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Markov Random Field-based Fitting of a Subdivision-based Geometric Atlas

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Abstract

An accurate labeling of a multi-part, complex anatomical structure (e.g., brain) is required in order to compare data across images for spatial analysis. It can be achieved by fitting an object-specific geometric atlas that is constructed using a partitioned, high-resolution deformable mesh and tagging each of its polygons with a region label. Subdivision meshes have been used to construct such an atlas because they can provide a compact representation of a partitioned, multi-resolution, object-specific mesh structure using only a few control points. However, automated fitting of a subdivision mesh-based geometric atlas to an anatomical structure in an image is a difficult problem and has not been sufficiently addressed. In this paper, we propose a novel Markov Random Field-based method for fitting a planar, multi-part subdivision mesh to anatomical data. The optimal fitting of the atlas is obtained by determining the optimal locations of the control points. We also tackle the problem of landmark matching in tandem with atlas fitting by constructing a single graphical model to impose pose-invariant, landmark-based geometric constraints on atlas deformation. The atlas deformation is also governed by additional constraints imposed by the mesh's geometric properties and the object boundary. We demonstrate the potential of the proposed method on the difficult problem of segmenting a mouse brain and its interior regions in gene expression images which exhibit large intensity and shape variability. We obtain promising results when compared with manual annotations and prior methods.

1. Introduction

With significant advancements in biomedical imaging technology, there is a growing interest in development of automated tools to spatially organize the observed information from the images within a common frame of reference. Such spatial organization enables a comparative analysis across images that provides meaningful information on the underlying phenomenon captured in the images. Most often, these images depict a common anatomical structure with multiple sub-anatomical structures of interest (e.g., the ventricles, atria, and arteries in the heart; or the hippocampus, cerebellum, and cortex in the brain (Fig. 1)). Such multi-part anatomical structures are non-rigid in nature, and are known to have significant

shape variations among different subjects. Furthermore, the image acquisition protocol may introduce variations in the observed intensity in these images (e.g., gene expression images), adding to the challenges involved in automated spatial organization.

One of the many biomedical applications with an urgent need for automated tools for spatial data analysis is gene expression analysis. Technological advancements in *in situ* hybridization techniques have enabled fast acquisition of large amounts of imaging data that represent cellular gene expression profiles [3]. Discovering the gene expression profiles and their functional relationship in different cell populations of the brain can significantly expand the knowledge of interaction of gene products, their role in biological processes, and their effects on diseases. However, each expression image only exhibits information about a single gene. To enable analysis of spatial relations between genes and reveal their functional relations, it is important to compare the expression profiles across images. For this, the structures have to be placed in a common spatial frame of reference using computer-assisted automated techniques. This task, however, is difficult because of the significant variations in the geometry and appearance of the brain structures in these images, and hence has not been sufficiently addressed.

The problem of organizing the spatial information in a common frame of reference is essentially a problem of correspondence mapping. One of the common methods to solve the correspondence mapping problem is to perform registration of a given image to the reference image or an atlas. The pre-defined anatomical labels on the reference image or the atlas can then be easily transferred to the given image through correspondence mapping for further comparative analysis. Image registration methods provide pixel-to-pixel correspondence but require image warping to determine the quality of mapping. An alternative solution is to fit a planar, multi-part, mesh-based deformable model to the data such that a common coordinate space is established within which the anatomical regions/sub-regions can be easily compared. The polygons of the deformable model can be pre-labeled with the names of the various anatomical regions/subregions to obtain an anatomical geometric atlas that enables label mapping directly through model-to-image registration. Subdivision meshes have been used to construct such an atlas because they can provide compact representation of a partitioned, multi-resolution, object-specific mesh structure using only a few control points [15, 1]. However, automated fitting of a subdivision mesh-based geometric atlas to an anatomical structure in an image is a difficult problem.

In this paper, we propose a novel method for model-to-image registration of a deformable, anatomical geometric atlas represented by a labeled subdivision mesh. The optimal fitting of the atlas is obtained by determining the optimal position of the control points. We formulate the problem of fitting a subdivision mesh as a discrete labeling problem, which is solved using the Markov Random Field (MRF) framework. Based on the discrete MRF formulation, the position of the control points is determined as an optimal label configuration in a graphical model. The solution to the labeling problem is obtained by minimizing the corresponding Gibbs energy function using efficient discrete optimization techniques. Among other constraints, we introduce a prior to preserve the convexity of the planar mesh polygons during deformation and a pose-invariant, landmark-based geometric constraint to drive the deformation towards the desired solution. In order to obviate the need

for *a priori* landmark correspondences, we solve the problem of landmark matching in tandem with atlas fitting in a single graphical model. This is inspired by the joint image registration and landmark matching approach [17]. However, we substitute the regular grid-based image registration layer with an irregular, object-specific grid-based subdivision mesh fitting that conforms well with the object boundary, and also obviates the need for image warping for correspondence mapping.

Our method uses the subdivision mesh as the geometric model for atlas fitting, similar to the method by Bello *et al.* [1]. However, the key differences between the two methods are the deformation formulations, the energies that can be used for fitting and the ability to capture the optimal solution. In Bello *et al.*'s method [1], the deformation is achieved through a modified iterated closest point (ICP) technique. This requires to explicitly pre-determine the expected locations or the correspondences of the mesh points (not the control points). Thus, the external energy has to be defined in the form of the distances between the current and the expected locations of the mesh points and it must be differentiable. Furthermore, ICP-based methods are known to be very sensitive to the initial matching conditions to erroneous correspondences and cannot provide guarantees on the optimality of the obtained solution due to their greedy optimization nature.

The proposed method achieves the deformation by solving a label assignment problem for the locations of the control points using a discrete MRF formulation. Therefore, it does not require pre-defined correspondences, inherits considerable flexibility in defining the energy terms (graph-based methods can encode any local metric), provides certain guarantees on the optimality properties of the obtained solution and is portable to other atlas-based deformation problems (e.g., face model fitting for recognition) with suitable modification of the energy terms. To the best of our knowledge, this is the first time that an MRF formulation is used in combination with subdivision meshes to fit a geometric atlas to the structure of interest.

The main contribution of this work is a novel MRF-based discrete formulation for deformable fitting of a subdivision-based geometric atlas. The advantages of our framework are: (i) a compact representation of the geometric atlas using a few control points for complete characterization of the anatomical object and its interior regions; (ii) derivative free optimization allowing considerable flexibility in the formulation of suitable energy functions; (iii) robustness to initialization as larger displacements can be captured through sub-optimal solutions of successive MRFs; and (iv) invariance to similarity transforms due to a higher-order MRF formulation for landmark matching problem.

2. Related Work

Contour-based models

Snakes or active contour models [16] and geodesic active contour model [4] are the popular learning-free deformable model fitting methods. Active shape and appearance models [7, 6] provide geometric and appearance constraints by learning the shape and intensity priors. Even though these models are suitable for many applications, they cannot be used to characterize the internal regions and their boundaries in a complex object.

Structured mesh-based models

In these models the object is embedded in a structured rectilinear mesh grid where the grid points are the control points for a tensor product spline. Deforming the mesh by moving the control points also deforms the embedded object. Mesh deformation, also known as free-form deformation, can be driven by either boundary- and region-based external forces from the same image [12] or by comparing the quality of the current deformation with a reference image [19, 10, 23, 17] or an atlas [9]. Since the whole embedding space is deformed in these methods, they directly provide the complete characterization of an object. However, the structured grid pattern does not naturally conform to the boundaries of the structures and hence, cannot account for local variations in shapes. This limitation can be overcome by increasing the number of mesh points. However, this will also increase the computational time required to compute deformations for a large number of points.

Unstructured mesh-based models

Unstructured simplex meshes [8] are more flexible to conform to a structure's boundaries and characterize the internal regions. However, due to their piecewise linear nature, they require a large number of mesh points to conform accurately to a curved object. Also, they require explicit constraints to maintain boundary smoothness. Subdivision meshes [22] provide an alternative to overcome such limitations and are inherently suitable for spatial organization of image data [15]. Recently, subdivision meshes were used for segmenting brain structures [1] where the optimal position of the control points was obtained using a modified ICP method. Further, a principle component analysis-based statistical shape model, landmark points, and learned internal boundaries were used to impose geometric constraints to the deformation of the mesh. However, this method has severe restrictions on the type of energy functions that can be used and is very sensitive to initialization.

3. Method

3.1. Subdivision Mesh for a Geometric Atlas

In this section, we review the concepts related to using a subdivision mesh as an atlas [15]. A geometric atlas can be represented as a planar mesh consisting of several connected polygonal elements. The mesh is further partitioned into sub-meshes that are defined by a set of partitioning polylines, which are referred to as *crease edges*. Such a partitioning of the mesh enables an accurate representation of an anatomical object and its interior sub-regions. The mesh is designed specifically for an object and its polygons are labeled to provide a geometric atlas for that object (Fig. 2).

A modified Catmull-Clark subdivision scheme [5] is used to obtain successively smoother meshes from an initial base mesh. The subdivision eventually converges to a limit mesh, which contains a network of smooth curves and accurately models the anatomical boundaries. The position of the vertices of the base mesh, M^0 , determines the shape of successive smooth meshes M^k , (at subdivision level k) and the limit mesh, M^∞ . Hence, the deformation of any smooth mesh entirely depends on the displacement of the vertices in the base mesh M^0 , which are relatively less in number when compared to the number of vertices in the smooth meshes.

The subdivision process consists of two simple transformation steps: (i) bilinear subdivision, and (ii) centroid averaging. Bilinear subdivision modifies the topology of the mesh, while centroid averaging refines the geometric positions of the resulting vertices. Specifically, bilinear subdivision involves splitting of each quadrilateral or *quad* of the mesh into four sub-quads such that the new vertices are placed at the midpoints of the quad edges and the centroids of the faces of the previous mesh. In centroid averaging step, each vertex is displaced towards the centroid of the centroids of the quads containing that vertex. To accurately model the smooth boundaries of an object, the process is slightly modified such that the vertices on the crease edges are processed using only the crease edges network and not the quads. Additionally, to impose further constraints on the atlas geometry, the positions of selected vertices are not changed during the subdivision process. These vertices are termed as *crease vertices*, and are selected from the vertices that are shared by two or more crease edges.

Due to the linearity of the subdivision process, the position of a vertex i in a mesh M^k at subdivision level k can be represented as a linear combination of vertices of the base mesh M^0 :

$$M^k(i) = \sum_j \eta_j^k(i) M^0(j),$$

where $\eta_j^k(i)$ is a subdivision-basis coefficient that represents the influence of the vertex j of the base mesh on the vertex i of a smooth mesh at subdivision level k . Thus, the vertices of the base mesh can be thought of as the control points that control the shape of the smoother meshes. To simplify the notation, the basis coefficients will be represented as $\eta_j(\cdot)$ assuming that they are computed for a subdivision level k , unless stated otherwise.

The subdivision-basis coefficients depend on the chosen subdivision scheme and the relative topological position of the vertices. They can be easily computed using the subdivision process. For instance, consider N control points and associate each i^{th} control point with a vector of length N , $\mathbf{v}_i = \{0, \dots, 1, \dots, 0\}$, that has value 1 at i^{th} position and 0 elsewhere. Then, apply the subdivision process to these vectors by treating them as the coordinates of each vertex in the coefficient space. After k subdivisions, each vertex of the subdivided smooth mesh will be represented by a vector of length N , which is the desired vector of the basis coefficients. Each i^{th} element of the basis vector associated with a particular vertex determines the influence of the i^{th} control point on this vertex. For more detailed information on subdivision meshes, the reader is referred to the book by Warren and Weimer [22].

Once a geometric atlas is constructed (manually), we only need to know the location of a few control points in an image to fit a high resolution mesh model to an object (i.e., its boundary and its internal regions), and obtain a correspondence mapping across images. Given an initial control mesh M^0 , the goal of model fitting is to estimate the locations of the control mesh vertices such that the limit mesh of the new deformed control mesh M^{0*} fits accurately to the object in the given image I :

$$M^{0*} = \arg \min_{M^0} E(M^0),$$

where $E(M^0)$ is the energy function consisting of an image-based external energy $E_D(M^0)$ that measures the quality of fit of the limit mesh to the given data I and a regularization energy $E_M(M^0)$ that constrains the deformation of the model based on prior knowledge of the model or the deformation space. In practice, the quality of fit of the limit mesh is approximated by a high resolution smooth mesh at a user-defined subdivision level k . In the following sections, we describe a novel method to determine the optimal location of these control points for a given image.

3.2. Discrete MRF Formulation

We propose a discrete formulation for model deformation in which the search space is discretized and the discretized displacements are associated with labels. The model is deformed under some constraints that are obtained from available prior knowledge about the data, model, and the deformation space. Thus, the problem of model fitting becomes a constrained discrete labeling problem, which can be solved using the MRF framework. Next, we describe the proposed discrete formulation and the constraints used to fit the mesh model. Consider a graph $\mathcal{G} = (\mathcal{V}, \mathcal{E})$ consisting of a set of nodes $\mathcal{V}$ and a set of edges $\mathcal{E}$ connecting the nodes. We define the nodes of the graph by the vertices of the base mesh and the edges are defined to represent the dependencies between the vertices. We also define a set of labels $\mathcal{L}$ where a label l_j represents a discretized displacement vector $\mathbf{d}_j$ corresponding to the deformation space $\mathcal{D}$. The goal is to assign a label f_i , which takes a value from the set $\mathcal{L}$ corresponding to a displacement vector $\mathbf{d}_{f_i}$, to each mesh vertex i such that the obtained deformation field is optimal given some criterion. Thus, the objective of the label assignment is to find a mapping $F : \mathcal{G} \rightarrow \mathcal{L}$. We denote a configuration of label assignment to the N nodes of graph $\mathcal{G}$ by $\mathbf{f} = \{f_1, f_2, \dots, f_N\}$ and the set of all possible configurations as $\mathcal{F}$. The total energy of the MRF:

$$E(\mathbf{f}|I) = \sum_{c \in \mathcal{C}} V_c(\mathbf{f}|I),$$

is essentially a sum of clique potentials $V_c(\mathbf{f}|I)$ over the set $\mathcal{C}$ of all possible cliques. A clique c is defined as a subset of the set $\mathcal{V}$ of sites such that each member of the clique is a neighbor of all the other members. The value of $V_c(\mathbf{f}|I)$ depends on the local configuration of the clique c . The number of sites in a clique defines the order of the clique and the corresponding clique potential.

3.3. Energy Functions

In this section, we describe the construction of the energy function, $E(\mathbf{f})$, which is basically a weighted sum of several energy functions each modeling a specific type of prior information. These functions are computed as the sum of unary, pairwise and/or higher-order potentials and are described in detail in the following sub-sections.

3.3.1 Boundary-based Energy—A suitable boundary energy has to be defined to drive the deformation of the subdivision mesh such that its boundary coincides with the object boundary. We weigh the contribution of each mesh vertex towards the displacement of the boundary control points in the boundary-based energy by a set of weight coefficients which are determined using the subdivision-basis coefficients. Assuming that the object boundary is known or can be computed *a priori* for a particular application, the boundary-based energy function $E_B(\mathbf{f})$ is defined as the sum of pairwise potentials that are defined as:

$$V_{ij}(f_i, f_j) = \begin{cases} \sum_m \hat{\eta}_{ij}(m) \psi(\hat{M}_{f_i, f_j}^k(m), C) & \text{if } m \in \mathcal{B}^k \\ 0 & \text{otherwise} \end{cases},$$

where $\hat{M}_{f_i, f_j}^k$ is the deformed mesh at subdivision level k obtained by simultaneously moving the control points i and j by displacement vectors $\mathbf{d}_{f_i}$ and $\mathbf{d}_{f_j}$, respectively, $\psi(\cdot)$ is a function of distance between a mesh vertex m and the object boundary C , $\hat{\eta}_{ij}$ is an inverse weight coefficient, and $\mathcal{B}^k$ is the set of vertices on the boundary of the smooth mesh. The new deformed mesh can be computed using the subdivision-basis coefficients as:

$$\hat{M}_{f_i, f_j}^k(m) = M^k(m) + \eta_i(m) \mathbf{d}_{f_i} + \eta_j(m) \mathbf{d}_{f_j}.$$

The inverse weight coefficient, $\hat{\eta}_{ij}$, measures the influence of a mesh vertex m on the pairwise energy of control points i and j , and is given by:

$$\hat{\eta}_{ij}(m) = \frac{\eta_i(m) + \eta_j(m)}{\sum_{a, b \in \mathcal{E}} (\eta_a(m) + \eta_b(m))}.$$

This is similar to the approach employed to approximate likelihood energy for a b-spline curve [11]. Alternatively, a unary potential can be defined to approximate the boundary likelihood but it will be less accurate than the pairwise formulation because the position of a mesh vertex is influenced by more than one control point in the subdivision scheme.

3.3.2 Landmark-based Energy—Landmarks provide geometric constraints to drive the solution towards *a priori* known locations. Subdivision meshes provide a natural way to incorporate such constraints. Any point within a mesh can be represented as a linear combination of the mesh control points and the subdivision-basis coefficients. The coefficients of a point can be computed through barycentric interpolation of the coefficients associated with the vertices of the quad in the mesh that contains the point [14]. Alternatively, they can be approximated by associating the coefficients of the nearest vertex in a high resolution subdivision mesh to the landmark point. Thus, the locations of landmark points can be defined in terms of the control points and the subdivision-basis coefficients as:

$$\mathbf{p}_i = \sum_j \eta_j^{\mathcal{P}}(i) M^0(j),$$

where $\mathbf{p}_i$ is the i^{th} landmark point on the geometric atlas and $\eta_j^{\mathcal{P}}(i)$ is the basis coefficient between the i^{th} landmark point and the j^{th} control point.

Single candidate: Assuming that a best corresponding candidate for each landmark has been determined in the given image using manual annotations or application specific techniques, the landmark point in the deformed mesh should coincide with the corresponding candidate on the image. This can be achieved by minimizing the distance between the two points. Using the properties of the subdivision-basis coefficients,

$\sum_j \eta_j^{\mathcal{P}}(\cdot) = 1$, and the triangle inequality, we obtain:

$$\|\hat{\mathbf{p}}_m - \mathbf{q}_m\| \leq \sum_j \eta_j^{\mathcal{P}}(m) \|\mathbf{d}_{f_i} - \mathbf{d}_m\|,$$

where $\mathbf{q}_m$ is the location of the corresponding landmark candidate, $\mathbf{d}_m = \mathbf{q}_m - \mathbf{p}_m$, and $\mathbf{p}_m$, $\hat{\mathbf{p}}_m$ are the locations of a landmark point in the current and deformed mesh, respectively. Thus, the landmark-based energy $E_L(\mathbf{f})$ can be approximated to minimize an upper bound of the energy from a unary potential defined as:

$$V_i(f_i) = \sum_m \eta_i^{\mathcal{P}}(m) \|\mathbf{d}_{f_i} - \mathbf{d}_m\|.$$

Multiple candidates: If the best corresponding candidate is not known *a priori* for each landmark point, it can be determined by the proposed framework from a pool of prospective candidates by solving the landmark matching problem in tandem with atlas fitting within a single optimization framework. Toward this, we add a layer of landmark-based subgraph to the existing graph to obtain a new set of nodes $\mathcal{V} = \mathcal{V}_m \cup \mathcal{V}_g$ and edges $\mathcal{E} = \mathcal{E}_m \cup \mathcal{E}_g \cup \mathcal{E}_{mg}$ where $\mathcal{V}_m$ and $\mathcal{E}_m$ belong to the mesh graph, $\mathcal{V}_g$ and $\mathcal{E}_g$ belong to the landmark graph, and $\mathcal{E}_{mg}$ connects the two graphs. We also append the label set with a set of new labels $\mathcal{L}_g$, where a label assignment l_j^g to the i^{th} node in landmark graph represents the selection of the j^{th} candidate as the best candidate for the i^{th} landmark. We define a unary, pairwise and higher order potentials to compute the landmark-based energy $E_L(\mathbf{f})$.

The unary potential for the landmarks is defined by:

$$V_i(f_i) = \phi(\mathbf{q}_{f_i}^i),$$

where $\mathbf{q}_{f_i}^i$ is a candidate for the i^{th} landmark and $\phi(\cdot)$ measures the candidacy strength of the candidate based on its appearance and/or boundary curvature. We define higher-order potentials for triplets of landmarks. The interdependencies between the landmarks in a triplet

can be modeled using the probability distribution of the relative lengths of triangles formed by them [21]. Each triplet forming the clique c is represented by a two element descriptor $\mathbf{r}_c = (r_{ij}, r_{jk})$, where r_{st} is the relative length of the side defined by the points s and t . This representation is translation, rotation, and scale-invariant. We learn a multivariate Gaussian distribution $\mathcal{P}_c(\mathbf{r}_c)$ for each $\mathbf{r}_c$ from a training set. The higher-order potential for landmark graph is then computed as:

$$V_c(\mathbf{f}_c) = -\log(\mathcal{P}_c(\mathbf{r}_c(\mathbf{f}_c))).$$

The interaction between the two graphs is represented by pairwise connections between the landmarks and the control points, and are defined using the subdivision-basis coefficients. A control point i and a landmark j are connected to form an edge if the basis coefficient of the control point for that landmark is non-zero (i.e., $\eta_i^{\mathcal{P}}(j) > 0$). Using the properties of the subdivision-basis coefficients and the triangle inequality, and considering each landmark candidate as the desired candidate, the pairwise potential is defined as:

$$V_{ij}(f_i, f_j) = \eta_i^{\mathcal{P}}(j) \|\mathbf{d}_{f_i} - (\mathbf{q}_{f_j}^j - \mathbf{p}_j)\|.$$

3.3.3 Label Regularization Energy—The label regularization energy E_R is included in the energy function to introduce smoothness in the label domain. It is defined as the sum of pairwise potentials that are defined as: $V_{ij}(f_i, f_j) = \|\mathbf{d}_{f_i} - \mathbf{d}_{f_j}\|$, where $\mathbf{d}_{f_i}$ is the displacement vector corresponding to the label f_i assigned to the i^{th} control point.

3.3.4 Internal Energy—The internal energy of the model constrains the deformation of the model based on the prior information on the set of feasible solutions. We propose a new prior for planar subdivision meshes that preserves the convexity of the mesh quads and is computed from the relative positions of their vertices. The cross-product of two vectors computed from any two connected sides of a convex quad should be in the same direction as the cross-product of vectors from the remaining two sides. Consider a mesh with M quads, where the vertices of each quad are given in either clock- or counter-clockwise order. Let's assume that the vertices of i^{th} quad are given as: $\{\mathbf{p}_1^i, \dots, \mathbf{p}_4^i\}$. Using the vectors $\mathbf{v}_1^i = \mathbf{p}_1^i - \mathbf{p}_2^i$, $\mathbf{v}_2^i = \mathbf{p}_3^i - \mathbf{p}_2^i$, $\mathbf{v}_3^i = \mathbf{p}_3^i - \mathbf{p}_4^i$, and $\mathbf{v}_4^i = \mathbf{p}_1^i - \mathbf{p}_4^i$, the directions of the resulting cross-product vectors can be compared by:

$$\begin{aligned} c_1^i &= (v_{1x}^i \cdot v_{2y}^i) - (v_{1y}^i \cdot v_{2x}^i), \\ c_2^i &= (v_{3x}^i \cdot v_{4y}^i) - (v_{3y}^i \cdot v_{4x}^i), \\ s(i) &= \begin{cases} 1, & \text{if } c_1^i \cdot c_2^i < 0 \\ 0, & \text{otherwise} \end{cases} \end{aligned}$$

where s is a binary vector indicating the non-convexity of the quads, and c_1^i and c_2^i are the signed magnitudes of the cross-product vectors. Thus, the unary potential that defines the internal energy $E_I(\mathbf{f})$ is given by:

$$V_i(f_i) = \sum_{m=1}^M \eta_i^{\mathcal{Q}}(m) s(m),$$

where M is the number of quads in the smooth mesh. The term $\eta_i^{\mathcal{Q}}(\cdot)$ is a basis coefficient measuring the influence of a quad on the control points and is computed as an average of the basis coefficients of its vertices:

$$\eta_i^{\mathcal{Q}}(m) = 0.25 \sum_{j \in \mathcal{Q}_m} \eta_i(j).$$

3.4. Optimization

Lastly, we need to define a method to optimize the MRF energy function. Our proposed graphical model has higher-order cliques that require special attention. Most of the optimization techniques solve for only unary and pairwise connections. In addition, the energy in our formulation is non-differentiable and non-submodular, which can be a problem with many optimization techniques. To this end, we adopt the general framework proposed by Ishikawa [13]. The optimization of the multi-label, higher order MRF is performed by: (i) transforming the multi-label MRF problem to a binary MRF problem, and (ii) transforming the binary higher-order MRF to a binary first-order MRF. Owing to the non-submodular nature of the MRF potentials, the optimization of the binary MRF is performed using a quadratic pseudo-boolean optimizer (QPBO)[18].

4. Results

We applied the proposed method on the challenging problem of segmentation of mouse brain gene expression images (Fig. 1). These images were acquired as part of a gene expression study [2]. The images and their corresponding manually fitted meshes used in the experiments were provided by Bello *et al.* [1]. These images depict sagittal sections of postnatal day-7 mouse brains at standard section 9, each revealing the expression of a single gene after *in situ* hybridization. The images were acquired using a light microscope at 3.3 μm per pixel resolution resulting in approximately $2,400 \times 4,000$ pixels image size (for details on the image acquisition, we refer the reader to [3]). The images were scaled down to 25% of the original size and globally aligned to a reference Nissl-stained image that was used to construct the atlas. The landmarks were identified by visual inspection of several images and were categorized into internal and boundary landmarks based on their positions [1] (Fig. 3 (top-left)).

Before applying the proposed method, we first segmented the images using histogram thresholding, flood-filling and morphological operations. Then, a border tracing algorithm was applied on the segmented region to obtain the boundary contour, which was further smoothed with a moving average filter. In each image, the candidates for each landmark were obtained from a local search region using appearance and/or curvature information. The appearance of the landmarks was characterized using gradient orientation histograms-

based descriptors that were partially normalized as proposed by Tola *et al.* [20]. The candidates were selected as the points having minimum descriptor distance when compared to the corresponding landmarks in the reference image, and those having minimum/maximum curvatures at the boundary. To capture the deformation of the model, we used multiple optimization cycles (10 iterations) to improve the approximation of the local deformations incrementally. In each iteration, the maximum displacement range for each control point was decreased by a scaling factor (10%) to improve the accuracy of fitting. The maximum displacement range was sampled along the major axes and diagonals to provide a set of 25 labels for each control point. The same weights were used in all the experiments and were determined empirically. Also, in the case of partial labeling by the QPBO, the labels of the unlabeled nodes are left unchanged.

We evaluated the proposed method on 100 available gene expression images. Figure 3 depicts the qualitative results for few sample gene expression images. For quantitative evaluation, the performance of the proposed method was compared with the provided manually fitted meshes. We used a spatial overlap measure, the Dice similarity coefficient (DSC), which was computed for two regions as the ratio of twice the area of shared region between them and sum of their areas. The DSC was computed for all the 14 sub-anatomical regions within the mouse brain. We compare the performance of our method with the method proposed by Bello *et al.* [1] referred to as *Bello*.

The mean and standard deviation values of the DSC for the 14 sub-anatomical regions for our method and *Bello* are depicted in Fig. 4. It is evident that our method performs comparable to *Bello* with less variance in the accuracy as measured by DSC. This is promising as our method uses much less information than *Bello*. It should be noted that, unlike *Bello*, our method does not use: (i) a sub-anatomical region boundary prior, or (ii) a deformation prior that penalizes non-affine deformation of the mesh. Furthermore, we tackle the problem of landmark matching and atlas fitting simultaneously, within the same discrete MRF framework.

The accuracy of the proposed method is dependent on the quality of the selected landmark candidates and can become worse in the absence of good candidates. This effect can be mitigated by not only improving the candidate detection but also by including/excluding the reliable/unreliable landmarks based on their consistency in being detected across a set of training images. Our method can also benefit significantly by incorporating prior information from the interior boundary likelihood and statistical deformation prior of the control mesh in the discrete formulation. We will be addressing these issues in the near future.

5. Conclusion

In this paper, we have introduced a novel method for fitting a geometric atlas, constructed using planar subdivision meshes, to segment the anatomical structures and its subregions. We formulated the problem of mesh fitting as a graph labeling problem which was solved using the MRF framework. The proposed method can also solve the problem of landmark matching, in tandem with the subdivision mesh fitting problem, to incorporate geometric

point constraints, and thus voiding the need to know the mapping between the corresponding landmark points *a priori*. We have demonstrated the suitability of the proposed method to the application domain of gene expression analysis for spatial data organization. The potential of our method is demonstrated by its promising results on the challenging gene expression image data.

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Figure 1.
Depiction of the anatomical regions in the sagittal section of a Nissl-stained mouse brain image (from [1]).

Figure 2.

A subdivision mesh representing the geometric atlas of a mouse brain at subdivision level-2, constructed from the control points depicted by '■' (*crease vertices* are depicted by '□'). The region boundaries are depicted in blue.

Figure 3.

Top: (left) Internal and boundary landmarks with their IDs (left) (from [1]), and (right) depiction of the results (control points and the corresponding mesh) obtained by our method on sample image. Middle/bottom: Comparison of the mesh boundaries obtained manually (blue) and by our method (red) overlaid on few example gene expression images, also depicting the effect of landmark bias in case of a bad candidate and lack of interior boundary prior.

Figure 4.

Comparison of mean (top) and standard deviation (bottom) of DSC computed for the 14 sub-anatomical regions from the results of the proposed method (bar-2 in green) and Bello (bar-1 in red). The region IDs on the x-axis correspond to the sub-anatomical regions: 1- cerebellum, 2-medulla, 3-pons, 4-midbrain, 5-cortex, 6-hippocampus, 7-thalamus, 8- hypothalamus, 9-olfactory bulb, 10-basal forebrain, 11-septum, 12-striatum, (13, 14)-ventral striatum.