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Multiscale 3D Shape Representation and Segmentation with Applications to Hippocampal/Caudate Extraction from Brain MRI

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Abstract

Extracting structure of interest from medical images is an important yet tedious work. Due to the image quality, the shape knowledge is widely used for assisting and constraining the segmentation process. In many previous works, shape knowledge was incorporated by first constructing a shape space from training cases, and then constraining the segmentation process to be within the learned shape space. However, such an approach has certain limitations due to the number of variations, eigen-shapemodes, that can be captured in the learned shape space. Moreover, small scale shape variances are usually overwhelmed by those in the large scale, and therefore the local shape information is lost. In this work, we present a multiscale representation for shapes with arbitrary topology, and a fully automatic method to segment the target organ/tissue from medical images using such multiscale shape information and local image features. First, we handle the problem of lacking eigen-shapemodes by providing a multiscale shape representation using the wavelet transform. Consequently, the shape variances existing in the training shapes captured by the statistical learning step are also represented at various scales. Note that by doing so, one can greatly enrich the eigen-shapemodes as well as capture small scale shape changes. Furthermore, in order to make full use of the training information, not only the shape but also the grayscale training images are utilized in a multi-atlas initialization procedure. By combining such initialization with the multiscale shape knowledge, we perform segmentation tests for challenging medical data sets where the target objects have low contrast and sharp corner structures, and demonstrate the statistically significant improvement obtained by employing such multiscale representation, in representing shapes as well as the overall shape based segmentation tasks.

Keywords

multiscale shape representation; shape-based segmentation

1. Introduction

Extracting anatomically and/or functionally significant regions from medical imagery, i.e., segmentation, is a challenging and essential task in medical image analysis. In the past two decades, a great deal of research has been devoted to the segmentation problem, especially

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the segmentation of medical imagery. Among them, various types of methods have been utilized ranging from linear filtering (Sobel and Feldman, 1968; Canny, 1986), graph theory (Boykov and Kolmogorov, 2004; Shi and Malik, 2000), stochastic processes (Geman and Geman, 1984; Panjwani and Healey, 1995), and active contour/deformable models (Kass et al., 1988; Mcinerney and Terzopoulos, 1996). Although a complete review of image segmentation is beyond the scope of this paper, we briefly review some of the relevant work using the active contour methods, with special emphasis on the shape-based active contour segmentation.

In (Kass et al., 1988), the authors proposed an active contour model that represents the object boundary using parametric splines. The contour then evolves to converge to the salient edges of the desired object. The method was extended to the 3D case in (Terzopoulos et al., 1988). However, due to the parametric representation of the contour (for simplicity we will use the term *contour* for both 2D curves and 3D surfaces in this work), such an approach has problems handling topological changes during the evolution process. In (Osher and Sethian, 1988), the contour is represented as the level set of a function defined on the image domain. Subsequently, researchers in (Malladi et al., 1995; Kichenassamy et al., 1995; Caselles et al., 1997; Yezzi Jr et al., 1997) adopted such a level set representation for implementing their active contour models. However, all the aforementioned active contour schemes utilize only the edge information of the image, which is prone to problems with noise. To solve this problem, several authors capture the object feature from a more global perspective of view by utilizing the image statistics inside and outside the evolving contour (Zhu and Yuille, 1996; Yezzi Jr et al., 1999; Chan and Vese, 2001; Michailovich et al., 2007).

Nevertheless, these algorithms only utilize the image information and are all “bottom-up” schemes. However, due to typical problems such as imaging noise, low contrast, and partial voluming effects, these “bottom-up” segmentation methods that solely rely on image information are not sufficient to obtain satisfying results. Accordingly, higher level shape knowledge is necessary to incorporate the necessary “top-down” information into the segmentation process for better performance. For example, Cootes *et al.* used a parametric representation for the shapes and constructed a point-wise correspondence among all the training shapes (Cootes et al., 1995). By assuming the distribution of corresponding points to be Gaussian, principal component analysis (PCA) was utilized to extract the eigenmodes of the variations. To extend such an approach to situations where the contour is implicitly represented, Leventon *et al.* performed PCA directly on the level set functions (Leventon et al., 2000). Furthermore, Tsai *et al.* employed PCA as the basis for the learned shape space with the subsequent image segmentation being carried out in a finite dimensional shape space setting (Tsai et al., 2003). Finally, Rousson *et al.* performed a similar principal component analysis, but then incorporated the shape constraint into a segmentation energy functional in order to guarantee that the final shape does not deviate too drastically from those in the learned shape space (Rousson et al., 2004).

1.1. Related Work

While the previous shape based segmentation methods achieved great success in solving segmentation problems where the image quality is suboptimal, they also have certain limitations. First, the number of eigen-shapemodes is limited by the number of training cases. Indeed, when performing PCA, the covariance matrix is of rank less than or equal to $N - 1$ when there are N training sets. Hence, the eigen-shapemodes have an upper limit of $N - 1$. More importantly, the eigen-shapemodes are encoded by the eigenvectors of the covariance matrix, which captures the most global modes of variations of the shape. In other words, small scale variance is very likely to be missed by such an analysis because its energy is overwhelmed by the global variance. However, especially for medical

applications, this global variance may be due to inter-subject differences not related with pathology, whereas a relatively small “bump” may be an important indicator of pathology.

In order to address this issue of “treating the shape as a whole”, a natural way is to decompose a single shape into several “sub-shapes”. For example, a surface may be decomposed into a linear combination of sinusoids using the Fourier transformation (Staib and Duncan, 1996). Later in (Davatzikos et al., 2003), Davatzikos *et al.* treat the coordinates of the points on the curve as 1D functions and perform wavelet decomposition on them. However, extending such a scheme to higher dimensions and more complicated topologies is not straightforward. More recently, Nain *et al.* extended such methods to 3D spherical shapes (Nain et al., 2007). In that work, the surface is parametrically represented and is mapped to a sphere using a conformal mapping (Angenent et al., 1999). By doing so the surface becomes a 3D function defined on a sphere and is then decomposed using spherical wavelets. Nevertheless, not only the spherical topology is a limitation, the conformal step in mapping a surface to a sphere needs the selection of some landmarks, which also induces arbitrariness into the procedure. Graphically, these most related previous works form a grid illustrated in Table 1. Naturally, filling the blank at the corner, is the objective of the present work.

1.2. Our Contributions

Inspired by (Nain et al., 2007), in this work we perform the wavelet decomposition on an implicit representation of the shape. More explicitly, we use a modified version of the level set function to represent the contour, and the subsequent wavelet decomposition is performed on such a level set function. This effectively removes the topological restriction on the contour. Further, without the spherical mapping step, the correspondence among shapes is more naturally handled.

Indeed, with the shape being learned at various scales, the subsequent shape based segmentation is performed by utilizing the image information as well as respecting the prior shape knowledge. In doing so, we provide a general 3D shape-based segmentation method which handles nonspherical topologies and respects fine scale structure of the shape. Moreover, not only do we learn the shape which is the binary segmentation of the training image, but also the entire training image information is utilized in a multi-atlas framework. This effectively automates the algorithm initialization and improves the consistency of the method.

In addition to the methodological contribution, the proposed method was motivated by problems in image guided radio therapy. Indeed, brain metastases constitute the most common manifestation of cancer involving the central nervous system: it has been estimated that over 170,000 cases of brain metastases are diagnosed annually in the United States alone (Patchell, 2003). During the past half-century, the cornerstone of treatment for this oncologic phenomenon has been whole brain irradiation (WBI) (Knisely, 2009). WBI has multiple salutary effects including rapid relief of neurological signs and symptoms as well as enhanced local control. Moreover, WBI represents an attractive clinical alternative because it can potentially suppress micrometastases that are undetectable with the current degree of resolution by MR imaging. Unfortunately, WBI may also engender side effects including memory deficits and decrements in quality of life (Aoyama et al., 2007).

Stereotactic irradiation is an option that has gained popularity in the management of brain metastases. Stereotactic irradiation is appealing because it is of short duration, uses multiple intersecting beams to augment the dose within the tumor volume and provides a rapid dose fall-off thereby optimizing the dosimetric gradient outside the tumor. This rationale allowed Chang *et al.* (Chang et al., 2009) to mount a trial comparing WBI to stereotactic techniques

for patients suffering from brain metastases. The results of the trial indicated less decline in learning and memory function within the stereotactic arm. In order for those receiving WBI to obtain the optimal intracranial control of disease while simultaneously preserving neurocognitive function, it is of strategic importance to recognize that the primary neurocognitive impairments are in memory. Since memory control is thought to be mediated by the hippocampus, attention has been turned to whole brain radiotherapeutic techniques that allow the sparing of the hippocampus. In order to be able to minimize dose deposition within the hippocampus, clinicians must be able to confidently identify that structure. However, manually tracing out the hippocampus for each patient is time consuming and subject to the individual bias. Therefore, one major application of the proposed method is to automate the hippocampus extraction process, which can be very useful for the radiation planning task.

The remainder of the paper is organized as follows. In Section 2, we demonstrate how to represent the shape in a multiscale fashion and how the shape prior is constructed. After that, the segmentation scheme which utilizes both the image information and the learned shape prior is detailed in Section 3. Next, the experiments and results are given in Section 4. Finally, future and ongoing work are discussed in Section 5.

2. Multiscale Shape Representation and Shape Learning

We begin by noting that the two concepts: “contour representation” and “shape representation” are distinct but closely related. In particular, the shape representation depends on the representation chosen for contours. In this section, we first give an appropriate representation for contours. Then, based on this, we provide the multiscale shape representation. Moreover, the training shapes are learned under such new representation.

2.1. Contour Representation Using the Modified Level Set Function

In this work, we choose a modified level set function as the representation for the contours. This choice will not only be suitable for the shape representation given below, but also it is a natural choice for the subsequent segmentation step. More explicitly, given the closed contour $C \subset \Omega \subset \mathbb{R}^3$, its signed distance function (SDF) $\tilde{L} : \Omega \rightarrow \mathbb{R}$ is defined as:

$$\tilde{L}(x) := \begin{cases} -\inf_{y \in C} \|x - y\|, & x \text{ inside } C \\ \inf_{y \in C} \|x - y\|, & x \text{ outside } C \end{cases} \quad (1)$$

where $\|\cdot\|$ is the Euclidean norm. Furthermore, the original SDF is modified to:

$$L(x) := \begin{cases} 3, & \tilde{L}(x) \geq 3 \\ -3, & \tilde{L}(x) \leq -3 \end{cases} \quad (2)$$

This is the level set function used in (Whitaker, 1998), which is called the Sparse Field Level Set (SFLS) function. Besides its being a natural choice for the subsequent segmentation process, it will also benefit the shape representation step detailed in the next section. In the subsequent sections, all the level set representation for the contours are using such SFLS functions.

2.2. Shape Representation Using Wavelet Coefficients

At this point, we are able to formulate the multiscale shape representation. In general, given an SFLS represented contour $L : \mathbb{R}^3 \rightarrow \mathbb{R}$, its wavelet decomposition is written as:

$$W(\mathbf{u}) := \mathcal{D}\mathcal{W}\mathcal{T}[L(\mathbf{x})] \quad (3)$$

where we assume the image size in each dimension of L is power of 2, and $\mathbf{u}$ is the independent variable in the wavelet domain. Different wavelet bases can be chosen. In fact, in this study we tested the orthogonal Daubechies wavelets $D4$, $D6$, and $D8$, with constant boundary condition but the final segmentation results were not significantly affected by the choice. Moreover, we can see the using of the SFLS instead of the original SDF eases the boundary handling. Indeed, if the regular SDF were used, the unbounded nature of it brings difficulties in choosing the appropriate boundary condition. But with SFLS, constant padding is an easy and natural choice.

Having set up like that, we note that the wavelet coefficients are stored in a 3D array. Next, in order to represent the shape in multiscale, the coefficients are decomposed into multiple bands corresponding to various scales. As is illustrated in Figure 1, the coefficients in each scale are concatenated to form a column vector, called a *band*, and all coefficients are rearranged into different bands. Formally, we write this operation as:

$$\mathcal{R}[W] = \{B_1, B_2, \dots, B_K\} \quad (4)$$

where K is the total number of bands. For example, in Figure 1 there are 13 bands. Note that in the sequel, we will need to “inversely rearrange” the wavelet coefficients from the bands and this process is denoted as:

$$\mathcal{R}^{-1}[\{B_1, B_2, \dots, B_K\}] = W \quad (5)$$

Up to this point, the contour embedded in the SFLS function $L(\mathbf{x})$ is now represented by the set of bands: $\{B_1, \dots, B_K\}$. A nice property of such multiscale representation derives from the fact that the shape variance in different spatial locations and frequency scales are now separated in various bands.

In Figure 2, we demonstrate the multiscale shape representation using a seahorse data set (AIM@SHAPE). This particular shape is chosen because it has rich shape features in both the large and small scales, which is suitable for demonstrating the algorithm’s multiscale shape representation property. The SFLS of the seahorse shape is 512^3 in size, and it is decomposed into 7 different scales. After the decomposition, we keep the coefficients at the coarsest scale and set all the others to zero. With the remaining coefficients, the shape (SFLS) is reconstructed and its zero level surface is shown in Figure 2(a). Subsequently, by adding in the wavelet coefficients of the next finer level and reconstructing the shape, we get the surface in Figure 2(b). Such process continues till all coefficients are added, and the original surface is obtained as shown in Figure 2(g). Figure 2 clearly demonstrates that the multiscale view for the shape meets the need of the shape analysis. Indeed, under such representation, the local shape changes, such as those pointed by the arrows, can now be separated from the large ones and are analyzed in its own scale. Otherwise, if the entire shape is analyzed as a single entity, such small feature is very likely to be overwhelmed by those global scale ones.

2.3. Shape Prior Construction in Wavelet Domain

Assume we are given a set of N training contours (shapes): $\hat{L}_1(\mathbf{x}), \hat{L}_2(\mathbf{x}), \dots, \hat{L}_N(\mathbf{x})$. Firstly, the shapes need to be co-registered so that the variance we learned in the subsequent

statistical learning step is only due to shape, but not pose. To this end, we randomly choose one shape, for example $\hat{L}_1$, as the fixed shape, and register all the others to it. This is done by seeking the optimal similarity transformation τ in order to minimize the mean-square-error energy E defined by:

$$E(L_i, \tau) := \int (\hat{L}_i(\tau(x)) - \hat{L}_1(x))^2 dx \quad (6)$$

In 3D, the similarity transformation consists of translation along $X/Y/Z$ axes, rotation around $X/Y/Z$ axes, and isotropic scale. The registered contours are denoted as $L_1, L_2, \dots, L_N$. For each registered contour, its shape representation, i.e., wavelet coefficients band structure is obtained as

$$\mathcal{B}^{(i)} = \{B_1^{(i)}, B_2^{(i)}, \dots, B_K^{(i)}\} \quad (7)$$

where $i \in \{1, 2, \dots, N\}$.

In order to statistically learn the shape variances existing in the training shapes, we apply principal component analysis (PCA) to each band in order to compute the statistical model of the shape. More explicitly, the mean band structure is computed as:

$$\overline{\mathcal{B}} = \{\overline{B}_1, \overline{B}_2, \dots, \overline{B}_K\} \quad (8)$$

$$= \left\{ \frac{1}{N} \sum_i B_1^{(i)}, \frac{1}{N} \sum_i B_2^{(i)}, \dots, \frac{1}{N} \sum_i B_K^{(i)} \right\} \quad (9)$$

The mean shape can be considered as the shape without any variations, regardless of the scale of the variance. Because of this, it is expected that the mean shape computed in this manner will be consistent with the mean shape from a non-multiscale shape representation. In fact, since the wavelet transform is a linear operator, it is easy to show that such mean shape, defined as:

$$M := \mathcal{W} \mathcal{T}^{-1} [\mathcal{R}^{-1} [\overline{\mathcal{B}}]] \quad (10)$$

is the same as the one computed in (Tsai et al., 2003; Leventon et al., 2000).

While the proposed shape representation does not affect the mean shape, the multiscale property is beneficial when the shape variances are analyzed. In order to utilize such property, PCA is performed in each band to capture the shape variance. Formally, the mean of each band is first removed as $\tilde{B}_k^i = B_k^{(i)} - \overline{B}_k$, $i \in \{1, 2, \dots, N\}$. The covariance matrix for the k -th band is then formed as:

$$C_k := \frac{1}{N} \sum_{i=1}^N \tilde{B}_k^i (\tilde{B}_k^i)^T \in \mathbb{R}^{l_k \times l_k} \quad (11)$$

where $l_k = |B_k^{(i)}|$ denotes the length of the k -th band. Furthermore, the eigen-decomposition of C_k gives:

$$C_k = Q_k \Lambda_k Q_k^T = (q_1^k, \dots, q_{p_k}^k) \text{diag}(\lambda_1^k, \dots, \lambda_{p_k}^k) Q_k^T \quad (12)$$

where $p_k = \min(N, l_k)$ and the vectors $\{q_j^k, j=1, \dots, p_k\}$ consist of the bases for this band.

In contrast to the PCA scheme used in (Cootes et al., 1995; Tsai et al., 2003; Leventon et al., 2000), where for N training shapes there are at most $N - 1$ linear independent eigenvectors for the whole learned shape space, here we have bases in each band to record the shape variance at the given scale. Specifically, since the band length is varying, in the k -th band, the number of bases does not exceed p_k . For instance a 2D image with size 16×16 shown in Figure 1, it can be seen that starting from the band B_{11} , the band lengths l_k 's are greater than or equal to 64. In most of the cases, the medical images are all larger than 16×16 .

Therefore except for the first few bands, we almost always have $p_k = N - 1$. Hence the total

number of bases is: $\sum_{k=1}^K p_k \approx K(N - 1)$. In comparison to $N - 1$, such enrichment of the eigenmodes in the shape space greatly enhances the capability of capturing the shape variances at multiple scales.

In order to construct the allowable shape space which restricts the subsequent segmentation, we assume the eigen-values obtained in Equation (12) are decreasingly ordered.

Furthermore, the first Y eigenmodes, $q_1^k, \dots, q_Y^k$ corresponding to the largest Y eigenvalues are picked to record the shape variance in this band (scale). In practice, we choose Y to be $\min(\tilde{Y}, l_k)$ where

$$\tilde{Y} = \arg \min_Y \left[\sum_{i=1}^Y \sqrt{\lambda_i^k} \geq 90\% \sum_{i=1}^{p_k} \sqrt{\lambda_i^k} \right] \quad (13)$$

Moreover, for every $k = 1, \dots, K$, the shape space in that band, $\mathcal{S}_k$ is defined as:

$$\mathcal{S}_k := \left\{ (q_1^k, \dots, q_Y^k) \text{diag}(\sqrt{\lambda_1^k}, \dots, \sqrt{\lambda_Y^k}) \cdot (a_1, \dots, a_Y)^T : a_i \in [-6, 6], \forall i \right\} \quad (14)$$

2.3.1. Characteristics of the shape space—The above formula defines a hyper-rectangular shaped region centered at the mean in each band, with axes of length 6 times the standard deviation. Equivalently, this imposes a uniformly distributed prior for the shapes. In most of the literature, however, the Gaussian distribution is used. We should note here that in order to maximize the shape likelihood in the Gaussian case, there is always a tendency of evolving towards the mean shape which eliminates the individual shape variance. This is not always a desired property. On the other hand, the uniform distribution does preserve the shape variances. Moreover, the “six standard deviation” is chosen so that any event outside this hyper-rectangular is a very rare event. Finally, we note that the “shape space” above is in fact topologically closed but not a mathematical vector space, because it is not closed under addition.

3. Multiscale Shape Based Segmentation

In this section, we describe our multiscale shape representation based segmentation strategy. Briefly, given the image to be segmented, we first use a multi-atlas method to estimate the target location in the new image. Then, a data driven segmentation scheme is applied to extract the initial estimate of the shape. Thirdly, the multiscale shape constraints are used to regularize the previously obtained shape in the learned shape space. The second and the third steps are iterated until arriving at a steady state, which provides the final segmentation. We now give the details.

3.1. Shape Initialization

Given a new image $I : \mathbb{R}^3 \rightarrow \mathbb{R}$, the objective of the present section is to provide an initial shape, which is to be used as the starting point for the subsequent segmentation process presented in the next section. Accordingly, an atlas-based segmentation approach is adopted (Rohlfing et al., 2005; Aljabar et al., 2009). That is, all of the training images are deformably registered to the new image by maximizing mutual information (MI) (Viola and Wells III, 1997; Rueckert et al., 1999). The affine transformation is followed by a B-spline free form deformation. Moreover, to mitigate the error resulting from the implementation, we opt to use the MI registration scheme found in the InsightToolkit (Ibanez et al., 2003). By using MI, the proposed method is capable of handling images of multiple modalities. Then, with the optimal deformable transformations (affine + B-spline) being computed and denoted by $T_1, \dots, T_N$, the initial shape $P(\mathbf{x})$ is then defined using the “majority rule”:

$$P(\mathbf{x}) = \begin{cases} 1, & \text{if } \sum_{i=1}^N \tilde{U}_i(T_i(\mathbf{x})) \geq \frac{N}{2} \\ 0, & \text{otherwise} \end{cases} \quad (15)$$

where $\tilde{U}_i$ is the i -th binary label image corresponding to the i -th training image. In many atlas based algorithms, P serves as the final results. However, in order to further improve the segmentation result by combining the capability of atlas method with the shape based active contour, P only serves as the initialization for the subsequent shape based active contour segmentation for the new image I .

3.2. Data Driven Segmentation

Given the initial shape P , the proposed segmentation method is an alternating data-driven and multiscale shape-based process that starts with a data-driven (not shape guided) algorithm. Specifically, we use the energy functional defined in (Lankton and Tannenbaum, 2008): Denote the initial contour, the level set representation of the initial shape $P(\mathbf{x})$ in the previous section, as ϕ . Then, the contour evolves to minimize the energy functional defined as:

$$E(\phi) := \alpha \int \delta\phi(\mathbf{x}) |\nabla\phi(\mathbf{x})| d\mathbf{x} + \int \delta\phi(\mathbf{x}) \int \chi(\mathbf{x}, \mathbf{y}) (\mathcal{H}(\phi(\mathbf{y}))(\mathbf{I}(\mathbf{x}) - u_x) + (1 - \mathcal{H}(\phi(\mathbf{y}))) (\mathbf{I}(\mathbf{y}) - v_x)) dy d\mathbf{x} \quad (16)$$

In equation 16, the $\mathcal{H}$ is the smooth Heaviside function defined as:

$$\mathcal{H}\phi(\mathbf{x}) := \begin{cases} 0, & \phi(\mathbf{x}) < -\varepsilon \\ 1, & \phi(\mathbf{x}) > \varepsilon \\ \frac{1}{2} \left(1 + \frac{\phi(\mathbf{x})}{\varepsilon} + \frac{1}{\pi} \sin\left(\frac{\pi\phi(\mathbf{x})}{\varepsilon}\right) \right), & \text{otherwise} \end{cases} \quad (17)$$

and δ is the derivative of $\mathcal{H}$. Moreover, χ denotes the characteristic function for the r -neighborhood around $\mathbf{x}$ and the radius r is fixed at 5, and the u_x and v_x are respectively the mean intensities outside and inside the current contour within the r -neighborhood. In addition, α is a positive curvature weighting parameter and it is fixed at 0.1 in our test. One can compute the first variation of E with respect to ϕ and we obtain the corresponding gradient descent flow for ϕ ; see (Lankton and Tannenbaum, 2008) for all the details. The evolution of ϕ is only performed for a few steps (not until convergence), and the resulting ϕ is then fed into the shape-filtering processing described in the next section.

3.3. Shape Filtering with Shape Prior

Since physical imagery is never perfect (noise, etc.), the data driven segmentation ϕ performed in the previous section usually suffers from under-segmentation, leakage, or a combination of both. To solve this problem, the extracted shape in the previous step is processed through a “shape filter” so as to fall into the admissible shape space. First of all, the current contour ϕ is registered to the mean shape M in Equation (10) by minimizing the following energy over all $\zeta \in \mathcal{T}$ the group of 3D similarity transformations:

$$E_M(\zeta) := \int (\phi(\zeta(\mathbf{x})) - M(\mathbf{x}))^2 d\mathbf{x}. \quad (18)$$

The optimal similarity transformation is denoted by ζ^* and the registered contour $\phi(\zeta^*(\mathbf{x}))$ is denoted by $\psi(\mathbf{x})$. Moreover, $\psi(\mathbf{x})$ is sampled on the same discrete domain as $M(\mathbf{x})$, so that they have the same dimensions. Then, the wavelet transform is applied to $\psi(\mathbf{x})$ to obtain its band structure as:

$$\mathcal{B}^\psi = \{B_1^\psi, B_2^\psi, \dots, B_K^\psi\}. \quad (19)$$

In a manner similar to that of the learning part of the algorithm, the mean bands are subtracted from $\mathcal{B}^\psi$ in order to obtain $\tilde{\mathcal{B}}^\psi$ as:

$$\tilde{\mathcal{B}}^\psi = \{B_k^\psi - \bar{B}_k : k=1, \dots, K\} =: \{\tilde{B}_k^\psi : k=1, \dots, K\}. \quad (20)$$

Next, in each of the K bands, the band $\tilde{B}_k^\psi$ is projected to the learned band space. Without loss of generality, we can take the k -th band. Accordingly, we project $\tilde{B}_k^\psi$ to the bases vector in the band $\{\mathbf{q}_j^k, j=1, \dots, p_k\}$ and we obtain the coefficients:

$$A_k = \left(\frac{\tilde{B}_k^\psi \cdot \mathbf{q}_j^k}{\sqrt{\lambda_j^k}} : j=1, \dots, p_k \right)^T =: (a_1, a_2, \dots, a_{p_k})^T \in \mathbb{R}^{p_k}. \quad (21)$$

In order to restrict the given novel shape to the learned shape space, the novel shape is mapped to its closest shape in the allowable shape space learned in Section 2.3. Hence, we adjust each A_k as:

$$\tilde{A}_k := \begin{cases} A_k, & \|A_k\| \leq 6 \\ 6A_k / \|A_k\|, & \|A_k\| > 6 \end{cases} \quad (22)$$

in which the number 6 is chosen because an event outside six standard deviation is a very rare one. After that, the adjusted band structure $\hat{\mathcal{B}}^\psi$ is obtained as:

$$\hat{\mathcal{B}}^\psi := \{(\mathbf{q}_1^k, \dots, \mathbf{q}_v^k) \text{diag}(\sqrt{\lambda_1^k}, \dots, \sqrt{\lambda_v^k}) \cdot \tilde{A}_k + \bar{B}_k, \forall k\} \quad (23)$$

and the filtered shape $\tilde{\psi}$ is then obtained as:

$$\tilde{\psi} = \mathcal{I} \mathcal{D} \mathcal{W} \mathcal{T}[\mathcal{R}^{-1}[\hat{\mathcal{B}}^\psi]]. \quad (24)$$

Finally, the filtered shape is transformed back to the new image domain using the inverse of the similarity transformation ζ^* described above. Thus $\psi((\zeta^*)^{-1}(\mathbf{x}))$ is used as the initial segmentation contour for the next-round data driven segmentation. These two steps alternate until convergence. Usually, it only takes two or three iterations for convergence on the data sets we used.

4. Experiments and Results

In this section, we first demonstrate the multiscale shape representation will provide better learning capability especially for the high resolution (small scale) shape variance. Then, the multiscale shape representation is used as a core component in the proposed shape based segmentation framework, and the segmentation is tested on the hippocampus data sets and caudate data sets. Furthermore, by replacing the shape representation in other well known general purpose shape based segmentation techniques with our multiscale one, those methods are also tested on the same data sets and statistical significant improvements are observed. By doing this, not only do we show the value of the proposed segmentation framework, but also the applicability of the multiscale shape representation as a component in many such techniques, hence its potential of being plugged into more application specific methods.

4.1. Eigen-Shape Comparison Using SFLS and Wavelets

We design the experiment to show that the learning using the proposed representation is consistent with the existing methods for large scale and moreover it has better differentiability for the small scale variances in the shapes.

24 segmented caudate shapes are registered and padded to have size $128 \times 128 \times 128$. For comparison, we directly learn the shapes using PCA and the mean and eigen-shapes are displayed in Figure 3. The blue shape in the bottom row of both sub-figures is constructed by adding the mean shape with the -3 times the standard deviation of the first eigen-shape (the eigenvector corresponding to the largest eigenvalue). The lighter blue one in the same row is similar but with -2 as the multiplier and this goes on till the red which has $+3$. The rows above repeat the same scheme for the second and the third eigen-shapes. In all rows, the middle one which is in green, is the mean shape.

One can also observe that due to the use of the level set formulation, the topology of the object is free to change. Therefore, in some shape eigenmodes, the tip of the tail is detached from the body. However, allowing change in topology bridges the gap between the previous multiscale shape representation/segmentation efforts, such as (Davatzikos et al., 2003; Nain et al., 2007) and the general (non-multiscale) shape based segmentation research, like (Leventon et al., 2000; Tsai et al., 2003; Rousson et al., 2004). Indeed, similar to the level set formulation, it only indicates the *capability* of accommodating topology change in the learned shape space, but does not predict a broken tail in the real segmentation tasks. Indeed, together with the image information, a broken tail is not observed in experiments with real data.

Shape learning using the proposed scheme with the Daubechies D8 wavelet is shown in Figure 4. The colors and orders are the same as Figure 3. Comparing to Figure 4, three things can be observed:

- 1. Identical mean shape**

The mean shapes obtained from the two learning process are the same. This verifies the claim in Section 2.3.

- 2. Similar for large scale shape variances**

For the head of the caudate which has large scale variances, the learning results are similar to that of Figure 3. This shows the consistence of this proposed method with the existing learning schemes.

- 3. Better capture of small scale shape variances**

On the other hand, the tail regions which have sharp tip and small scale features are smoothed out in the previous learning but are successfully captured here.

With enhanced shape learning capability, in what follows we show the performance of the proposed multiscale shape based segmentation method, applied on medical image data sets.

4.2. Hippocampus

The hippocampus is a part of the limbic system and is a major component for long-term memory and spatial navigation. As discussed in Section 1, in the process of radiation planning, it is of great importance to investigate the whole brain radiotherapeutic techniques that allow sparing of the hippocampus, in order to be able to minimize dose deposition within the hippocampus. For this purpose, clinicians must be able to confidently identify that structure. On the other hand, the segmentation of the hippocampus from the MRI images without shape prior knowledge is a difficult task due to its low contrast with the surrounding tissue. Moreover, the sharp tips in its shape are usually not well captured by the previous shape based methods. The multiscale shape based method proposed in this work is a suitable way to handle both these problem. Therefore, in this section, we report the results of 24 spoiled gradient-recalled (SPGR) coronal-plane volumetric T1-weighted images acquired in the Brigham and Women's Hospital, Harvard Medical School. The ages of the subjects range from 28 to 55 with mean 43.6 and standard deviation 7. The image resolution is $0.938 \times 0.938 \times 1.5\text{mm}^3$. Fortunately, we have all the images segmented by a radiologist at the Brigham and Women's Hospital. In order to make full use of all the data, we choose the leave-oneout strategy to perform the shape learning and segmentation. That is, 23 out of 24 images as well as their segmented shapes are used for learning and the image left is segmented and the result is compared with its expert hand segmentation. On an Intel 2.8GHz quad-core machine with 8G memory, segmenting one volumetric image takes about 20 minutes, and the segmentation is fully-automatic, so that no human interaction is needed.

In Figure 5 we show the segmentation result of one randomly chosen data set in axial slice views. In this result, the hippocampus boundary generated by the proposed automatic algorithm is colored in yellow whereas the manual boundary, drawn by an expert radiologist at the Brigham and Women's Hospital, is colored in red and used as the reference. As can be observed from the comparison, the two sets of contours match very well in all the slices. Due to space constraints, only one case is shown here. However, note that all the 24 experiments work consistently, and the detailed statistical analysis is given below.

Furthermore, in order to demonstrate the performance of the algorithm in 3D, in this section we show the surfaces of the segmented hippocampi. In Figure 6, all the 24 hippocampal surfaces are shown. From Figure 6, we can observe that the manual delineated hippocampal surfaces may have many discontinuities. This is mainly due to the fact that the contours are traced out slice-by-slice. Thus, although in that process the image information in the adjacent slices is utilized, nevertheless, the resulting surfaces still have a jagged appearance. On the other hand, the proposed 3D segmentation method achieves better continuity and smoothness in all the three spatial dimensions, and the jagged appearance is avoided.

Moreover, in order to quantify the differences between the two sets of results, the difference maps are computed: Given any point on the manual surface, the difference map value is the closest distance to the automatically generated surface. Altogether, they form a scalar function defined on the manually generated surface. The difference maps are illustrated as the colors on the manual surfaces: Given any location on the surface, the red/blue color means that there exists a relatively large/small difference between the surface generated by expert and the algorithm, respectively. As can be seen in Figure 6, except at few isolated regions, the automatic results are very consistent with the expert manual results.

In order to further analyze the results quantitatively, the Dice coefficients (Dice, 1945) and the Hausdorff distances with respect to the expert segmentation results are provided in Table 2 and are also plotted as the red bar in Figure 7. Furthermore, to demonstrate the improvement of employing the multiscale scheme in the shape-based segmentation, we replaced the multiscale shape representation/learning/segmentation in the proposed method by the ordinary PCA based shape learning and segmentation. That is, the shape is represented by the SFLS, the learning (PCA) is directly performed on the SFLS, the segmentation is based on such non-multiscale scheme, but everything else is unchanged. As a result, the Dice coefficients and the Hausdorff distances of these experiments are given as the purple bar (the second bar in each group of four) in Figure 7.

Furthermore, the method in (Tsai et al., 2003) (denoted as "SASMI" hereafter), which is another widely used shape based active contour segmentation technique, is also tested to show the wide applicability of the multiscale shape representation scheme. Similar to above, we test their original algorithm and then replace their non-multiscale shape representation with the multiscale one proposed here. The results are shown in the third (with multiscale) and the fourth (original algorithm, without multiscale) bars in Figure 7.

In addition to visual inspection, we perform the *t*-test on the Dice coefficients of the segmentation methods with and without the multiscale scheme. At a significance level of 0.01, the null hypothesis that the mean Dice coefficient is higher in the multiscale version is accepted for both the proposed method and the SASMI method. Similarly and with the same significance level, the null hypothesis that the mean Hausdorff distance is larger in the multiscale version, is rejected for both the proposed method and the SASMI.

4.3. Caudate

The caudate nucleus is also an important part for the learning and memory functions of the brain. Similar to the hippocampus, the segmentation of the caudate nuclei is challenging due to low contrast with the surrounding tissues. Moreover, the sharp corner at the tail of the caudate is difficult to be captured by the ordinary PCA based shape learning procedure because the energy contribution there are usually overwhelmed by the shape variation with larger energy at the caudate head, and this was shown in Figure 3. Furthermore, equipped with the proposed multiscale shape representation, the better learning capability leads to better segmentation. The leave-one-out testing is performed for the same data set used in Section 4.1 (different data set from those in Section 4.2): the MR images are spoiled gradient-recalled (SPGR) coronal-plane volumetric T1-weighted images which are acquired in the Brigham and Women's Hospital, Harvard Medical School. After segmentation, the Dice coefficients are computed. Among them, the image with the median Dice coefficients is selected and the slices containing automatic and manual contours are shown in Figure 8. Furthermore, similar to the Figure 6, the distance map is computed for each manual/automatic segmentation pair, and the result is rendered on the surface of the manual segmentation, shown in Figure 9.

In addition, all the Dice coefficients and the 95% Hausdorff distances are computed, shown in Table 3, and plotted as the red bars in Figure 10. Furthermore, similar to the hippocampus case, in order to demonstrate the improvement by employing the multiscale scheme in the shape-based segmentation, we replace the multiscale shape representation/learning/segmentation in the proposed method by the ordinary PCA based shape learning and segmentation. The resulting Dice coefficients and the Hausdorff distances of this experiment are drawn as the purple bars (the second bar in each group of four) in Figure 10. After that, the tests using the SASMI method in (Tsai et al., 2003) are also conducted, with and without the multiscale shape representation. Their results are shown in the third (with multiscale) and the fourth (original algorithm, with-out multiscale) bars in Figure 10. As expected, they also indicate significant improvements over the non-multiscale version.

In addition to visual inspection, the t -test between the Dice coefficients of the segmentation methods with and without the multiscale scheme is performed. With a significance level at 0.01, the null hypothesis that the mean Dice coefficient is higher in the multiscale version is accepted for both the proposed method and the SASMI method in (Tsai et al., 2003). Moreover, with the same significance level, the null hypothesis that the mean Hausdorff distance is larger in the multiscale version, is rejected for both the proposed method and the SASMI for the caudate case.

5. Conclusion and Discussion

In the present work, we described a multiscale shape based framework to automatically extract the objects with sharp shape features from MR brain imagery. First, we proposed a multiscale representation for the shape using the wavelet transform. In doing so, we were able to take advantage of the multiscale property of the wavelet representation. In particular, in learning the shapes, small-scale shape variances were not overwhelmed by large ones. Moreover, in the segmentation step, we combined an atlas-based scheme and an active contour method to provide an automatic and robust segmentation algorithm to extract the hippocampus. Having set up like that, the algorithm was tested on a total of 48 T1 MR brain images and the results were analyzed.

Furthermore, we show the applicability of the multiscale shape representation by replacing the shape representation part in other well known shape based segmentation methods in the field and achieved statistical significant improvement. With such advantage, the multiscale

shape representation can be plugged into the more application specific methods, targeting at various organs.

This methodology can now be incorporated into existing treatment planning approaches. In this manner, the objective of assessing the merits of whole brain irradiation with hippocampal avoidance can be pursued. With time, the neuro-oncologic community will be able to determine whether control of microscopic disease can be achieved without significant compromise of neurocognitive function.

Further work includes investigating the number of training shapes needed for learning as well as the atlas-based initialization, in order to achieve optimal efficiency and accuracy. Moreover, in the data driven segmentation step, the local image mean intensity is used as the criterion in separating the hippocampus with its surrounding tissue. However, since the training images are available, one promising alternative would be learning the image information of hippocampus region in the training images, and use such information to drive the segmentation.

- A multiscale shape representation scheme is proposed.
- A fully automatic multiscale shape-based segmentation framework is proposed.
- The multiscale shape representation can be used with other shape analysis and shape-based techniques.

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Figure 1. Decomposition of wavelet coefficients into various bands. The band structure of wavelet coefficients for an image having size 16×16 . The coefficients in different scales are rearranged into different vectors (bands).

Figure 2.

Multiscale decomposition of the seahorse shape. In subfigure (a), the shape is reconstructed from the coefficients in the coarsest scale. Then, the wavelet coefficients in each scale are successively added, and the reconstructed shapes are shown in subfigure (b) through (g). In the finest two scales, some of the nuances are indicated by the arrows.

Figure 3.
Shape learning using PCA. Details are given in text.

Figure 4.
Shape learning using proposed method. Details are given in text.

Figure 5.

Axial slices of a segmentation result. The yellow contours are generated by the proposed automatic segmentation algorithm, while the red contours are drawn manually by an expert radiologist in BWH.

Figure 6.

The surfaces of all the 24 testing hippocampi. The yellow ones are generated by the proposed method and the ones below are the corresponding manual results. On the manual surfaces, the color shows the difference between the automatic and manual surfaces.

Figure 7.

Bar plot of the (a) Dice coefficients and (b) Hausdorff distances using the different methods for the hippocampus data sets. In particular, we see that with the multiscale shape representation, the Dice coefficients are higher while the Hausdorff distances are lower than the ones without.

Figure 8.

Axial slices (odd ones) of one segmentation result whose Dice coefficient is the median among all. The yellow contours are generated by the proposed automatic segmentation algorithm, while the red contours are drawn manually by an expert radiologist in BWH, and the green contour is where the automatic ones coincide with the manual ones.

Figure 9.

The surfaces of all the 24 testing caudate nuclei. The yellow ones are generated by the proposed method and the ones below are the corresponding manual results. On the manual surfaces, the color shows the difference between the automatic and manual surfaces.

Figure 10.

Bar plot of the (a) Dice coefficients and (b) Hausdorff distances using the different methods for the caudate data sets. In particular, we see that with the multiscale shape representation, the Dice coefficients are higher while the Hausdorff distances are lower than the ones without.

Table 1

The relative location of the proposed work in the grid of the most related shape-based segmentation schemes. The framework proposed in this work aims to fill in the blank at the corner.

	Fixed topology	Flexible topology
Non-multiscale	Cootes et al. (1995)	Leventon et al. (2000) Tsai et al. (2003) Rousson et al. (2004)
Multiscale	Davatzikos et al. (2003) Nain et al. (2007)	

Dice coefficients and the 95% Hausdorff distances between the expert segmentation and the automatic result generated by the proposed method for the **hippocampi**. The unit for the Hausdorff Distance is mm.

Table 2

Patient ID	#1	#2	#3	#4	#5	#6	#7	#8	#9	#10	#11	#12	#13
Dice Coef	0.835	0.842	0.776	0.843	0.819	0.774	0.789	0.812	0.847	0.847	0.779	0.848	0.847
95% HD	2.904	3.025	3.067	3.276	3.243	3.351	3.336	3.112	3.378	3.931	4.476	2.684	2.889
Patient ID	#14	#15	#16	#17	#18	#19	#20	#21	#22	#23	#24	Mean	STD
Dice Coef	0.807	0.833	0.777	0.801	0.843	0.833	0.847	0.821	0.768	0.837	0.845	0.820	0.028
95% HD	3.570	3.817	2.981	3.643	3.863	2.633	3.215	3.082	3.538	3.211	3.445	3.320	0.423

Dice coefficients and the 95% Hausdorff distances between the expert segmentation and the automatic result generated by the proposed method for the **caudate nuclei**. The unit for the Hausdorff Distance is mm.

Table 3

Patient ID	#1	#2	#3	#4	#5	#6	#7	#8	#9	#10	#11	#12	#13
Dice Coef	0.924	0.857	0.903	0.927	0.917	0.942	0.919	0.882	0.913	0.916	0.920	0.907	0.899
95% HD	1.593	3.512	1.290	1.594	1.289	3.353	2.401	0.937	3.371	1.849	3.897	3.599	3.484
Patient ID	#14	#15	#16	#17	#18	#19	#20	#21	#22	#23	#24	Mean	STD
Dice Coef	0.915	0.928	0.910	0.894	0.934	0.886	0.914	0.876	0.855	0.943	0.920	0.908	0.023
95% HD	1.326	2.485	2.301	3.542	4.194	3.434	1.852	1.287	1.290	1.500	1.290	2.361	1.057