Connectivity-Based Parcellation of Functional Sub-Regions from Brain fMRI Signals

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Outline

- Motivation
- Functional Sub-Regions Parcellation
  - Connectivity Network Generation
  - Community Detection
- Results
  - Synthetic Dataset
  - fMRI Dataset
- Conclusion & Future Works

Motivation

- Our brain consists of structurally and functionally interconnected regions-of-interest (ROIs)
- Many literature-based studies prefer regions-of-interest (ROI) based connectivity analysis to understand the underlying interactions between brain regions.
- In some cases several functional sub-regions-of-interest (subROIs) exist within one anatomically defined ROI, e.g. striatum (putamen and caudate)

Motivation

- Exploration of the connectivity patterns of the functional subROIs inside striatum, could be of great importance in
  - Developing more detailed models of whole-brain connectivity networks [1]
  - understanding degenerative basal ganglia disorders such as Parkinson's disease, Huntington's disease [2]
  - evaluating hypotheses about healthy aging [3] and cortical-basal ganglia circuitry in typical development [4].

[1] Butts, science 325 (5939) (2009). [2] Barnes et al., Frontiers in systems neuroscience 4 (2010).[3] Hedden et al., Nature reviews neuroscience 5 (2) (2004). [4] Rubia et al., Human brain mapping 27 (12) (2006).

Motivation

Literature-based approaches can be roughly divided into two categories-

- Clustering based approach
- Graph-theory based approach

Motivation

Literature-based approaches can be roughly divided into two categories-

- Clustering based approach
  - Considers connectivity of the ROI with other brain regions
  - Needs rigorous preprocessing and denoising steps to obtain spatially continuous results.
- Graph-theory based approach

Motivation

Literature-based approaches can be roughly divided into two categories-

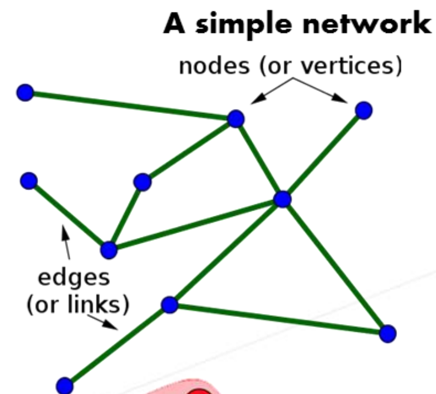
- Clustering based approach
- Graph-theory based approach
  - Considers connectivity within ROI
  - fMRI data of spatially distant voxels sometimes are grouped together.
  - Most cases do not impose spatial continuity , and where considered, parameter tuning remains a challenge

Motivation

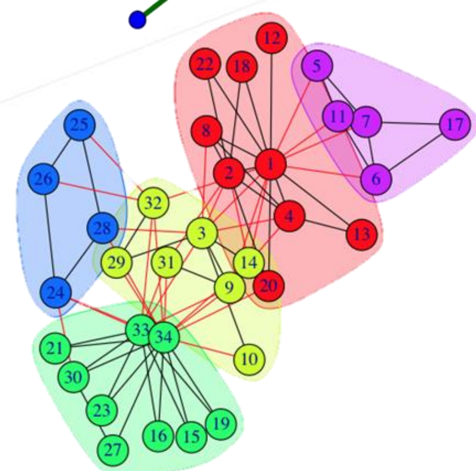
- To develop a data-driven graph-theoretic technique for parcellation of functional sub-regions (subROI) from brain fMRI signals

Functional Sub-Regions Parcellation

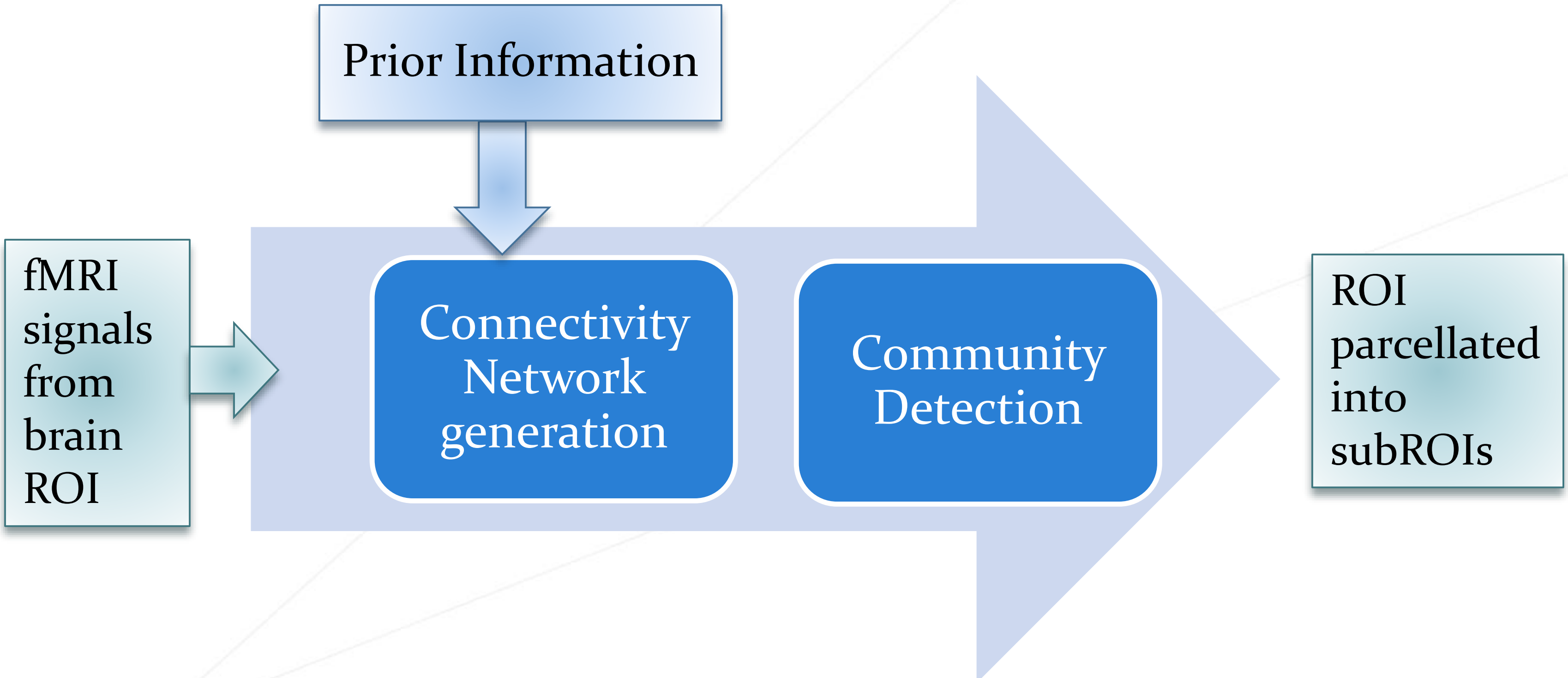
- We propose a connectivity network generation approach that incorporates both the inter-ROI and intra-ROI connectivity patterns while imposing spatial continuity for subROIs



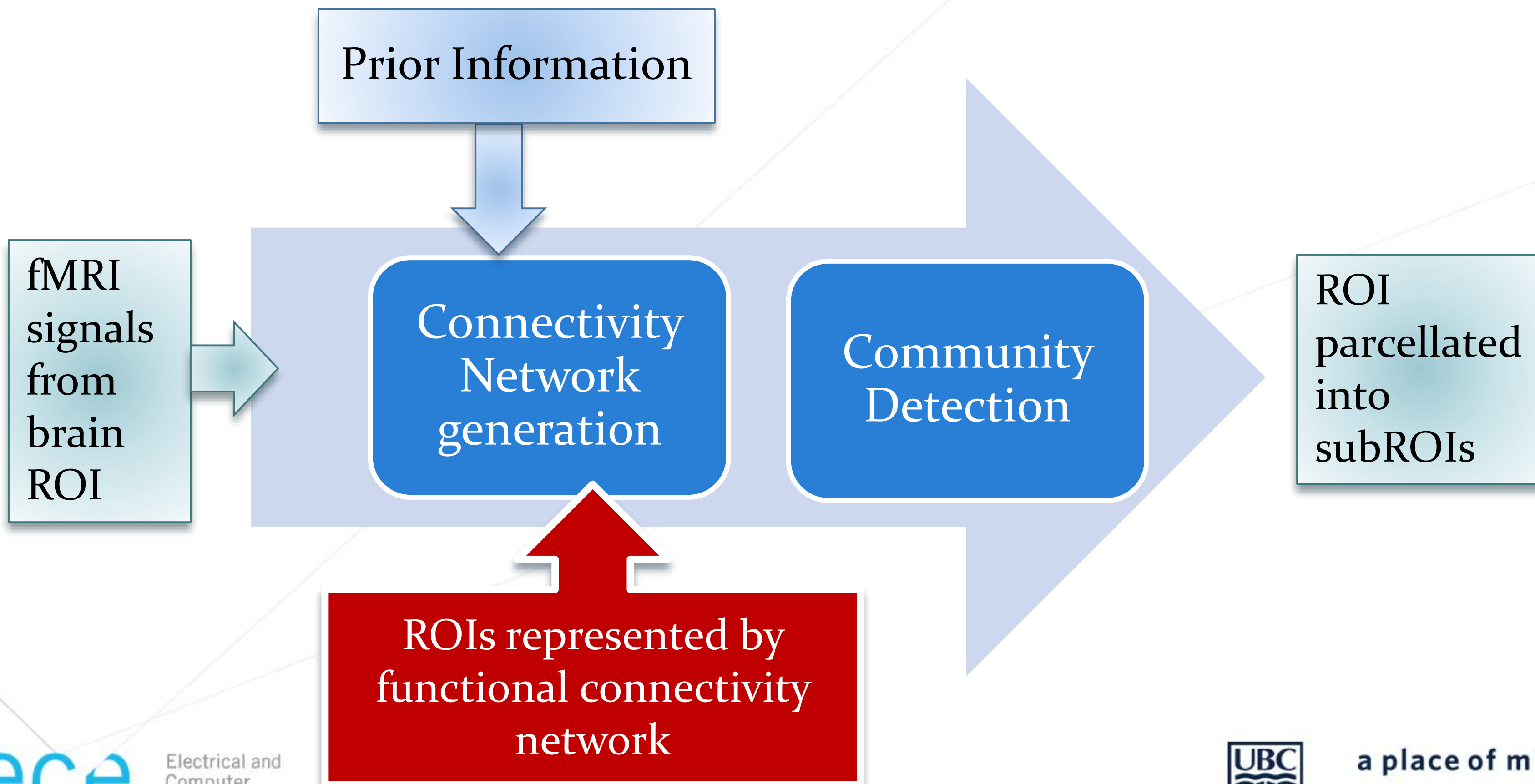
- A community detection based approach is then adapted to sub-divide the connectivity network into two spatially continuous subROIs.



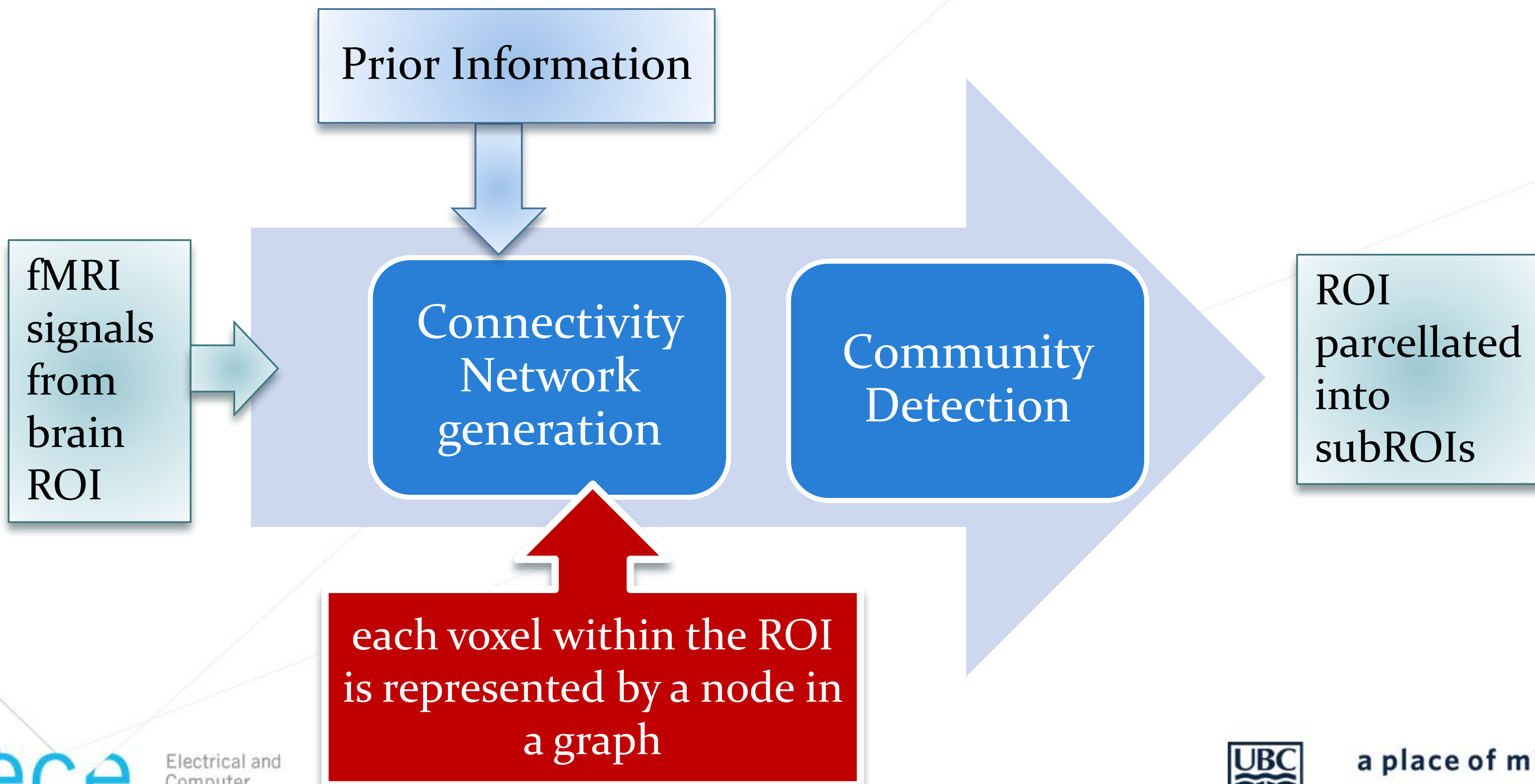
Functional Sub-Regions Parcellation



Functional Sub-Regions Parcellation



Functional Sub-Regions Parcellation



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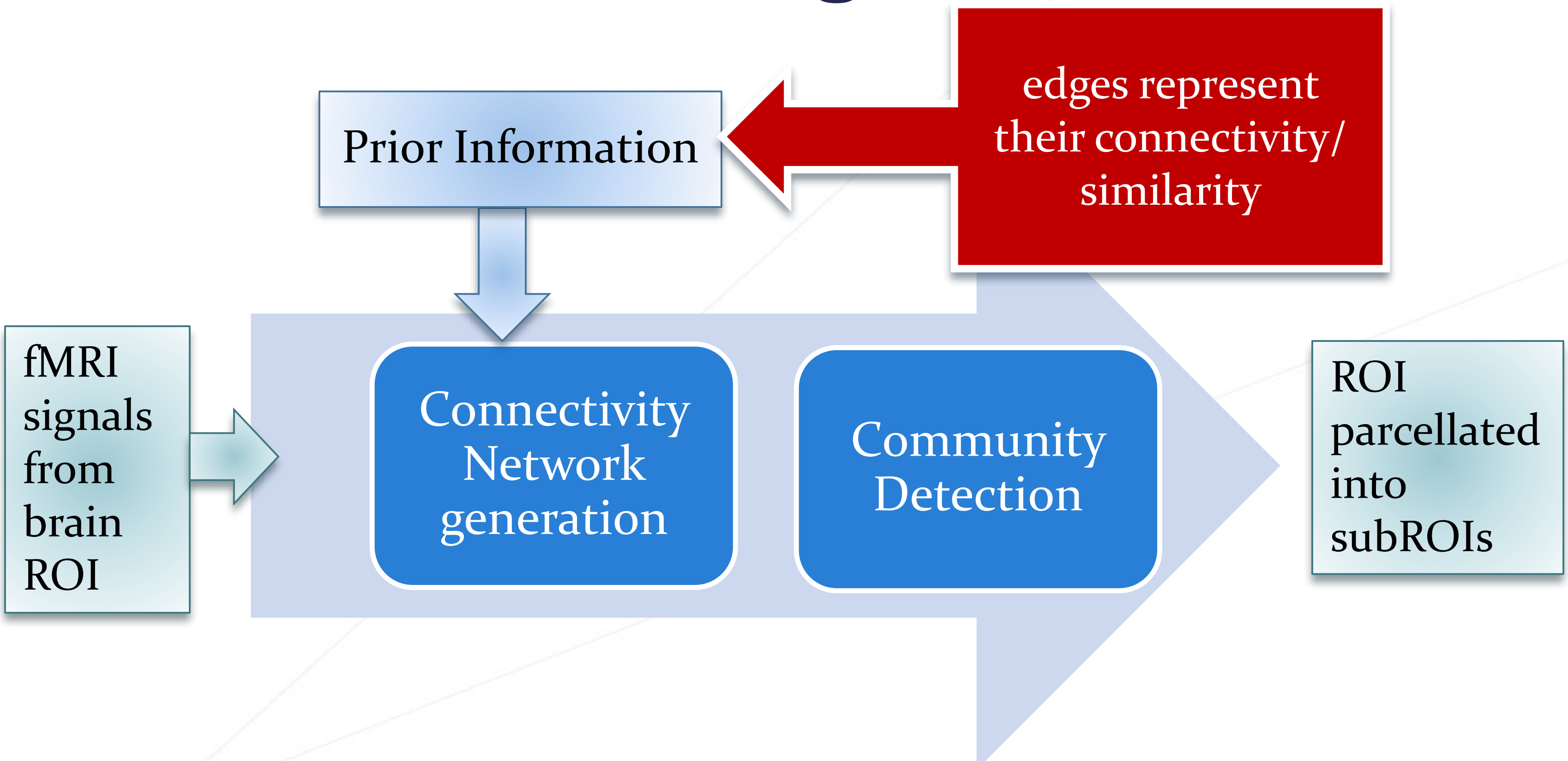
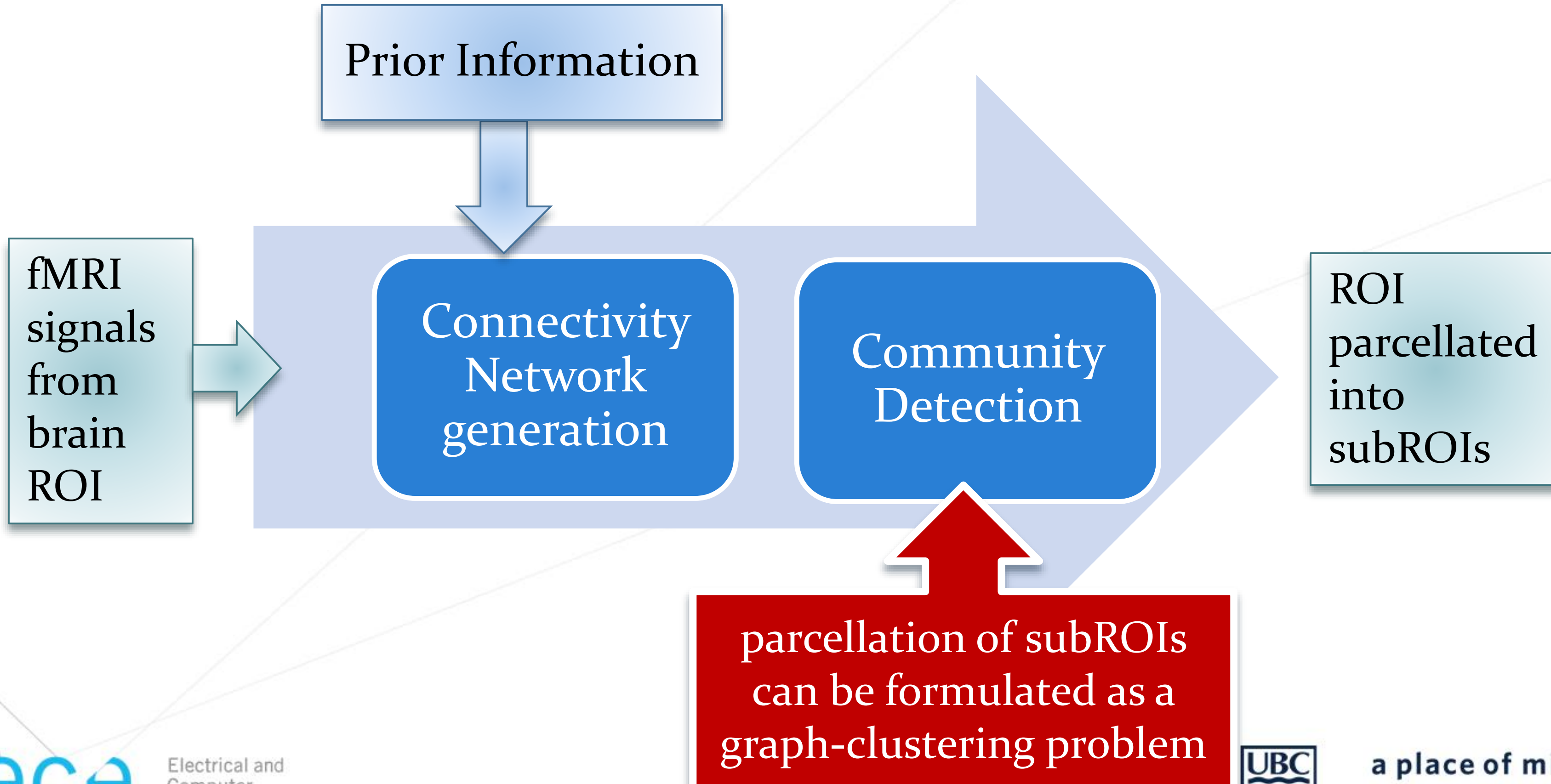
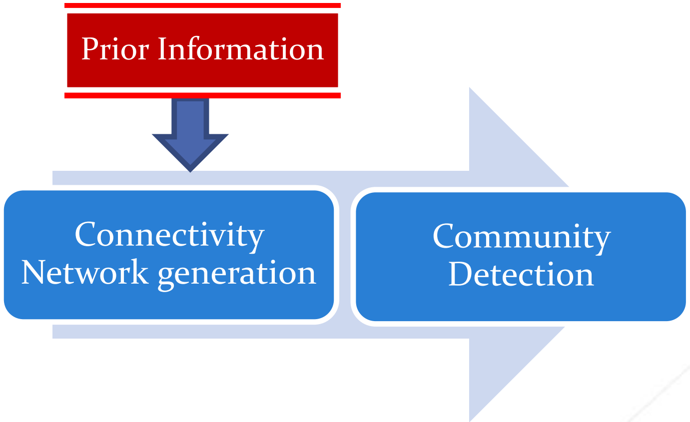
Functional Sub-Regions Parcellation



Functional Sub-Regions Parcellation



Connectivity Network Generation



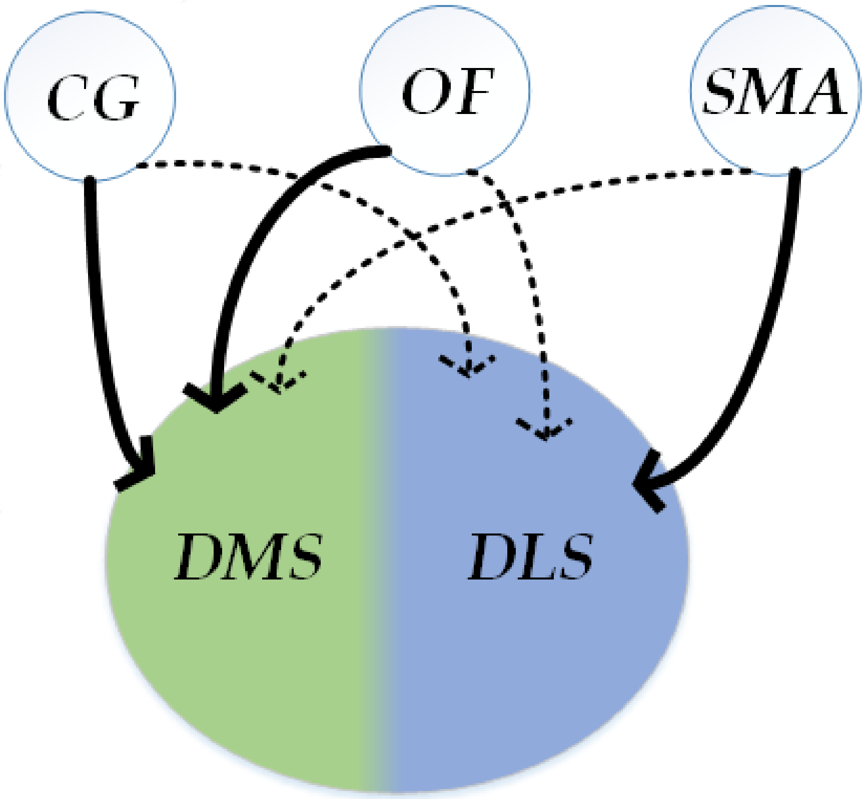
DLS : Dorsomedial Striatum

DMS : Dorsomedial Striatum

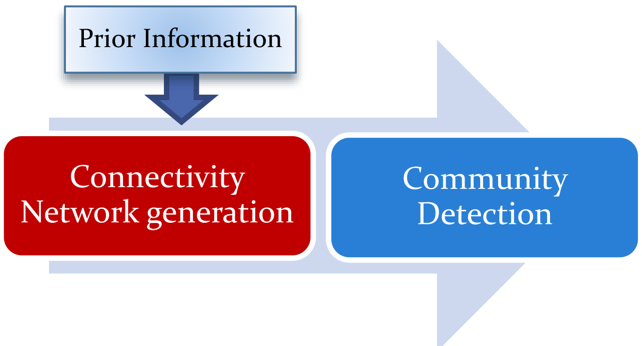
OF : Orbitofrontal Cortex

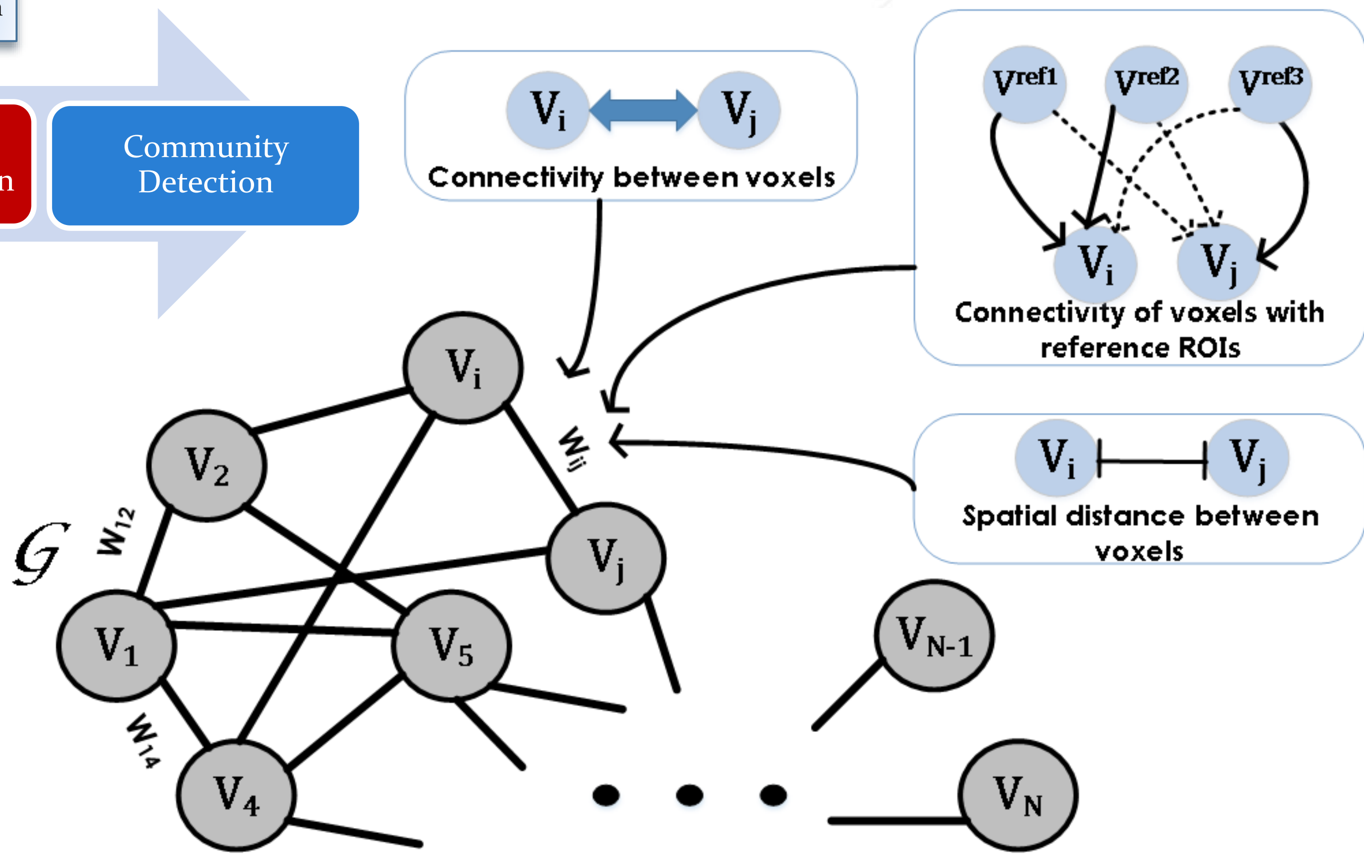
CG : Cingulate Gyrus

SMA : Sensorimotor Cortex Area

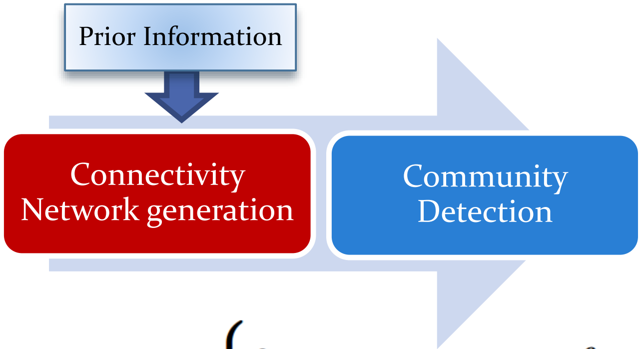


Connectivity Network Generation

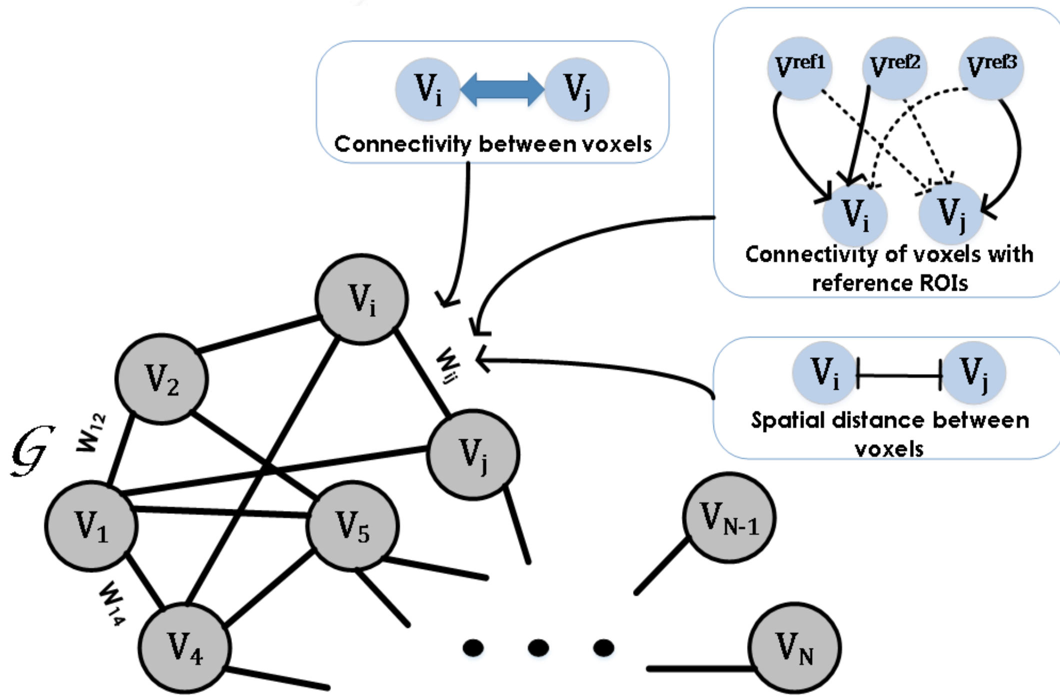




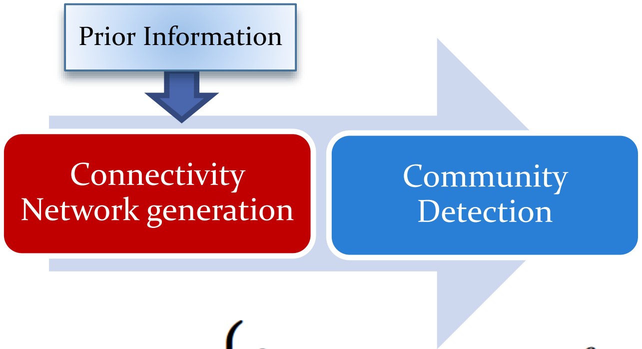
Connectivity Network Generation



$$W_{ij} = \begin{cases} 0 & \text{for } i = j \\ W_{ij}^{task} \times W_{ij}^{ref} & \text{for } i \neq j \end{cases}$$

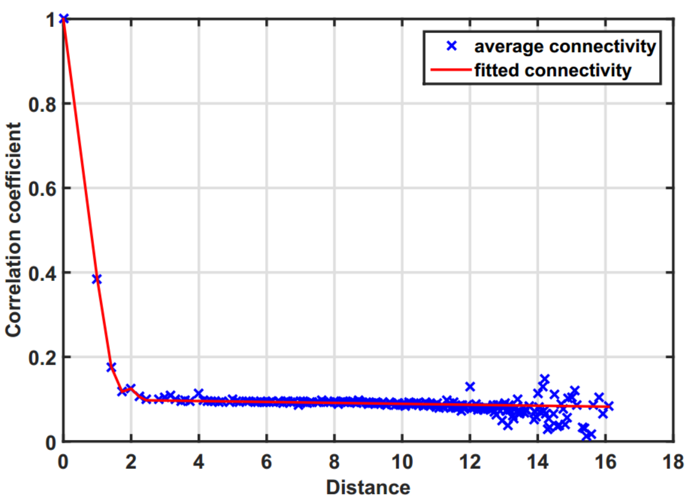


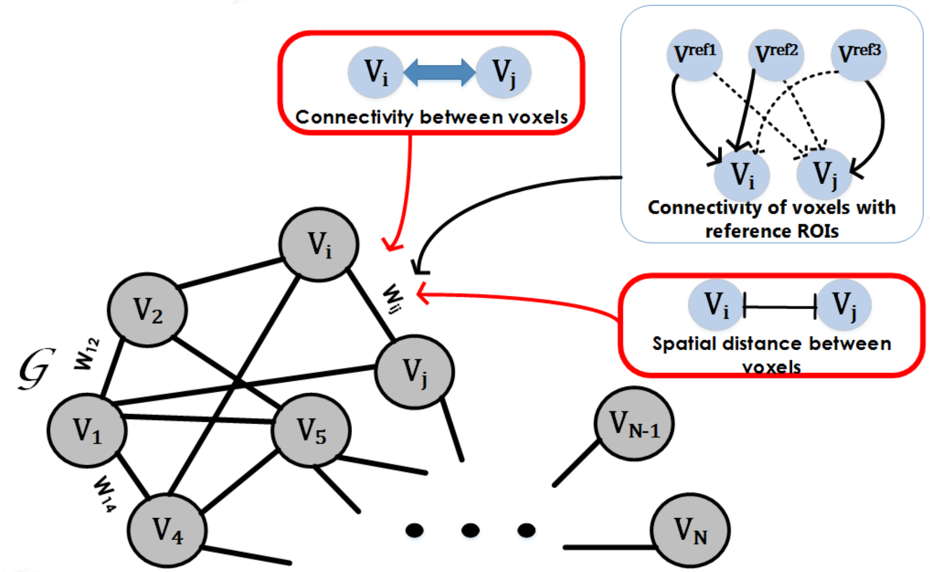
Connectivity Network Generation



$$\mathcal{W}_{ij} = \begin{cases} 0 & \text{for } i = j \\ W_{ij}^{task} \times W_{ij}^{ref} & \text{for } i \neq j \end{cases}$$

$$W_{ij}^{task} = \delta_D^T(||\mathbf{r}_i - \mathbf{r}_j||) \times C^{task}(||\mathbf{r}_i - \mathbf{r}_j||); \quad i \neq j$$





$$\delta_D^T(d) = \begin{cases} 1, & \text{if } d \leq T \\ 0, & \text{otherwise} \end{cases}$$

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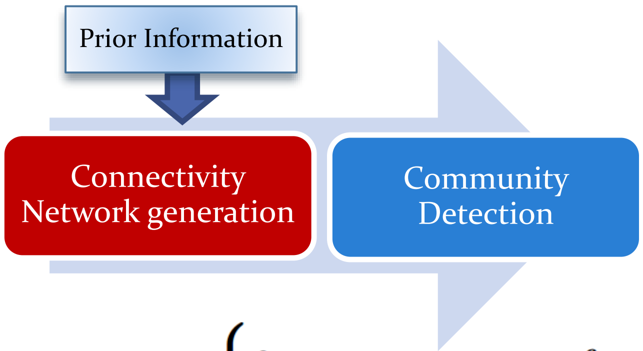
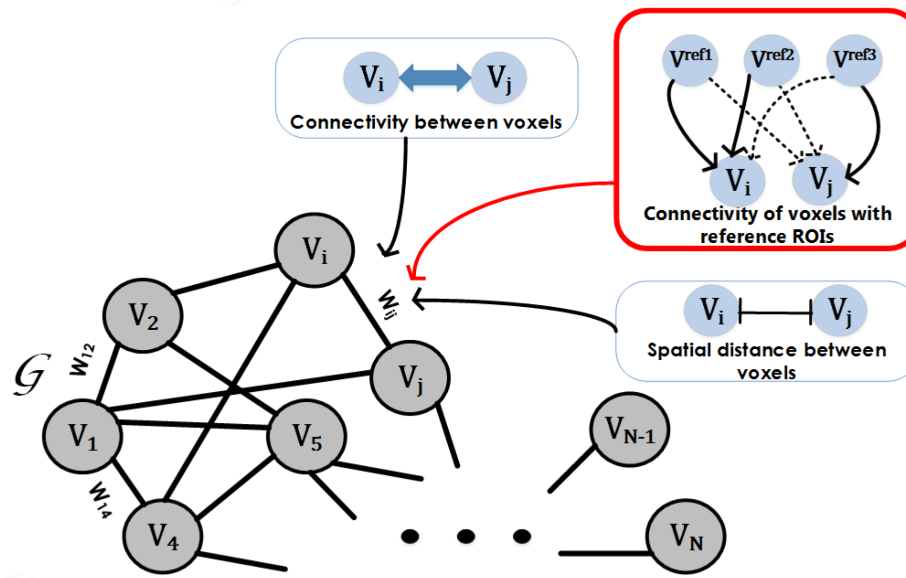
Connectivity Network Generation



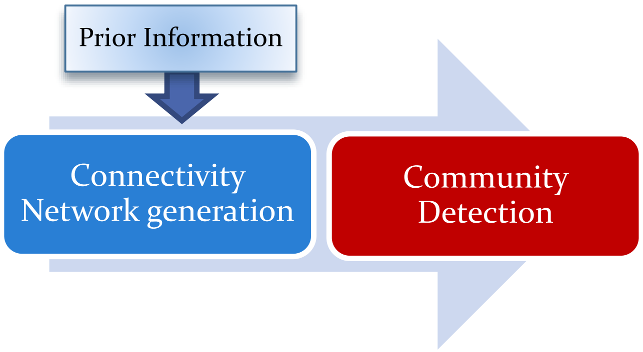
$$W_{ij} = \begin{cases} 0 & \text{for } i = j \\ W_{ij}^{task} \times W_{ij}^{ref} & \text{for } i \neq j \end{cases}$$

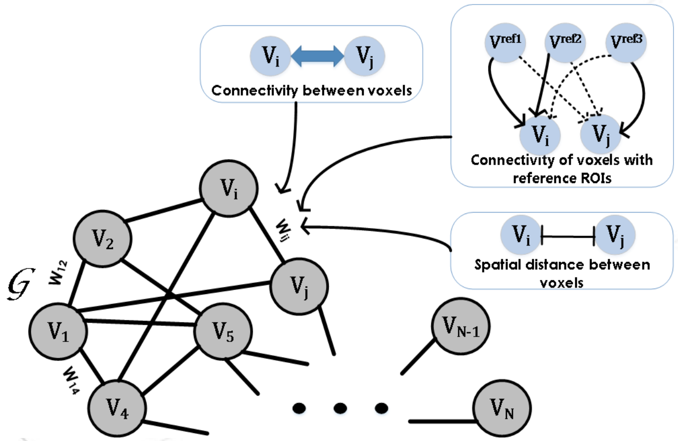
$$W_{ij}^{ref} = 1 - \frac{\sum_{m=1}^{M} |C_{m,i}^{ref} - C_{m,j}^{ref}|}{M}; \quad i \neq j.$$

$$C_{m,i}^{ref} = |\rho_{partial}(y_i, y_m^{ref} | y_1^{ref}, \ldots, y_{m-1}^{ref}, y_{m+1}^{ref}, \ldots, y_M^{ref})|.$$



Community Detection

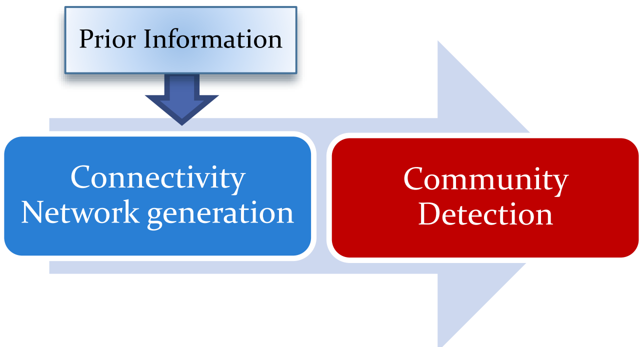


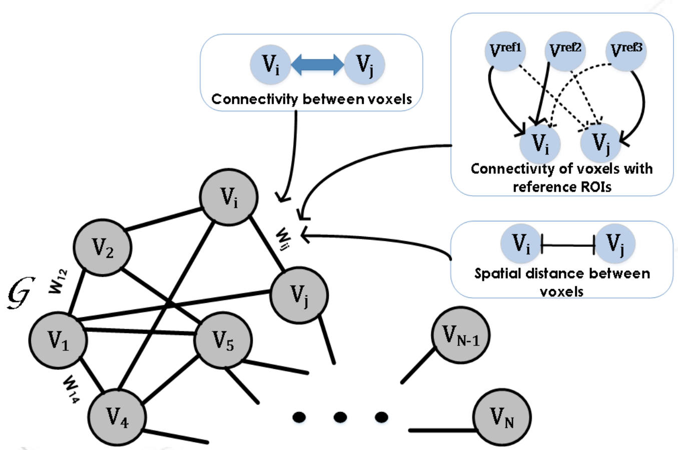


- Community detection method – Spatial Clustering On Ratio of Eigenvectors[1]
- Assumes number of community, K to be known
- Outperforms other methods on benchmark graphs
- Can detect communities of variable sizes
- Computationally efficient

[1]Jin, Annals of Stat 43.1 (2015): 57-89

Community Detection





- Calculate K leading eigenvectors of adjacency matrix, say, η1, . . . , ηK
- Calculate Rn × (K – 1) matrix such that R(i, k) = ηk+1(i)/η1(i),

  $1 \leq i \leq n, \;\; 1 \leq k \leq K - 1$

- Use R for clustering by applying the k-means method.

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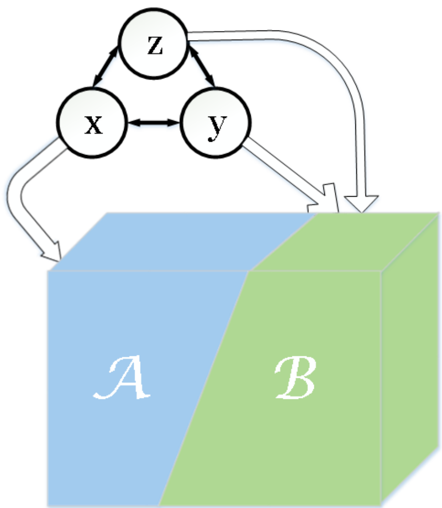
[6]Jin, Annals of Stat 43.1 (2015): 57-89

Results: Synthetic Dataset



Dataset	Description	Signal to Noise Ratio (SNR)
IA	Two subROIs, no outliers	$\text{SNR}_{data} = 6$ dB
IB	Two subROIs, 100 outliers in each ROI	$\text{SNR}_{data} = 6$ dB, $\text{SNR}_{outlier} = -3$ dB
IC	Two subROIs, 100 outliers in each ROI	$\text{SNR}_{data} = 6$ dB, $\text{SNR}_{outlier} = -10$ dB

$$r_X = \theta_1 m_s + (1-\theta_1) l_s + \epsilon_1$$
$$r_Y = \theta_2 n_s + (1-\theta_2) l_s + \epsilon_2$$
$$r_Z = \theta_3 n_s + (1-\theta_3) l_s + \epsilon_3$$
$$x_A = \alpha[\theta_A m_s + (1-\theta_A) l_s] + (1-\alpha) k_s + \epsilon_A$$
$$x_B = \beta[\theta_B n_s + (1-\theta_B) l_s] + (1-\beta) r_s + \epsilon_B$$
$$l_s, m_s, n_s, k_s, r_s \sim \mathcal{N}(0,1)$$
$$\epsilon_1, \epsilon_2, \epsilon_3, \epsilon_A, \epsilon_B \sim \mathcal{N}(0, \sigma_N^2)$$
$$\theta_1, \theta_2, \theta_3, \theta_A, \theta_B, \alpha, \beta \sim \mathcal{U}[0.5, 0.9].$$

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[7] Kahnt *et al.*, J.NeuroSc.2012;32(18):6240-6250. [8] Barnes *et al.*, Front.Sys.NeuroSc.2010; 4:7-11. [9] Zhang *et al.*,Biomed.Sys.Proc.Contrl.2016; 27:174-183

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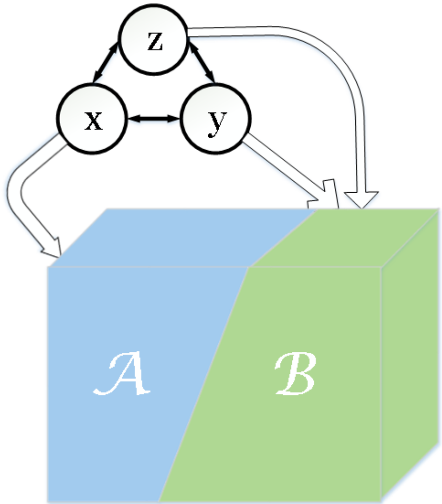
Results: Synthetic Dataset



$$
\begin{gathered}
r_X = \theta_1 m_s + (1-\theta_1) l_s + \epsilon_1 \\
r_Y = \theta_2 n_s + (1-\theta_2) l_s + \epsilon_2 \\
r_Z = \theta_3 n_s + (1-\theta_3) l_s + \epsilon_3 \\
x_A = \alpha[\theta_A m_s + (1-\theta_A) l_s] + (1-\alpha) k_s + \epsilon_A \\
x_B = \beta[\theta_B n_s + (1-\theta_B) l_s] + (1-\beta) r_s + \epsilon_B \\
l_s, m_s, n_s, k_s, r_s \sim \mathcal{N}(0,1) \\
\epsilon_1, \epsilon_2, \epsilon_3, \epsilon_A, \epsilon_B \sim \mathcal{N}(0, \sigma_N^2) \\
\theta_1, \theta_2, \theta_3, \theta_A, \theta_B, \alpha, \beta \sim \mathcal{U}[0.5, 0.9].
\end{gathered}
$$

Percentage of errors for synthetic datasets

	Two subROIs		
	IA	IB	IC
Proposed method	**0%**	**0.32%**	**2.50%**
k-means clustering	0%	1.50%	9.99%
Modularity detection	0%	0.002%	5.97%
Spatially regularized regression	2.87%	3.80%	2.90%

$$
Error = \frac{Total\ number\ of\ misclassified\ voxels}{Total\ number\ of\ voxels\ in\ \mathcal{V}} \times 100\%
$$

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L-means: Kahnt *et al.*, J.NeuroSc.2012;32(18):6240-6250.
Modularity method - Barnes *et al.*, Front.Sys.NeuroSc.2010; 4:7-11.
Spatial regression - Zhang *et al.*,Biomed.Sys.Proc.Contrl.2016; 27:174-183

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Results: fMRI Dataset

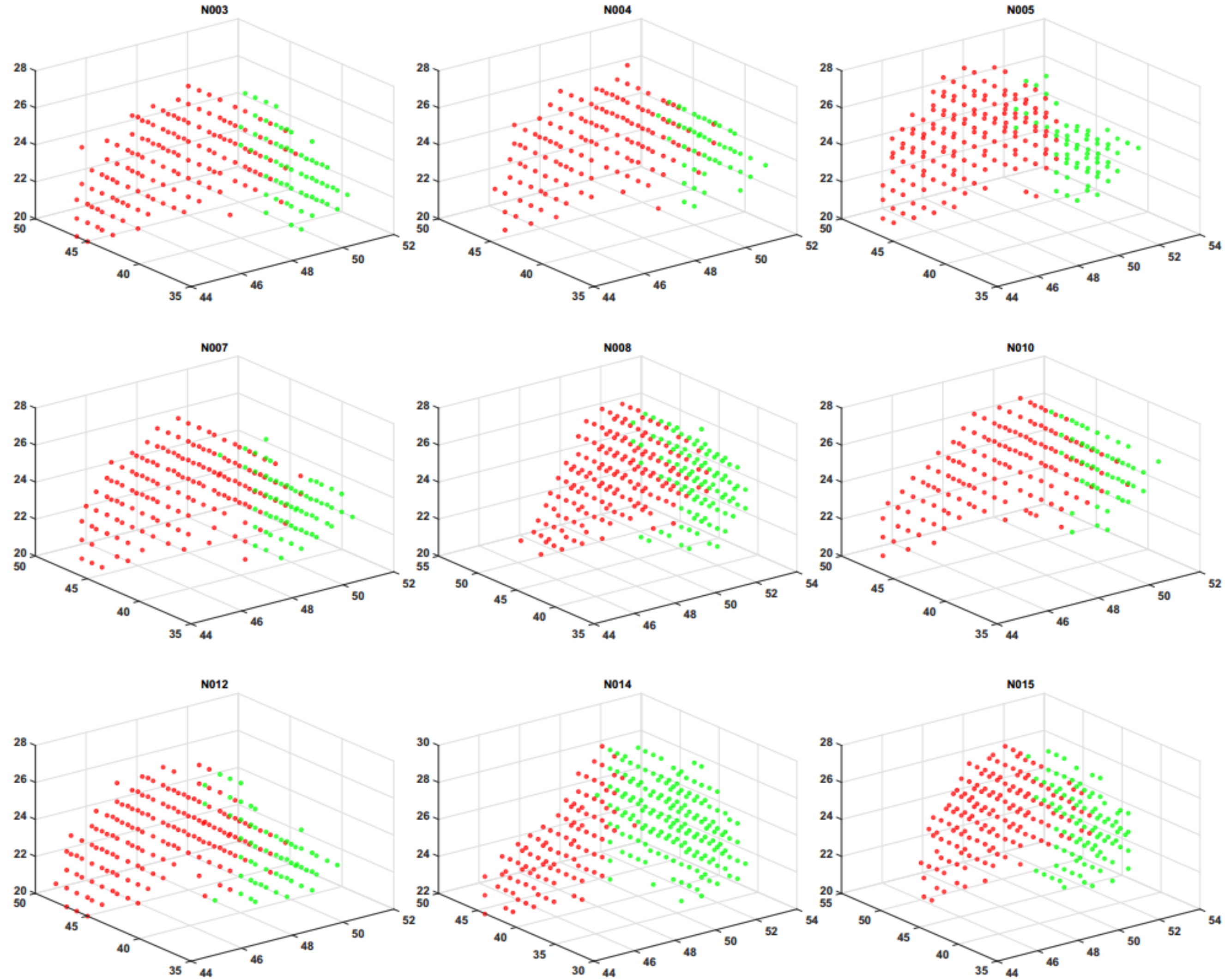

Figure : Putamen parcellation results using the proposed framework for nine healthy subjects. The red dots represent the dorsomedial striatum (DMS) subROI and the green dots represent the dorsolateral striatum (DLS) subROI.

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Results: fMRI Dataset

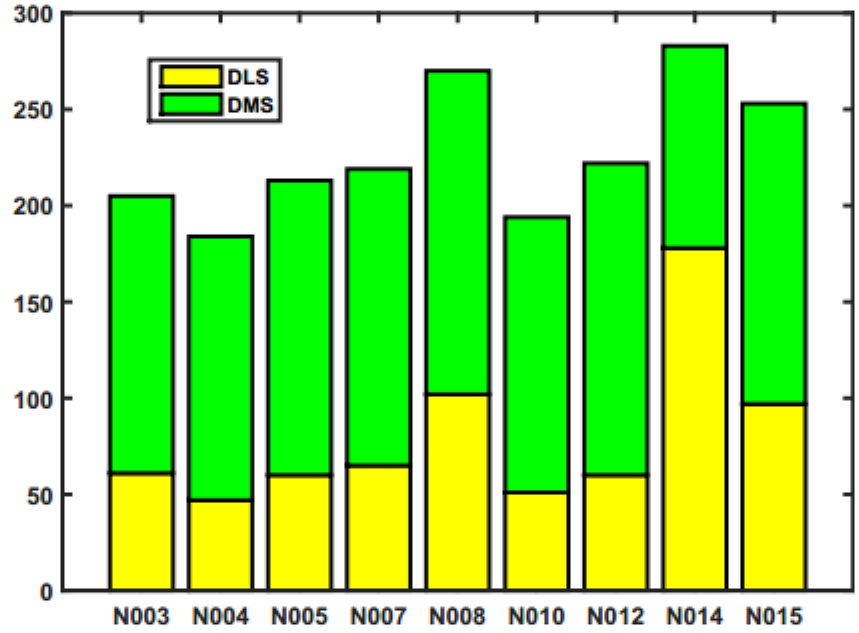

Figure : Bar graph of DLS and DMS voxels in left-putamen region. The yellow bar represents the total number of DLS voxels and green bar represents the total number of DMS voxels.

Results: fMRI Dataset

Two versions of fMRI

- Odd time points: t=1,3,5,…
- Even time points: t =2,4,6,…

Results: fMRI Dataset

- To compare the clustering results we define the percentage of similarly classified voxels as:

$$\epsilon = \frac{S}{N} \times 100\%$$

S : total number of voxels that belong to the same cluster for both cases
N : the total number of voxels in putamen

Results: fMRI Dataset

- To compare the clustering results we define the percentage of similarly classified voxels as:

$$\epsilon = \frac{S}{N} \times 100\%$$

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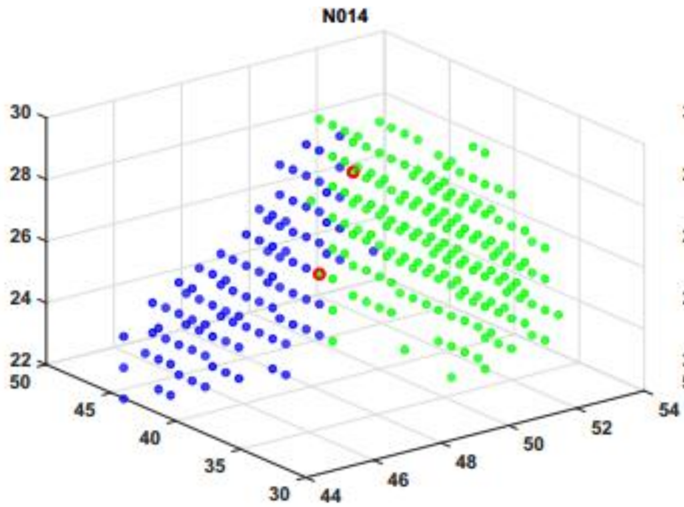
Percentage of similarly clustered voxels (ϵ) in two downsampled fMRI datasets.

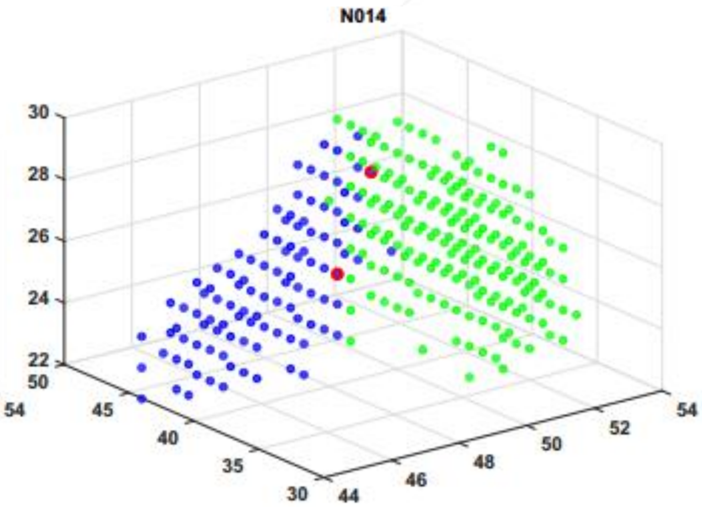
Subject	N003	N004	N005	N007	N008	N010	N012	N014	N015
Similarly clustered voxel percentage, ϵ	99.02%	100%	98.12%	100%	98.89%	98.45%	99.10%	99.29%	98.81%

Average ϵ 99.08%

Results: fMRI Dataset



(a)



(b)

Figure : One example of the robustness analysis. (a) Parcellation using the odd time-points of the fMRI signals from the putamen voxels. (b) parcellation using the even time-points of the fMRI signals from the putamen voxels. The blue dots represent the dorsomedial striatum (DMS) subROI and the green dots represent the dorsolateral striatum (DLS) subROI. The voxels that belong to different clusters in these two cases are outlined with red color.

Conclusion & Future Works

- We proposed a connectivity network generation idea that takes into account the connectivity and spatial distance between voxels in the target ROI as well as their dissimilarity in connectivities with other brain reference ROIs.
- A community detection algorithm based on the ratio of eigenvectors of the associated adjacency matrix is then applied to sub-divide the network into several functionally connected and spatially continuous subROIs.

Conclusion & Future Works

- Putamen/caudate parcellation for patients with Parkinson's disease
  - Analysis of DLS/DMS ratio
  - Analysis of overlapping voxels

Thank You!