HHS Public Access
Author manuscript
IEEE Comput Graph Appl. Author manuscript; available in PMC 2017 May 01.

Published in final edited form as:
IEEE Comput Graph Appl. 2016 ; 36(3): 60–71. doi:10.1109/MCG.2015.70.

Evaluating Alignment of Shapes by Ensemble Visualization

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Abstract

The visualization of variability in surfaces embedded in 3D, which is a type of ensemble *uncertainty visualization*, provides a means of understanding the underlying distribution of a collection or ensemble of surfaces. Although ensemble visualization for isosurfaces has been described in the literature, we conduct an expert-based evaluation of various ensemble visualization techniques in a particular medical imaging application: the construction of atlases or templates from a population of images. In this work, we extend contour boxplot to 3D, allowing us to evaluate it against an enumeration-style visualization of the ensemble members and other conventional visualizations used by atlas builders, namely examining the atlas image and the corresponding images/data provided as part of the construction process. We present feedback from domain experts on the efficacy of contour boxplot compared to other modalities when used as part of the atlas construction and analysis stages of their work.

I. Introduction

As computational tools for simulation and data analysis have matured, researchers, scientists, and analysts have become interested in understanding not only the *deterministic* output of these tools, but also the *uncertainty* associated with their computations and/or data collection. Consequently, there is an increasing interest in uncertainty quantification (UQ) as an integrated part of simulation and data science in a wide variety of science and engineering disciplines. UQ views the simulation and data science pipelines as a random process containing possibly both epistemic (i.e., reducible) and aleatoric (i.e., by chance) uncertainty. Quantification efforts in this random process are divided into roughly two categories: (1) efforts to understand the uncertainty and/or variability of the process through examination of instances (samples) of the process; and (2) efforts to determine models (e.g., probability theory) that capture the nature of the process. The first of these categories, and the focus of this study, utilizes an *ensemble* of solutions meant to capture the inherent variability or uncertainty in a computational or data science pipeline. Although we assume that the variability seen in the ensemble can be attributed to some condition or property of the generating process, we do not assume that articulation of the process via a mathematical model is straightforward, and hence we have only the ensemble members themselves to gain insight into the originating process.

Studying an ensemble in terms of the *variability* or dispersion between ensemble members can provide useful information and insight about the underlying distribution of possible outcomes. Correspondingly, ensemble visualization can be a powerful way to study this variability; however, a key challenge here is to be able to convey the variability among ensemble members while preserving the *main features* they share. Preservation of these features is particularly challenging in cases where the ensemble members are not *fields* over which statistical operations such as mean and variance are well-defined, but instead are derived or extracted features such as isosurfaces.

In this article, we examine the effectiveness of the contour boxplot technique [1], a descriptive summary analysis and visualization methodology, in the context of a particular medical data science application: brain atlas construction and analysis. We conducted an expert-based evaluation of the visualization of ensembles generated through the alignment of shapes using the deformation of images in the construction of atlases (or templates) for brain image analysis. To accomplish this evaluation, we constructed a prototype system for visualizing and interacting with ensembles of 3D isosurfaces through a combination of 3D rendering (isocontouring) and cut-planes (slices through 3D volumetric fields). In addition, we generalized the algorithm in [1] to three dimensions as a direct extension of their analysis of isocontours to isosurfaces – that is, from co-dimension one objects embedded in 2D to co-dimension one objects embedded in 3D. This generalization allows us to compare contour boxplot summaries of an ensemble to both full enumeration of the ensemble as well as other traditional means of atlas evaluation (e.g., qualitative visual inspection of slices of the atlas image or individual volumetric images used for construction of the atlas). We employ this system to explore, in collaboration with domain experts, the efficacy of using ensemble visualization techniques for evaluating 3D shape alignment of brain MRI images.

The purpose of this paper is to study and evaluate the use of contour boxplots in a real-world data science application, the alignment of 3D shapes or surfaces in a population-based ensemble. Our hypothesis is that the contour boxplot will allow users to summarize their data in a meaningful way that allows either better or more efficient (faster) assessment of the atlas construction as compared to explicit enumeration of the ensemble (i.e., looking at each member image individually) or through more coarse-grained characterizations such as examination of the average intensity image or label (segmentation) probability maps. As our evaluation results will show, the contour boxplot methodology has the potential to significantly benefit the application under study by providing a visualization of the quantitative summaries of the ensemble. Although we have formulated our hypothesis in the context of a particular application, we believe that our evaluation may provide insight into other arenas where visualization and analysis of ensembles of shape is desired. Examples of such applications will be discussed in the conclusion section.

To begin, we give a brief introduction to the process of brain atlas construction and the evaluation process used by domain experts.

A. Brain Atlas Construction

Construction of an anatomical *atlas* for a collection of brain images is an important problem in medical image analysis. The goal of various atlas construction schemes is to construct a statistical *representative image* and associated set of *coordinate transformations* (i.e., deformations) from an ensemble of images [2]. Anatomical atlases provide a common coordinate system (atlas space) in which to define reference locations of brain structures. As part of the atlas construction process, nonlinear registration techniques generate deformations that can map the anatomies in an individual image to the atlas space (see Figure 1). The atlas construction process jointly estimates a representative image defining the atlas space (the *atlas image*) and the deformations aligning individual images to this atlas image (i.e., mapping the image individually to the atlas space). The atlas image generated by these techniques then represents the *average* (or normal) anatomy of this population. Such atlases help domain experts characterize expected anatomical structure and variability of a population and compare different populations in terms of their group atlases (for example, healthy and unhealthy groups). Differences in the atlas anatomy can be identified both *qualitatively* by inspecting unaligned structures (when mapped to the atlas space) and *quantitatively* by analyzing the deformations, quantifying the amount of change necessary to bring individual ensemble member into alignment.

Atlas generation is an automated process, but it is not parameter-free, and the choice of parameters can greatly influence the quality of the result. In particular, nonlinear deformations computed for medical image registration are a tradeoff between image matching and *plausible* deformations. For example, the deformation should not result in the elimination of anatomical features or noninvertible transformations. Hence, the deformation is often controlled by tuning parameters to find a compromise between the mismatch between images and the regularity (e.g., smoothness) of the transformation. Due to the regularization of the deformations and the inherent anatomical differences between ensemble members, not all features will be perfectly aligned. This imperfect alignment is manifested as *blurring* in the atlas image where there is disagreement regarding voxel intensity among ensemble members when mapped to the atlas space.

Correct tuning of the regularization parameters allows the deformations to account for as much anatomical variability as possible by correctly aligning the corresponding anatomy, and not simply matching similar intensities. This alignment of corresponding anatomy is essential for an atlas to be effective in later statistical analysis of the population. Convergence of the optimization can be easily checked, but the degree of alignment of particular structures is analyzed qualitatively by observing the amount of *blurring* in the atlas image and by checking the alignment of each ensemble member (deformed to atlas space) to the atlas image. The initial alignment is often unsatisfactory, which results in an iterative process of parameter tuning and rerunning the atlas generation process.

In addition, due to problems with image scans, extreme variability among the ensemble members, or incorrect preprocessing, it may not be possible to achieve reasonable alignment to the atlas image for some set of *outlier* images. Identification and removal of such images is often another part of the atlas generation procedure. Automated measures of global image alignment are available, but they do not give insight into why or in which spatial regions particular ensemble members have poor alignment. Depending on the proposed application of the atlas, these insights may be pertinent to the decision to prune or keep particular images (ensemble members).

This manual iteration of parameter tuning/pruning and atlas generation eventually yields the final atlas to be used in further analysis. There are two important points to be noted about the final atlas image. The first is this *representative* image/segmentation is not a member of the ensemble itself, but rather an image/segmentation generated through statistical operations on the deformation fields. That is to say, it is not a member of the population that best represents the population, but rather an attempt at statistically characterizing a representative image. Second, as noted above, the iterative process does not guarantee that the resulting atlas image is crisp – that is, that there are no blurry regions in the image. The ensemble of images compared to the atlas image scenario is similar in spirit to the feature-space averaging issue highlighted in [1]; the analogy is that the isosurface (e.g., segmentation) of the average field is oftentimes not equivalent to a representative of a set chosen from isosurfaces of the individual fields. As per the rationale given in [1], the avoidance of feature-space averaging is why we believe the contour boxplot methodology provides a useful way to summarize the type of ensemble data where analyzing feature-sets and their representatives is important. Since the manual, qualitative evaluation of shape alignment (as a result of image registration) is a challenging task, quantifying the variability of the shape alignment and visualizing this variability can facilitate the domain experts' ability to effectively validate the atlas construction scheme.

In Section II, we introduce a prototype system that uses various uncertainty visualization schemes to enhance the study of variability in an ensemble of shapes. Before introducing our prototype system, we first provide an overview of the data used as well as a high-level description of our expert evaluation study.

B. Data Preprocessing for Atlases

The images analyzed in this article are 3D MRI images obtained from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database [3]. Each brain image in our ensemble was also provided with a corresponding label map volume with various anatomical structures segmented and marked, with each brain region having a unique integer value. In order to analyze a specific structure within the brain anatomy, we used the label assigned to that structure to select it and mask out the remaining region in all members of the ensemble. The atlas construction scheme we used is the unbiased diffeomorphic atlas proposed by Joshi et al. [2], implemented as part of an open source medical image atlas construction package called AtlasWerks [4]. We constructed atlases from ensembles of MRI images using different choices of parameters and/or different ensembles (i.e., subject groups). In each case, after constructing the atlas using the MRI images, the corresponding label map images were transformed to the common (atlas) coordinate space using deformation fields calculated during the atlas construction process as described in Section I-A. These transformed label maps were then passed as input to the preprocessing pipeline (described in Section II) for visualization. For a well-constructed atlas, we can expect the anatomical structures in the brain to have a relatively small amount of variability after being transformed to the atlas space. We selected two anatomical structures in the brain expected to pose different levels of difficulty during atlas construction, namely the left ventricle and the cortex. The ventricle is often considered as a very distinct structure (i.e., high contrast) in the brain image and, therefore, can be expected to exhibit good alignment among ensemble members in the atlas space (if all goes well). The cortex was selected as an example of an anatomical structure with a complex shape (see Figure 2), a significant challenge for registration/alignment.

C. Expert Evaluation Study Details

Domain experts use various open source or commercial packages to visualize slices from *individual* volumetric images or simply from the average of the aligned images, but to the best of our knowledge, ours is the first attempt to study the alignment of shapes in atlas construction using ensemble visualization techniques. For our evaluation study, we had access to a group of five domain experts who work with atlases on a regular basis and who volunteered to participate in our expert evaluation study. This group included graduate students, staff researchers, and faculty who use atlases and medical image ensembles in their research projects.

We asked the participants to explain their current methodology for evaluating the atlas construction scheme as well as the quality of the atlas in terms of being a representative of the ensemble. As mentioned earlier, we learned that this process is often performed *qualitatively*. A visual inspection is carried out to ascertain whether the shapes of the anatomical structures in the atlas space are realistic. Experts also mentioned that in order for an atlas to be helpful for different medical imaging applications such as segmentation of a specific structure in the brain, they need the atlas image and the anatomical structures therein to have sufficient contrast. For example, they expect to see a crisp boundary (in terms of the average combined image intensities) between gray and white matter in the brain. Therefore, the sharpness of the boundaries of the anatomical structures in the atlas image is another criterion examined qualitatively to evaluate the alignment of the ensemble. These qualitative evaluations are often performed on a subset of the ensemble of images (in the atlas coordinate system), because visualizing the entire ensemble results in too much clutter and blurriness. Figure 3 shows a snapshot of a slice of the brain atlas image used as a common (atlas) coordinate system to register individual label maps from the ensemble.

II. Our Visualization Pipeline

In this section, we discuss the visualization pipeline of our prototype system. We first start with a brief summary of various ensemble visualization strategies that we have considered and incorporated into our prototype system. We then provide an overview of the pipeline and our design choices to mitigate the challenge of visualizing and rendering an ensemble of 3D isosurfaces.

A. Ensemble Visualization Overview

Visualization is often data-driven, and therefore uncertainty visualization schemes are typically designed to deal with the type of data being visualized. For scientific data, users are often interested in visualizing derived *features* of their data, such as transition regions (or edges), critical points, or isosurfaces (of volumetric data) and the uncertainty associated with such feature sets. A thorough review of the rich literature on uncertainty visualization is beyond the scope of the current manuscript. However, interested readers can consult [5], [6] for further details on recent advancements on this topic. The focus here is visualization of isosurfaces in the context of uncertain scalar fields, which has been studied somewhat extensively. Most relevant to the application under study (i.e., atlas construction) is the visualization of uncertain isosurface extracted from an *ensemble* of scalar fields.

Here we provide a brief summary of three classes of popular techniques for visualization of uncertain isosurfaces that are extracted from ensembles of scalar fields. These techniques were chosen to represent the range of strategies for representing an ensemble (as discussed in Section I)—namely, (1) enumeration of all ensemble members, (2) visualization of the statistical summaries induced from parametric uncertainty modeling, and (3) descriptive nonparametric summaries:

1. **Enumeration:** A widely used approach for ensemble visualization is the direct visualization of all ensemble members. Direct visualization of ensembles has gained significant interest in applications such as weather forecasting and hurricane prediction [7]. *Ensemble-vis* [8] is an example of the data analysis tools designed to visualize ensemble data. Ensemble-vis uses multiple views of fields of interest to enhance the visual analysis of ensembles. We incorporate direct visualization of 3D ensemble members (see second column in Figure 5) by rendering the curves formed by the region of intersection of the codimension one isosurface of each ensemble member with a cut plane. Note that as long as the isosurface embedded in 3D is closed, closed curves will be generated when the isosurface is sliced for visualization purposes. We refer to this visualization as a **spaghetti plot**. In order to facilitate the interpretation of the individual ensemble members, each of these curves has been rendered with distinct and random colors. There are a variety of options for rendering the enumeration of all 3D surfaces, including transparency, but clutter is a significant challenge [7]. For this work, we present the surfaces of the inner- and outermost volumetric bands formed by all ensemble members. User studies have suggested the effectiveness of direct ensemble visualization techniques [7]. However, direct visualization of the ensemble does not provide any quantitative information about the data uncertainty, and relies solely on the user for interpreting data.

2. **Parametric Probabilistic Summaries:** Many uncertainty visualization schemes use probabilistic modeling to convey *quantitative* information regarding data uncertainty. These techniques often rely on a certain kind of statistical model such as multivariate normal distributions. As a representative of such techniques, we have chosen to consider the concept of *level-crossing probabilities* (LCP) [9]. For visualization, we implemented the 3D **probabilistic marching cubes**

algorithms (proposed based on LCP) [10] as part of our initial visualization system. Probabilistic marching cubes rely on approximating and visualizing the probability map of the presence of the isosurface at each voxel location. However, the use of parametric modeling can limit the capability of this techniques. Approximating the underlying distribution giving rise to the ensemble and presenting the user with *only* aggregated quantities of the inferred distribution can be misleading in some applications. For instance, this approach can often hide or distort structures that are readily apparent in the ensemble.

3. **Nonparametric Descriptive Summaries:** An alternative strategy that relies on neither enumeration nor parametric modeling of the underlying distribution is to form *descriptive statistics* of an ensemble. Descriptive statistics offer an ensemble visualization paradigm for understanding or interpreting uncertainty from the structure of an ensemble. The notion of *centrality* is a natural approach to understanding the structure of an ensemble. Because an ensemble is an empirical description of its distribution, some instances from an ensemble are more central to the distribution, and therefore more typical within the distribution. The notion of *data depth* provides a formalism for characterizing how *central* a sample is within an ensemble. Data depth provides a natural generalization of rank statistics to multivariate data [11]. The univariate boxplot (or whisker plot) is a conventional approach to visualize order statistics. Boxplot visualizations provide a visual representation of the main features of an ensemble, such as the most representative member (i.e., the median), quartile intervals, and potential outliers. The notation of data depth has been generalized for ensembles of isocontours [1]. The authors also propose *contour boxplot* as a visualization technique to summarize robust and descriptive statistics of ensembles of 2D isocontours [1]. In our system, we algorithmically extend and implement the **contour boxplot** analysis for isosurfaces embedded in 3D (see Figure 5, first column) as an example of visualization techniques based on nonparametric descriptive statistical summaries of an ensemble.

In order to analyze the alignment, or lack thereof, of shapes in an ensemble, we incorporated representative members of the aforementioned ensemble visualization technique categories as part of our prototype system.

B. Ensemble Visualization Prototype System

At a high level, our prototype system consists of two stages (see Figure 4):

1. **Data Preprocessing:** When visualizing isosurfaces of a binary 3D segmented image, it is often necessary to perform smoothing to reduce aliasing artifacts and facilitate 3D rendering/shading. We perform this smoothing in a two-step preprocessing stage. In the first step, the binary partitioned image is antialiased using an iterative relaxation process described in [12]. Next, a very small amount of mesh smoothing is performed on the isosurface mesh generated from the antialiased binary image. All visualization preprocessing operations occur on the

3D volume (and corresponding codimension one isosurfaces) prior to cut-plane extraction.

2. **Visualization:** This stage includes some visualization strategies to facilitate the perception and navigation of the rendered 3D objects. In order to improve the perception of shape in our application, we include interactivity with renderings of 3D objects as part of the visualization system. In our settings, the user is able to rotate the object displayed on the screen using the standard trackball interaction mechanism. The system allows the user to select cutting planes, which clip a portion of the volume displayed on the screen, to render cross section views of surfaces embedded in 3D. The user can also interactively orient and translate the cutting plane. Additionally, the system provides the flexibility of having one or multiple cutting planes and interactively adjusting their position and orientation. The interface of the system allows the user to interactively select various features of interest for rendering in order to focus on any particular feature of interest. For example, the user can select specific ensemble members to be rendered individually.

In the case of 3D contour boxplots, the analysis has been performed on the 3D binary segmented volumetric data (in the preprocessing stage), and the results are rendered interactively. While the analysis has been performed on the volumetric data leading to volumetric 50- and 100 percent bands, we render the visualization of the statistical summaries only on chosen cut planes to deal with the issue of occlusion. For instance, in absence of a cut plane the 100 percent band entirely occludes the median shape as well as the 50 percent band.

III. Evaluation

In this section, we demonstrate the efficacy of using ensemble visualization techniques to study the alignment of MRI brain images during brain atlas construction by gathering feedback as part of an expert evaluation study of the proposed prototype system. We refer to our expert evaluators as *participants*. All the visualizations presented were part of the prototype system introduced in Section II. We described the prototype system to the participants after a walk-through presentation of the different ensemble visualization techniques. The participants were able to interact with the system and switch through the various visualization methods as explained in Section II. For our study, we solicited their feedback on the visualization of the two anatomical structure presented below: the left ventricle and the cortical surface. We paid particular attention to the participants' comments concerning the suitability of ensemble visualization for this application. A summary of our interactions with the participants follows. We start by describing three examples where useful insights into the atlas data were gained by the participants on interacting with the system.

In our first example, we focus on analyzing the *variability within an ensemble* of different regions of brain ventricles transformed to a common atlas space using the unbiased, diffeomorphic approach in [2]. Ensemble visualization not only helps general users identify regions that are either well or poorly aligned, but also provides insight regarding whether the variability is due to differences in shape, position, or both.

Figure 5 shows the three approaches to visualizing the aligned ventricles for an ensemble of 34 brains. From the contour boxplot in Figure 5a, one can immediately identify regions of high variability such as Region A, which is highlighted in the figure. In this specific region, most of the variability is outside the 50 percent band, which means that less than half the ensemble members contributed to this variability. Looking at the spaghetti plot in Figure 5b, we see there are, in fact, only two ensemble members that significantly differ from the other members in Region A. These results show that the variability is due to overall position as well as shape in this region. In Region B (Figure 5a), we notice that the variability can be attributed to significantly different shapes of the isocontours, and that these shapes would not easily be aligned through the smooth transformations in this atlas, and may require parameter tuning to achieve alignment. By observing Region C (Figures 5a–b), we see that the variability comes mostly from the positions of the isocontours. Results in Region C also show that no particular ensemble member is disproportionately responsible for the variability—the width of the 50 percent band is nearly that of the 100 percent band in this region, and outliers align well with the median contour.

Finally, Region D (Figure 5a) demonstrates an area of very low variability across the ensemble and provides an example of good alignment of all the ventricles, which is confirmed by the spaghetti plot in Figure 5b. Figure 5c shows a volume-rendered 3D version of the average intensity image for comparison. The average intensity image is an essential part of the atlas, but it does not provide the same insights for *debugging* the atlas in a detailed way.

We also showed the participants volume renderings of level-crossing probability values, as suggested in [10]. The participants noted that the level-crossing probability visualization shows almost the same information as the average intensity image (Figure 5c), which is already used extensively during atlas construction. They did not feel that further exploration of this form of ensemble uncertainty visualization for evaluating atlases would be useful, and therefore we did not include comprehensive results from level-crossing probability renderings in this study.

The second example was chosen to evaluate whether ensemble visualization can also provide insight into the *overall variability* between the members of an ensemble of aligned shapes. An understanding of the overall variability (as opposed to local variability) is useful not only to understand how well a particular atlas was constructed, but also to compare different atlases. For this example, we have constructed three atlases, each with an ensemble of size 30. The first atlas was constructed with a high value of regularization (transformation smoothing), $\lambda = 1.0$; a second atlas was constructed for the same ensemble while using a low regularization value, $\lambda=\frac{1}{9}$; and a third atlas was constructed from a different ensemble (i.e., subject group) with the regularization/smoothing at $\lambda=\frac{1}{9}$.

Figure 6 shows slices of intensity atlases and contour boxplot visualizations for each of the three cases (columns from left to right). The first row presents a slice of the intensity image for each atlas, and the second row demonstrates the 3D contour boxplot visualization of the cortical surfaces for atlases corresponding to the intensity image above.

Using a high value for the regularization parameter enforces high smoothness of the deformation fields, which in turn makes it harder to arrive at a set of deformations that would perfectly align all the individual images. The lack of alignment leads to high variability between isosurfaces in the ensemble. Such high variability is easily visible by looking at region E in Figure 6d where the 50- and 100 percent bands are wider than in the corresponding region of the atlas with low regularization (Figure 6, middle column). Better image alignment when the atlas is constructed with low regularization is also evident in region E by comparing contours of the median and outlier shapes rendered on the cut plane in Figures 6c and d. We see that the median and the outlier shapes are poorly aligned for images aligned with an atlas constructed with high regularization (Figures 6, first column), while the alignment is much better when the atlas is constructed with low regularization.

Finally, the third atlas (right column of Figure 6) in this example demonstrates the effect of inherent variability between the ensemble members (i.e., brain images) on the atlas construction process. We see that in many regions of Figure 6f, for instance in region F, the 100 percent band is significantly wider than the 50 percent band, indicating a significant spread in the distribution of surfaces, which is different from the variability seen in the corresponding region in Figure 6e, where both bands nearly overlap. Furthermore, in the third atlas we see that the outlier is well aligned with the median in some regions (see region G), but poorly aligned in others (see region H). This example demonstrates that shape/ surface variability in atlases depends, in addition to parameters of construction, on the inherent variability of shapes in the ensemble. Thus, the contour boxplot, as part of the atlas construction process, can help users tease apart these different aspects of variability.

In addition to aiding in the understanding of the general alignment of shapes in an ensemble, the contour boxplot is also useful in conveying to the general user how well a particular shape is aligned with respect to the rest of the ensemble. Such knowledge is particularly useful in the case of *outlier shapes*. Atlas construction is often an iterative process, and identification of outlier images that do not align sufficiently with the atlas is an important intermediate step in the process. In the contour boxplot shown in Figure 7c, we see a single outlier shape and its alignment relative to the ensemble. In comparing this visualization with an average intensity image of the left ventricle region Figure 7a, we see that an anomaly in Region I (Figure 7c) shows as a barely perceivable increase in intensity in Figure 7a. A similar observation can be made from the intensity image slice of the outlier member shown in Figure 7b. However, the anomaly shows up clearly in the contour boxplot, and because it is outside the 100 percent band, we know that the degree of misalignment of this shape is rare within the ensemble of ventricles. Region I also demonstrates the challenges of assessing geometry in 3D, because distances between surfaces can be exaggerated when viewing them on a single cut. However, interacting with the visualization by moving and rotating the cut plane can help verify the 3D shapes of rank statistics and the surface geometries and separation distances.

In some cases, aligned shapes can differ in *size* from the rest of the ensemble. For instance, Figure 7c shows that the outlier ventricle is noticeably smaller than the median ventricle in regions J and K, which is not the case in the region L. This observation is not possible in the corresponding intensity images. These size differences occur for several reasons. In this example, for instance, the outlier ventricle may have been different and irregular to begin with. Another reason could be mislabeling of the ventricular region during the segmentation process to generate the labels for that image. Finally, the process of generating deformations during the atlas construction might fail, leading to irregularities for an ensemble member when mapped onto the atlas space. The contour boxplot can provide information that can help the user decide whether or not any particular outliers need to be removed from the ensemble or if further investigation is necessary to identify causes of possible misalignment.

At the conclusion of our study, we asked the participants to comment about their experience with the system, including the applicability of such a system if integrated into an atlas construction software. They were also asked to compare the ensemble visualizations to the evaluation techniques they currently use. As mentioned in Section I, the two main techniques currently used for atlas evaluation are inspecting unaligned structures (when mapped to atlas space) or analyzing the deformations, quantifying the amount of change necessary to bring individual ensemble member into alignment. Here we summarize the observations of the participants in this study:

- The participants pointed out that being able to visualize the *extent* of the variation among the ensemble of aligned shapes in terms of quantitative percentile information using the contour boxplot visualization was helpful for comparing various atlas construction schemes (or comparing atlases that were constructed from different ensembles or parameter settings). They also mentioned that the contour boxplot has the potential to help reduce the time needed for the user of the atlas construction software to gain insights regarding the quality of the atlas.
- The participants noted that state-of-the-art techniques for evaluation/visualization of atlases provided limited information about the variability that remained within an ensemble after transforming it to atlas space. Deformation and image match energies (quantities that are optimized during registration of images in atlas construction) are not able to provide insight into the geometric discrepancies that are crucial to understanding atlas quality.
- The participants noted that the capability of the contour boxplot to effectively locate and characterize different types of variability was valuable in atlas construction.
- The participants pointed out that an automated and statistically robust way of identifying and visualizing outliers in an ensemble can play a major role in construction of an atlas.
- The spaghetti plot was found to be helpful to view the contours of specific ensemble members other than the median or outliers.

- The participants noted that both the contour boxplot and the spaghetti plot were able to convey important details pertaining to the variability in an ensemble, whereas the average intensities had limited utility because of their general fuzziness.

We conclude this section by summarizing our findings from this study and the interview process. The goal of the application described in this manuscript is to evaluate the alignment of 3D shapes, in particular the alignment of 3D MRI images that have been transformed to a common atlas space, using various ensemble visualization methods. It is observed that the ensemble visualization methods are helpful in characterizing the alignment of shapes, and furthermore, provide insights that are useful in understanding the variability in alignment. An understanding of the type or location of the variability can be helpful in tuning parameters used in atlas construction and/or removal of outliers to achieve better alignment. We observed that the contour boxplot emerged as a clear favorite of our participants. One of the salient features of the contour boxplot that makes it distinct from the other ensemble visualization approaches is its ability to convey an aggregated result from the analysis of all regions of shapes in the ensemble on any arbitrary cut plane. For example, visualizing a slice of the intensity image, or contours on a cut plane using the spaghetti plot, conveys the variability for *only* the region intersecting the cut plane whereas a contour boxplot visualization using the same cut plane also provides information about the median and outlier contours that are calculated from a global analysis of contours. The contour boxplot, however, has a drawback in that it does not give the user much information about specific ensemble members, other than the median or the outliers. For such cases, the spaghetti plot with interactivity that allows highlighting of specific ensemble members can augment the contour boxplot by providing more detail if the general user wishes to focus on very specific anatomical areas or members of the ensemble.

IV. Conclusions

In this article, we introduce a new approach to study alignment of shapes. We demonstrate the efficacy of using the 3D contour boxplot ensemble visualization technique to analyze shape alignment and variability in atlas construction and analysis as a real-world application using a prototype system. The system was evaluated by medical imaging experts and researchers working with medical image atlases in an expert evaluation study that was conducted to examine the applicability of ensemble visualization for studying shape alignment and variability. We find that providing the user with both quantitative and qualitative visualization of variability can yield better understanding of the main features of the ensemble and the atlas construction quality.

Future work for our system in the context of the current application includes refining the system in order to address the suggestions provided by the participants, such as viewing the specific structures in the context of the whole brain and more interaction options. Furthermore, ensemble visualization approaches discussed in this article can be integrated into an atlas construction package in order to provide the users the capability of interactively inspecting the shape alignments and the variability among ensemble members after atlas construction. Motivated by the feedback from the participants, a more comprehensive study is required to examine the applicability of ensemble visualization to *compare* different atlas construction schemes.

In addition, studying shape variability has applications in various branches of science. In molecular dynamics, researchers study different types of molecular structures and the shapes of their potential fields in solutions (which vary stochastically) in order to understand, for instance, their biochemical properties [13]. Scientists are also interested in the evolution of the shape of molecules. For example, the surfaces of 3D molecular chains are of significant interest for comparison of various types of protein structures [13]. In Figure 8a, the contour boxplot visualization of the surface of an ensemble of simulated HIV molecules is shown. The ensemble members underwent a Procrustes alignment (translation, rotation, scale) using the positions of the underlying molecules. The potential fields that form these contours are inherently smooth, and thus there was no need for preprocessing of this volume data.

Another application where the study of shape variability and alignment is of significant interest is fluid mechanics. In fluid mechanics, when developing models of vortex behavior, scientists oftentimes study the variability of the shape of vortex structures among different simulations (e.g., using slightly different parameter settings or boundary conditions) to confirm that their observations are repeatable [14], rather than a numerical artifact of a particular simulation. The center of an eddy corresponds to low pressure values in the flow and hence studying the pressure field of a fluid flow can help detect the position of the eddies and regions of high vortices. We have used the 2D incompressible Navier-Stokes solver as part of the open source package Nektar++ [15] to generate an ensemble of 28 fluid flow simulation runs. These simulations have been designed for a steady fluid flowing past a cylindrical obstacle. For each of the ensemble members, we randomly perturbed the initial conditions such as inlet velocity and Reynolds number. For this example, the pressure dependence in the third dimension was computed analytically. The contour boxplot visualization of the isosurfaces of the pressure volume is shown in Figure 8b. There are many possible applications beyond the ones showcased that could benefit from the contour boxplot summary and visualization technique.

Acknowledgments

The authors would like to thank Clement Vachet and Dr. Sarang Joshi for discussions on atlas construction. The authors would also like to thank Dr. Lee Makowski and Dr. Jaydeep Bardhan for providing the HIV molecule data and Dr Shireen Elhabian for help in processing the HIV molecule data. The authors received valuable feedback from Theresa-Marie Thyne for improving the visualizations. This work was supported by National Science Foundation (NSF) grant IIS-1212806.

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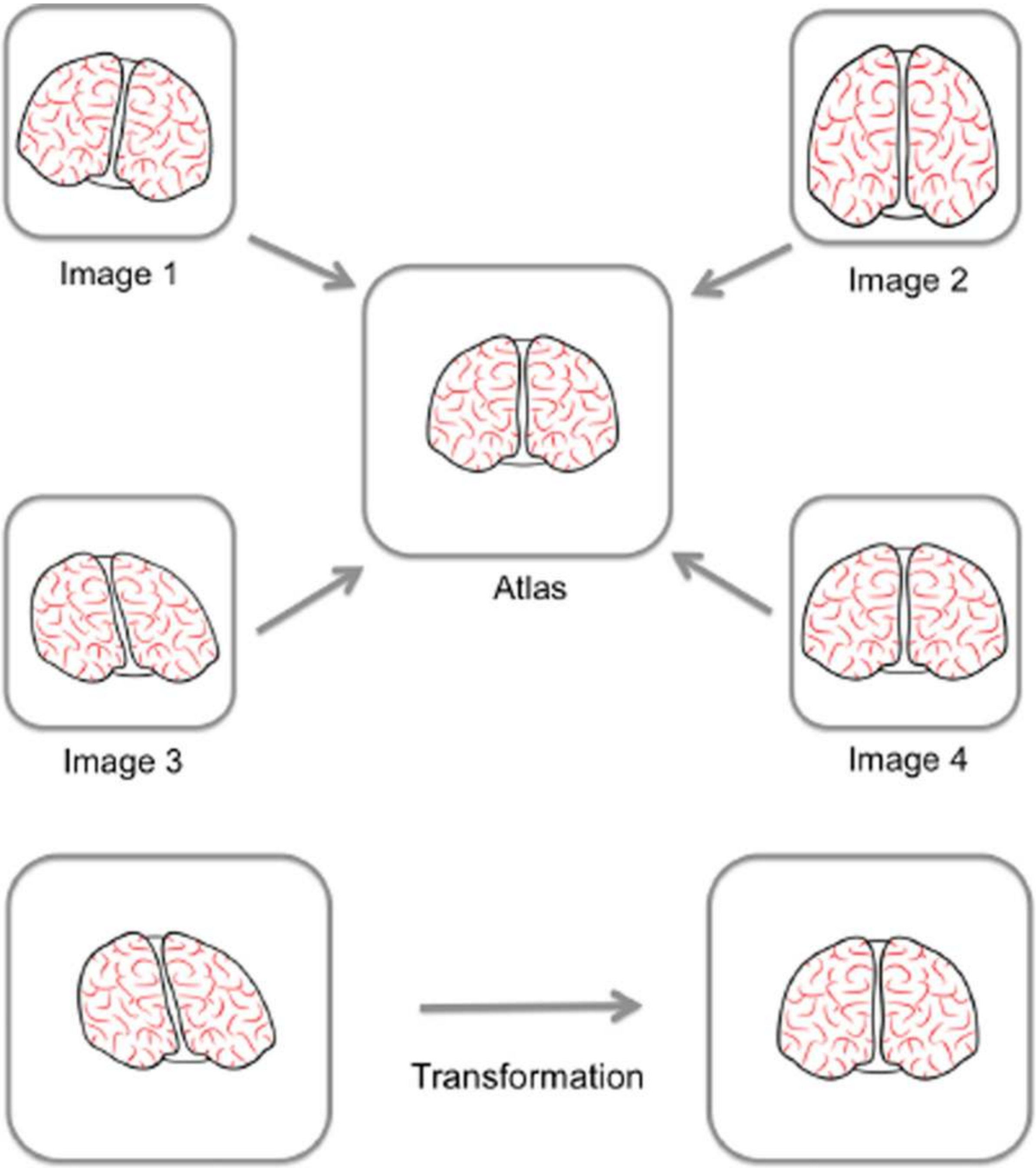
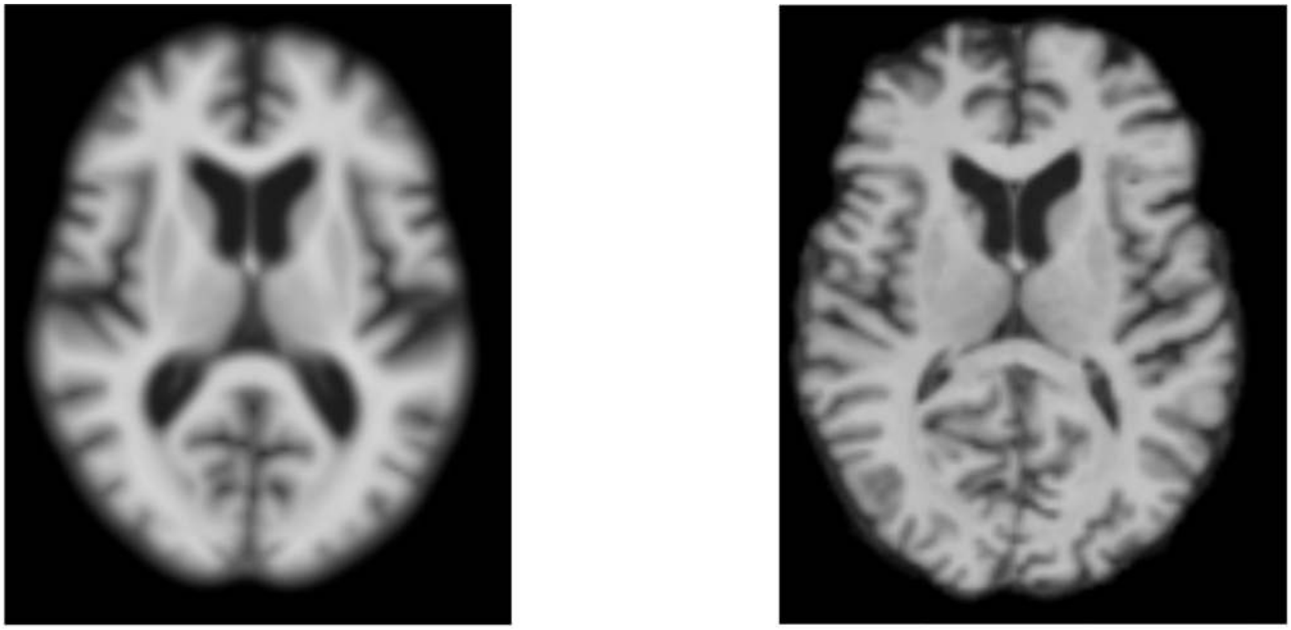


Fig. 1.

An atlas construction scheme involves deformation and registration of all ensemble members to the atlas. The process of deformation and registration of ensemble members is called transformation to the atlas coordinate system or the atlas space.

Fig. 2.

Illustration of the cortex (green) and the ventricle (red). This image shows the segmentation provided by the label map volume for a typical ensemble member. The coarseness of the segmentation seen in this label map is mitigated by smoothing for the final visualization.



(a) Atlas image slice (b) An MRI image slice

Fig. 3.

Illustration of the atlas image slice constructed using AtlasWerks [4]. The anatomical structures in the atlas image usually have lower contrast and fuzzier edges as compared to an original MRI image. This fuzziness results from performing averaging while constructing the atlas.

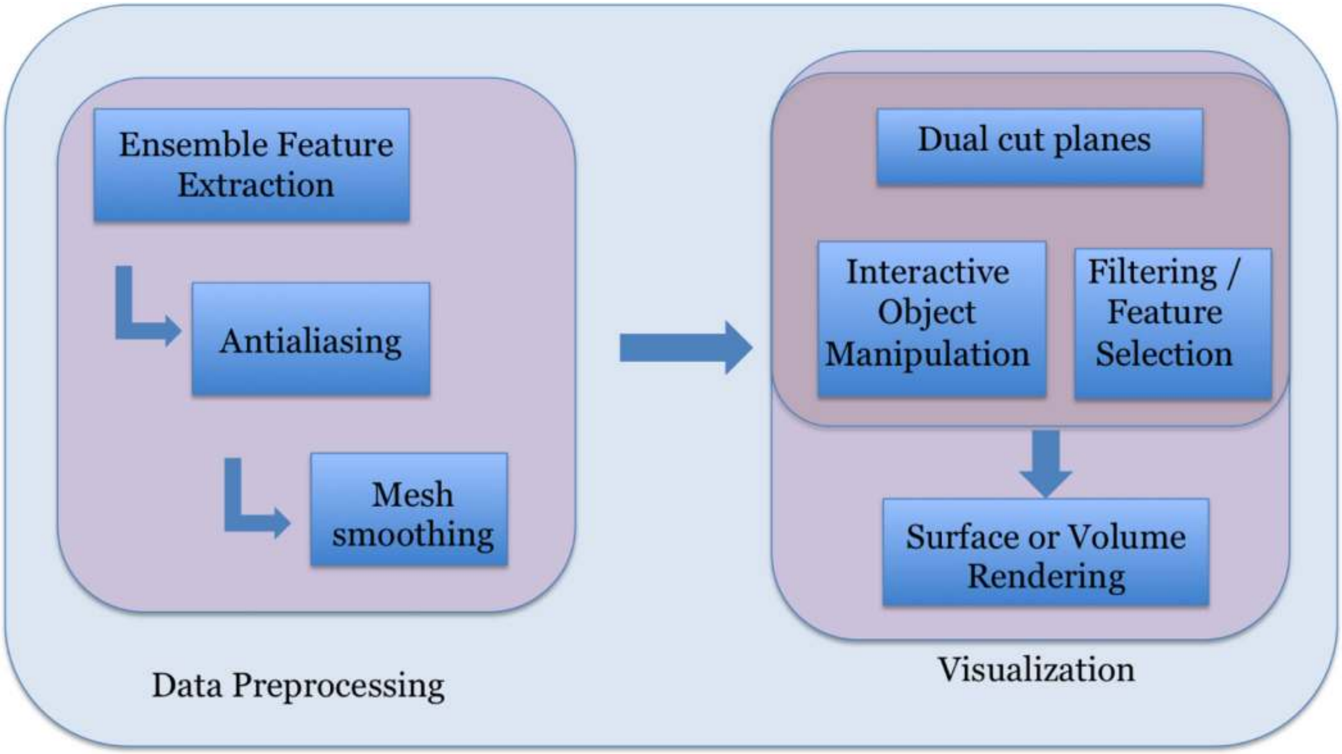
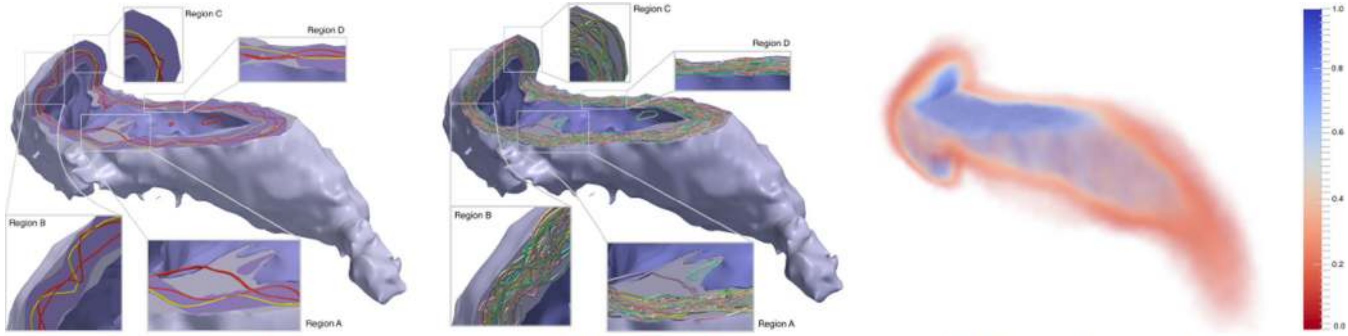


Fig. 4.
Overview of prototype system designed for shape alignment evaluation using ensemble visualization.



(a) 3D Contour Boxplot (b) Spaghetti Plot (c) 3D Average Intensity Image

Fig. 5.

Three visualizations of ventricles from an ensemble containing 34 images from the ADNI dataset transformed to a common atlas space. Left: the contour boxplot visualization in 3D, with 50 percent volumetric band dark purple, 100 percent band volume in light purple, median in yellow, and outliers in red (on the cutting plane). Middle: direct visualization of the ensemble members (spaghetti plot). Right: 3D average intensity image.

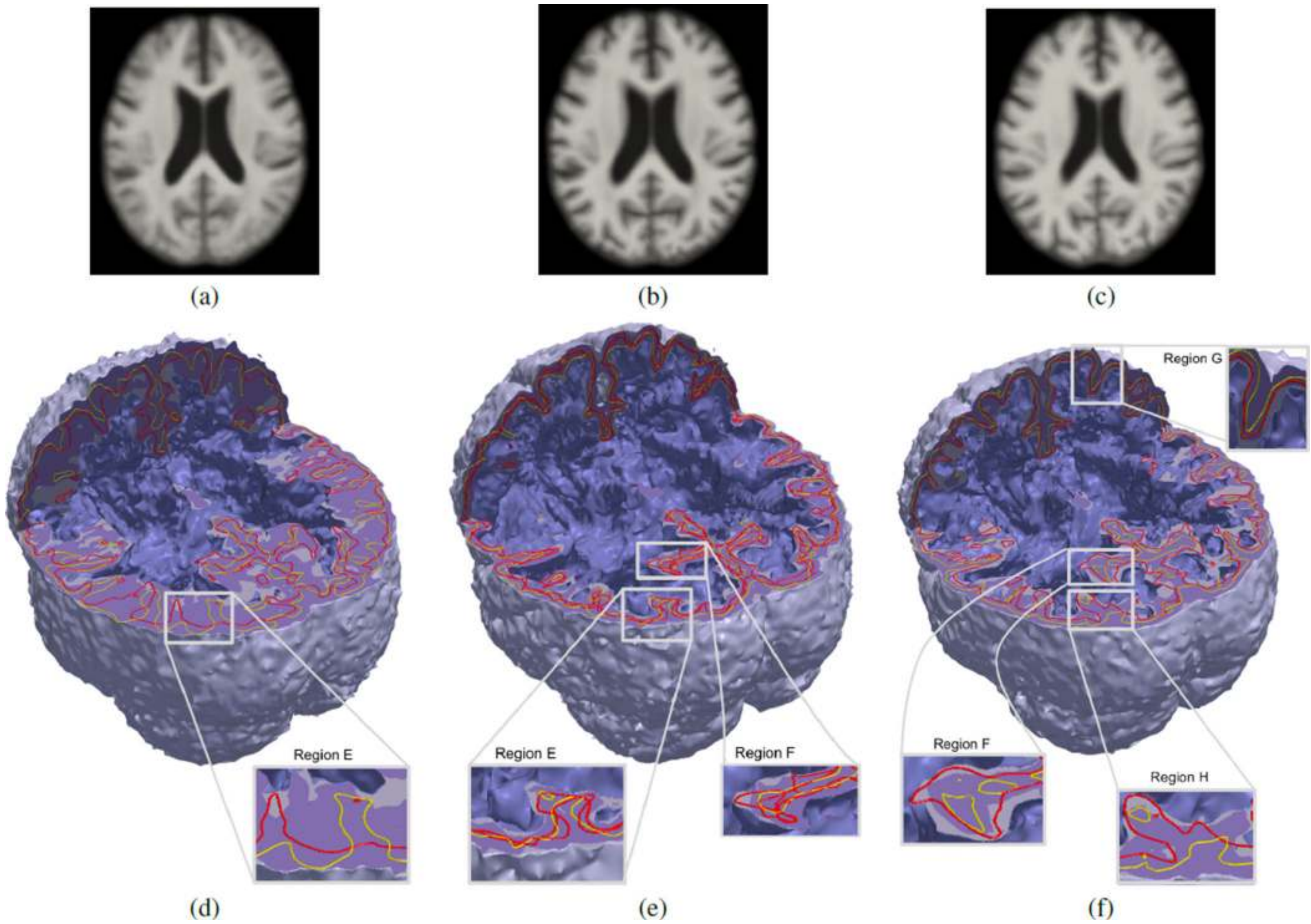


Fig. 6.

Top: slices of average intensity atlases for ensembles of 30 brain images. Bottom: associated contour boxplot visualizations for cortical surfaces. Left: atlas constructed with high regularization of deformation. Middle: atlas constructed with low regularization. Right: atlas with low regularization using a different ensemble than in the other columns.

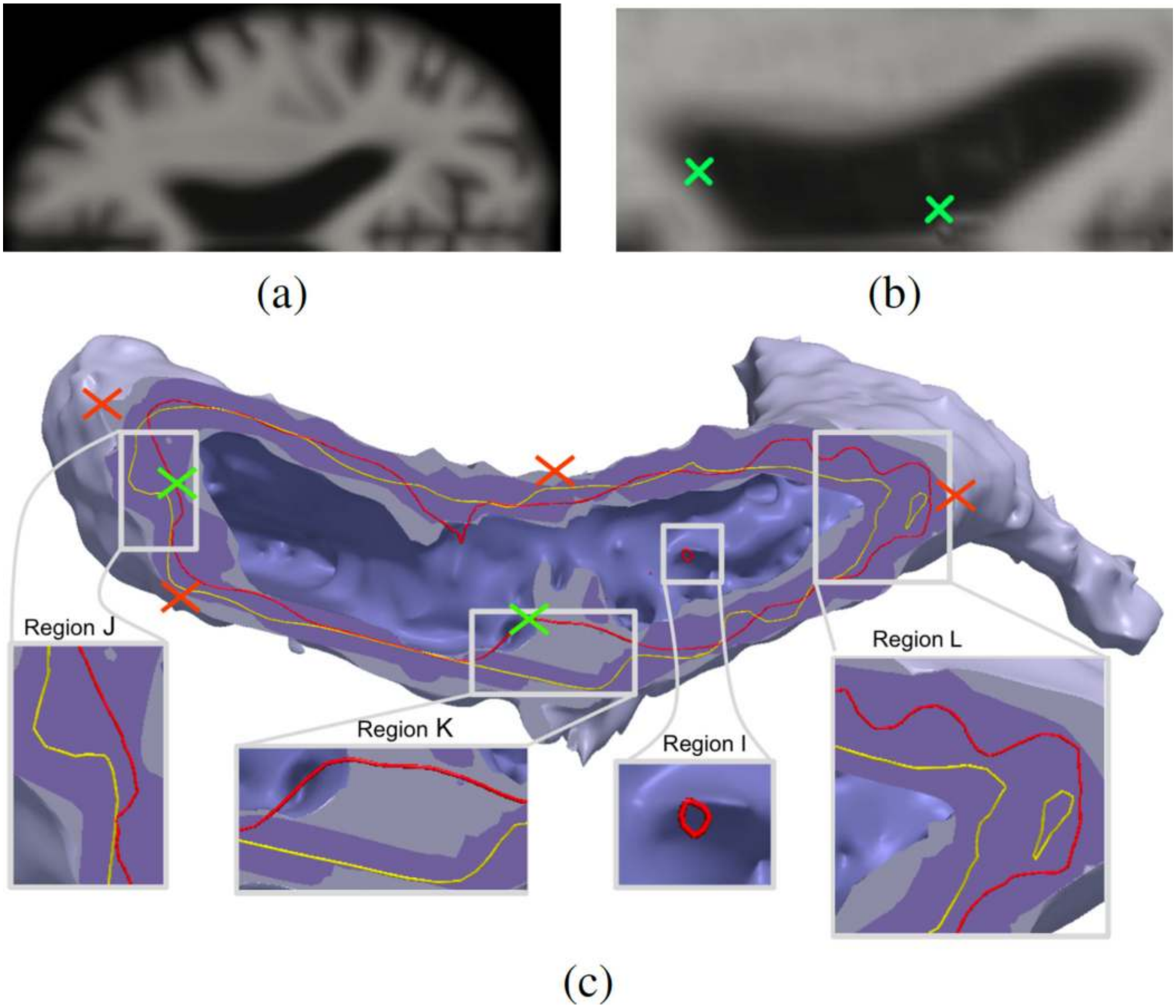


Fig. 7.

Visualizations of left ventricles. Crosses mark the correspondence between the images. (a) Left ventricle slice from an intensity image of the atlas. (b) Left ventricle slice of an ensemble member identified as an outlier by data depth analysis (c) Contour boxplot visualization of an ensemble of 34 ventricles in atlas space.

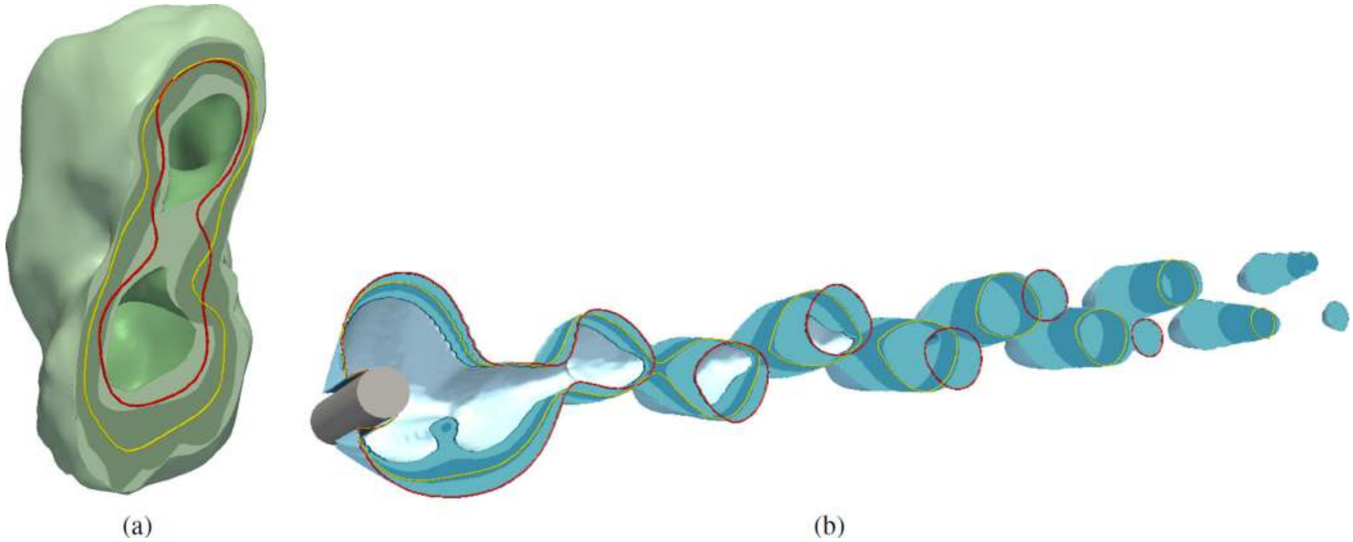


Fig. 8.

(a) Contour boxplot visualization for an ensemble of size 100 simulated HIV protein. Here, we see the median contour in yellow and the outlier contours in red. (b) Contour boxplot visualization of the isosurface of pressure field of a fluid flow. The pressure is considered as a function of depth to generate a 3D pressure volume. The median contour is drawn in yellow and the outlier contours are drawn in red.