K-parcel: Spatially-Continous Brain Parcellation

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ABSTRACT

Functional parcellation purposes to divide a spatial activity map, such as brain images, into homogeneous and functionally coherent regions, which serve with fundamental importance as applications to analysis and interpretation.

Previous practice on this task choose to do clustering in the feature space while ignoring the spatial proximity, and consider features by calculating simple statistical measure such as correlation. We argue that those widely adopted clustering methods often results in not spatially continous and unsatisfactory parcellations in inevitable noisy settings in brain images, questioning the reliability of parcellation.

We propose K-parcel, a simple clustering algorithm which could be viewed as a constrained K-means that guarantee to obtain spatially-connected and highly coherent functional parcellations on a spatial activity map. K-parcel is able to group voxels with coherent feature patterns and robust to noisy signals which leads to the aforementioned problems in practice.

The proposed method is compared with several alternative approaches through simulation studies, and is applied to real brain images. Experimental results demonstrate the superiority and robustness of K-parcel algorithm that it could find spatially-connected and homogeneous parcellation even in high noisy settings.

KEYWORDS

brain image, clustering, brain parcellation

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1 INTRODUCTION

Analysis and interpretation of complex spatial-temporal system often requires to divide the whole system into functional parcellations a priori. Take an instance in neuroimaging-based brain research, analysis are rarely done on voxel-level descriptions, but often at the level of many voxels constituting a coherently functioning brain region. The brain could be viewed a complex network with macroscopic organization at the level of functional areas and subcortical nuclei, but the number, shapes, locations of these regions in humans are largely unknown [Power et al. 2011]. Functional brain parcellations aim at dividing the brain's spatial map into partitions of non-overlapping regions within which voxels shows coherent temporal activities, upon which further advanced analyses are performed by neuroscientists.

Anatomical brain parcellation often fails to capture the functional coherence and thus comes the rise of data-driven parcellation methods. Traditonally, neuroscientists use predefined ontology of brain, such as current anatomical knowledge, results from previous experiments or brain atlases, to determine a functional ROI (region of interest) for brain-connectivity and high-level cognitive task analysis. This approach has been very successful but do not adapt in every flexible experimet settings, because these predefined parcellation may not fit the current experiment data well [Bohland et al. 2009] and thus might fail to fully capture the intrinsic coherent functionality. Brain parcellations are therefore often derived from specific clustering algorithms.

Clusteing algorithms are widely used for data-driven parcellation in fMRI research community only recently, but due to the inherent noisy nature of fMRI data, existing methods often expose very severe problems. As in [Thirion et al. 2014] and a more recent systematic comparison [Arslan et al. 2018], the dominant clustering algorithms are comprehensively compared and the authors point out that those methods generally do not give accurate clustering result, fail to reproduce parcellation among multi-subjects, producepoor partitions of unsatisfactory inner-homogeneity, and are also not very robust in the low Signal-To-Noise ratio (SNR) given the current technologies, and thus often require several data processing technique such as smoothing.

We argue that key point of a desirable clustering algorithm for functional parcellation is that it must take into consideration coherent temporal patterns and spatial proximity at the same time. Most methods consider the temporal information by an explicit usage of calculating Pearson correlation as well as an extra spatial regularization term. The parcels could be of arbitray shape, making this task even harder.

We propose K-parcel, a simple clustering algorithm which could be viewed as a constrained K-means that guarantee to obtain spatially-connected and highly coherent functional parcellations on a spatial activity map. K-parcel finds parcels that preserve spatial continuity with voxels having coherent feature patterns and the shape of parcels could be arbitray. K-parcel is also robust to noisy signals which leads to the aforementioned problems in practice.

The proposed method is compared with several alternative approaches, including K-means, spectral clustering, DBSCAN, Ward's algorithm, through simulation studies. K-parcel is also applied to

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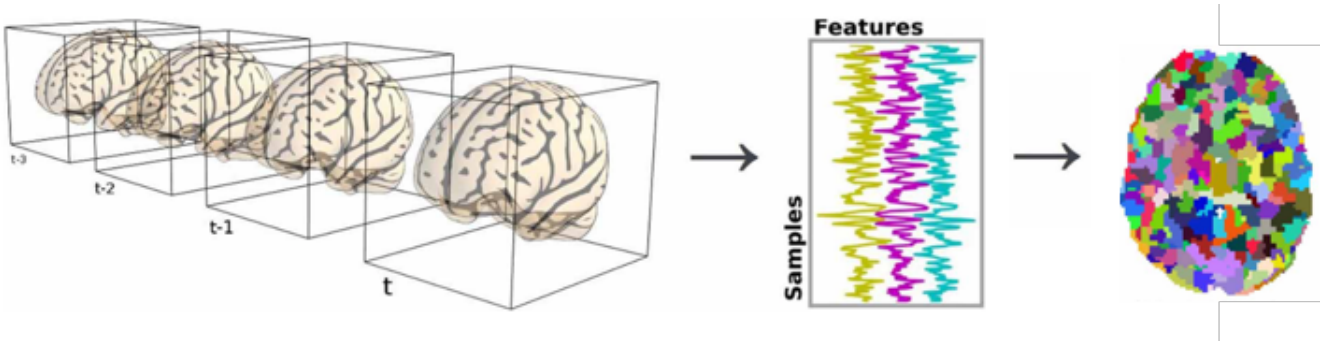


Figure 1: *What is brain parcellation* We take a sequence of brain images as input and preserve the temporal order, the signals for each voxel are preprocessed and then feeded into the clustering algorithm, the output is a collection of partitions (brain regions) that show homogeneous and coherent activities within the same parcel.

real brain images. Experimental results demonstrate the superiority and robustness of K-parcel algorithm that it could find spatially-connected and homogeneous parcellation even in high noisy settings.

2 NOTATION

In a subject-level functional parcellation setting, we start with a given set of functional images that represent e.g., different timestamps for one subject. we denote n to be the number of functional images acquired from ths subject. these images are typically the results of first-level analysis (standardized effects) and are sampled on a grid of Q voxels. starting from a fmri volumes $y = y_1, \ldots, y_q \in r_{n\dot{q}}$ that consist of Q voxels, we seek to cluster these voxels so as to produce a partition of y.

we denote the spatial cordinate of y_i as x_i, which would be a 2-d or 3-d coordinate.

3 RELATED WORK

3.1 Clustering for Brain Functional Parcellation

Although the problem of functional parcellation has been studied more than a century in the field of neuroscience, finding parcellation though a data-driven clustering approach has only begun recently. Instead of using anatomy knowledge, this clustering approach has been proved to give more useful and parcellation across a wide range of studies.

Typically, functional connectivity are estimated from rest-state functional MRI (rs-fMRI) to provide meaningful subdivisions of the brain into homogeneous and coherent regions that are specialised in a certain function. Upon this goal, various methods has been proposed but basic clustering methods such as K-means and Ward's algorithm are still the dominant clustering method due to its robust performance.

3.2 Brief introduction to clustering methods

Each clustering algorithm comes with advantages and limitations, and thus inevitably bias the parcellations in different aspects, including the shape, number, size, and spatial contiguity of the parcels [Eickhoff et al. 2015].

We briefly review some representative clustering methods widely used for brain parcellation.

k-means. K-means is arguably the most used clustering technique for vector data. It consists of an alternate optimization of (1) the assignment $u_{\mathrm{k-means}}$ of samples to cluster :

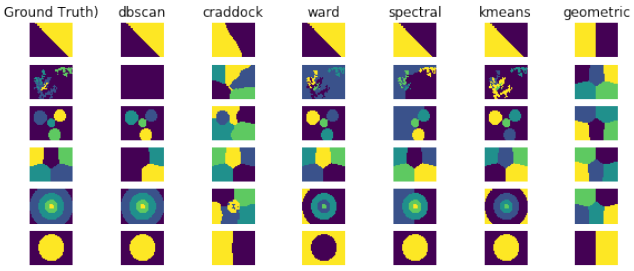
$$\forall j \in [1, \ldots, Q], u_{\mathrm{k-means}}(j) = \underset{c \in [1,\ldots,K]}{argmin} ||Y_c - y_j||$$

and (2) the estimation of the cluster centroids.

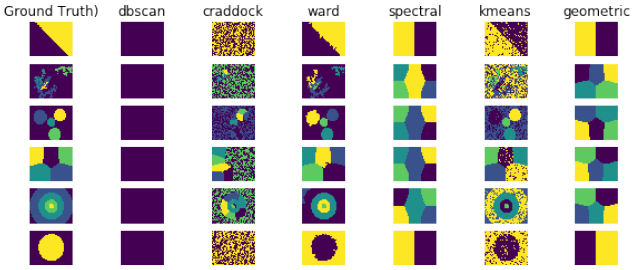
$$Y_c = \frac{1}{|c|} \sum_{u_{\mathrm{k-means}}(j)=c} y_j$$

It explicitly minimizes the inertia, i.e., the sum of squared differences between the samples and their representative cluster centroid. A widely-adopted approach [Thirion et al. 2014] is to use an approximation for the sake of efficiency: the whole set of feature data used in clustering reduced by PCA to $m = 100$ components prior to clustering, capturing about 50% of the variance. It is important to note that k-means clustering of fMRI data are used without explicitly considering their spatial structure, although spatial smoothing prior to clustering can indirectly provide spatial regularization.

It is also possible to add spatial coordinated x_j into the feature so that x_j and y_j is concatenated with custominzed weight to enforce spatial continousity along with functional features'similarity. However, such approach is still constrained to find spherical-shape parcels which is not a desirable property.



(a) No noise



(b) $\frac{A}{\sigma} = 1$ which is a mild condition in fMRI

Figure 2: *On a Synthetic dataset* When there is no noise in the synthetic dataset, i.e., σ are all set to zero, all methods performs just well.
When given a noise level of 1 defined as $\frac{A}{\sigma}$, This SNR is a widely used amplitude measurement to the standard deviation of the noise, a defination of SNR in fMRI as in [Welvaert and Rosseel 2013] varies from 0.5 to 1.8 in real fMRI data, as reported in a more detailed experiment, at average 0.48 (from 0.01 to 95.73).
As shown in the figure, spectral clustering methods start to fail, normalsized cut with correlation (Craddock's method) [Craddock et al. 2011] are giving very unstable parcellation and spectral clustering [Thirion et al. 2014] are giving very conservative results. On the other hand, K-means are giving also very unstable result. Wards seems to be the most robust algorithm.

Spectral clustering. We introduce two spectral clustering methods [Craddock et al. 2011; Thirion et al. 2014] for brain parcellation using different distance metrics.

Spectral clustering consists in performing k-means clustering on a representation of the data that preserves the spatial structure yet represents the functional features'similarity. This representation is typically obtained by using the first eigenvectors of the Laplacian matrix of the graph that encodes the spatial relationships weighted by the functional features similarity between adjacent locations. In [Thirion et al. 2014], for all voxel pairs $(i, j) \in [1, \ldots, Q]$, Let

$$W_{ij} = \exp(-\frac{||y_i - y_j||^2}{2\sigma^2})$$

if i and j are neighbours where $\sigma = mean_{i,j}\,||y_i - y_j||^2$ where the averaging is performed over all pairs of adjacent voxels. σ^2 is thus the average squared distance between the data across neighboring voxels. We use $W_{ij} = 0$ if i and j are not neighbours. In [Craddock et al. 2011], w_ij is measured as the pearson correlation.

W is the adjcency matrix weighted by the functional distance between voxels. We denote Σ_W the diagonal matrix that contains the sum of the rows of W. Then, let $\{\xi_1, \xi_2, \ldots, \xi_m\}$ denotes the first m solutions of $W\xi = \lambda\Sigma_W\xi$, the spectral clustering is defined as $u_{spectral} = k - means(\{\xi_1, \xi_2, \ldots, \xi_m\})$

We will consistently denote the first spectral clustering [Thirion et al. 2014] using the first normalsize squared distance as 'spectral-clustering' and the second spectral clustering [Craddock et al. 2011] using pearson correlation as 'Craddock' or normalsize cut with correlation.

other methods. We also use DBSCAN, Ward's hierarchical clustering and a baseline called geometric which perform k-means clustering only on the spatial coordinates x_j as for comparison.

3.3 Performance of Clustering Algorithm

Consistent results have been reported in comprehensive systematic comparisions in [Arslan et al. 2018; Eickhoff et al. 2015; Thirion et al. 2014] that k-means generally provides the most robust and best performing parcellation with high-homogeneity within parcels, but suffers from low reproducibility among multiple experiments from, for example rs-fMRI from different subjects, due to the fact that it does not consider hard spatial constraints. On the other hand, spectral techniques, which are usually dominated by spatial constraints, capture stable features regarding the geometry of the cortical mesh (Thirion et al., 2014). This appears to confer a strong advantage for reproducibility, but also leads to an inaccurate alignment with the brain's underlying functional organisation. Hierarchical clustering such as Ward's algorithm often yields a more balanced performance in-between: it offers the advantage of generating spatially contiguous parcels, which can contribute to yielding more reproducible parcellations, while still capturing the functional features with high fidelity.

It is also worth mentioning that, anatomical parcellations yield the poorest performance in terms of parcellation quality. However, they allow a more intuitive neuro-biological interpretation which can make network analysis more insightful.

More recently proposed algorithms [Arslan and Rueckert 2015; Baldassano et al. 2015; Gordon et al. 2016; Power et al. 2011] are not giving much improvement and give generally poor performance in various metrics compared with aforementioned methods like k-means and ward's algorithm.

The widely-adapted K-means algorithm still outperforms all other methods in terms of both the homogeneity and Silhouette analysis, while give extremely poor reproducible results among different subjects and poorest overlaping agreement of parcellations with the Brodmann cytoarchitectonic areas.

As shown in results Figure 2 in a synthetic dataset , most methods perform quite well when there is no noise, while in noisy conditions most of these methods (fine-tuned with the right parcel number and other hyperparameters for each method) do not find spatial-continous parcels anymore. Details about the synthetic is introduced Section 5.1.

4 METHOD

4.1 Heuristic and overview of K-parcel algorithm

K-means outperforms other clustering methods for brain parcellation in many aspects but do not guarantee to find spatially-continous parcellations. We intend to extend it into a constrained iterative clustering algorithm that preserves the spatial continuity.

We use graph-edge to define space adjcency, for distance of functional feature we use squared eucliean distance to be the distance function d, although theoretically we could also use other distance measures such as pearson correlation.

The overall clustering would take a region growing approach. We first initialize the mean vector Y_c for $c \in [1, \ldots, K]$ and its spatial location as X_c. Then we consider the neighbours around X_c and assign the neighbour with least distance compared with Y_c into parcel c. This procedure is iterated till all voxels are assigned into parcels.

The method is formulated as a iterative algorithm.

Require: brain image data Q voxels: its spatial coordinates x and its functional feature y and the spatial adjcency map M. Number of parcels wished to find K

$f \leftarrow 0$ // *failure count*
initialize Y_c for $c \in [1, \ldots, K]$ with K-means++
find $X_c = x_j$ that $j = argmin_i\, d(i, Y_c)$ for $c \in [1, \ldots, K]$
while parcels Y_c not converge or maximum iteration is not achieved **do**
  $\mathcal{S} \leftarrow \emptyset$ // *processed voxels*
  initialize K priority queue P_c for $c \in [1, \ldots, K]$
  add neighbours of X_c into P_c with priority computed by distance function d to Y_c
  while $\mathcal{S}$ do not cover all Q **do**
    find $c^* = \mathrm{K} - parcel(j) = argmin_c\, min_j(d(j, Y_c))$
    pop j out of P_{c^*} and assign $u_{\mathrm{K}-parcel}(j) = c^*$
    add j's neighbour into P_{c^*} with priority $d(y_j, Y_{c^*})$
  end while
end while
return $u_{\mathrm{K}-parcel}(j)$ for each $j \in Q$

Algorithm 1: *K-parcel Algorithm* This is the pseudo-code for K-parcel Algorithm to find spatially continous parcellations.

Initialization. Initialization plays an important role in k-means algorithm, so does it in our K-parcel algorithm. In fact, good initialization will not only prevent it converge in a bad local minima, but also makes the clustering converge faster. We use K-means++ to initialize to find K initial points, and take its functional feature as Y_c, then we take the corresponding spatial location X_c.

Iterative Procedure. For each parcel c with a spatial location X_c and its functional feature Y_c, we initialize a priority queue P_c. For initialization, we add every neighbour j of X_c into P_c where the priority is computed as $d(j, Y_c)$.

For each iterative, we find the voxel that has the highest priority (the least distance) and assign it to a pacel c^* anywhere

$$c^* = u_{\mathrm{K}-parcel}(j) = \underset{c}{argmin}\, \underset{i}{min}(d(i, Y_c))$$

When j is assign to parcel c, neighbours of j that currenly have not been assigned into any parcels are added into the priority queue P_c where the priority is also computed using the distance function d.

This procedure is iterated till all voxels are assigned to a parcel.

After all voxels have been assigned into one of the parcels, we re-estimate the parameters Y_c and X_c of this parcel. Y_c is re-estimated as the mean value of all voxels in the same parcel c that

$$Y_c = \frac{1}{|c|} \sum_{u_{k-means}(j)=c} y_j$$

and we find X_c to be the spatial location of a voxel j that has the least distance with Y_c that

$$j = \underset{i}{argmin}\, d(i, Y_c)$$

.

We then re-initialize the algorithm with X_c and Y_c and repeat the above mentioned procedure.

Termination Criteria. The iterative procedure is terminated when one of these two criterias are met: when the algorithm exceeds the maximum iteration number or the parcels converge.

5 EXPERIMENTS

Comparing methods. We compared our new proposed K-parcel methods (denote as 'new' in figures) with several alternative clustering methods for brain parcellation.

- k-means (tested in [Thirion et al. 2014]). Combinations of different extension of K-means are all tested on whether PCA is used and whether distance is computed in frequency domain obtained by fast fourier transformation
- wards algorithm (tested in [Thirion et al. 2014])
- DBSCAN.
- spectral clustering as in [Thirion et al. 2014]

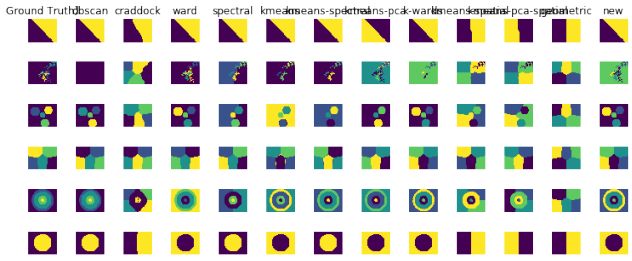


Figure 3: *parcellation on a Synthetic dataset with mild-condition noise* As shown in this figure, even in this mildly noisy synthetic dataset, k-means (see the 6-th column) already can not find spatially continous parcels. And both spectral clustering methods [Craddock et al. 2011; Thirion et al. 2014] (see the 5-th and 3-rd column) can not find satisfactory parcellation even the ground truth parcel number is known.

- N-cut:Spectural Clustering with constrainted normalsized cuts with pearson correlation [Craddock et al. 2011] (also tested in [Arslan et al. 2018; Thirion et al. 2014])
- geometric clustering (do not consider functional information) as baseline.

5.1 Synthetic Dataset

Synthetic Data: Periodic Signal Mixed-effect model. We construct a synthetic dataset that takes noise into account.

We models the signals in a specific parcel P_k where $k = 1, 2, \ldots, K$ using a periodic signal. Let p_k be the number of voxels in the k-th parcel P_k, let y be a p-dimensional vector that denotes the scalar signal in this parcel, we model it through the following periodic signal mixed-effect model.

$$y_k^t = (\mu_k + A_k sin(\frac{2\pi}{T}(\phi + t))) + \sigma_k$$

where y_k^t is the signal of parcel P_k at time t. μ, A, T and ϕ are the mean, amplitude, period length and the phase shift of this parcel's periodic signal. σ_k is the temporal parcel noise.

As for noise in spatial space, we randomly perturb 5% of voxels in one parcel to be of random value such that

$$y_k^t \sim N(0, 1)$$

.

We tested all these methods mentioned above in 5 mild noisy synthetic dataset and visualize the parcellation in Figure 3.

Quantitative metrics. Since in synthetic dataset we have the ground truth parcellation, we could compare the result parcellation using clustering methods with the ground truth. We use normalsize mutual information (or known as adjusted mutual information in [Thirion et al. 2014]) to measure the mutual information of two discrete assignment of voxels to parcels, which is corrected for chance: two statistically independent assignments should have an AMI value of 0, while two identical assignments should have an AMI value of 1. Normalsized mutual information (NMI) is upper bounded by 1.

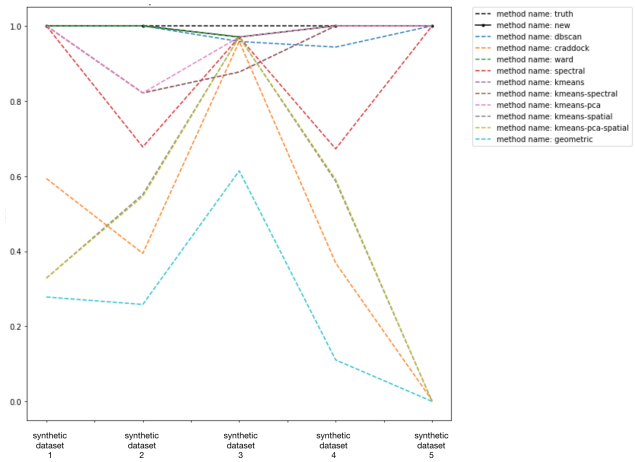


Figure 4: *normalsize mutual information on 5 Synthetic dataset with mild-condition noise*
y-axis is the mutual information where *x*-axis denotes five of different ground truth parcellations (consistent as in Figure 3). Our proposed K-parcel algorithm consistently outperform other methods and are very stable in synthetic dataset with different shaped parcels.

As one can see in Figure 4, our new proposed methods outperforms all these methods in terms of normalsized mutual information compared with ground truth. Note that the original K-means and its variants are all not as good as our new proposed K-parcel algorithm, and do not guarantee to find spatially continous parcellation (ignoring spatial coordinates) or find arbitray shape parcellation (with concatenated spatial coordinates). Our K-parcel can not only find spatially continous parcellations with arbitray shapes, and also outperforms in terms of quantitative evaluation.

Our method also have disadvanges. Its performance is only slightly better than applying Ward's algorithm in the synthetic dataset, which also finds spatially continous when only neighbour clusters are merged. Ward's algorithm is also more efficient to use in size of typical brain images and much faster than our K-parcel algorithm.

5.2 Real Dataset

We use a resting-state dataset from test-retest study performed at NYU. Note that since we do not consider group-level effects, we only use the brain image from the same subject (same person). We fetch the data from Internet and apply our K-parcel algorithm to find 2000 parcels. The algorithm takes no more than 15 seconds in a macbook pro without any heavy efficiency optimization.

As one can see in Figure 5, the K-parcel algorithm finds spatially continous parcellation. Next, to test whether the voxels in found parcellations are coherent.

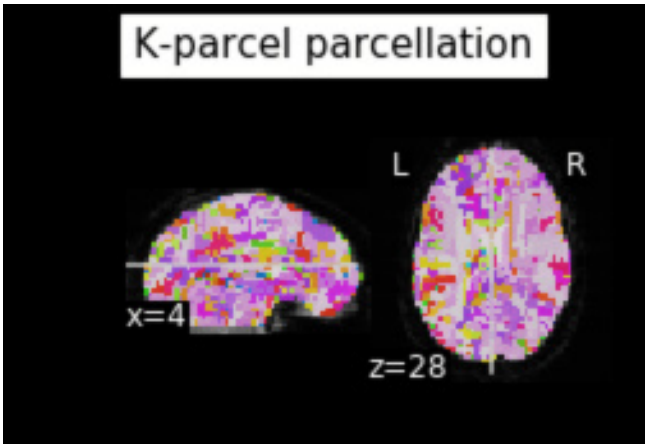
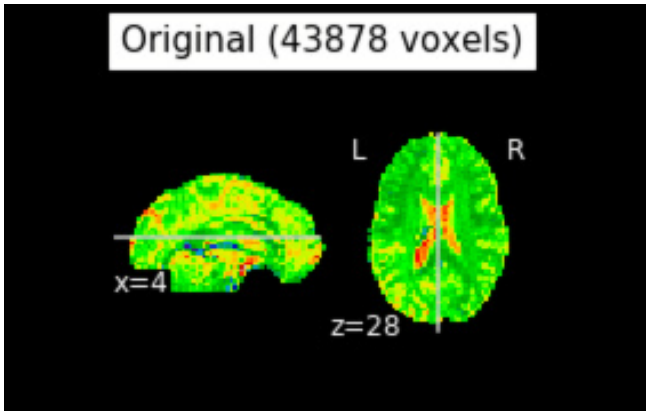
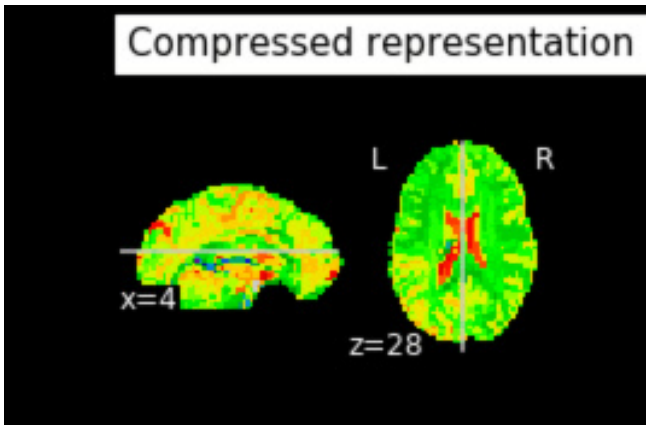


Figure 5: ***parcellation on NYU dataset***



(a) original data



(b) Compressed representation

Figure 6: ***Compressed Representation of the original brain images***

We transform the original brain image into a compressed representation where the value of each parcel is replaced by the parcel mean Y_c. The compressed image as well as the orignal one is shown in fig. 6. We examine the "goodness" of parcellation by evaluating how much of the data variance is captured by the parcels. We measure it as the fraction of variance in the full $Q \times Q$ correlation matrix which is captured by the correlation between parcels (consisting of only tens of thousands of connections).

We find that 83.2 % of the data variance is obtained by the compressed image by 2000 parcels , indicating that the compressed image is a good approximation of the original brain images. K-means needs to use about 2347 parcels to capture the same varaince of data (83.2 %), while our K-parcel method uses only 2000. This means K-parcel algorithm needs about 300 fewer parcels to explain the same variance, indicating that K-parcel algorithm does find good quality parcellations.

6 CONCLUSION

We propose K-parcel, a clustering algorithm for brain parcellation which finds spatial-continous parcellation of arbitray shapes. This is import because the orignal K-means algorithm is the robusted method as tested in [Arslan et al. 2018; Thirion et al. 2014] in terms of finding parcellations of coherent voxels for brain parcellation but it do not explicitly consider spatial continuity. Regularizing k-means with concatenated spatial coordinates is a simple solution but can only finds parcellation of spherical shapes. Our K-parcel algorithm is demonstrated to find spatial-continous parcellation of arbitray shapes. Experimental results even suggest that K-parcel finds better parcellations than k-means, where K-means do not find spatially continous parcels.

Summary of advantages of K-parcel algorithm:

- find parcellations that preserve spatial continuity.
- shape of parcels could be arbitray.
- robust to noise (as low SNR is inevitable in fMRI).

K-parcel also has limitations. It is not as efficient as K-means and its variants, along with other alternative algorithms such as Ward's algorithm and DBSCAN.

But K-parcel outperforms spectral clustering methods [Craddock et al. 2011; Thirion et al. 2014] by a large margin, in terms of both the quality of result parcellations and computational efficiency.

As for future work, we are going to do more further experiments on various brain image data and evaluate our K-parcel algorithm in a more systematic way.

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