Automated Feature Selection for the Classification of Meningioma Cell Nuclei

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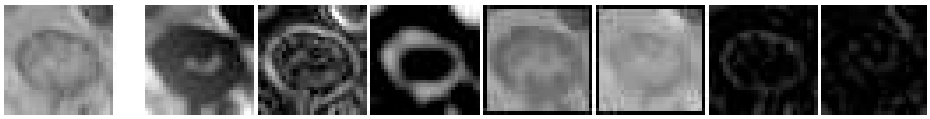
Abstract. A supervised learning method for image classification is presented which is independent of the type of images that will be processed. This is realized by constructing a large base of grey-value and colour based image features. We then rely on a decision tree to choose the features that are most relevant for a given application. We apply and evaluate our system on the classification task of meningioma cells.

1 Introduction

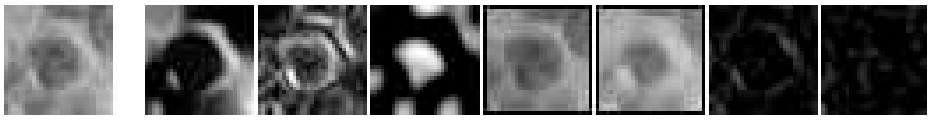
Computerized image analysis has emerged as a powerful tool for objective and reproducible quantification of histological features. DNA ploidy measurement, quantification of immunohistochemical markers, nuclear quantification, texture analysis of chromatin, and morphological diagnostic based on algorithms applied to multiple descriptors of tumor cells are the main application areas of computerized microscopy in pathology. For example, according to the grading system of the World-Health-Organization (WHO) of brain tumors, quantification of histologic features (mitotic index, cellular density, and Ki-67 labelling-index) are essential in the grading of meningiomas. Computerized image analysis may enable an objective, standardized, and time-saving assessment of these prognostic features. However, pixel-based methods at present are still afflicted by segmentation and classification problems. We have recently proposed a classification approach for Ki-67 antibody-labelled cells in meningiomas [1]. We here propose a method for computer-aided classification of tumor cell nuclei in routinely hematoxylin-eosin (HE)-stained slides from resected meningioma samples.

The proposed processing method is a general, supervised learning approach. It relies solely on a given training data set. Thus, we are working directly on the image data, without any need for preprocessing. Most researchers in the field for cell classification take a different approach: They first binarize the image and then use shape or texture features to classify cell types within an image, e.g. [2,3,4,5]. A similar approach to ours relies on a grey-scale image feature to train a Support Vector Machine (SVM) as classification method [6].

We will first describe the constructed feature space and outline the basic mechanisms of CART (Classification and Regression) trees. Then, we will apply and evaluate our method on the task of classifying meningiomas.



(a) Meningioma tumor cell



(b) Normal cell

Fig. 1. The original intensity images and the computed features for two typical representatives of the tumor and nontumor classes. Color channels are not shown, here.

2 Features

The first step in our system consists of computing a set of features from the given input images. For the results presented in this paper, we chose a linear scale-space representation of the image, first and second order edge features, morphological features (minimum and maximum masks, white and black tophat transformations) and the three color channels (red, green and blue). All combined yields a 10-dimensional feature vector in each pixel.

Extension or modification of this particular choice of features is easily done and does not change the setup of our method. In order to smooth out noise effects, we averaged each feature vector over a small local window. Fig. 1 shows two cells from the data along with their feature spaces.

3 A Brief Review of the CART Algorithm

Having constructed such a high dimensional feature space, we apply a machine learning method to extract class information. For this purpose, we have chosen the CART classification tree, see [7] and [8], which also discusses trees in the context of ensemble learning techniques. In brief, the goal in classification trees is to construct a series of decisions, which are arranged in a hierarchical manner, namely a tree.

The CART algorithm has two stages: Tree growing and tree pruning. The growing stage recursively splits the training samples until the GINI diversity index,

$$i(t) = \sum_{i \neq j} p(j|t)p(i|t), \tag{1}$$

is minimized in each terminal node. Here, t is a node and $i, j \in C$ are class labels. $p(i|t)$ is therefore the conditional probability of observing a sample from class i at node t. The rationale behind the GINI index is that the probability of seeing two different classes in one node should be minimal.

Once (1) is minimized for all leaves, the pruning stage begins. CART pruning is a risk minimization approach penalized by tree complexity:

$$\min R(T) + \alpha|\tilde{T}|, \tag{2}$$

where $T = \{t_1, t_2, \ldots\}$ is a tree and R is the misclassification rate. By $|\tilde{T}|$, we denote the number of terminal nodes in T. The problem is that the regularization parameter α is unknown, a priori. But for CART, there exists a procedure of optimizing (2) without being explicitly given α.

4 Application to Cell Classification

We applied the CART classification method to the feature space described in Sec. 2. We tested the method on 6 microscopic color images of surgically resected and HE-stained meningioma samples.

Each of the six images is assigned a ground-truth, as is shown in Fig. 2(b), which depicts the image that was used for training the classifier. The remaining five images were used for testing only. There were up to 400 labelled tumor cells in each of the six images. Not all types of cells were present in all six images with around 50 nontumor locations marked in each image.

5 Results

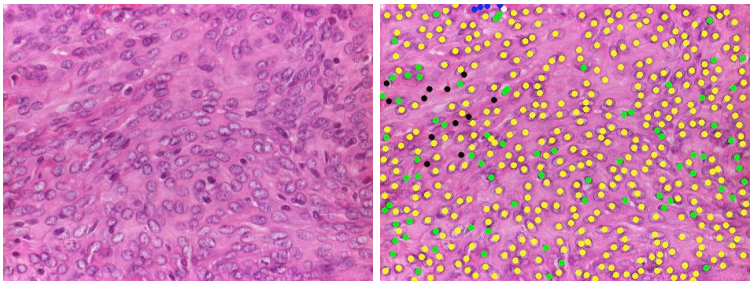
Results obtained by our classification algorithm are expressed as true and false positive rates. These are usually presented in Receiver-Operator Characteristic (ROC) plots such as Fig. 2(d), which is plotted over the posterior class probabilities which are the results of CART, c.f. Sec. 3. In our evaluation, we considered any occurence of labels within one pixel distance as a detection and averaged over all according class posteriors in that area.

We show performance of the tumor class against all other available labelled points combined in Fig. 2(d). The classification performance against all other types of cells in the data is summarized in terms of true and false positive rates at the optimal operating point in the table in Fig. 3.

One of the most frequent arguments for the use of decision trees for classification is that their structure is often comprehensible and interpretable for humans. The quantity of interest is the split dimension that was chosen in each tree node. In our experiments, the tree classifier used mainly edge information and the red color channel.

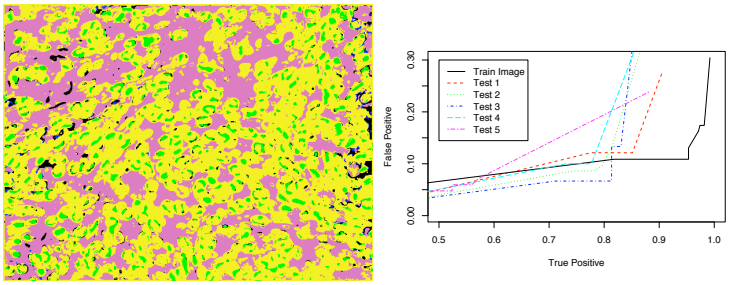
6 Discussion

With detection rates of usually well above 80%, our classifier is capable of localizing meningioma tumor cell locations in HE stained microscopic images. The ROC plots in Fig. 2(d) show good generalization properties of our method, being stable in terms of false positive errors, in particular.



(a) The original image which was used for training

(b) Labelled ground-truth of the training image



(c) CART classified training image

(d) Receiver-Operator Characteristic (ROC) of our classifier on the training image and all five testing images

Fig. 2. Original data and classification results of our classifier. Color-codes of the different classes in these images are as follows: tumor cells (green), normal cells such as fibroblasts (yellow), collagen (black) and erythrocytes (blue).

However, the classified image in Fig. 2(c) indicates that our results are noisy and that the tumor class is overestimated. This is also apparent in the ROC results, which show false positive rates around 10%. We attribute these results to the pixel-wise approach that we took, here.

7 Conclusions

We proposed a method that could be helpful during the examination of histopathological samples. Results from our method are promising and could lead to a system for computer-aided diagnostics. The tree-structure of the CART classifier is also useful for data exploration: The path along which a sample is passed down a tree for classification contains information about which types of features are discriminant characteristics of a certain type of cell.

	normal		endothelial		erythrocyte		collagene		all combined	
	TP	FP	TP	FP	TP	FP	TP	FP	TP	FP
Train	0.95	0.09	0.99	0.00	0.98	0.25	0.98	0.17	0.95	0.11
Test 1	0.85	0.14					0.90	0.00	0.85	0.12
Test 2	0.80	0.11	0.78	0.22	0.81	0.00			0.78	0.09
Test 3	0.81	0.07							0.81	0.07
Test 4	0.78	0.14	0.78	0.00	0.88	0.00			0.77	0.10
Test 5	0.88	0.23	0.88	0.60	0.88	0.13			0.88	0.23

Fig. 3. True and false positive (TP,FP) rates at the optimal operating point of the classifier on all six images of the class tumor vs. all other classes. Column "all combined" matches Fig. 2(d). Empty fields mean that a cell type was not present in the image.

We expect to be able to reduce false detection errors by segmenting individual cells from these images and this is also the track we are following in our current research.

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