PARCELLATION OF BRAIN IMAGES WITH ANATOMICAL AND FUNCTIONAL CONSTRAINTS FOR FMRI DATA ANALYSIS

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ABSTRACT

In this paper we propose a methodology for brain parcellation with anatomical and functional constraints dedicated to fMRI data analysis. The aim is to provide a representation of fMRI data at any intermediate dimensionality between voxel and region of interest. In order to fill in the gap between these two approaches we developed an automatic parcellation of the 3D cortex with an adjustable resolution. The algorithm relies on an adaptation of the K-means clustering in a non convex domain with geodesic distances. Fine anatomical or functional constraints can be embedded through the use of weighted geodesic distances. The applications of such a method are principally connectivity studies, multivariate analyses and fusion with other modalities.

1. INTRODUCTION

We introduce this work by first giving some rationales for our application domains namely the functional brain imaging and cognitive neuroscience. We then briefly give a first idea on the image analysis tools used in the proposed method.

Functional Magnetic Resonance Imaging (fMRI) is a recent technique that allows the study of the relation between function and anatomy in the human brain. fMRI measures in vivo a physiological parameter related to the concentration of deoxyhemoglobin (Blood Oxygen Level Dependent - BOLD contrast) with a spatial resolution of a few millimeters and a temporal resolution of a few seconds, while a subject is performing a task or presented with stimuli. Series of functional images are typically acquired for 5-15 minutes leading to series of several hundreds of 3D scans. During the same MR session, a T_1-weighted image with high resolution (around 1 mm) informing on the anatomy of the brain is also acquired and, if necessary, coregistered with the functional images.

Two main approaches have been designed in the past for the analysis of these data. The most common approach is to treat each (functional) voxel separately and test for correlation between time series at each and every voxel with the predicted response given by the experimental paradigm and localize the "activated" voxels on the anatomical image [1]. The second approach consists in defining regions of interest using either functional or anatomical a priori information and test for the activation signal within these regions [2].

The former approach is limited in several ways. First, the dimensionality of the data is very high while the resolution needed to understand the brain function may not require such a number of locations. In other words, it might be enough in some situations to have a coarser resolution when analyzing cognitive processes. This coarser resolution is often reached through spatial filtering. Second, the resolution of the voxel may not be adapted when functional images have to be put in correspondence with other modalities used in the neuroimaging field such as EEG (typically, the number of dipoles that can be reconstructed from the signal measured on the scalp is limited) [3]. Third, when investigating the relations between brain regions (connectivity), one would like to be able to construct a region per region correlation matrix, for which the voxel resolution is much too high [4, 5]. Lastly, since there are many more voxels than measures in the time domain, the use of some multivariate techniques that require the inversion of a (here rank deficient) matrix is precluded [6, 7].

On the other hand, regions-of-interest-based techniques are in practice difficult to implement for two main reasons. First they are difficult to define a priori, because the automatic labeling of many sulci is still an open problem. Second, tools for defining 3D volumes on the cortex are difficult to use (a manual parcellation can take many hours or days) and require an important expertise. Generally, only a limited number of large regions are delineated (for instance regions corresponding to lobes are defined) and therefore the relation between anatomy and function is addressed with a very rough resolution.

We therefore propose a method to automatically parcel the brain volume at any specified resolution. This parcellation can take into account not only anatomical information such as the position of sulci but also any other information that could influence the definitions of the parcels (or

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region of interest). For instance, parcels position may be influenced by functional information.

The method relies on the definition of geodesic distances over the cortical ribbon embedded in a spatial K-means clustering algorithm. For instance, 3D discrete geodesic Voronoï diagrams are used to define such parcels. Anatomo-functional constraints can be included via weighted geodesic distances in order to favor or penalize specific areas.

2. A GENERAL DESCRIPTION OF THE PARCELLATION METHOD

In this section, we describe the desired features of the brain parcellation in the context we just settled in the introduction.

Firstly, the parcellation has to be defined at an anatomical resolution to tackle the rough spatial resolution of fMRI and to be able to take into account fine anatomical details such as sulci. The parcels are then defined as connected clusters of anatomical voxels.

A second desired feature is to obtain an "homogeneous" parcellation where parcels regularly pave the volume of interest. This means that parcels should have similar volumes, but should also be somehow similarly compact.

Lastly, the parcellation must be generic enough to allow the inclusion of additional constraints. For instance, the crossing of a sulcus should be penalized in order to obtain parcels well localized on each side. Similarly one may want to impose a parcel centered on a specific locus such as a local maximum of a t-map resulting from a previous functional analysis or provided by the literature.

To meet these goals, we propose a fully automatic method where the number of parcels is provided by the user (depending on the particular application for which the parcellation is dedicated). The main steps of the algorithm are:

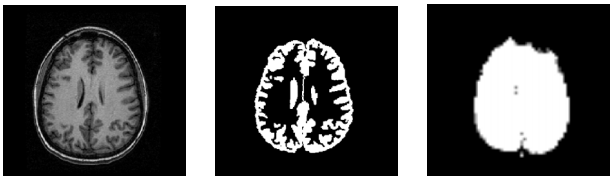
1. Define the global volume of interest (e.g. the gray matter), and the required parcellation resolution (input of the user).
2. Find a first solution yielding "homogeneous" parcels within the (non-convex) volume of interest.
3. Improve this first parcellation by adding the constraints coming from anatomy or function.

3. ALGORITHMS

We provide here a more detailed description of each step of the algorithm presented in the previous section.

3.1. Definition of the volume of interest

The first step of our algorithm is to define what is the domain to parcel, i.e. the global volume of interest. For instance, we want to confine in this article the functional data analysis to the cortical ribbon. Such an anatomical representation of the cortex can be obtained from segmented T_1-weighted images [8]. To overcome the artifacts and distortions problems in the fMRI sequence, this segmentation of the cortex is combined (logical `and`) with a functional mask of the whole brain performed in the averaged fMRI image (thresholding of a Gaussian fit of the histogram). The resulting volume of interest is a set of voxels at the anatomical resolution corresponding to the part of the cortex that can be analyzed in functional images.



(a) (b) (c)

Fig. 1. (a) Axial T_1-weighted MRI and its cortex segmentation (b). (c) Brain mask of functional images.

3.2. Parcellation of a convex domain: K-means

To define "homogeneous" parcels, one could rely on a volume criterion. However, this would not prevent the algorithm from finding very elongated or complex cells, and there can be multiple solutions (e.g. two cells in a square). A more interesting idea is to try to minimize the inertia of each cell, which introduces an idea of compactness combined with the volume (the disc minimizes the inertia of a cell at a fixed volume). This corresponds to the minimization of the intra-class variance in the classification context, efficiently solved using the K-means algorithm [9].

In our case, the data $\{x_i\}$ to classify are the 3D coordinates of the voxels defining the volume of interest and the cells are defined by their positions $\bar{x}_j$. The problem is then to find simultaneously a partition of the voxels $\{x_i\}$ into k classes C_j and the cell positions $\bar{x}_j$ minimizing the intra-class variance:

$$I_{intra} = \sum_{j=1}^{k} \sum_{i \in C_j} d^2 \left(x_i, \overline{x}_j\right)$$

In this context, the resolution of our parcellation is naturally parameterized by the number k of classes used.

If the volume of interest is convex, the distance d is the standard Euclidean distance, and the criterion is solved using an alternated minimization of I_{intra} over:

1. The partition of the data (given cell positions): each voxel x_i is assigned to the class C_j that minimizes the distance to its position $\bar{x}_j$. This is usually realized through a Voronoï diagram.
2. The cell positions (given a data partition): the position $\bar{x}_j$ minimizing the variance of the x_i's assigned to this class is simply their barycenter.

Fig. 2. Example of a 2D geodesic Voronoï diagram with 50 seeds (black dots). Left: random initialization. Right: after convergence of the K-means algorithm.

The K-means algorithm simply consists in an iterated loop of these two estimations until convergence, i.e. when assignments are the same at two consecutive steps. To initialize the algorithm, we simply randomly select k distinct voxels in the volume of interest as the initial cell positions. Notice that the number of classes k, which is usually very difficult to optimize, is in our case a user input defining the resolution of the parcellation.

In the general Euclidean case, minimizing the intra-class variance turns out to maximizing the inter-class variance $I_{inter} = \sum_{j,l=1}^{k} d^2(\overline{x}_j, \overline{x}_l)$ because the total variance is constant (thanks to Huygens theorem). Thus, the optimized criterion can be interpreted as providing a low within-class variance (compactness) and a high distance between class centers (isolation), which were desired features.

3.3. A modified K-means for the geodesic distance

In our case, the volume of interest is not convex, and the choice of the distance d is a crucial issue. In order to be more compliant with the highly convoluted structure of the cortex, the geodesic 3D distance [10] (the shortest path entirely within the volume of interest) is more suitable than the Euclidean distance. Indeed two points on opposite sides of a sulcus are close together in Euclidean terms but may be geodesically far apart.

The main difference with the Euclidean case is that we do not have any more the strict equivalence with the maximization of the inter-class variance. However, the convergence is still ensured for a compact and connected domain since we are minimizing a positive function.

The algorithm is thus modified as follows: the initial k seeds are distributed to the different connected components (according to their volume ratio). Then, the two steps of the K-means algorithm become:

Step 1 (partition): the class assignment is now realized using a 3D discrete Voronoï diagram with geodesic distances. A fast implementation using region growing and hierarchical queues is described in [11]. A more accurate implementation could be realized using Fast Marching [12].

Step 2 (cell positions): there is no closed-form solution for the "geodesic barycenter", but we may compute it by a gradient descent on the intra-class variance. In practice, most of the cells are still convex (even within a highly non convex domain) and the standard barycenter is a good approximation. In our implementation, we use the Euclidean barycenter as far as it stays within the cell, and a gradient descent otherwise.

3.4. Incorporating constraints

After a first unconstrained parcellation (in order to obtain an homogeneous repartition of the cells), additional constraints can be enforced through the use of weighted geodesic distances. By defining the cost required to move to each voxel (the local metric), we may penalize or favor specific connections between neighboring voxels. Such an information can be embedded in a weight map (a 3D image) for which each value is a multiplicative factor that must be applied over classical geodesic distances during the region growing process (step 1 of the K-means algorithm).

One interesting anatomical constraint is to penalize the crossing of sulci. To do so, sulci are first automatically extracted from a T_1-weighted MRI [8] then labeled by a neural network as explained in [13]. Sulci of interest are selected and the resulting binary map is smoothed to allow a small uncertainty in their position. This map is then used to weight geodesic distances in a K-means algorithm initialized by an unconstrained parcellation.

Another constraint is to impose a parcel centered on a specific locus such as a local maximum of a t-map resulting from a previous functional analysis or provided by the literature. This can be easily realized by constraining the position of the current cell containing this position to the desired value, and adapting neighboring cell positions accordingly.

4. RESULTS

The theoretical convergence is owed to the minimization of the same distance in the two steps of the K-means algorithm. In our case, the geodesic distances and the barycenters are approximated via discrete transformations so that the convergence is not guaranteed. In practice, we observed that the algorithm always converges in a reasonably low number of iterations (a few dozen). Thus, thanks to the efficient implementation of geodesic Voronoï diagram, we obtain very

low computation times (typically a few minutes). This is indeed an important issue for our application domains.

The well-known sensitivity of the K-means clustering to the initial conditions leads in our case to different but always satisfying parcellations: Fig. 3 presents the results of two parcellations with anatomical constraints and 50 to 500 seeds. One can see that the cells are well distributed and correctly respect the geometric sulcal constraints depending on the required resolution.

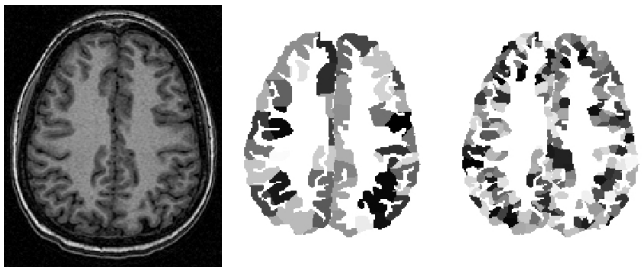


Fig. 3. Axial slice of a 3D parcellation of the cortex: original T_1 MR slice (left) and parcellation with 50 (middle) and 500 parcels per hemisphere (right).

5. DISCUSSION

This work is a first important step toward a generic and automated parcellation of brain images for fMRI data analysis at a user defined resolution, between voxel and region of interest. It currently incorporates anatomical constraints such as the penalization of sulci crossings and anatomo-functional constraints such as centering a cell on a predefined location.

The next step will focus on how to interpolate the functional signal on each cell. The first idea is indeed to average the time courses of all functional voxels of each cell, oversampled at the anatomical resolution. This is based on the hypothesis of a spatially consistent signal within the parcel. In this context, one important improvement could be the use of more functional constraints for the definition of the parcels via the definition of a distance depending on the temporal correlation between functional signals.

Although this approach was not designed in the first place with this goal in mind, it will be interesting to evaluate it for the detection of fMRI activations in order to exhibit the effect of the anatomical constraints.

The adjustable representation of fMRI data provided by a parcellation allows for the application of numerous techniques that were difficult or impossible to implement on the whole brain, due to the large dimensionality of the data. The main research tracks opened by this work are of course connectivity studies, multivariate analyses (e.g. CVA) and fusion with other modalities (such as MEG/EEG, diffusion MRI), which will be investigated.

Another very interesting future work will deal with the intersubject problem and how to define homologous cells across subjects.

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