resulting skeleton for a hippocampus s-rep.

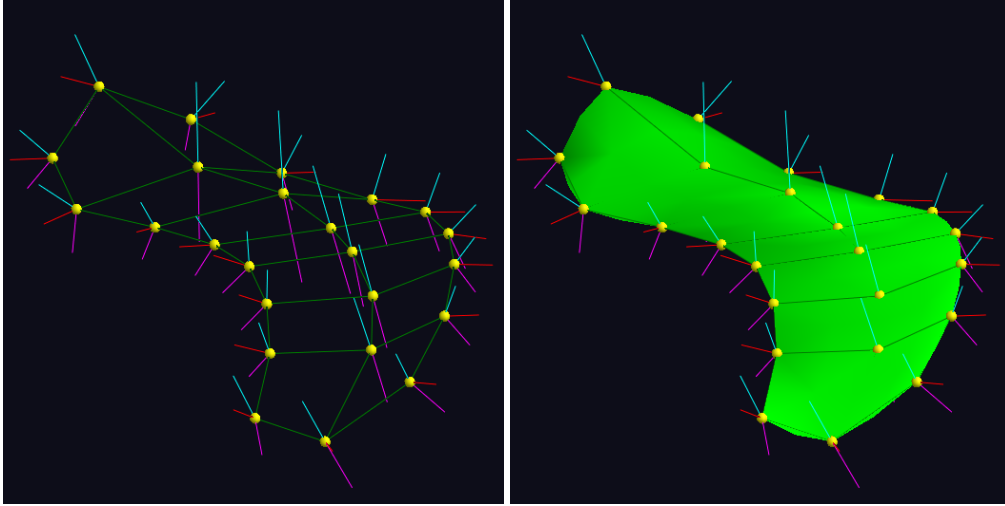


Figure 3.3: An s-rep of a hippocampus (left) and the interpolated skeleton (right).

### 3.4 Spoke Interpolation

We wish to interpolate an unknown spoke  $\mathbf{S}(u_1^*, u_2^*)$ . If the sampled hubs have integer parameter values,  $(u_1^*, u_2^*)$  can be written as

$$(u_1^*, u_2^*) = (u_1^0 + \delta u_1, u_2^0 + \delta u_2); \quad \delta u_1, \delta u_2 \in [0, 1) \quad (3.3)$$

where  $(u_1^0, u_2^0)$  is the top left corner of the quad containing the desired value. Figure 3.4 gives an illustration of this configuration.

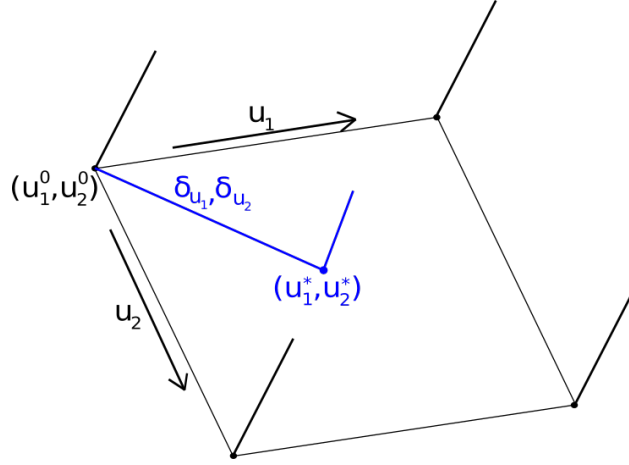


Figure 3.4: An s-rep quad, with the desired spoke in blue.

I then interpolate the spoke  $\mathbf{S}(u_1^*, u_2^*)$  by beginning from the known spoke  $\mathbf{S}(u_1^0, u_2^0)$  and integrating the derivatives of  $\mathbf{S}$  from  $(u_1^0, u_2^0)$  to  $(u_1^*, u_2^*)$ . This approach yields the equation

$$\mathbf{S}(u_1^*, u_2^*) = \mathbf{S}(u_1^0, u_2^0) + \oint_{(0,0)}^{(\delta u_1, \delta u_2)} \left( \frac{\partial \mathbf{S}}{\partial u_1} du_1 + \frac{\partial \mathbf{S}}{\partial u_2} du_2 \right) \quad (3.4)$$

for the desired spoke. This means that, to interpolate  $\mathbf{S}(u_1^*, u_2^*)$ , I must be able to compute partial derivatives of  $\mathbf{S}$  at every point along the path from  $(u_1^0, u_2^0)$  to  $(u_1^*, u_2^*)$ . These partial derivatives can be written as

$$\mathbf{S}_{u_i} = r \mathbf{U}_{u_i} + r_{u_i} \mathbf{U}. \quad (3.5)$$

Thus, to compute  $\mathbf{S}_{u_i}$ , we must be able to compute  $\mathbf{U}_{u_i}$  and  $r_{u_i}$  at arbitrary positions within a quad.

In s-reps, changes to the spoke length  $r$  at some point depend on the changes in the skeleton  $\mathbf{p}$  and boundary  $\mathbf{B}$ . Damon's compatibility condition [52][53] for skeletal models is given by

$$-r_{u_i} = \mathbf{p}_{u_i} \cdot \mathbf{U} + \mathbf{B}_{u_i} \cdot \mathbf{U}, \quad (3.6)$$

where  $\mathbf{B}_{u_i} = \mathbf{p}_{u_i} + \mathbf{S}_{u_i}$  are derivatives of the object's boundary. Substituting equation 3.6 into 3.5,

we obtain the expression

$$\begin{aligned} \mathbf{S}_{u_i} &= r\mathbf{U}_{u_i} - (\mathbf{p}_{u_i} \cdot \mathbf{U} + (\mathbf{p}_{u_i} + \mathbf{S}_{u_i}) \cdot \mathbf{U}) \mathbf{U} = r\mathbf{U}_{u_i} - (2\mathbf{p}_{u_i} + \mathbf{S}_{u_i}) \mathbf{U}^\top \mathbf{U} \\ &= (r\mathbf{U}_{u_i} - 2\mathbf{p}_{u_i} \mathbf{U}^\top \mathbf{U}) (\mathbf{I} + \mathbf{U}^\top \mathbf{U})^{-1} \end{aligned} \quad (3.7)$$

for the partial derivatives of  $\mathbf{S}$ . This equation allows for the computation of the spoke derivative at any point  $(u_1^*, u_2^*)$  given derivatives of the skeletal surface  $\mathbf{p}_{u_i}$ , which we can compute using the method described in section 3.3, and the spoke direction  $\mathbf{U}_{u_i}$  at that point.

### 3.5 Estimation of Spoke Direction Derivatives via Quaternion Splines

The partial derivatives of the spoke direction vector field  $\mathbf{U}_{u_i}$  are needed to solve equation 3.7. Because  $\mathbf{U}$  is a unit vector field, changes in  $\mathbf{U}$  can be represented as rotations. For this reason, I use a quaternion-based interpolation to compute these derivatives.

Each spoke at the corner of a quad is represented by a quaternion. Each unit vector  $\mathbf{U} = (U_x, U_y, U_z)$  is represented by the unit quaternion  $\mathbf{q} = 0 + U_x i + U_y j + U_z k$ . From the four spoke direction quaternions bounding a quad, the spoke directions on the interior of the quad must be interpolated.

A computationally inexpensive method for this interpolation is spherical linear interpolation (slerp) [54]. Using slerp, the quaternion that is  $\lambda \in [0, 1]$  of the distance between two adjacent quaternions  $\mathbf{q}_i$  and  $\mathbf{q}_{i+1}$  is given by

$$SL(\mathbf{q}_i, \mathbf{q}_{i+1}, \lambda) = \mathbf{q}_i (\mathbf{q}_i^* \mathbf{q}_{i+1})^\lambda. \quad (3.8)$$

However, as its name suggests, this method would only have  $C^0$  continuity across quad boundaries. For this reason, a higher order method is needed.

Instead of this analogue of linear interpolation, I use an extension of the cubic Bézier curve to the surface of a sphere called *squad* [55] to interpolate quaternions in a quad interior. To ensure  $C^1$  continuity between adjacent Bézier curves, the four control points driving the Bézier curves

must be chosen carefully. For a curve, two of the control points ( $q_i$  and  $q_{i+1}$ ) are the two points between which we are interpolating. The other two points,  $a_i$  and  $a_{i+1}$ , are computed by considering not only  $q_i$  and  $q_{i+1}$  but also  $q_{i-1}$  and  $q_{i+2}$  to ensure  $C^1$  continuity. The computation for  $a_i$  is thus [55][56]:

$$\mathbf{a}_i = \mathbf{q}_i \exp \left( -\frac{\log(\mathbf{q}_i^{-1}\mathbf{q}_{i+1}) + \log(\mathbf{q}_i^{-1}\mathbf{q}_{i-1})}{4} \right)$$

Given these control points, De Casteljau's algorithm can be used to efficiently compute a Bézier curve as a sequence of linear interpolations. Given a set of 4 control points, the algorithm proceeds as follows:

1. Connect the control points to form an open polygon with 3 sides.
2. Subdivide each segment into two pieces with length ratio  $t : (1 - t)$ .
3. Connect the points from step 2 to form two line segments.
4. Subdivide the two new segments as in step 2 and connect these points to form a single line.
5. Subdivide this line. The resulting point is on the curve.

Figure 3.5 shows the application of this algorithm to a simple example.

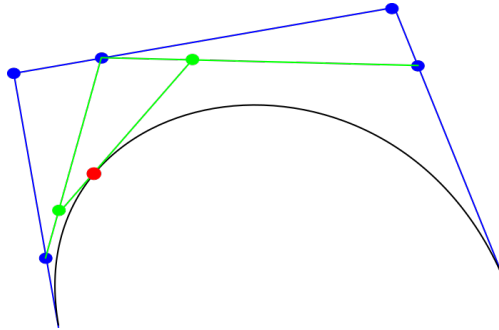


Figure 3.5: An example of the use of De Casteljau's algorithm to compute a Bézier curve. First, the control points are connected (blue) and subdivided; then, the resulting points are connected (green) and subdivided again. The result of connecting and subdividing the final line segment yields a point on the curve (red).

A similar approach allows for computation of squad by leveraging slerp (equation 3.8), giving the quaternion equation

$$SQ(\mathbf{q}_i, \mathbf{q}_{i+1}, \mathbf{a}_i, \mathbf{a}_{i+1}, \lambda) = SL(SL(\mathbf{q}_i, \mathbf{q}_{i+1}, \lambda), SL(\mathbf{a}_i, \mathbf{a}_{i+1}, \lambda), 2\lambda(1 - \lambda)) \quad (3.9)$$

Differentiating equation 3.9 with respect to  $\lambda$  yields [56]

$$\begin{aligned} SQ'(\mathbf{q}_i, \mathbf{q}_{i+1}, \mathbf{a}_i, \mathbf{a}_{i+1}, \lambda) = \\ SL(\mathbf{q}_i, \mathbf{q}_{i+1}, \lambda) \log(\mathbf{q}_i^* \mathbf{q}_{i+1}) \mathbf{g}_i(\lambda)^{2\lambda(1-\lambda)} + SL(\mathbf{q}_i, \mathbf{q}_{i+1}, \lambda) (\mathbf{g}_i'(\lambda)^{2\lambda(1-\lambda)}) \end{aligned} \quad (3.10)$$

where  $\mathbf{g}_i(\lambda) = SL(\mathbf{q}_i, \mathbf{q}_{i+1}, \lambda)^* SL(\mathbf{s}_i, \mathbf{s}_{i+1}, \lambda)$ .

The derivative  $\mathbf{U}_{u_1}(u_1^*, u_2^*)$  within a quad is computed by first using equation 3.9 to estimate  $\mathbf{U}(u_1^{-1}, u_2^{\delta u_2})$ ,  $\mathbf{U}(u_1^0, u_2^{\delta u_2})$ ,  $\mathbf{U}(u_1^1, u_2^{\delta u_2})$ , and  $\mathbf{U}(u_1^2, u_2^{\delta u_2})$  via the  $4 \times 4$  surrounding grid spokes. Equation 3.10 on the resulting quaternions then yields the desired derivative. The computation is similar for  $\mathbf{U}_{u_2}$ .

### 3.6 Interpolation of the Crest

The method described in the previous sections works without modification on quads adjacent only to quads on the same side of the object. However, interpolating quads which go around the crest from the top to the bottom of the object requires special consideration because their geometry differs from that of other quads. The major difference in the s-rep structure at the crest is that adjacent spokes can emanate from the same hub. This yields degenerate quads which are collapsed into lines, causing difficulties in the direct application of equation 3.7.

We address this problem by dilating the crest curve as shown in figure 3.6 to regain the quad structure on the skeleton. The crest is dilated by a small fraction  $\theta$  of the length along each spoke, forming an elliptical tube around the crest curve. The end points for the spokes on the crest are set to be the points where they intersect this tube. From this new structure, interpolation of the skeleton and spoke directions proceeds as described in section 3.4. When the final spoke is computed, its

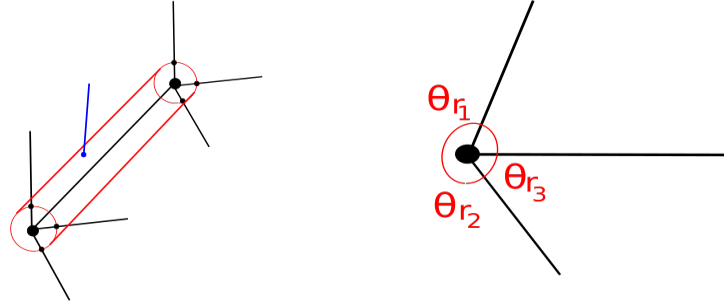


Figure 3.6: Left: The dilated crest curve with desired spoke in blue. Right: A cross-section of the crest showing the radius-relative dilation.

end point is set back to be on the original crest curve.

### 3.7 Spoke Computation via Integration of Derivatives

With the  $\mathbf{p}_{u_i}$  and  $\mathbf{U}_{u_i}$  values from sections 3.3 and 3.5, we can start from the quad corner  $(u_1^0, u_2^0)$  and integrate equation 3.7 numerically. Using Euler's method for the integration, taking a step of length  $h$  yields  $\mathbf{S}(u_1^h, u_2^h) = \mathbf{S}(u_1^0, u_2^0) + h(\delta u_1 \mathbf{S}_{u_1}(u_1^0, u_2^0) + \delta u_2 \mathbf{S}_{u_2}(u_1^0, u_2^0))$ . From  $(u_1^h, u_2^h)$ , we can take another step towards  $(u_1^*, u_2^*)$  and iterate until  $(u_1^*, u_2^*)$  is reached.

An alternative approach which yields better accuracy is to use a more sophisticated predictor-corrector method for the integration. In particular, I use the Adams method, consisting of an Adams-Bashforth predictor followed by an Adams-Moulton corrector [57]. Because the Adams-Bashforth predictor for computing a value  $y_{i+1}$  requires  $y_i, y_{i-1}, y_{i-2}$  and  $y_{i-3}$ , Euler's method is used until enough previous steps have been computed to bootstrap the Adams method.

In this formulation, the choice of the origin corner  $(u_1^0, u_2^0)$  is arbitrary. We can interpolate  $\mathbf{S}(u_1^*, u_2^*)$  using this method starting from any of the four quad corners. I have found that the stability of the interpolations is increased when I interpolate each  $\mathbf{S}(u_1^*, u_2^*)$  from all four corners and compute the final result as a weighted average of the four interpolations, with the weights being the relative distance of  $(u_1^*, u_2^*)$  from each corner.

Figure 3.7 shows the results of interpolating the spokes on the top side of a lateral ventricle s-rep. It is difficult to assess the accuracy of this interpolation method because it is typically used to interpolate objects where the exact answer is not known. In order to assess the accuracy I applied



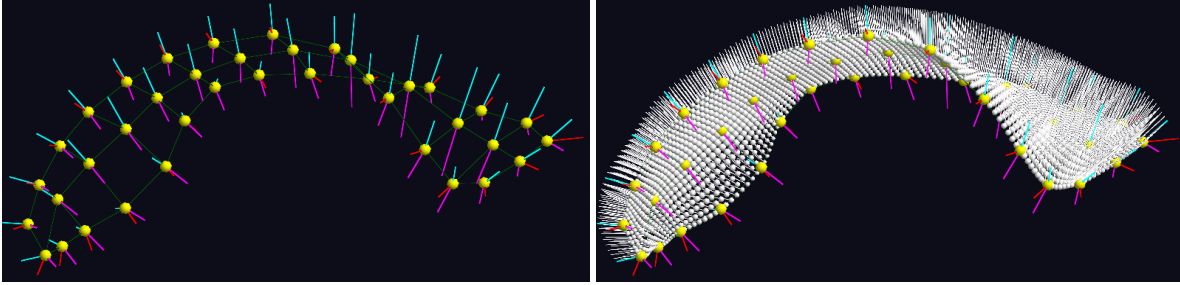


Figure 3.7: A lateral ventricle s-rep and a dense interpolation of its top side spokes.

this method to an s-rep of an ellipsoid where the medial sheet can be computed analytically. In this ellipsoid, interpolated spokes along the top and bottom differ by no more than  $5^\circ$  from their computed counterparts. Spokes along the crest, particularly in the four corners of the s-rep grid, have higher errors but none more than  $10^\circ$ .

### 3.8 Discussion

This chapter presents a geometrically-based method for continuously interpolating discrete s-reps. While it is difficult to evaluate my method’s accuracy due to the lack of ground truth values to compare against, it has produced smooth and reasonable surfaces for a variety of anatomical objects, including objects where older m-rep and s-rep interpolation methods failed. Having an accurate interpolation method is useful in a variety of tasks. It makes s-rep fitting more accurate, it can be used to optimize correspondence over a population of s-reps by shifting spokes to interpolated positions, transfer labels from one s-rep to another via object-relative coordinates, and it can be used to generate s-rep-relative appearance models such as the one described in chapter 5.

A benefit of this interpolation method is that it is highly parallelizable. Currently, the interpolations from each corner described in section 3.7 are done in parallel for each spoke. Because the interpolation is used in the inner loop of Pablo for many tasks, it would be desirable to further leverage the fact that each spoke can be interpolated independently of the others and implement a fully parallel interpolation over the entire s-rep.

## 4 PROBABILITY DISTRIBUTION ESTIMATION OF SHAPE DIFFERENCES

### 4.1 Introduction

A common approach in segmenting a structure from a medical image is to use prior knowledge of the shape of that structure. One way to incorporate this prior knowledge, given a training set of instances of the object, is to estimate the probability distribution of that shape and only choose potential segmentations either directly from this distribution or based on their closeness to it.

In the segmentation problem I am considering in this dissertation, however, I already have specific prior knowledge of the shape of the prostate in a patient's ultrasound from their planning-time MRI, so I have less need to estimate the possible distribution of all prostate shapes. Rather, I wish to model a distribution which allows for the use of this patient-specific knowledge. Because of this, I choose to model the effect of the transducer-induced deformation on the prostate in order to best leverage the prior knowledge given by the MRI for estimating the prostate shape in TRUS.

In order to effectively estimate the probability distribution on these shape differences, careful consideration must be given to the method by which the objects and their differences are analyzed. As discussed in section 2.1, shapes are best thought of as non-linear entities, so typical Euclidean statistical methods such as PCA are ill-suited for direct application to shape data. This is particularly the case with s-reps. Because the space of shapes is curved, the difference between a pair of shapes in the space will be a curve along the manifold, such as a geodesic connecting the two shapes. The problem then becomes estimating a probability distribution of geodesics in this curved space.

Instead of directly analyzing these geodesics, I develop a method which uses the ideas of Euclideanization to analyze a population of shape differences. By turning the manifold-resident shape representations into a form which can be treated as Euclidean, the differences between pairs

of points become line segments which can be analyzed using standard statistical techniques. I apply this method to PDMs in several toy experiments as well as to s-reps fit to clinical prostate data.

I consider this modeling of the difference between pairs of shapes (in this case, the prostate shapes from a single patient’s planning-time MRI and biopsy-time TRUS) as a restricted form of the general problem of longitudinal shape analysis. While the goal of longitudinal analysis is to learn the various ways in which a population of objects change over various time points, I am only concerned with the effect of a specific process on pairs of prostate shapes at a given time pair. However, many of the techniques discussed in this chapter could be applied to a more general longitudinal problem.

## **4.2 Related Work**

Early work on this problem includes the work by Mardia and Walder [58] on so-called paired shape distributions, where they consider two shape distributions with different means and variances but correlation between the two classes. They use maximum likelihood estimation to estimate unknown parameters of this correlation and to determine if there are statistically significant differences between the two classes.

I contrast the problem being considered here - statistical analysis of the differences between pairs of objects - with the class of methods where the change between shapes is the base object being considered, such as the methods based on Large Deformation Diffeomorphic Metric Mapping (LDDMM). There are two general ways in which statistics on such objects is done: either on the full deformation fields themselves or on their initial momentum. Methods in the first category [59, 60] involve performing PCA on these deformation fields. While not theoretically ideal, these methods often perform adequately well in practice, though they are not guaranteed to yield smooth or invertible transformations.

The second class of methods [61, 62] applies PCA to the initial momentum rather than the full deformation fields. Because the initial momentum fully describes the resulting geodesic and they

lie in a tangent space, they provide a linear representation of the non-linear deformation between two shapes so linear statistical methods can be applied.

There is already an established method for analyzing s-reps while taking into account their underlying manifold structure. PNS-based Euclideanization has been shown to produce compact statistics of s-reps (and PDMs) for tasks such as hypothesis testing [10], classification [5], and producing correspondencing objects [6]. For this reason, I choose to study s-rep differences within this framework rather than adapting another approach to work with s-reps directly.

As mentioned, I am only concerned with changes between a starting and ending shape, each of which is at a known time point. This is contrasted with the more general area of longitudinal analysis, where there are often more than two shapes in a sequence and their exact time points relative to the underlying change are unknown. A detailed review of general longitudinal shape analysis methods can be found in [63].

### **4.3 Methodology**

In this section I describe the methodology by which I compute probability distributions on changes of pairs of shapes. The first several sections describe the general analysis methodology which can be applied to various shape representation while the latter sections deal specifically with initialization of s-reps for analysis.

#### **4.3.1 Euclideanization**

The first step I take is to convert shape representations which live on manifolds into a form on which more standard Euclidean statistical techniques may be applied. To do this I use principal nested spheres (PNS) as described in section 2.2.3 to compute a polar system (consisting of pole/angle pairs for each subsphere) which can be used to create Euclideanized versions of the input shapes.

Before performing the PNS analysis, the question of which set of shapes to use in this analysis must be addressed. In the case where the data being analyzed are pairs of shapes, there seem to be three reasonable choices: computing the polar system on the set of starting shapes, the set of

ending shapes, or the union of all of the shapes.

I choose to base the PNS calculation on the union of all training shapes for several reasons. First, if the training were based only on one of the two sets of shapes, instances from the other set may be outliers in the estimated shape space and thus have unstable representations (if much of the variation is captured in the low-variance spheres of the PNS computation, for example). Using a larger training set is also advantageous in situations where the amount of training data is limited as is typical in medical applications. This approach is not suited to situations where the expected deformations are very large, however. In such cases, using one class of shapes as the basis for the PNS calculation may be preferable.

#### 4.3.2 Probability Distribution Estimation

Once the PNS polar system has been computed, I subtract the starting shape from the ending shape to get the difference of their Euclideanized values. I then apply PCA to these values to estimate the probability distribution of these differences.

This subtraction can be thought of as a transport, where subtracting the starting shapes from the ending shapes is analogous to transporting each starting shape to a common point and transporting each corresponding ending shape in the same way. If this analysis were performed directly on the curved manifold, the non-trivial problem of how to transport the geodesic connecting two shapes to a common location would have to be addressed. I avoid the problems inherent of transports on general curved spaces by performing this transport in the Euclideanized space.

### 4.4 Evaluation

First, I evaluate the performance of my proposed approach on a set of ellipsoid boundary PDMs which are deformed by twisting and/or bending. The results of the proposed method are compared to results computed by directly taking pointwise differences between the PDMs in Euclidean space followed by PCA. I then show the result of applying the Euclideanization-based method to ellipsoid s-reps.

The data used for the following experiments consist of sets of 100 ellipsoids which are bent

and/or twisted following a specific distribution. Each set of ellipsoids has principal radii following Gaussian distributions with means 40, 20, and 15 and standard deviations 3, 2, and 1.5 respectively. For each group of 100 ellipsoids, a mean bend angle  $\theta$  and mean twist angle  $\phi$  are selected. The 100 ellipsoids are then bent and twisted by angles randomly generated from Gaussian distributions with those means, generating the pairs of ellipsoids on which my analysis is done. Deformations are done by first twisting the ellipsoid boundary about the long axis followed by a bending of the long axis.

#### 4.4.1 Single Mode of Change

For ellipsoids with single (either bending or twisting alone) modes of change, both my method and standard PCA were able to identify a single dominant mode of variation. For bending, distributions with means of 0 and  $\pi/6$  yield a distribution whose first principal variance accounts for 98% of the total variance using both methods of analysis. For twisting, a 0 mean distribution yields a similar 98% principal variance for both analyses, while a  $\pi/3$  mean distribution yields 93%. In all cases, the Euclideanization-based method yields deformations which, when visualized, move more naturally and follow curved paths than using PCA alone, which produces linear deformations.

I also study how well the mean deformation computed by each method recovers the expected bending or twisting angle. To do this, I apply the mean deformation to an undeformed ellipsoid and compare the average angle the points are bent or twisted by to the expected angle. Figure 4.1 shows the results of this experiment. Both methods are able to accurately recover the bending and twisting angles, though the Euclideanization-based method is slightly more accurate.

Figure 4.1: Bending (left) and twisting (right) angles estimated from computed mean deformations compared to ground truth.

Actual	Eucl.	PCA	Actual	Eucl.	PCA
30	29.87	28.50	30	33.53	34.18
45	43.67	42.73	45	47.70	48.09
60	59.67	57.45	60	58.48	57.83

#### 4.4.2 Composed Bending and Twisting

Next I consider ellipsoids whose deformations are a combination of a twisting followed by a bending. Both methods are able to separate bending and twisting deformations into separate eigenmodes. However, the estimated principal variances can be very different.

In order to test which method's estimated principal variances are more accurate, I designed an experiment where the relative size of the bending and twisting variances should be equivalent and compare the results of both methods to the expected results. Because twisting is done about the longest principal radius while bending transforms it, a twist of some angle  $\theta$  produces less change to the points of the PDM than a bend of the same angle. For a twisting angle of  $\pi/3$ , the parameters for the bending angle distribution are computed to yield approximately the same change to each point's position (and thus the total variance should be approximately even between the two modes). This scaling is done by using the knowledge that bending is applied in the plane which intersects the ellipsoid in its two largest radii, while twisting is applied in the plane of the two smallest. Once the twisting angle is chosen, a bending angle which will move points on the ellipsoid boundary by the same Euclidean distance as the twisting angle can be computed. For this data, PCA yields two large principal variances which account for 65% and 28% of the total variance. The Euclideanization-based method yields principal variances of 49% and 46%, which are much closer to the expected values. Furthermore, the dominant mode of the PCA distribution is a bending deformation rather than a twist, even when the angles are adjusted so that the twisting deformation should be slightly larger, showing that PCA tends to overestimate the effect of the bending transformation relative to the twisting.

The mean deformations produced by the Euclideanization-based method are closer to the expected deformations than their PCA counterparts. To demonstrate this, I generated 5 sets of 100 ellipsoids with mean bending/twisting angles of 30/45, 45/45, 45/60, 60/45, and 60/60. I then computed the pointwise mean squared error (MSE) between the expected PDM (computed analytically) and the PDM resulting from applying the learned deformation to the same undeformed ellipsoid

for each set. The five ellipsoids resulting from the mean PCA deformations have an average MSE of 1.038 from the expected result while the five deformations produced by the Euclideanization-based method have an average MSE of 0.664. Figure 4.2 shows the results for each individual experiment.

Bending	30	45	45	60	60
Twisting	45	45	60	45	60
PCA MSE	0.62	1.13	0.90	1.52	1.02
CPNS MSE	0.31	0.87	0.59	0.71	0.84

Figure 4.2: MSE between the estimated mean deformations of PCA and CPNS compared to the expected mean deformation.

#### 4.4.3 Application to S-reps

This approach of first Euclideanizing a shape representation before then estimating probability distributions of their differences can also be applied to s-reps. Because the s-rep manifold is a product of various spaces (some spherical and some not), a single PNS can not be used for an entire s-rep. Instead, the various components of the s-rep are Euclideanized separately and these Euclideanized values commensurated and combined into a single vector in a process called compositing. The details of this method are given in section 2.2.4. Differences between these Euclideanized representations can then be computed and their probability distribution can be estimated. Figure 4.3 shows the result of applying a computed mean of bending and twisting deformations with twisting angle  $\pi/3$  and bending angle  $\pi/6$  to an ellipsoid s-rep. Figure 4.4 shows the result of deforming the s-rep along the first two eigenmodes of this deformation, with the first principal component being mostly twisting and the second mostly bending, showing good separation of the two types of deformation into separate principal components.

## 4.5 Discussion

In this chapter, I introduced a method to estimate probability distributions of paired shape differences by first Euclideanizing the shape representation so that differences between pairs of shapes can be easily computed and analyzed. I've shown that this approach, when applied to deformed ellipsoid PDMs, more accurately estimates both the correct types of change as well as the correct



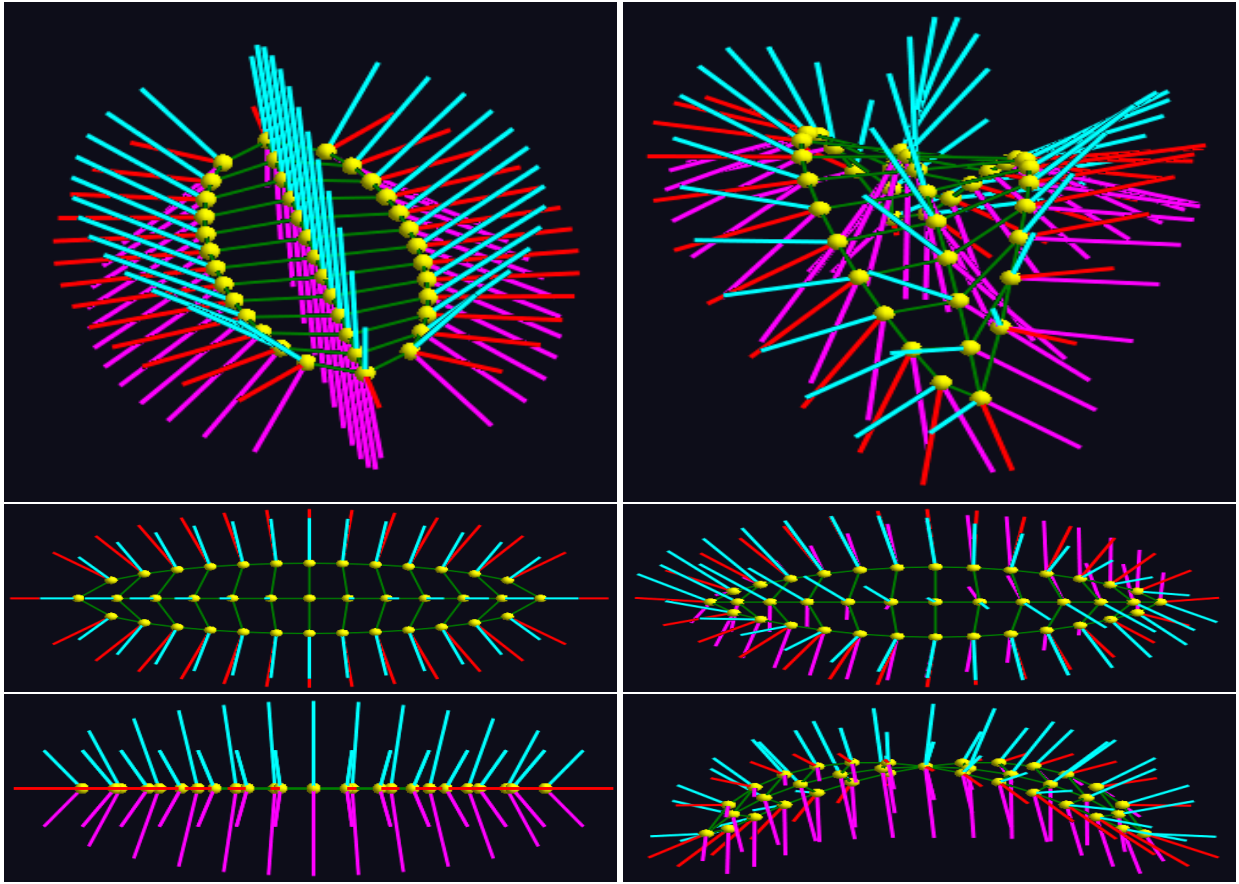


Figure 4.3: Three views of an ellipsoid s-rep before (left) and after (right) application of computed mean deformation. As expected, both bending and twisting can be seen in the mean

magnitude of these changes relative to applying PCA directly on PDM differences. When applied to s-reps of deformed ellipsoids, the Euclideanization approach computes a reasonable mean deformation and correctly separates the components of the deformation into separate eigenmodes.

This method could be extended to more general longitudinal analysis problems. Once a sequence of multiple shapes has been Euclideanized, standard techniques such as regression could be used to estimate how shapes are changing over time.

In chapter 6 I show results of performing this analysis on a population of prostate s-reps in the form of a mean change and its modes of variation as well as its application in segmenting the prostate in TRUS.

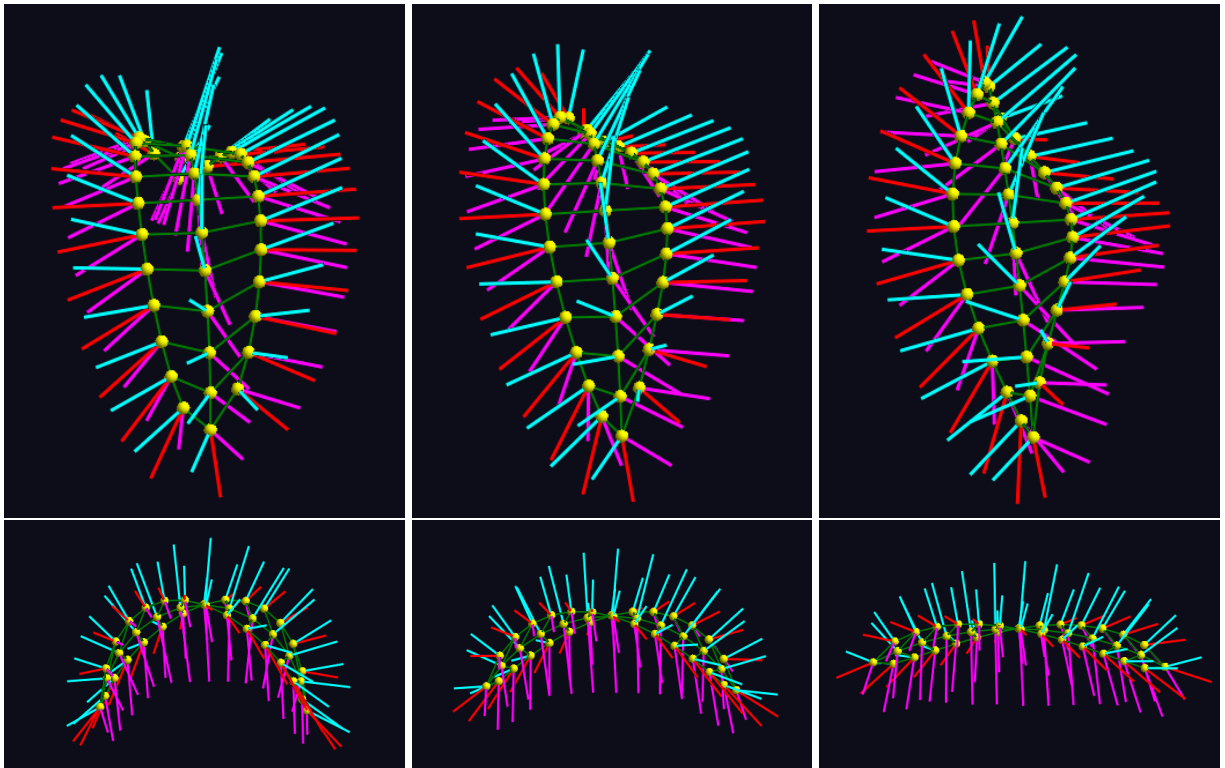


Figure 4.4: An ellipsoid deformed  $-1.5$  (left),  $0$  (middle), and  $1.5$  (right) standard deviations along its first (top) and second (bottom) principal components. The first component is dominated by a twisting deformation, while the second is dominated by a bending.

## 5 MODELING TRUS APPEARANCE VIA REGIONAL TEXTURE CLASSIFIERS

### 5.1 Introduction

As mentioned previously, deformable model segmentation involves deforming an object representation so that it better matches the boundary of the desired object in the image. A common approach is to build a statistical model of the appearance of an object in a particular modality and use this model in driving the optimization. Building a single, global model for appearance can be successful when an object’s appearance is relatively uniform or it has strong contrast with the neighboring anatomy. When these properties do not hold, however, a more fine-grained approach is required.

Segmentation of the prostate from TRUS is challenging in part because of the difficulties in discerning the edges of the prostate in ultrasound images. The appearance of both the prostate and its surrounding anatomy varies widely around its boundary, making the use of a single global appearance model insufficient and motivating the use of a locally-defined one. In addition, issues of contrast and noise-like speckle present in the ultrasound images makes direct analysis of ultrasound intensity unreliable. Instead, we define appearance in a local fashion using derived texture features. S-reps provide a convenient method for defining local boundary patches that correspond across multiple cases. For each patch we take the approach of training a classifier on both texture and intensity to distinguish between the appearance of voxels just inside the prostate boundary in that region from those just outside.

From these classifiers we can compute the probability that a voxel in a new image came from inside the prostate. We then use these probabilities in a new objective function to drive prostate segmentation. The appearance model itself is the subject of this chapter, while its use in the segmentation framework is described in chapter 6.5.

This overall approach shares several similar characteristics with many of the methods discussed in section 2.2.6, but it has several important characteristics which none of the other methods fully capture. Some of the classification-based methods discussed previously perform segmentation based on the binary decisions output by the classifier, while others turn the classifier outputs into continuous values using various methods such as application of a sigmoid function to map outputs to  $[0, 1]$ . Instead, I use an application of Bayes' theorem to further leverage the training data in order to better understand what the likely distribution of classifier outputs will be when applied to a new image.

Perhaps the most important characteristic that my method uses for modeling ultrasound appearance is the strong level of localization used in the training of the appearance classifiers. While other methods, most notably those of Zhan et al. [40] and Yang et al. [46] use locally trained classifiers of prostate appearance, they train over many fewer and much larger regions (15 and 6, respectively). This means that their regions often contain many disparate types of tissue and textures which can lead to poorer classification results, particularly if there is tissue which is relatively similar to prostate texture. In contrast, I am able to leverage the strong correspondences provided by s-reps to train much more localized texture classifiers, allowing for these classifiers to be more finely tuned for the specific regions of the image in which they will be applied. Because s-reps have been shown to produce stronger correspondence than the PDMs typically used in ASM-based segmentations, these classifiers can be consistently applied on voxels in the correct regions, minimizing the main drawback of such a scheme.

## 5.2 Materials

The data used for this work consists of a set of 29 manually segmented 3D TRUS images of the prostate. We divide the cases into 16 for training and 13 for testing. Each of the prostates from the training set has been fit with an s-rep using the procedure described in section 2.1.2. Using the probability distribution computed from the 16 training s-reps, the remaining cases are then fit with s-reps for use in testing. Each s-rep has 7 rows and 6 columns, resulting in 106 total spokes.

### 5.3 Methodology

In order to build a local appearance model, we must be able to define local regions of the object boundary which correspond across the training cases. Given a set of such regions, the voxels just inside the boundary at a region form one class, while the voxels just outside the boundary make up the other.

For each voxel we have a feature tuple  $\mathbf{f}$  consisting of some combination of intensity, texture, or other derived features. For each patch we pool together the inside and outside features from each training case to form overall inside and outside classes for that patch. From these two classes we use distance-weighted discrimination (DWD) [64] to compute a separation direction  $\mathbf{v}$  in feature space which best separates the appearance of voxels inside and outside the prostate boundary.

Given a separation direction  $\mathbf{v}$ , we project each training point  $\mathbf{f}$  onto  $\mathbf{v}$  yielding a value  $d$ . If we consider the threshold on the separation direction to be at  $d = 0$ , the sign of  $d$  indicates to which class  $\mathbf{f}$  has been assigned, while its magnitude is distance from the separating hyperplane and thus indicates confidence in this assignment under the assumption that points further from this hyperplane are more likely to be correctly classified than those nearer to it. We form two histograms of  $d$  values, one for those voxels from inside the boundary and one for voxels outside the boundary. These histograms represent the probability distributions  $p(d|in)$  and  $p(d|out)$ , respectively.

Given a new feature tuple, such as one from an image to be segmented, we wish to determine whether it is more likely that this feature tuple came from inside or outside of the prostate. Assuming we know which regions of the prostate the voxel came from, we can project it along the  $\mathbf{v}$  for that region and get its  $d$  value. From this  $d$  value we wish to know  $p(in|d)$ . Using Bayes rule we have

$$p(in|d) = \frac{p(d|in)p(in)}{p(d|in)p(in) + p(d|out)(1 - p(in))}$$

where  $p(in)$  is the prior probability of being inside the object and is a parameter that must be set. If we assume equal probability of coming from inside and outside of the object, this reduces to

$$p(in|d) = \frac{p(d|in)}{p(d|in) + p(d|out)} \quad (5.1)$$

This allows for the computation of the probability that any particular voxel came from inside the prostate.

## 5.4 Application

To build a local appearance model, we must first be able to define local regions around the prostate boundary which are in correspondence across the training cases. The s-rep fitting process ensures that each prostate's s-rep comes from the same shape space and produces reasonable correspondence across cases.

Given a set of fit s-reps, we define a local boundary region to be centered at the end of a spoke and extend halfway to neighboring spokes in each direction, forming a quadrilateral on the boundary. By moving some distance along the spoke in either direction, we can form inside and outside regions for the voxels near the boundary.

### 5.4.1 Ultrasound Appearance Model

As a preprocessing step, each of the TRUS images is *unfanned* so that the insonation direction, the direction along which the sound propagates, runs along one of the major axes while the others represent two axes orthogonal to it. This is done under the observation that much of the texture information happens either along or orthogonal to the insonation direction. Figure 5.1 shows an example of the original ultrasound and its unfanned counterpart. In order to decrease the variance in the ultrasound intensity and to better separate texture and intensity, we run speckle-reducing anisotropic diffusion [21] on each image. This produces a smoothed intensity image. The difference between the original image and the smoothed one yields a texture image upon which we can do texture-based analysis. Figure 5.2 shows an ultrasound image along with its derived intensity and texture images.

The choice of the feature tuple  $f$  that represents each voxel is important to the success of the

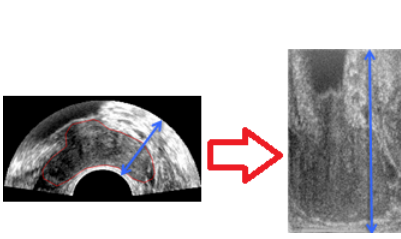


Figure 5.1: An original, fanned ultrasound on the left and its defanning on the right.

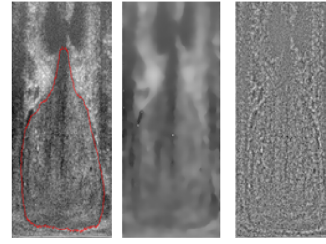


Figure 5.2: The unfanned ultrasound on the left, despeckled intensity image in the middle, and texture image on the right.

method. As noted in section 2.2.6, previous work has been done on ultrasound prostate segmentation making use of either 2D or 3D Gabor filters, and this is what we choose to use here. At each voxel in the image, we compute 2D Gabor features in 6 orientations, 2 scales (5 and 10 voxels), and 2 phases in each of the 2 orthogonal planes which include the insonation direction. Combining these 48 values together with the voxel’s intensity yields a 49-dimensional feature tuple for analysis. In chapter 6 I show how these feature tuples, after being converted into probabilities, can be used to drive the image match term of a deformable-model based segmentation.

## 5.5 Evaluation

Here I evaluate the effectiveness of the appearance model specifically in how well the local classifiers can classify inside from outside without regard to its ultimate application of segmentation, which will be discussed in chapter 6.5.

To analyze the effectiveness of the local texture classifiers, I first test to see if there are meaningful differences found between the inside and outside classes in each region. To test this, each region was subjected to a Direction-Projection-Permutation (DiProPerm) [65] hypothesis test. In this test, all training features from a given region are projected onto that region’s separation direction. Then, the difference of the mean of the two distributions of  $d$  values is computed. The region’s training points are then randomly relabeled and a new classifier is computed, followed by a reprojection and recomputation of the mean difference. Iterating this process yields a null distribution of these mean differences, and we can then check the z-score of the mean difference for the original labelings.

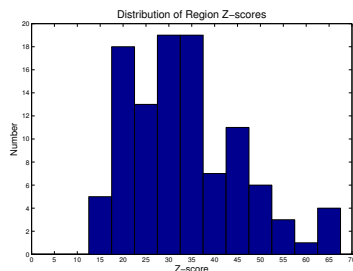


Figure 5.3: Histogram of z-scores resulting from DiProPerm tests. These scores show strong significance for all regions.

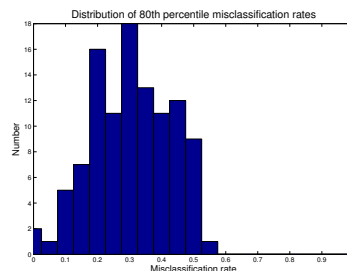


Figure 5.4: Histogram of 80th percentile misclassification rates. Most of the regions perform well most of the time.

Figure 5.3 shows the resulting z-scores for each of the 106 local classifiers. As we can see, the original labeling’s mean difference lies greater than 3 standard deviations from the mean of the null distribution in every region. This indicates that every region finds truly separable classes.

This evaluation is useful for determining if a region truly has two separable classes, but it does not directly indicate how well each of the trained classifiers does in separating these two classes. For this, we look directly at the misclassification rates of the classifiers applied to the s-reps fit to the 13 images left out of training. Figure 5.4 shows that 73 of the 106 regions have lower than 30% misclassification on at least 80% of the test data, showing that most of the classifiers do well most of the time. More importantly, the regions where the classifiers perform poorly are spread out around the boundary of the prostate, so that no large region always performs badly.

Using the fitted s-reps, we can classify all voxels near the s-rep boundary and compute the probability that they came from inside the prostate. Doing this for every voxel yields an image I call a  $p$ -image. These images generally show high probabilities of inside on the inside and lower probabilities of inside on the outside of the object, indicating they could be used as a basis for a good segmentation.

## 5.6 Discussion

This chapter introduced a novel method for modeling appearance of the prostate in TRUS by defining local classifiers based on s-rep correspondence which allow for the computation, at any voxel, of the probability that it came from inside the prostate based on its texture features. The



majority of the local classifiers are able to accurately classify inside from outside in unseen testing cases and produce reasonable probability images which can be used for segmentation.

One failing of the method in its present form is the use of hard boundaries (i.e., no overlap between neighbors) on the regions. While the s-rep correspondence behaves adequately in most cases, the most problematic regions in terms of quality of model tend to be those near the locations of the prostate boundary where the appearance of the neighboring anatomy changes. The use of fuzzy region boundaries, such as the considering of neighboring regions texture features when training the classifiers, could decrease the effect of small correspondence problems and would be an interesting avenue for future work.

Another place where the method could be improved is the use of the 48 Gabor texture features. To my knowledge, there is no work that definitively shows that Gabor texture features are better than other methods for modeling the appearance of the prostate in ultrasound, such as other image-derived features or physically-based features, though it does appear to be overwhelmingly the most common approach in the literature. There is also no indication that all 48 features are needed in every region, and reducing the feature dimension could be useful in reducing computational load and bringing the method to clinical use.

## **6 SEGMENTATION OF THE PROSTATE FROM TRUS**

### **6.1 Introduction**

As discussed in chapter 1.7, there are a number of factors which make prostate segmentation from 3D TRUS difficult. One of these is the difference in prostate shape caused by the introduction of the ultrasound transducer, while another is the difficulty in modeling the highly variable appearance around the prostate boundary in ultrasound images.

In chapter 4.5 I developed a method for estimating probability distributions on deformations between pairs of shapes. Chapter 5.6 described a method that uses s-reps to define local regions of the prostate boundary on which classifiers specific to that region's appearance can be trained, providing a locally-based appearance model for the prostate boundary in TRUS images. This chapter describes how these two techniques are used in a deformable model-based segmentation framework to segment the prostate from TRUS images.

### **6.2 Materials**

As in chapter 5.6, the data used for this work consists of a set of 29 manually segmented 3D TRUS images of the prostate. I divide the cases into 16 for training and 13 for testing. Each of the prostates from the training set has been fit with an s-rep using the procedure described in section 2.1.2.

I proceed with the discussion of the segmentation method in this chapter assuming that the training both of the shape deformation probability distribution from chapter 4.5 and of the local classifiers described in chapter 5.6 has already been done.

### **6.3 Segmentation Methodology**

This section describes the methodology I use to apply the techniques in chapters 4.5 and 5.6 to segment the prostate from TRUS images. I perform segmentation using a deformable model-based

segmentation framework. The objective function for a deformable segmentation has the general form

$$f(x) = P(x) + \omega I(x) \quad (6.1)$$

where  $x$  are the parameters of the model's current state,  $P$  measures the log-likelihood of having the particular model given by  $x$ ,  $I$  measures how well the model matches the image data, and  $\omega$  is a parameter used to control the relative weights of the two terms. The objective is to maximize  $f$ .

### 6.3.1 Model Deformation and Probability

In segmenting the prostate from TRUS, a patient's prostate starts in a normal state and is deformed by the TRUS transducer. Chapter 4.5 describes a method for learning a probability distribution on these deformations using a set of pre- and post-deformation prostate s-reps. This method yields a mean deformation  $\hat{D}$  and a set of shape change eigenvectors  $v$  together with their variances  $\sigma^2$ , all in the Euclideanized s-rep space, which together define the shape space I will optimize over.

Given a new case to segment, I assume the existence of a pre-segmented planning-time MRI of the patient's prostate with an s-rep fit to it. I apply the learned mean deformation  $\hat{D}$  to the patient's initial model  $M_{MRI}$  to yield  $M_{US}^0$ , the initial guess for the patient's prostate shape in ultrasound. Because this mean (and its eigenmodes) are learned in Euclideanized rather than ambient space, the actual computation is

$$M_{US}^0 = DE \left( E(M_{MRI}) + \hat{D} \right),$$

where  $E$  and  $DE$  Euclideanize and de-Euclideanize, respectively, based on the polar system computed via PNS on the group of prostate s-reps.

The parameters  $x$  from equation 6.1 of the model deformation are the coefficients for the eigenmodes of the deformation distribution. For any iteration  $k$  of the optimization, the current candidate model is given by

$$M_{US}^k = DE \left( E(M_{MRI}) + \hat{D} + \sum_i x_i^k \sigma_i v_i \right),$$

where  $i$  ranges over the modes of variation being considered.

### 6.3.2 Probability Images and Image Match

Given a current guess for the patient's prostate s-rep in the TRUS image, I use the appearance classifiers described in chapter 5.6 to create a probability image or *p-image*. These classifiers are trained on patches of voxels near the boundary, where patches are formed based on neighborhoods around s-rep spokes. Every voxel within a certain distance of the s-rep boundary has an s-rep spoke which it is nearest to and so falls within that spoke's patch. Associated with each voxel is a 49-dimensional vector of Gabor texture features as described in section 5.4. This feature vector can be projected onto the DWD separation direction for that patch, giving a value  $d$ . From this  $d$  value the probability that that voxel came from inside the prostate,  $p(in|d)$ , can be computed using equation 5.1. A p-image is created by performing this computation on every voxel within a certain distance of the s-rep's boundary. Figure 6.1 shows an example p-image.

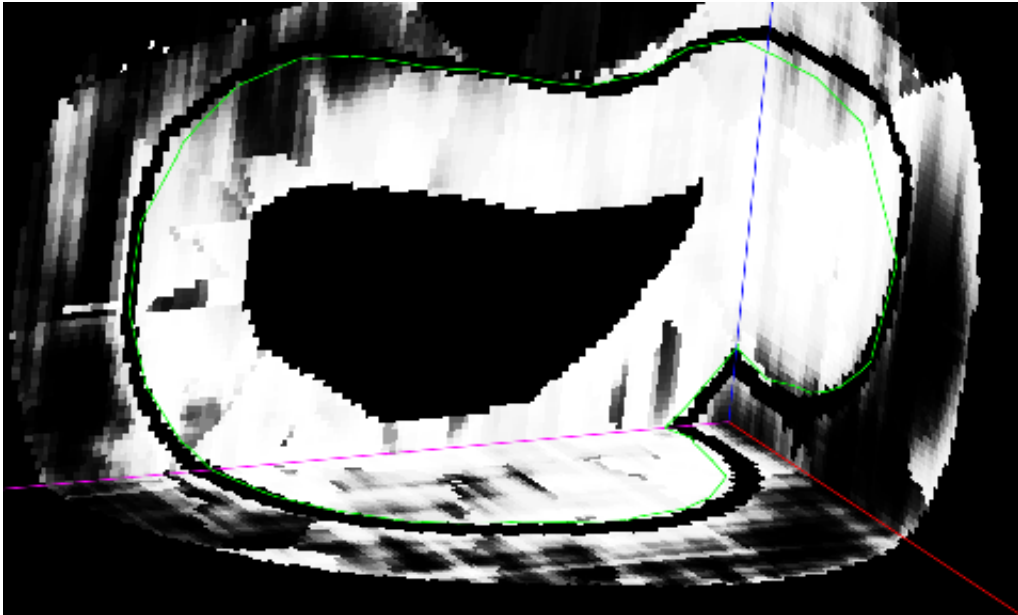


Figure 6.1: An example p-image of a prostate. High intensities reflect high  $p(in|d)$  for that voxel.

Intuitively, a good segmentation should have voxels with high average  $p(in|d)$  inside the candidate boundary and low average  $p(in|d)$  values outside it. I define the match value  $I$  from equation

6.1, for an object with  $k$  regions, as

$$I = \sum_{\Omega_i=1\dots k} [(\rho_i^{in} - \rho_i^{out}) - |\rho_i^{in} + \rho_i^{out} - 1|] . \quad (6.2)$$

where  $\rho_k^{in}$  and  $\rho_k^{out}$  are the average  $p(in|d)$  values for the regions inside and outside, respectively, the  $k^{th}$  patch. The first term encourages large differences in the means for the inside and outside patches ( $\rho^{in} = 0.7$  and  $\rho^{out} = 0.2$  is better than  $\rho^{in} = 0.6$  and  $\rho^{out} = 0.35$ ) while the second encourages the midpoint of  $\rho_k^{in}$  and  $\rho_k^{out}$  to be near 0.5 ( $\rho^{in} = 0.7$  and  $\rho^{out} = 0.3$  is better than  $\rho^{in} = 0.9$  and  $\rho^{out} = 0.5$  even though the separation is the same.)

### 6.3.3 Optimization

The optimization of equation 6.1 proceeds via a standard conjugate gradient optimization of  $x$ , deforming the prostate to more closely match the current p-image. After each iteration, the p-image is recomputed using the new candidate model.

## 6.4 Results

### 6.4.1 Estimation of Prostate Deformation Distribution

The mean and modes of variation of the prostate's deformation from planning-time MRI to biopsy-time TRUS were computed from the 16 training cases using the method described in chapter 4. The computed mean deformation shows the denting characteristic of the effect of the TRUS transducer, and the eigenmodes show various other changes in the TRUS dent and thus the shape of the prostate. Figure 6.2 shows an example of the computed mean deformation applied to a single prostate case. Videos of deformation along the first few eigenmodes are available online [66]. For segmentation, I optimize over the first 10 eigenmodes, which capture 93% of the total variance.

### 6.4.2 Segmentation

The shape space described in section 6.4.1 can be used to segment the prostate in TRUS. In each of the 13 test cases, an initial prostate is obtained by applying the mean deformation to an s-rep fit to that patient's pre-segmented planning-time MRI, serving as the initial guess for that patient's deformed prostate shape. This s-rep is then manually aligned into the TRUS image,

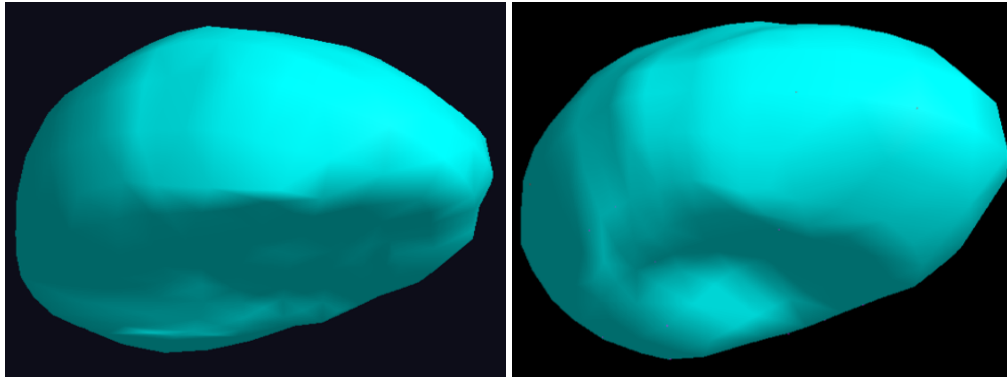


Figure 6.2: A prostate segmented from planning-time MRI (left) and this prostate with the mean deformation applied (right). Notice the large dent in the post-deformation model. This is similar to the typical dents caused by the TRUS transducer.

although an automatic method, such as one which matches the dent in the prostate to the location of the TRUS transducer, could be used. From this initial aligned s-rep, a p-image is calculated, and the s-rep is deformed along the eigenmodes of the deformation distribution to better match the image. From this new s-rep a new p-image is computed, and the process is iterated. I evaluate the quality of these segmentations based on two metrics: Dice Similarity Coefficient (DSC) and mean absolute distance (MAD) between my segmentation and a ground truth manual segmentation. The computations are performed via MeshValmet [67].

This procedure yields segmentations with an average DSC of 0.783 and MAD of 2.76 compared to ground truth manual segmentations. While these results are not unencouraging, this global optimization clearly does not do well enough to be clinically useful on its own. The need for further refinement is typical of the case when a global optimization over a limited number of eigenmodes is performed.

#### 6.4.3 Refinement

This segmentation via global deformation of the s-rep comes as close as it can to match the p-image by staying within the shape space, but some areas of the prostate will be more well-segmented than others. To address this issue, I include a refinement step to the segmentation following the global optimization. In this stage, spokes in regions where the classifiers are known to perform well are either lengthened or shortened to better match the p-image (note that, because

there are no angular changes to spokes, the s-rep region a voxel falls in does not change at this stage). The voxels near the s-rep boundary at each such spoke are then examined to see how well the segmentation is doing in that region.

In regions where there are high probabilities inside and low probabilities outside, the spoke stays as is. In regions where there are all high probabilities, the spoke is gradually lengthened until it finds an outside region with low probabilities, and a similar approach is taken for spokes which have low probabilities everywhere. Spokes are constrained to not gain or lose more than 25% of their original lengths. In order to maintain smooth s-rep boundaries, the change in a spoke's length is propagated to its neighbors, falling off quickly so as to only change nearby spokes.

Using this approach, the segmentations described in section 6.4.2 can be improved to have an average DSC of 0.903 and MAD of 1.4, both of which are competitive with state of the art. A comparison to the accuracies reported for other methods is given in table 6.3. These methods each require a small amount (typically the marking of a few points) of user interaction and were tested on similar sized datasets of 25-30 prostates.

Method	Year	DSC	MAD
Tutar[45]	2006	.835	1.3
Garnier[32]	2011	.864	0.8
Mahdavi[20]	2011	-	0.7
Qiu[23]	2013	.932	1.1
Proposed	2015	.903	1.4

Figure 6.3: Results of the proposed method compared with other recently published methods.

This refinement approach is simply an initial attempt to refine the segmentations and as such is not yet fully developed or claimed as a contribution of this dissertation. Nevertheless, it shows that the combination of the shape space developed in chapter 4 and the appearance model developed in chapter 5 form a promising basis for performing good segmentations.

## 6.5 Discussion

The segmentation method presented in this chapters shows an ability to accurately segment the prostate from TRUS by combining the appearance model proposed in chapter 5 with the method

for estimating an individual's prostate shape from chapter 4. The results obtained by a simple optimization over the shape space show promise, while a simple refinement method produces segmentations which are competitive with other recently published methods.

It is interesting to compare these results to a previous attempt, with the most notable difference being that the old attempt used a different method for estimating prostate shape. Instead of the method described in chapter 4, it used a different s-rep-based metric (spoke direction changes as rotations, radius changes as scalings, and hub position changes as regular Euclidean differences), applied each computed deformation to a single reference case, and then computed statistics on these deformed references. To apply to a new case, the reference case would be subtracted from the mean of the deformed cases and the resulting difference would be applied to the new case. In this previous try, the initial segmentation was much worse (0.718 vs 0.783 DSC) while the final segmentations (0.893/1.7 vs 0.903/1.4) are closer. This shows that the proposed method for estimating probability distributions on shape differences is superior to the previously used method, but that both segmentations seem to be reaching the limit of the current appearance model's ability to produce better p-images.

There are two factors currently limiting the usefulness of the appearance model's application to the segmentation problem: the use of hard patch boundaries and the density of the base s-rep used. The regions where the segmentation performs worse tend to be regions where the appearance of the tissue outside of the prostate changes, which would be alleviated by moving to fuzzy patch boundaries so that the appearance of neighboring patches would be considered when training each classifier. Increasing the s-rep density would allow for more closely matching the s-rep boundary by giving the s-rep the ability to have more finely grained local changes, but this would increase the previously described problem if it was not also paired with fuzzy patch boundaries.



## 7 CONCLUSIONS & DISCUSSION

This dissertation presented a method for segmentation of the prostate from TRUS during biopsy using a novel statistical model for how the TRUS transducer affects the prostate shape as well as novel learned regional classifiers on prostate appearance. S-reps provide a rich object representation well suited to both of these tasks. I described a method for learning a probability distribution on how an individual's prostate is deformed by the TRUS during image-guided biopsy and provided a means for leveraging the inherent localization ability of s-reps to train local classifiers for corresponding regions across a set of patients. Chapter 6.5 used these methods in a deformable segmentation framework to produce prostate segmentations which are competitive with the latest methods from the literature.

The contributions of this dissertation are as follows:

1. The development and implementation of a method for producing smooth continuous skeletal models from discrete s-reps. I used the extension to skeletal models of the mathematics of medial models to create a geometrically-based interpolation of discrete s-reps.
2. The development of a method using s-reps for computing probability distributions of how a shape changes from one state to another. Using representations of pairs of before/after objects, I use Euclideanization to transform the representations into a space where Euclidean statistical methods can be used to analyze the difference between before and after objects, avoiding the pain that comes with dealing with shape representations on the curved spaces in which they actually live.
3. The use of s-reps as a basis for the training of localized classifiers of object intensity and texture.

4. The computation of the probability that a new voxel from a particular region came from inside the prostate.
5. The combination of the previously mentioned techniques into a deformable segmentation framework to segment the prostate from biopsy-time TRUS images.

From these contributions I derive the following thesis:

*Thesis: Segmentation of an object deformed from a base state in a systematic way with appearance that varies around its boundary benefits from combining the following two approaches:*

- 1. Statistical analysis of the object deformation by a method suited for analysis in curved spaces*
- 2. Regionally trained appearance models to distinguish voxels inside and outside of the object's boundary in a classification-based approach.*

*Instead of the more typical boundary-based approach, continuously interpolated skeletal models form a strong basis for the training of statistics of object deformation as well as the creation of object-relative regions on which to train appearance models.*

## **7.1 Discussion and Future Work**

### **7.1.1 S-reps and Fitting**

The work in this dissertation as well as various related works [10, 5, 6] in the past few years have shown that s-reps are a powerful representation for modeling object shape. One of the major hurdles to s-reps gaining more widespread use is the various difficulties associated with using the related software. Steps have been taken recently to reduce these problems, but there is much work still to be done.

A major barrier to beginning to use s-reps has been the process used to fit s-reps to binary images. The fitting process in Pablo is driven through the use of plain-text configuration files, which are lists of various penalty terms which are used to weight various parts of the fitting optimization's objective function. The best values for these weights depend on a number of things, including the

particular object, the base s-rep grid size, and which of the various properties are desirable for that model to have.

Typically, creating a good configuration file consists of modifying one or more weights, re-running the fit, checking the result visually, changing some weights to correct some problem, and iterating. This is a tedious process that can result in a configuration file that is overly tuned for the specific case or cases used in the creation, so sometimes the file must be retuned after a population-wide fit is done.

The fitting process has been somewhat marginalized by the development of the thin plate spline (TPS)-based initialization method used to fit the s-reps described in chapter 4.5, which in many applications can replace the old initial fitting step called the *atom stage*, which greatly reduces the amount of work needed to create an initial set of s-reps. This TPS-based method requires a set of initial correspondences for the template model as well as each individual case. Currently, these correspondences can come from any source that produces corresponding PDMs. Early work used SPHARM-PDM [7] to generate these correspondences, but this method can produce unreliable correspondences when there is an ambiguity in the fitting of an ellipsoid to the object, such as when there is strong rotational symmetry. For this reason, I instead used the method of thin-shell demons [9] to register PDMs representing two objects and used the correspondence implied by this registration to fuel the TPS. While this method worked well for the prostates, it is unclear if it would be suitable for objects which had larger expected deformations.

### 7.1.2 Interpolation

The s-rep interpolation method presented here has been quite successful in producing qualitatively (and quantitatively in those objects where a ground truth is known) good s-reps. The method tends to produce high quality interpolation except in those regions where the spokes change direction rapidly, most notably at the corners of the s-rep grid, a problem which could be alleviated by moving away from the rectangular grid as the basis for s-rep representation. From what I have been able to tell, this is caused largely by the use of Bezier curves in the interpolation, which can curve

more wildly than is desired in such cases. Using a different set of basis functions could improve the accuracy of the interpolation in these regions.

This interpolation is highly parallelizable on a quad-by-quad basis, and because the s-reps are reinterpolated frequently in the core of many of the presented algorithms, it is necessary to leverage as much parallelism as possible. Currently, the averaging process described in section 3.7 is done in parallel for each spoke, but there is no spoke-level or quad-level parallelism as of yet.

Some work has been done on finding a closed-form solution for the interpolation which would allow for much more efficient computation, but it has not yet been carried to a usable state.

This interpolation is extendable to quasitubular s-rep models, though this work has not yet been performed.

### 7.1.3 Statistics on Shape Differences

The presented method for computing probability distributions of shape deformations proved powerful for accurately recovering underlying deformations in synthetic ellipsoid data, both for PDM and s-rep representations. It also showed the ability to represent the deformation caused by the TRUS transducer to the shape of the prostate and provide a basis for an accurate prostate segmentation. The method currently relies on a pooled set of before and after shapes to compute the PNS polar systems that allow for Euclideanization, but it is unclear whether this technique would be applicable if the underlying deformations were larger. In cases where the before and after shapes are too far separated, the PNS computation on two separate groups can produce results which do not accurately represent either.

I believe that this method is applicable in situations beyond simply estimating probability distributions for use in segmentation. Future work could include using the differences of the Euclideanized shapes in other tasks, such as categorizing the progression of an anatomical object as either normal or pathological.

#### 7.1.4 Appearance Model

The presented appearance model is able to accurately classify the texture of voxels inside the prostate from those outside the prostate in a large majority of the prostate boundary, providing a basis for an accurate segmentation. The appearance model could potentially increase performance even further with the use of features other than 2D Gabor features for modeling texture. In particular, the exploration of features which take into account the physics of the TRUS image acquisition could be powerful. It would also be desirable to explore using a reduced set of particularly informative features to ease computational load.

The prostate boundary patches with low classification performance tend to come from the regions surrounding areas of the boundary where the appearance changes. This is caused by training linear classifiers for data which may have more than two clusters, such as the inside appearances vs 2 or 3 different classes of outside appearances, some of which may be close to the inside appearances and thus produce a higher rate of misclassifications. This problem could potentially be solved using a non-linear kernel for the classifier.

There is nothing about this appearance model that is specific to the task of prostate segmentation from ultrasound. While the specific features used for classification will likely be different for other objects or modalities, the underlying strategy of using s-reps to heavily localize the object boundary, train classifiers to tell inside from outside appearance, and use the learned distribution of each region's features during classification to produce probabilities, could be adapted to many different scenarios.

#### 7.1.5 Segmentation

The segmentation method presented shows promising results, able to produce segmentations whose accuracy is competitive with other recently published TRUS prostate segmentation algorithms. However, there are several potential areas of improvement.

One problem, related to a problem mentioned for the appearance model, is that because the candidate segmentations are only guesses for the actual shape of the model, the s-reps regions

are not precisely in the prostate regions they are during training. Because of the hard boundary constraints between regions, a classifier may be seeing appearance it has never seen before and thus perform poorly. However, it is likely that, if the initial alignment is good, each spoke of the s-rep is near its correct region. By changing the hard boundary constraints in the training to fuzzy ones, so that the appearance of the regions neighboring region  $k$  are taken into account when training region  $k$ , it is less likely that the classifier is seeing something new so the expected accuracy should increase.

While the focus of this dissertation was on the methodological pieces which make up the segmentation algorithm rather than the segmentation itself, an initial try at a method for refining the initial segmentation is presented. This method shows good results, but further work is needed to address some of its drawbacks. For shapes which are very different in some region than the initial guess, the capture distance for the refinement step can be difficult to tune. Accurately finding the boundary means having some inside and some outside voxels in a region so that the boundary between the two shows up in the p-image. A naive scheme where, if the region is seeing only high  $p(in)$  values it looks farther out and vice versa, was applied, but more sophisticated methods, such as local histogram analysis or machine learning approaches to learn where to search for the boundary, could make this process both faster and more accurate. There are also still issues of the refinement of one spoke changing the position of neighboring spokes, which can pull those spokes to less desirable places in their own regions. There is a difficult balance to strike between accuracy of one spoke and its effect on its neighbors, though moving to using fuzzy regions for the appearance model could alleviate this somewhat.

A major hurdle in making this segmentation method clinically usable is the speed. Currently, the time taken to perform a single segmentation is on the order of an hour, whereas it would need to run in a few seconds at most to be used during a biopsy procedure. There are, however, several areas where this speed could be improved. As mentioned previously, the interpolation method could be greatly sped up by taking advantage of the highly parallel nature of the computation.

Another area where the speed could be improved is in the computation of the texture features, which currently requires 48 separate computations at every voxel in the image. Because the values computed for each voxel are independent of the values computed for neighboring voxels, this process is also highly parallelizable. Choosing a smaller set of more representative features would also make this computation more efficient. Finally, only computing them in the regions of the image where the prostate is most likely to be (or alternatively only in the areas currently being considered by the candidate segmentation) may also be useful, though the TRUS images do not typically capture anatomy very far from the prostate.

#### 7.1.6 Conclusions

While this chapter has focused mainly on the drawbacks and future improvements to be made to the various pieces of methodology presented here, the prostate segmentation method as it currently stands seems sound and has been able to produce quality results. While here the pieces of the method are applied to a prostate segmentation, none of these methods are specific to this ultimate goal and could be applied, either individually or collectively, to other problems. In particular, the method for producing statistics on shape differences could be applied to any task where the change in a shape from one time to another is of interest and the appearance model could be applied in any case with an object representation that supports localization. It is my hope that these methods will be applied to other problems in the future.

## REFERENCES

- [1] A. C. Society, “Cancer Facts & Figures 2016,” *American Cancer Society*, 2016.
- [2] J. Bax, D. Cool, L. Gardi, K. Knight, D. Smith, J. Montreuil, S. Sherebrin, C. Romagnoli, and A. Fenster, “Mechanically assisted 3D ultrasound guided prostate biopsy system. ,” vol. 35, no. 12, pp. 5397–5410, 2008.
- [3] T. F. Cootes, C. J. Taylor, D. H. Cooper, and J. Graham, “Active shape models-their training and application,” *Computer vision and image understanding*, vol. 61, no. 1, pp. 38–59, 1995.
- [4] S. M. Pizer, S. Jung, D. Goswami, J. Vicory, X. Zhao, R. Chaudhuri, J. N. Damon, S. Huckemann, and J. Marron, “Nested sphere statistics of skeletal models,” in *Innovations for Shape Analysis: Models and Algorithms* (M. Breuss, A. Bruckstein, and P. Maragos, eds.), pp. 93–113, Springer, 2013.
- [5] J. Hong, J. Vicory, J. Schulz, M. Styner, J. Marron, and S. M. Pizer, “Non-euclidean classification of medically imaged objects via s-reps,” *Medical Image Analysis*, vol. 31, pp. 37–45, 2016.
- [6] L. Tu, J. Vicory, S. Elhabian, B. Paniagua, J. C. Prieto, R. Whitaker, M. Styner, and S. M. Pizer, “Entropy-based correspondence improvement of interpolated skeletal models,” *Computer Vision and Image Understanding*, 2016.
- [7] M. Styner, I. Oguz, S. Xu, C. Brechbühler, D. Pantazis, J. J. Levitt, M. E. Shenton, and G. Gerig, “Framework for the statistical shape analysis of brain structures using spharm-pdm,” *The insight journal*, no. 1071, p. 242, 2006.
- [8] J. Cates, P. T. Fletcher, M. Styner, M. Shenton, and R. Whitaker, “Shape modeling and analysis with entropy-based particle systems,” in *Information Processing in Medical Imaging*, pp. 333–345, Springer, 2007.
- [9] Q. Zhao, T. Price, S. Pizer, M. Niethammer, R. Alterovitz, and J. Rosenman, “Surface registration in the presence of missing patches and topology change,” in *Proceedings of the 19th Conference on Medical Image Understanding and Analysis*, 2015.
- [10] J. Schulz, S. M. Pizer, J. S. Marron, and F. Godtlielsen, “Non-linear hypothesis testing of geometric object properties of shapes applied to hippocampi,” *Journal of Mathematical Imaging and Vision*, vol. 54, no. 1, pp. 15–34, 2016.
- [11] J. Damon and J. S. Marron, “Backwards principal component analysis and principal nested relations,” *Journal of Mathematical Imaging and Vision*, vol. 50, no. 1-2, pp. 107–114, 2014.
- [12] P. Fletcher, C. Lu, S. Pizer, and S. Joshi, “Principal Geodesic Analysis for the Study of Non-linear Statistics of Shape,” *IEEE Transactions on Medical Imaging*, vol. 23, no. 8, pp. 995–1005, 2004.
- [13] S. Huckemann, T. Hotz, and A. Munk, “Intrinsic shape analysis: Geodesic pca for riemannian manifolds modulo isometric lie group actions,” *Statistica Sinica*, pp. 1–58, 2010.



- [14] D. G. Kendall, "Shape manifolds, procrustean metrics, and complex projective spaces," *Bulletin of the London Mathematical Society*, vol. 16, no. 2, pp. 81–121, 1984.
- [15] S. Jung, I. L. Dryden, and J. Marron, "Analysis of Principal Nested Spheres," *Biometrika*, pp. 1–27, 2010.
- [16] S. Ghose, A. Oliver, R. Mart, X. Llad, J. C. Vilanova, J. Freixenet, J. Mitra, D. Sidib, and F. Meriaudeau, "A survey of prostate segmentation methodologies in ultrasound, magnetic resonance and computed tomography images," *Computer Methods and Programs in Biomedicine*, vol. 108, no. 1, pp. 262 – 287, 2012.
- [17] J. A. Noble and D. Boukerroui, "Ultrasound image segmentation: a survey," *Medical Imaging, IEEE Transactions on*, vol. 25, no. 8, pp. 987–1010, 2006.
- [18] R. Aarnink, S. D. Pathak, J. J. de la Rosette, F. M. Debruyne, Y. Kim, and H. Wijkstra, "Edge detection in prostatic ultrasound images using integrated edge maps," *Ultrasonics*, vol. 36, no. 1, pp. 635–642, 1998.
- [19] S. D. Pathak, D. Haynor, and Y. Kim, "Edge-guided boundary delineation in prostate ultrasound images," *Medical Imaging, IEEE Transactions on*, vol. 19, no. 12, pp. 1211–1219, 2000.
- [20] S. S. Mahdavi, M. Moradi, X. Wen, W. J. Morris, and S. E. Salcudean, "Evaluation of visualization of the prostate gland in vibro-elastography images," *Medical image analysis*, vol. 15, no. 4, pp. 589–600, 2011.
- [21] Y. Yu and S. T. Acton, "Speckle Reducing Anisotropic Diffusion," *IEEE Transactions on Image Processing*, vol. 11, no. 11, pp. 1260–1271, 2002.
- [22] M. Zouqi and J. Samarabandu, "Prostate segmentation from 2-d ultrasound images using graph cuts and domain knowledge," in *Computer and Robot Vision, 2008. CRV'08. Canadian Conference on*, pp. 359–362, IEEE, 2008.
- [23] W. Qiu, J. Yuan, E. Ukwatta, Y. Sun, M. Rajchl, and A. Fenster, "Prostate segmentation: An efficient convex optimization approach with axial symmetry using 3-d trus and mr images," *Medical Imaging, IEEE Transactions on*, vol. 33, no. 4, pp. 947–960, 2014.
- [24] A. Zaim, "Automatic segmentation of the prostate from ultrasound data using feature-based self organizing map," in *Image Analysis*, pp. 1259–1265, Springer, 2005.
- [25] A. Zaim, T. Yi, and R. Keck, "Feature-based classification of prostate ultrasound images using multiwavelet and kernel support vector machines," in *Neural Networks, 2007. IJCNN 2007. International Joint Conference on*, pp. 278–281, IEEE, 2007.
- [26] S. Mohamed, A. Youssef, E. El-Saadany, and M. Salama, "Prostate tissue characterization using trus image spectral features," in *Image Analysis and Recognition (A. Campilho and M. Kamel, eds.)*, vol. 4142 of *Lecture Notes in Computer Science*, pp. 589–601, Springer Berlin Heidelberg, 2006.

- [27] W. D. Richard and C. G. Keen, "Automated texture-based segmentation of ultrasound images of the prostate," *Computerized Medical Imaging and Graphics*, vol. 20, no. 3, pp. 131–140, 1996.
- [28] M. Kass, A. Witkin, and D. Terzopoulos, "Snakes: Active contour models," *International journal of computer vision*, vol. 1, no. 4, pp. 321–331, 1988.
- [29] A. Jendoubi, J. Zeng, and M. F. Chouikha, "Segmentation of prostate ultrasound images using an improved snakes model," in *Signal Processing, 2004. Proceedings. ICSP'04. 2004 7th International Conference on*, vol. 3, pp. 2568–2571, IEEE, 2004.
- [30] C. Knoll, M. Alcañiz, V. Grau, C. Monserrat, and M. C. Juan, "Outlining of the prostate using snakes with shape restrictions based on the wavelet transform (doctoral thesis: Dissertation)," *Pattern Recognition*, vol. 32, no. 10, pp. 1767–1781, 1999.
- [31] A. Zaim and J. Jankun, "An energy-based segmentation of prostate from ultrasound images using dot-pattern select cells," in *Acoustics, Speech and Signal Processing, 2007. ICASSP 2007. IEEE International Conference on*, vol. 1, pp. I–297, IEEE, 2007.
- [32] C. Garnier, J.-J. Bellanger, K. Wu, H. Shu, N. Costet, R. Mathieu, R. De Crevoisier, and J.-L. Coatrieux, "Prostate segmentation in hifu therapy," *Medical Imaging, IEEE Transactions on*, vol. 30, no. 3, pp. 792–803, 2011.
- [33] S. Lobregt and M. A. Viergever, "A discrete dynamic contour model," *IEEE transactions on medical imaging*, vol. 14, no. 1, pp. 12–24, 1995.
- [34] K. Li, X. Wu, D. Z. Chen, and M. Sonka, "Efficient optimal surface detection: theory, implementation, and experimental validation," in *Proceedings of SPIE*, vol. 5370, pp. 620–627, 2004.
- [35] H. M. Ladak, F. Mao, Y. Wang, D. B. D. B. Downey, D. Steinman, and A. Fenster, "Prostate segmentation from 2d ultrasound images," in *Engineering in Medicine and Biology Society, 2000. Proceedings of the 22nd Annual International Conference of the IEEE*, vol. 4, pp. 3188–3191, IEEE, 2000.
- [36] M. Ding, C. Chen, Y. Wang, I. Gyacskov, and A. Fenster, "Prostate segmentation in 3d us images using the cardinal-spline-based discrete dynamic contour," in *Medical Imaging 2003*, pp. 69–76, International Society for Optics and Photonics, 2003.
- [37] D. Shen, Y. Zhan, and C. Davatzikos, "Segmentation of prostate boundaries from ultrasound images using statistical shape model," *IEEE Transactions on Medical Imaging*, vol. 22, pp. 539–551, 2003.
- [38] N. Betrouni, M. Vermandel, D. Pasquier, S. Maouche, and J. Rousseau, "Segmentation of abdominal ultrasound images of the prostate using a priori information and an adapted noise filter," *Computerized Medical Imaging and Graphics*, vol. 29, no. 1, pp. 43–51, 2005.

- [39] Y. Zhan and D. Shen, "Automated segmentation of 3d us prostate images using statistical texture-based matching method," in *Medical Image Computing and Computer-Assisted Intervention-MICCAI 2003*, pp. 688–696, Springer, 2003.
- [40] Y. Zhan and D. Shen, "Deformable Segmentation of 3-D Ultrasound Prostate Images Using Statistical Texture Matching Method," *IEEE Transactions on Medical Imaging*, vol. 25, no. 3, pp. 256–272, 2006.
- [41] F. A. Cosío, "Automatic initialization of an active shape model of the prostate," *Medical Image Analysis*, vol. 12, no. 4, pp. 469–483, 2008.
- [42] T. Cootes, G. Edwards, and C. Taylor, "Active Appearance Models," in *Proc. European Conference on Computer Vision*, 1998.
- [43] R. Medina, A. Bravo, P. Windyga, J. Toro, P. Yan, and G. Onik, "A 2d active appearance model for prostate segmentation in ultrasound images," in *27th Annual international conference of the IEEE engineering in medicine and biology society*, pp. 3363–3366, 2005.
- [44] S. Ghose, A. Oliver, R. Martí, X. Lladó, J. Freixenet, J. C. Vilanova, and F. Meriaudeau, "Texture guided active appearance model propagation for prostate segmentation," in *Prostate Cancer Imaging. Computer-Aided Diagnosis, Prognosis, and Intervention*, pp. 111–120, Springer, 2010.
- [45] I. B. Tutar, S. D. Pathak, L. Gong, P. S. Cho, K. Wallner, and Y. Kim, "Semiautomatic 3-d prostate segmentation from trus images using spherical harmonics," *Medical Imaging, IEEE Transactions on*, vol. 25, no. 12, pp. 1645–1654, 2006.
- [46] X. Yang, D. Schuster, V. Master, P. Nieh, A. Fenster, and B. Fei, "Automatic 3d segmentation of ultrasound images using atlas registration and statistical texture prior," in *SPIE Medical Imaging*, pp. 796432–796432, International Society for Optics and Photonics, 2011.
- [47] S. Martin, J. Troccaz, and V. Daanen, "Automated segmentation of the prostate in 3d mr images using a probabilistic atlas and a spatially constrained deformable model," *Medical physics*, vol. 37, no. 4, pp. 1579–1590, 2010.
- [48] Y. Gao, Y. Zhan, and D. Shen, "Incremental learning with selective memory (ilsm): Towards fast prostate localization for image guided radiotherapy," *IEEE transactions on medical imaging*, vol. 33, no. 2, pp. 518–534, 2014.
- [49] J. R. C. Crouch, *Medial techniques for automating finite element analysis*. PhD thesis, Cite-seer, 2003.
- [50] Q. Han, S. M. Pizer, and J. N. Damon, "Interpolation in discrete single figure medial objects," in *Computer Vision and Pattern Recognition Workshop, 2006. CVPRW'06. Conference on*, pp. 85–85, IEEE, 2006.

- [51] J. Damon, “Smoothness and Geometry of Boundaries Associated to Skeletal Structures I: Sufficient Conditions for Smoothness,” *Annales de l’Institut Fourier*, vol. 14, no. 6, pp. 1941–1985, 2003.
- [52] K. Siddiqi and S. M. Pizer, *Medial representations: mathematics, algorithms and applications*, vol. 37. Springer, 2008.
- [53] J. N. Damon. personal correspondence, 2014.
- [54] K. Shoemake, “Animating rotation with quaternion curves,” in *ACM SIGGRAPH computer graphics*, vol. 19, pp. 245–254, ACM, 1985.
- [55] K. Shoemake, “Quaternion calculus and fast animation, computer animation: 3-d motion specification and control,” *Siggraph*, 1987.
- [56] E. B. Dam, M. Koch, and M. Lillholm, *Quaternions, interpolation and animation*. Datalogisk Institut, Københavns Universitet, 1998.
- [57] S. M. Pizer, *To compute numerically: Concepts and strategies (Little, Brown computer systems series)*. Little, Brown & Co. Inc., 1983.
- [58] I. L. Dryden and K. V. Mardia, *Statistical shape analysis*, vol. 4. J. Wiley Chichester, 1998.
- [59] J. G. Csernansky, L. Wang, S. C. Joshi, J. T. Ratnanather, and M. I. Miller, “Computational anatomy and neuropsychiatric disease: probabilistic assessment of variation and statistical inference of group difference, hemispheric asymmetry, and time-dependent change,” *Neuroimage*, vol. 23, pp. S56–S68, 2004.
- [60] L. Wang, J. S. Swank, I. E. Glick, M. H. Gado, M. I. Miller, J. C. Morris, and J. G. Csernansky, “Changes in hippocampal volume and shape across time distinguish dementia of the alzheimer type from healthy aging,” *Neuroimage*, vol. 20, no. 2, pp. 667–682, 2003.
- [61] M. Vaillant, M. I. Miller, L. Younes, and A. Trouvé, “Statistics on diffeomorphisms via tangent space representations,” *NeuroImage*, vol. 23, pp. S161–S169, 2004.
- [62] L. Wang, F. Beg, T. Ratnanather, C. Ceritoglu, L. Younes, J. C. Morris, J. G. Csernansky, and M. I. Miller, “Large deformation diffeomorphism and momentum based hippocampal shape discrimination in dementia of the alzheimer type,” *Medical Imaging, IEEE Transactions on*, vol. 26, no. 4, pp. 462–470, 2007.
- [63] S. Durrleman, X. Pennec, A. Trouvé, J. Braga, G. Gerig, and N. Ayache, “Toward a comprehensive framework for the spatiotemporal statistical analysis of longitudinal shape data,” *International journal of computer vision*, vol. 103, no. 1, pp. 22–59, 2013.
- [64] J. Marron, M. Todd, and J. Ahn, “Distance Weighted Discrimination,” *Journal of the American Statistical Association*, vol. 102, pp. 1267–1271, 2007.

- [65] S. Wei, C. Lee, L. Wichers, and J. Marron, “Direction-projection-permutation for high dimensional hypothesis tests,” *Journal of Computational and Graphical Statistics*, no. just-accepted, 2015.
- [66] “Prostate eigenmode videos.” <https://dl.dropboxusercontent.com/u/12881668/prostatemodes.html>.
- [67] “Meshvalmet.” <https://www.nitrc.org/projects/meshvalmet/>.