

Parcellating whole brain for individuals by simple linear iterative clustering

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Abstract. This paper utilizes a supervoxel method called simple linear iterative clustering (SLIC) to parcellate whole brain into functional subunits using resting-state fMRI data. The parcellation algorithm is directly applied on the resting-state fMRI time series without feature extraction, and the parcellation is conducted on the individual subject level. In order to obtain parcellations with multiple granularities, we vary the cluster number in a wide range. To demonstrate the reasonability of the proposed approach, we compare it with a state-of-the-art whole brain parcellation approach, i.e., the normalized cuts (Ncut) approach. The experimental results show that the proposed approach achieves satisfying performances in terms of spatial contiguity, functional homogeneity and reproducibility. The proposed approach could be used to generate individualized brain atlases for applications such as personalized medicine. The source codes of this study have been made publicly available at https://github.com/yuzhounh/SLIC_individual.

Keywords: whole brain parcellation; supervoxel; resting-state fMRI; functional connectivity; individualized brain atlas

1 Introduction

Since the manifestation of brain functional connectivity [1], studies have shown that the brain could be characterized as a network. To construct the brain network, an atlas should be defined in prior. It is usually chosen from the standardized atlases such as the automated anatomical labeling (AAL) atlas [2] and the Harvard-Oxford (HO) atlas. However, these atlases are generated based on structural criteria, and cannot guarantee the functional homogeneity of the fMRI time series in each node. Parcellating the brain based on resting-state functional connectivity (RSFC) could avoid the problem, and has attracted exploding attentions in recent years.

The majority of studies concerning RSFC-based parcellation are focusing on a region of interest (ROI) rather than the whole brain. Only a few studies [3-7] generate whole brain atlases. Among them, the normalized cuts (Ncut) [8, 9] is one of the most successful approaches and being widely applied.

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This paper employs a supervoxel method called simple linear iterative clustering (SLIC) [10, 11] to parcellate whole brain for individuals. By varying the initialized cluster number, we generate brain atlases with multiple granularities. The Ncut approach is also applied to parcellate the same dataset. Finally, we make a comparison between the two kinds of parcellation approaches under different evaluation metrics.

2 Materials and methods

2.1 Subjects

In the study, we use data from the 1000 Functional Connectomes Project (http://www.nitrc.org/projects/fcon_1000/) [12] that is publicly available online. Specifically, we use the structural and resting-state fMRI data acquired from 18 subjects in the Beijing_Zang dataset. The demographics of the subjects could be found online. The dataset is preprocessed by the Data Processing Assistant for Resting-State fMRI (DPARSF) [13]. The preprocessing steps include: discarding the first ten volumes, slice timing correction, motion correction, coregistration, segmenting the structural images, normalizing the functional images to the Montreal Neurological Institute (MNI) space at $4 \times 4 \times 4 \text{ mm}^3$ resolution; smoothing with a 6 mm FWHM Gaussian kernel; linear detrending; bandpass filtering with passband 0.01~0.08 Hz; regressing out nuisance covariates. No subject is excluded due to excessive head motion under the excluding criteria 2.0 mm and 2.0 degree. The global signal regression (GSR) is not included since its effect is still controversial.

2.2 Simple linear iterative clustering (SLIC)

SLIC could be used as a superpixel method [10] or a supervoxel method [11], which is determined by whether the target image is 2D or 3D. The common idea is to separate an image into perceptually meaningful patches. SLIC is actually an adaptation of K-means. Two important differences between SLIC and K-means are that SLIC limits the search space to the neighborhood of a cluster center and creates a unified distance by integrating the intensity distance and the spatial distance. SLIC has become very popular in the field of computer vision in recent years due to its simplicity, effectiveness and good clustering performance. In this study, we apply it on resting-state fMRI data to carry out whole brain parcellation.

The algorithm procedure of SLIC is stated as follows. To parcellate the brain into K clusters, we first initialize K cluster centers periodically in the 3D space, as shown in Fig. 1A. Assume that the number of voxels in the gray matter is N . Then the average length of a supervoxel is $S = \sqrt[3]{N/K}$. For each voxel in the $3S \times 3S \times 3S$ region around a cluster center, a distance between the voxel and the cluster center is calculated. This distance is assigned to the voxel as a measure to judge which cluster it should belong to. If the distance decreases comparing to the result in the previous iteration, then associate the voxel to the current cluster center. This procedure is repeated for all cluster centers. Once completed, each cluster center is updated to be a vector formed by averaging the fMRI time series and coordinates of voxels in that cluster. The above assignment and update steps are repeated until the change of the cluster centers is lower

than a certain threshold. The resultant clusters or supervoxels make up the final brain atlas. The algorithm procedure is summarized in Table 1. An illustration of the initializing and searching steps is shown in Fig. 1.

Table 1. The algorithm procedure of the SLIC approach

Input: the resting-state fMRI time series and the initialized cluster number.

Output: the cluster labels.

Initialize the cluster centers.

Initialize label $l(i) = -1$ for each voxel i .

Initialize distance $d(i) = \infty$ for each voxel i .

while not converged **do**

for each cluster center C_k **do**

for each voxel i in the $3S \times 3S \times 3S$ region around C_k **do**

 Compute the unified distance D between C_k and i .

if $D < d(i)$ **then**

 Set $l(i) = k$.

 Set $d(i) = D$.

end if

end for

end for

 Compute new cluster centers.

end while

How to define the unified distance is very important in the clustering procedure. For the i th voxel, assume that its fMRI time series is v_i and its coordinates in the MNI space is u_i , $i = 1, 2, \dots, N$, then the unified distance between two voxels could be defined as

$$d_{ij} = \sqrt{\frac{\|v_i - v_j\|_2^2}{m^2} + \frac{\|u_i - u_j\|_2^2}{s^2}}, \quad (1)$$

where m and S are two tuning parameters which normalize the functional distance and the spatial distance respectively. The parameter m could be chosen around the median of all functional distances, and we fix it to be 40 empirically. The parameter S is fixed to be the average length of the supervoxels. Though the algorithm in [11] and in this study are targeting at parcellating the 3D space, a major difference exists between them. That is, the functional distance is calculated between the image intensity of two voxels in [11] while it is calculated between the fMRI time series of two voxels in this study. Since the functional distance is incorporated in the clustering procedure, the proposed approach could be regarded as a RSFC-based parcellation approach.

We choose Ncut as the competing approach because it has achieved great success in whole brain parcellation. For that approach, the definition of the individual subject level weight matrix and the implementation of the multiclass spectral clustering (MSC) algorithm [14] are kept the same as in [4] in order to make a fair comparison. Only the individual subject level parcellations of the two approaches are generated and compared in this study. A comparison of the pipeline of the Ncut approach and the SLIC approach

is shown in Fig. 2. Without confusion, we use MSC to denote the clustering algorithm that operates after extracting features by Ncut. Since SLIC is directly applied on the fMRI time series, it only needs a single step to generate parcellations.

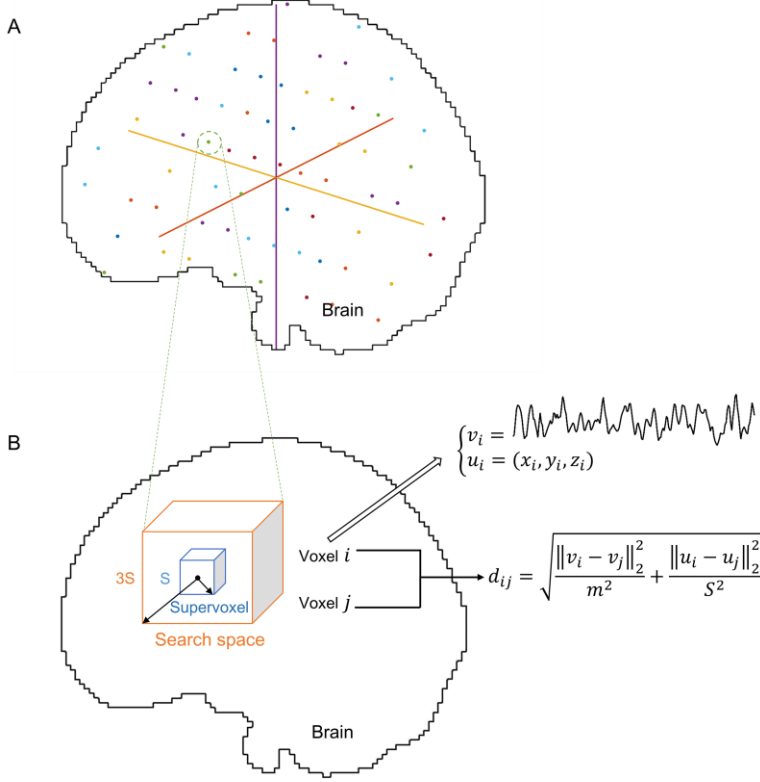


Fig. 1. Illustration of the SLIC approach on whole brain parcellation. (A) Initializing the cluster centers periodically in the 3D space. The three straight lines denote the xyz-axis system. (B) For each cluster, SLIC searches in the $3S \times 3S \times 3S$ region around its center to update the labels of all voxels in the search space. A unified distance is calculated between each voxel and the cluster center to judge whether the voxel should belong to the cluster. The unified distance is composed of the functional distance and the spatial distance, wherein the functional distance is calculated between the fMRI time series of two voxels. Note that the supervoxel is unnecessary to be a cube. It is displayed as a cube for simplicity.

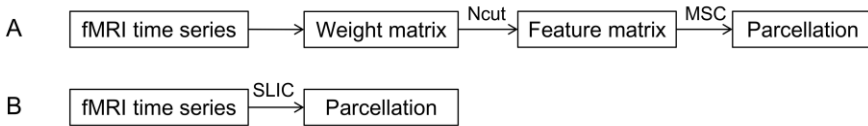


Fig. 2. The pipeline of the two parcellation approaches. (A) Ncut. (B) SLIC.

2.3 Evaluation metrics

The clusters in a brain parcellation result should be spatially contiguous, functionally homogeneous and reproducible [4, 5]. For spatial contiguity, we treat the spatially discrete regions that belong to the same cluster as separate clusters and count the increased cluster number. The increased cluster number is referred to as the spatial discontiguity index. For functional homogeneity, we first average similarities across all pairs of voxels within a cluster and then average the obtained results across clusters. Assume that the voxel number in the k th cluster C_k is n_k , $k = 1, 2, \dots, K$. The similarity between voxels i and j is s_{ij} , $i, j = 1, 2, \dots, N$. The average similarity within the k th cluster is

$$a(k) = \frac{1}{n_k(n_k-1)} \sum_{i,j \in C_k, i \neq j} s_{ij}. \quad (2)$$

Then the functional homogeneity of the brain atlas is

$$\frac{1}{K} \sum_{k=1}^K a(k). \quad (3)$$

To avoid circular analysis, we train an atlas on one subject and calculate the functional homogeneity based on this atlas and the resting-state fMRI data of other subjects. For reproducibility, we calculate the Dice coefficient between different brain atlases that are generated from different subjects. As a prior step, we should calculate an adjacency matrix for each brain atlas. An adjacency matrix A is a $N \times N$ symmetric matrix that is calculated by setting its elements a_{ij} to be one if voxels i and j belong to the same cluster in the brain atlas, and zero otherwise. For two adjacency matrices A and B derived from two atlases, the Dice coefficient between them is

$$\frac{2|A \cap B|}{|A| + |B|}, \quad (4)$$

where $|\cdot|$ denotes the number of ones in an adjacency matrix, $A \cap B$ denotes the union of the two adjacency matrices.

3 Experimental results

In the experiment, we use the fMRI data from 18 subjects. The Ncut approach and the SLIC approach are employed to do parcellation. Then the parcellation results are compared under different evaluation metrics. The initialized cluster number is set to be [50:50:1000] in order to generate parcellations with multiple granularities. For each subject, each parcellation approach and each cluster number, one atlas is obtained. Fig. 3 shows the atlases when the first subject is parcellated into 100, 300 and 800 clusters by Ncut and SLIC.

For a brain parcellation approach, the actual cluster number should be close to the initialized cluster number in order to obtain the granularity we have expected. By subtracting the initialized cluster number from the average actual cluster number for each parcellation approach, we could obtain their differences, as shown in Fig. 4A. The results show that SLIC outperforms Ncut in approximating the initialized cluster number.

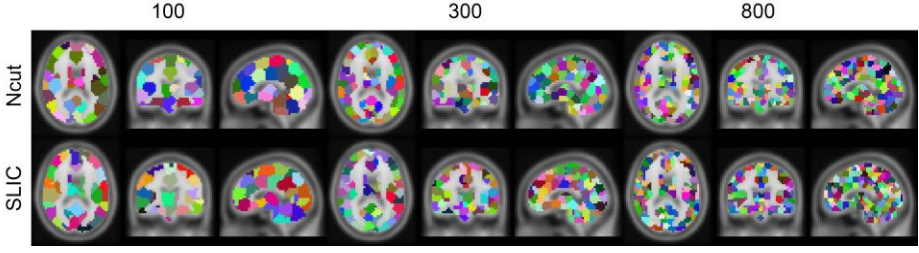


Fig. 3. Illustration of the atlases generated by Ncut and SLIC. Each atlas is represented by its three orthogonal cross sections. The initialized cluster numbers are 100, 300 and 800 from left to right. The colormap for each atlas is randomly generated, and each color represents a cluster.

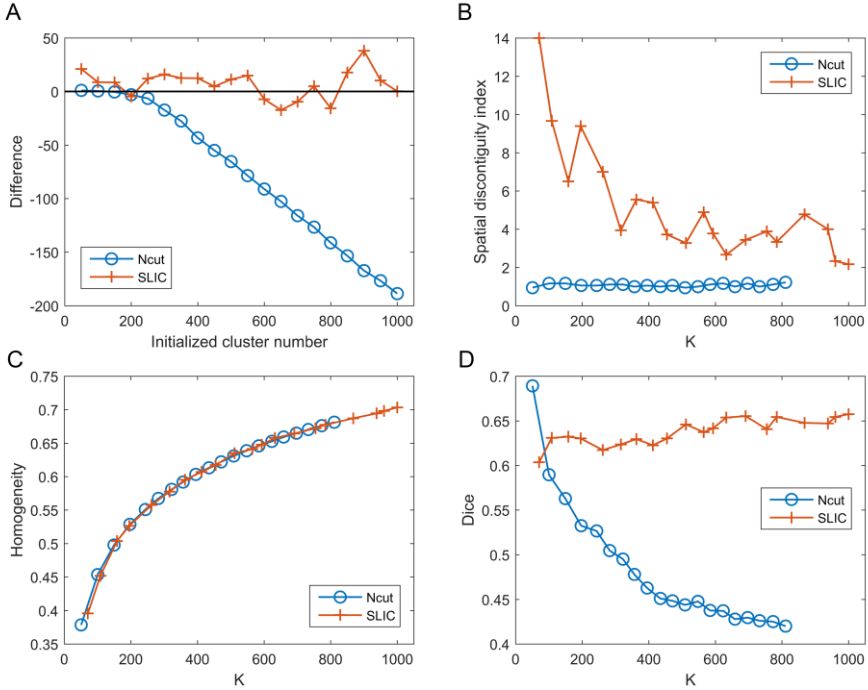


Fig. 4. The results of different evaluation metrics for Ncut and SLIC. (A) The difference between the initialized cluster number and the actual cluster number. (B) Spatial discontinuity index. (C) Functional homogeneity. (D) Dice coefficient. The first metric is plotted against the initialized cluster number while the other three metrics are plotted against the actual cluster number that is denoted by K.

To evaluate spatial contiguity, we calculate the spatial discontinuity index for each brain atlas and then average the results across subjects, as shown in Fig. 4B. A smaller result indicates that the brain atlases are more spatially contiguous. Ncut outperforms SLIC in spatial contiguity. The reason is that Ncut incorporates spatial constraint in the parcellation procedure that could guarantee to obtain spatially contiguous clusters [4].

The spatial constraint is a strong spatial structure, which weakens the influences of data structure and renders the generated atlases to have comparable shapes and sizes, as displayed in Fig. 3. This brings quite a lot of doubts to the Ncut approach [3, 5]. For SLIC, the spatial discontinuity index generally decreases with increasing cluster number. When the actual cluster number is larger than 200, there are only few spatially discontinuous regions in each atlas, which is also satisfactory.

To evaluate functional homogeneity, we train a brain atlas on one subject and calculate homogeneity based on this atlas and the resting-state fMRI data of the remaining subjects. The homogeneity results of each parcellation approach and each cluster number are averaged, as shown in Fig. 4C. The curves correspond to the two approaches are very close, which indicates that the two approaches obtain similar homogeneity results. Homogeneity increases with increasing cluster number. This is consistent with [4, 5, 15].

To evaluate reproducibility, we randomly choose two from the eighteen subjects and calculate Dice coefficient between their corresponding atlases when the parcellation approach and the initialized cluster number are fixed. This procedure is repeated for twenty times. The twenty results are averaged to yield a single Dice coefficient for each parcellation approach and each cluster number. The averaged results are shown in Fig. 4D. The Dice coefficients of SLIC are higher than the Dice coefficients of Ncut except when the initialized cluster number is 50. The result demonstrates that the atlases generated by SLIC have higher reproducibility across individuals than the atlases generated by Ncut. The Dice coefficient of Ncut decreases with increasing cluster number, which is consistent with [3-5].

For reproducibility, the source codes of this study have been made publicly available at https://github.com/yuzhounh/SLIC_individual.

4 Conclusion and future directions

This paper applies SLIC to generated individualized brain atlases. The algorithm is directly applied on resting-state fMRI time series without feature extraction in prior. The experimental results show that the proposed approach obtains satisfying results in terms of spatial contiguity and functional homogeneity, and outperforms Ncut in terms of reproducibility. It demonstrates the rationality of the proposed approach. For future directions, the individualized brain atlas might find its application in fields such as personalized medicine [16]. In addition, the proposed approach has the potential to be extended from individual subject level to group level as the Ncut approach [4].

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References

1. Biswal, B., Zerrin Yetkin, F., Haughton, V.M., Hyde, J.S.: Functional connectivity in the motor cortex of resting human brain using echo-planar mri. *Magn Reson Med* 34, 537-541 (1995)
2. Tzourio-Mazoyer, N., Landeau, B., Papathanassiou, D., Crivello, F., Etard, O., Delcroix, N., Mazoyer, B., Joliot, M.: Automated anatomical labeling of activations in SPM using a macroscopic anatomical parcellation of the MNI MRI single-subject brain. *Neuroimage* 15, 273-289 (2002)
3. Blumensath, T., Jbabdi, S., Glasser, M.F., Van Essen, D.C., Ugurbil, K., Behrens, T.E.J., Smith, S.M.: Spatially constrained hierarchical parcellation of the brain with resting-state fMRI. *Neuroimage* 76, 313-324 (2013)
4. Craddock, R.C., James, G.A., Holtzheimer, P.E., Hu, X.P.P., Mayberg, H.S.: A whole brain fMRI atlas generated via spatially constrained spectral clustering. *Hum Brain Mapp* 33, 1914-1928 (2012)
5. Shen, X., Tokoglu, F., Papademetris, X., Constable, R.T.: Groupwise whole-brain parcellation from resting-state fMRI data for network node identification. *Neuroimage* 82, 403-415 (2013)
6. van den Heuvel, M., Mandl, R., Pol, H.H.: Normalized Cut Group Clustering of Resting-State fMRI Data. *PloS one* 3, (2008)
7. Moreno-Dominguez, D., Anwender, A., Knosche, T.R.: A Hierarchical Method for Whole-Brain Connectivity-Based Parcellation. *Hum Brain Mapp* 35, 5000-5025 (2014)
8. Shi, J.B., Malik, J.: Normalized cuts and image segmentation. *IEEE T Pattern Anal* 22, 888-905 (2000)
9. von Luxburg, U.: A tutorial on spectral clustering. *Stat Comput* 17, 395-416 (2007)
10. Achanta, R., Shaji, A., Smith, K., Lucchi, A., Fua, P., Susstrunk, S.: SLIC superpixels compared to state-of-the-art superpixel methods. *IEEE T Pattern Anal* 34, 2274-2282 (2012)
11. Lucchi, A., Smith, K., Achanta, R., Knott, G., Fua, P.: Supervoxel-Based Segmentation of Mitochondria in EM Image Stacks With Learned Shape Features. *IEEE T Med Imaging* 31, 474-486 (2012)
12. Biswal, B.B., Mennes, M., Zuo, X.N., et al.: Toward discovery science of human brain function. *P Natl Acad Sci USA* 107, 4734-4739 (2010)
13. Yan, C.G., Zang, Y.F.: DPARSF: a MATLAB toolbox for “pipeline” data analysis of resting-state fMRI. *Frontiers in systems neuroscience* 4, 1-7 (2010)
14. Yu, S.X., Shi, J.B.: Multiclass spectral clustering. In: *Proceedings of IEEE International Conference on Computer Vision*, pp. 313-319. (2003)
15. Gordon, E.M., Laumann, T.O., Adeyemo, B., Huckins, J.F., Kelley, W.M., Petersen, S.E.: Generation and evaluation of a cortical area parcellation from resting-state correlations. *Cereb. Cortex* 26(1), 288-303 (2016)
16. Wang, D.H., Buckner, R.L., Fox, M.D., et al.: Parcellating cortical functional networks in individuals. *Nat Neurosci* 18, 1853-1860 (2015)