Adaptive Template Moderated Spatially Varying Statistical Classification

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Abstract. A novel image segmentation algorithm was developed to allow the automatic segmentation of both normal and abnormal anatomy. The new algorithm is a form of spatially varying classification (SVC), in which an explicit anatomical template is used to moderate the segmentation obtained by k Nearest Neighbour (k-NN) statistical classification. The new algorithm consists of an iterated sequence of spatially varying classification and nonlinear registration, which creates an adaptive, template moderated (ATM), spatially varying classification (SVC).

The ATM SVC algorithm was applied to several segmentation problems, involving different types of imaging and different locations in the body. Segmentation and validation experiments were carried out for problems involving the quantification of normal anatomy (MRI of brains of babies, MRI of knee cartilage of normal volunteers) and pathology of various types (MRI of patients with multiple sclerosis, MRI of patients with brain tumours, MRI of patients with damaged knee cartilage). In each case, the ATM SVC algorithm provided a better segmentation than statistical classification or elastic matching alone.

Keywords: template moderated segmentation, elastic matching, nearest neighbour classification, knee cartilage, neonate, brain, tumour

1 Introduction

The segmentation of structures or types of tissue from medical images is still a difficult problem. In particular, the segmentation of pathology often requires intensive manual interaction to achieve good, or even acceptable, segmentations. Our goal was to develop a generally applicable segmentation algorithm that could aid in the automation of medical image analysis tasks by successfully segmenting both normal anatomy and common types of pathology.

A strategy of feature detection and classification (spectral segmentation) has been widely used for the identification of tissue types. When spatial information (such as shape and spatial relationships between structures) is significant, a variety of deformable models have been proposed. Some segmentation problems can be solved simply by feature identification and classification. In this case, there is no need to make use of an anatomical template, and the segmentation is a straightforward process. Similarly, some segmentation problems can be solved by matching deformable models directly to the image data [1, 2, 3]. Here we deal with those segmentation problems for which feature identification and classification, or matching deformable models alone, are insufficient.

These different segmentation strategies are often complementary, both in the tasks where they succeed and in the tasks where the fail. For example, classification is often successfully applied for the global segmentation of major tissue types. Deformable models have been successfully applied to the localization of particular anatomical structures. Tissue classification is unsuccessful when different structures to be identified have the same or overlapping spectral properties. Deformable models often need accurate initialization and are usually optimized for particular structures (sometimes with a single closed boundary), and can fail in the presence of abnormal anatomical variability (or even in the presence of normal but highly variable structures, such as the cortex). Optimization strategies have usually been driven by local gradient information which is often insufficient to distinguish particular structures of interest.

We developed a new algorithm, ATM SVC, by embedding a traditional multiple feature k-NN classification into a higher dimensionality problem space. The additional dimensionality is derived from an anatomical template, and acts to moderate the statistical classification. In the special case of the classification problem involving separable classes with nonoverlapping anatomy accurately described by the anatomical model, the ATM SVC solution is the same as the original k-NN classification problem. In the common case involving some spectral overlap, the ATM SVC resolves the ambiguity of the feature space with anatomical context.

ATM SVC integrates an individualized explicit anatomical model with statistical classification. This allows the generation of a spatially varying classification, so that spectral overlap can be remedied through spatial information. In turn this generates a classification of the data which is a more reliable and robust source of information than the raw imaging data for the fast nonlinear registration to operate upon, allowing more accurate nonlinear registration than is possible from greyscale image data alone. By iterating these steps, we have found it possible to segment normal and abnormal anatomy from a range of locations in the body.

2 Method

Our algorithm iterates between a classification step to identify tissues and an elastic matching step to align a template of normal anatomy with the classified tissues. The template of anatomy is used to modify the classification to produce a spatially varying, rather than global, classification. The steps are iterated to improve the final segmentation. Figure 1 illustrates the ATM SVC algorithm.

2.1 The ATM SVC algorithm

When we come to segment a particular patient, several steps are involved in the initialization of data for the algorithm. We choose to represent normal anatomy with a 3D volumetric digital template. The template consists of a 3D volume with each voxel labelled according to the anatomical structure present [4]. Initialization involves the application of feature detection or image enhancement algorithms to construct images that have improved contrasts for the structures of interest (e.g. nonlinear diffusion for noise smoothing [5], local structure enhancement), the execution of an initial alignment

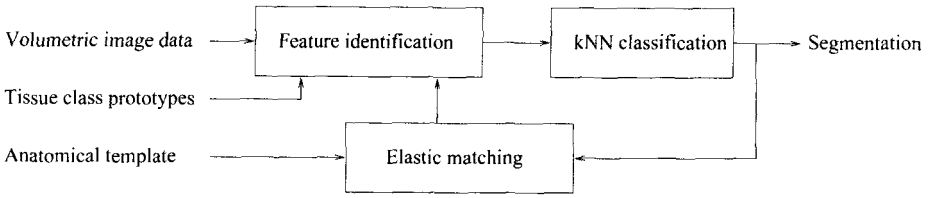


Fig. 1. Schema for Adaptive Template Moderated Spatially Varying Classification. Initialization consists of image acquisition, tissue class prototype selection and linear registration of a template of normal anatomy to the image data. Feature identification is problem dependent and often the image data alone is used. Local filtering strategies for feature enhancement can be motivated by the anatomical template. The anatomical template is converted into a set of features describing anatomical localization with a distance transform. A segmentation based upon these features is done with k-NN classification. The segmentation is then put through a feedback path that is used to refine the segmentation. A fast elastic matching algorithm is used to refine the alignment of the template of normal anatomy to the classified patient data. The anatomical localization is recomputed with the refined atlas, and the process is iterated.

strategy to align the template to the patient scan, and the selection of prototype voxels for tissue classes of interest to allow the construction of a statistical model for the distribution of features for each tissue class.

The initial alignment strategy depends upon whether the anatomy to be aligned is rigid or piecewise rigid, and examples are presented in Section 3. For brain MR, the usual rigid registration techniques are suitable, and we have used volumetric alignment of classified data sets [6]. For the knee joint, we use a piecewise rigid registration by manual alignment of each of the bones.

Spatially Varying Classification The k-Nearest Neighbour (k-NN) classification rule is a technique for nonparametric supervised pattern classification. Efficient techniques for k-NN classification have been developed [7, 8, 9]. Distance is measured with a distance metric appropriate to the problem domain. The main characteristic of the ATM SVC algorithm is to use Euclidean distance in a modified feature space.

We have a template aligned with the data. If this template was precisely aligned and modelled all of the structures present (including pathology) there would be no need for further segmentation. We would just use the model directly. However, the initial alignment of the template captures only global scale, rotation and translation parameters, and local shape differences remain. The relevant local shape differences may require more than one iteration of elastic matching to capture, particularly in the presence of pathology that distorts the patient anatomy significantly away from the normal anatomy of the template.

In order to improve the segmentation, we make use of the approximately aligned template to create a spatially varying classification. The template is used to provide anatomical localization for the classification. We can consider a range of confidence in our anatomical localization, ranging from the regions we have reason to suspect are far away from the anatomical structure, to those regions we suspect are very likely to be the anatomical structure. The nature of the misalignment of the nonlinear registration

makes our confidence in the anatomical localization weakest at the boundary of the model. A potential distance metric is:

$$d^2 = \sum_{a=1}^{M}(v_a - p_a)^2 + \sum_{f=1}^{D}(v_f - p_f)^2$$

where we have added M features of spatial information to the usual D features, and $(v_a - p_a)^2$ represents the difference in anatomical localization of the voxel to be classified and the prototype. Qualitatively, when v and p are from the same anatomical region, v_a and p_a will vary together, leading to a small addition (ideally zero) to the overall distance, and so the distance will be mainly determined by the original features. When v and p are from different anatomical regions, v_a and p_a will vary differently, leading to a large change to the overall distance, causing the distance to be large irrespective of the values of the original features.

We generate anatomical localization features by converting each of the structures of an aligned template into a distance map. We model the uncertainty of anatomical localization, which depends upon the size of the potential error in elastic matching. A straightforward model of error is to use a penalty of 0 where labels for the matched structure is present, and increase the penalty linearly or quadratically with distance from the anatomical template until saturating it. When better error bounds on the anatomical localization are known, they can be directly incorporated by modifying the penalty in the relevant regions.

Nonlinear Registration We achieve fast nonlinear registration with an elastic matching algorithm based upon that of Dengler [10]. The goal of the matcher is, given a source data set $g_1(x)$ and a target data set $g_2(x)$, to find a deformation vector field $u(x)$ such that the function $g_1(x - u(x))$ is as similar to the function $g_2(x)$ as possible.

The basic method of computing u is: for a fixed value of x, consider the problem of finding the value of u that minimizes

$$E_x(u) = \int w(x' - x)(g_2(x') - g_1(x' - u))^2 dx'.$$

The resulting value of u is taken as the value of $u(x)$. Here, w is a window function whose width determines the size of the region used to compute $u(x)$.

We compute a classification, and use the classification to update the template alignment. The updated template is then used to generate a new anatomical localization and used to compute a new classification. For the segmentation problems described in Section 3, the algorithm converges to a satisfactory segmentation around five or fewer iterations of this process.

2.2 Summary

The ATM SVC algorithm generates a sequence of segmentations $s^{(j)}$ given both a (multi-modality) data set g and an anatomical template t. The classification of a particular voxel v from a set of training prototypes P with classes $w_i, i \in 1..C$ for C

classes, is determined with a modified k-NN estimate $P(w_i|v) = \frac{k_i}{k}$,

$$s^{(j+1)}(v) = \max_i P^{(j)}(w_i|v) = \max_i \frac{k_i^{(j)}}{k^{(j)}} = \max_i \frac{\#N_{v,w_i}^{(j)}}{\#N_v^{(j)}} \ .$$

N_v is the subset of prototypes (drawn from the set of training prototypes P), with distance less than or equal to the distance to the kth nearest prototype, d_k. The ATM SVC algorithm differs from the usual k-NN classification by modifying the set of k nearest prototypes, at each iteration, in a manner that depends upon the anatomical template. The usual distance metric is extended to be

$$N_v^{(j)} = \{p \in P : d_k^2 \geq \sum_{f=1}^{D}(v_f - p_f)^2 + \sum_{a=1}^{M}(m(t^{(j)}(v_a)) - m(t^{(j)}(p_a)))^2\} \ ,$$

where N_{v,w_i} is the subset of N_v which consists of prototypes of class w_i, and $\#$ is the cardinality operator for counting the number of elements in a set. D is the dimensionality of the feature space derived from g, M is the number of spatial localization features derived from the anatomical template, $m(t^{(j)}(v_a))$ is the saturated distance transform of structure a of the anatomical template $t^{(j)}$ at voxel v, and

$$t^{(j)}(v) = t^{(j-1)}(v - u^{(j)}(v))$$

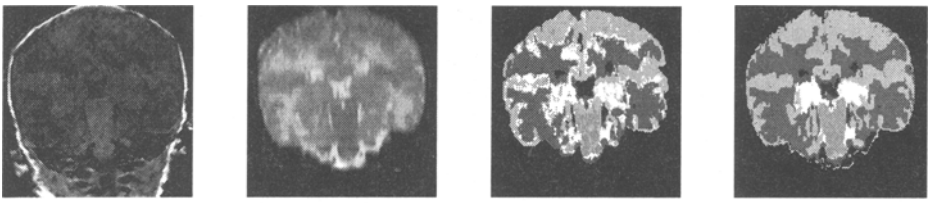
where $u^{(j)}(v) = u$ represents the nonlinear registration of the anatomical template $t^{(j-1)}$ to the data g and is obtained by minimizing the elastic matching constraint.

3 Results

In this section the application of ATM SVC to segmentation problems involving both normal anatomy and pathology is presented. For each of these problems, segmentation with a global (non-spatially varying) classification was also carried out (either k-NN classification [9] or the EM algorithm [11]) and a visual comparison was made. In each case the spatially varying classification generated by ATM SVC better reflects the underlying anatomy than global classification techniques.

Classification of Cortical and Subcortical Grey Matter from MR of Neonates In the developing brain rapid changes in the amount of cortical grey matter occur. These changes can be studied with MR imaging [12]. However, because the brain is still developing, the signal intensity characteristics of different parts of the brain can be quite similar, making it difficult to apply conventional classification techniques.

We applied the ATM SVC algorithm to this problem with the goal of improving the segmentation of cortical grey matter and subcortical grey matter. These have similar intensity ranges, but different spatial locations, and accurate measurement of cortical grey matter is a clinically interesting problem. Figure 2 illustrates the improvement in the segmentation that is achieved with ATM SVC.



(a) Single slice of baby brain SPGR MR

(b) Single slice of baby brain T2 weighted MR

(c) k-NN classification

(d) ATM SVC classification

Fig. 2. MRI of baby brain, k-NN classification and ATM SVC segmentation. Cortical grey matter is shown in light grey, and subcortical grey matter is shown as white. The quantification of cortical grey matter is a clinically important problem, but it is difficult to distinguish from subcortical grey matter because of the similarity of MR intensity. The ATM SVC algorithm allows the spatial distribution of grey matter to be modelled, and as shown, generates an improved segmentation of cortical and subcortical grey matter over that of k-NN classification alone.

Segmentation of Brain MR of Patients with Multiple Sclerosis White matter lesions appear in the brain of patients with multiple sclerosis and evolve over time. During the lifetime of a lesion some parts of the lesion develop signal intensity characteristics that overlap those of normal grey matter on conventional spin echo MR images [13]. A conventional spin echo MR image was segmented using a statistical classification with intensity inhomogeneity correction using the EM segmentation method of Wells et al. [11], and a spatially varying classification of a slice from a brain MR scan of a patient with multiple sclerosis. Comparison of the segmentations indicated ATM SVC improved the segmentation of normal white matter, the lesions and the grey matter over that of statistical classification alone.

Brain Tumour Segmentation A comparison of manual and ATM SVC segmentation of a brain tumour was carried out. An SPGR MRI of a patient was obtained and segmented with an interactive volume editing segmentation routine (requiring about 60 minutes of operator time). Independently, the SPGR MRI was segmented using ATM SVC (requiring about 5 minutes of operator time, for initial alignment of the template and for prototype selection). The results of the segmentations were very similar. On a voxel to voxel comparison the agreement was over 85%. The primary differences were due to over-smoothing of the boundary of the tumour in the manual segmentation.

Segmentation of Knee Cartilage from MRI ATM SVC was compared with manual outlining for the segmentation of knee cartilage from MRI of a patient with a focal cartilage defect. ATM SVC provided a close match of the cartilage segmentation to the cartilage seen in the MR, particularly in the region of the defect [14]. A quantitative assessment was carried out and the use of the ATM SVC was found to greatly reduce the variability of the segmentation (Table 1).

Observer	1	2	3	4	ATM SVC
C.V. (%)	7.2	9.6	6.6	7.0	3.9

Table 1. Coefficient of variation of volume of manual and ATM SVC femoral cartilage segmentation. Four experts segmented a single MR image with a single focal defect, 5 to 10 times on separate occasions over a period of one month. One of the experts also carried out repeated initializations of the automatic segmentation, so the variability induced in the segmentation by differences in initialization could be determined. The volume of the femoral cartilage was recorded, and the coefficient of variation of the volume for each of the experts and the automatic segmentation is shown. The use of the ATM SVC was found to greatly reduce the variability of the segmentation.

4 Discussion and Conclusion

We have developed a new algorithm which is an adaptive template moderated spatially varying statistical classification. The examples presented in Section 3 demonstrate that ATM SVC can achieve better segmentations than either statistical classification or nonlinear registration alone for the illustrated problems. These problems involve both normal anatomy and also certain types of pathology. The ATM SVC algorithm may fail when structures to be segmented have similar characteristics in all features and are also not spatially distinct. When the structures to be segmented have similar characteristics in all features the classification is strongly dependent upon the spatial localization that can be derived from the nonlinear registration (that is the point of the ATM SVC algorithm). The classification is then strongly dependent upon the boundaries identified by elastic matching. If the structures to be segmented have a boundary that cannot be discerned by elastic matching, the segmentation in the region of the boundary can be wrong, up to the size of the error of the spatial localization.

Related work has examined different types of adaptation in the classification problem. The segmentation of tissue classes in the presence of intensity inhomogeneity and variation of intensity over time was the motivation for the development of an adaptive tissue classification algorithm by Wells et al. [11]. This method iteratively adapts a model of intensity inhomogeneity to drive a tissue classification algorithm. This has the advantage of making it possible to classify patient scans without per-patient prototype selection. For the ATM SVC, we do per-patient training and iterate the classification with respect to an adaptive anatomical model. For the examples of Section 3, we have found it unnecessary to explicitly include estimation of intensity inhomogeneity, although it would be straightforward to incorporate.

An alternative modification to the usual classification model is to use a spatially varying a priori probability field. Kamber et al. [15] built a probabilistic spatially varying a priori model which was successful at reducing the number of false positives in a lesion classification problem. However, this algorithm did not adapt the spatially varying model to the particular patient being segmented and consequently was not able to reduce the number of false negative lesion classifications.

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