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# Applying spatial distribution analysis techniques to classification of 3D medical images

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**Summary**

*Objective:* The objective of this paper is to classify 3D medical images by analyzing spatial distributions to model and characterize the arrangement of the regions of interest (ROIs) in 3D space.
*Methods and material:* Two methods are proposed for facilitating such classification. The first method uses measures of similarity, such as the Mahalanobis distance and the Kullback—Leibler (KL) divergence, to compute the difference between spatial probability distributions of ROIs in an image of a new subject and each of the considered classes represented by historical data (e.g., normal versus disease class). A new subject is predicted to belong to the class corresponding to the most similar dataset. The second method employs the maximum likelihood (ML) principle to predict the class that most likely produced the dataset of the new subject.
*Results:* The proposed methods have been experimentally evaluated on three datasets: synthetic data (mixtures of Gaussian distributions), realistic lesion-deficit data (generated by a simulator conforming to a clinical study), and functional MRI activation data obtained from a study designed to explore neuroanatomical correlates of semantic processing in Alzheimer's disease (AD).

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*Conclusion:* Performed experiments demonstrated that the approaches based on the KL divergence and the ML method provide superior accuracy compared to the Mahalanobis distance. The later technique could still be a method of choice when the distributions differ significantly, since it is faster and less complex. The obtained classification accuracy with errors smaller than 1% supports that useful diagnosis assistance could be achieved assuming sufficiently informative historic data and sufficient information on the new subject.


## 1. Introduction

Current advances in medical image acquisition techniques have made available enormous amounts of remarkable high-resolution three-dimensional (3D) image data. In particular, the wide availability of non-invasive methods for capturing structural (e.g., magnetic resonance imaging (MRI), computed tomography (CT)) and functional/physiological (e.g., positron emission tomography (PET), functional MRI (fMRI)) information that complement clinical assessment, have opened new horizons towards a deeper understanding of the human body and its functionality. In addition to the continuous development of improved imaging techniques, greater computer capabilities and improvements in analysis techniques are leading to the creation of large repositories of medical image data. The work presented in this paper addresses problems related to the classification of 3D medical images.

Although significant research has been done in content-based image retrieval and classification for general types of images (see [1,2] for comparative surveys), progress in this type of analysis for medical images has been very slow. Global signatures [3–5] that are usually employed in the content-based image retrieval and classification do not work well in the medical imaging domain where the regions of interest (ROIs) occupy a small portion of the image. In this case, usually a distinction between important and unimportant features or among multiple objects in an image has to be made. We propose to overcome these problems by performing analysis focusing on the ROIs and their spatial distribution. Characterization of an image based only on regions that are of interest to an expert seems to be more meaningful in applications dealing with medical decision making [6–8]. The 3D images or volumes we consider here consist of *region data* that can be defined as sets of (often connected) voxels (volume elements) in three-dimensional space that form 3D structures (or objects). We actually focus on 3D binary volumes, where information is provided only with respect to whether a particular voxel is part of a certain ROI or not (voxel values $\in \{0, 1\}$). This assumption is often made in medical image analysis applications, since it simplifies the processing without being very restrictive. Examples of binary ROIs in medical images are lesions, tumors, areas of brain activity, etc.

In this study, we are given a set of 3D medical image data and an assignment of these images to a number of classes based on certain non-spatial attributes (e.g., normal versus disease states). The objective is to derive a classification scheme that will correctly assign a new 3D image to a particular class (e.g., normal or disease) according to spatial information only. A specific example of this task from the brain imaging domain is the following: Given an MR image of the brain of a new subject that contains lesions, determine whether it belongs to a group of subjects who did or did not develop a particular disorder (e.g., attention-deficit hyperactivity disorder (ADHD) after closed head injury).

We suggest two approaches for automatic classification of ROIs and quantitative measurement of their levels of similarity. Unlike existing techniques where ROIs are considered individually (see Section 2 for an overview), we propose methods that classify ROIs based on their global spatial arrangement taking into account the co-existence of multiple ROIs. The methods presented here are based on measures of similarity between 3D spatial probability distributions. In particular, we suggest applying distance based techniques and maximum likelihood (ML) criteria to facilitate the classification of 3D ROI distributions. One of the main advantages of these approaches is that they can be applied directly on the 3D space preserving the spatial locality of the ROIs. Hence, we avoid the loss of information and complexity encountered in approaches originally developed for 2D slices (applied to pixels instead of voxels) that are repeated for each slice of a 3D volume.

We perform an evaluation of the proposed classification framework based on synthetic and realistic datasets. The realistic datasets conform to MRI studies and have been used in lesion-deficit analyses. In addition, we include experiments on clinical data to demonstrate the applicability of the proposed methodology in real-world problems. The clinical data are obtained from a study [9] on Alzheimer's disease (AD), consisting of fMRI contrast