Network Modeling and Functional Data Methods for Brain Functional Connectivity Studies

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Brain connectivity studies

"Over the past 20 years, neuroimaging has become a predominant technique in systems neuroscience. One might envisage that over the next 20 years the neuroimaging of distributed processing and connectivity will play a major role in disclosing the brains functional architecture and operational principles." – Friston 2011, Brain connectivity

Brain connectivity studies

- Human connectome project (HCP): publicaly available data sets, processing pipelines and code.
- Structure connectivity, functional connectivity, effective connectivity.

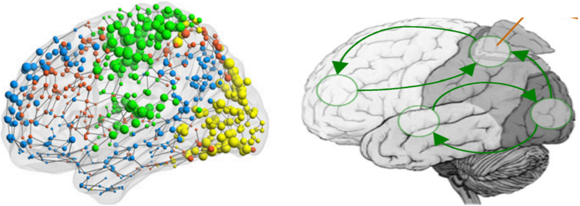


Figure: Crossley 2013, Friston 2011

- Functional connectivity is some type of statistical dependence among measured time series.

Functional connectivity measure

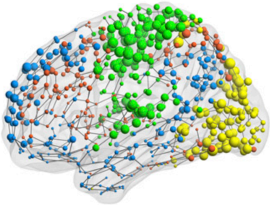
- Various methods have been proposed to characterize the functional connectivity measured with different modalities (EEG/MEG, fMRI etc).
- Correlation, partial correaltion, mutual information, coherence, phase locking values, among others.
- Functional data approach for correlation (He et al. 2016).
- Wang et al. 2014 (Frontiers in neuroscience): 42 methods, no-single measure is optimal for all types of data.
- Bastos et al. 2016 (Frontiers in systems Neuroscience): more on neuronal oscillartory.

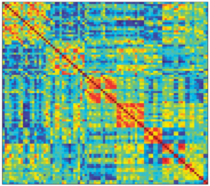
Brain segregation and integration

- Long history of functional segregation and the localization of function.
- Accurate parcellation provides
  - efficient comparisons across subjects and studies.
  - a foundation for illuminating the functional and structural organization of the brain
  - a means to reduce data complexity while improving statistical sensitivity and power for many neuroimaging studies.
- A single function may involve many specialized areas and their functional integration among them.
- Areas differ from their neighbors in microstructural architecture, functional specialization, connectivity with other areas.
- (Glasser 2016, Nature) used multi-source and multi-methods to detect 180 areas.

Community detection & brain parcellation

- $G = (V, E)$, represented by an adjacency matrix $A = (a_{ij})_{m \times m}$
- Node: depends on resolution
- Edge: depends on the measure and threshold
- Most modularity based approaches: more inter-community links, less intra-community links
- Stochastic block model: the connectivity patten is similar within communities.





Special features in brain connectivity problem

- The nodes are naturally embedded in a three-dimensional brain space
- Connectivity between adjacent nodes is sometimes over-represented due to technical reasons.
- Account for the spurious connectivity in adjacent nodes by removing the effect of spatial location so as to recover functionally distinct brain regions (“communities”).
- Especially relavant when doing subdivision parcellation (small areas).
- Feature adjusted stochastic block model (FASBM)

The stochastic block model

- Data: adjacency matrix $A \in \{0,1\}^{n\times n}$, where A_{ij} indicates the presence/absence of an edge between node i and node j.
- $A_{ii} = 0$, $A_{ij} = A_{ji}$, $\forall\ i,j$.
- Each node i belongs to a community with label $r_i \in \{1,\ldots,K\}$.
- Given $R = (r_1,\ldots,r_n)$ and B,

$$A_{ij} \sim \text{Bernoulli}(B_{r_i,r_j}), \ \ \text{independently}.$$

- $B \in [0,1]^{K\times K}$, symmetric, is the community-wise connectivity.
- Nodes in the same community have similar connectivity patterns.

Feature adjusted stochastic block model

The network Y is generated by

$$Y_{ij} = \begin{cases} \text{exponential family with mean } \mu_{ij} & \text{if} \quad i < j \\ 0 & \text{if} \quad i = j \\ Y_{ji} & \text{if} \quad i > j \end{cases}$$

FASBM is formulated as

$$E(Y_{ij}) = \mu_{ij} = g^{-1}(\theta_{r_i r_j} + f(\beta^T z_{ij})), \quad \text{with } \|\beta\| = 1.$$

Feature adjusted stochastic block model

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- SBM is a special case of FASBM
- Model relational data with single parameter exponential family; allow for a scaling parameter.
- Nonparametric estimation of the node feature effect.
- Can take multiple node features.

Model Fitting

- Maximum likelihood estimation in terms of (g, θ, β, f) : but no close form solution.
- Alternates between two stages of maximization:
  1. First with respect to the parameters in the block model component, g and θ,
  2. and then with respect to the parameters in the single-index model component, f and β.
- We adapt the labeling switch algorithms (Bickel& Chen 2009) for the SBM to stage 1 and the estimation procedures for fitting single-index models (Carrol et al 1997) to stage 2.
- Paper and matlab package available upon request.

Simulation setting

- Generate network with m nodes and K community.
- $Y_{ij} \sim \text{Bernoulli}(g^{-1}(\theta_{r_i r_j} + f(d_{ij})))$.
- $\theta = \text{logit}\begin{pmatrix} 0.5 & 0.2 \\ 0.2 & 0.2 \end{pmatrix}$ and $\theta = \text{logit}\begin{pmatrix} 0.5 & 0.2 & 0.2 \\ 0.2 & 0.3 & 0.2 \\ 0.2 & 0.2 & 0.1 \end{pmatrix}$.
- Compute d_{ij} as distance between node i and node j
- Let $f = a\sin(-8d_{ij})$, with a taking different values, $0, 1.4$ or 1.8

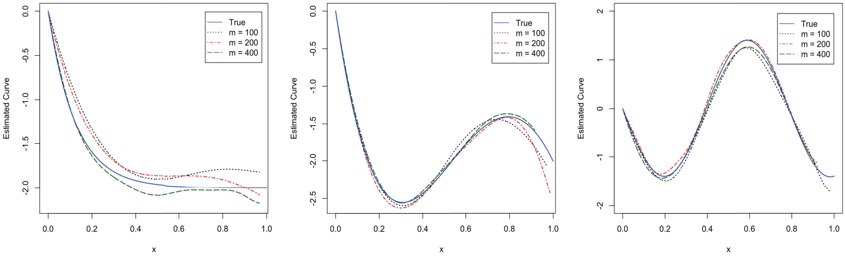
Simulation result for $K = 2$

		$m = 100$			$m = 200$			$m = 400$		
		FASBML	SBML	SPEC	FASBML	SBML	SPEC	FASBML	SBML	SPEC
$a = 0$	$\overline{Mis_p}$	**0.012**	**0.012**	0.041	**0.0004**	**0.0004**	0.006	**0**	**0**	0.0003
	NMI	**0.924**	**0.924**	0.783	**0.997**	**0.997**	0.955	**1**	**1**	0.998
$a = 1.4$	$\overline{Mis_p}$	0.157	0.443	**0.128**	**0.012**	0.469	0.079	**0.0001**	0.481	0.045
	NMI	**0.592**	0.038	0.470	**0.962**	0.005	0.625	**0.999**	0.002	0.75
$a = 1.8$	$\overline{Mis_p}$	**0.174**	0.461	0.182	**0.036**	0.469	0.132	**0.005**	0.482	0.105
	NMI	**0.524**	0.007	0.349	**0.908**	0.004	0.464	**0.989**	0.002	0.549

Simulation result for $K = 3$

		$m=100$			$m=200$			$m=400$		
		FASBML	SBML	SPEC	FASBML	SBML	SPEC	FASBML	SBML	SPEC
$a=0$	$\overline{Mis_p}$	**0.262**	0.265	0.298	**0.073**	0.075	0.185	**0.011**	**0.011**	0.074
	NMI	**0.546**	0.544	0.404	**0.825**	0.824	0.545	**0.954**	0.953	0.753
$a=1.4$	$\overline{Mis_p}$	**0.380**	0.535	0.407	**0.167**	0.524	0.352	**0.038**	0.534	0.335
	NMI	**0.332**	0.099	0.272	**0.682**	0.117	0.331	**0.910**	0.117	0.351
$a=1.8$	$\overline{Mis_p}$	**0.421**	0.566	0.450	**0.197**	0.573	0.434	**0.020**	0.592	0.436
	NMI	**0.260**	0.053	0.209	**0.625**	0.050	0.244	**0.919**	0.038	0.270

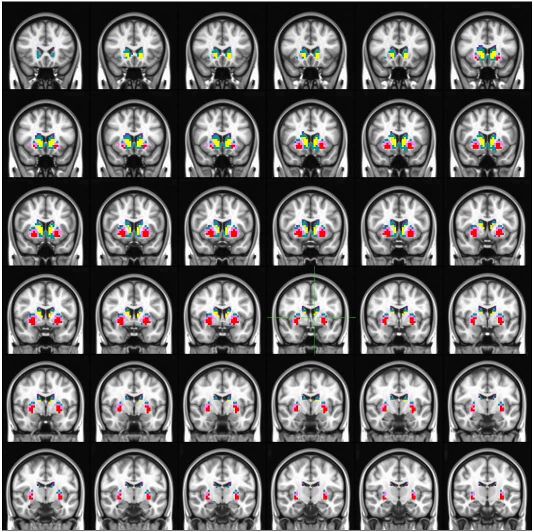
Fitted nonparametric functions

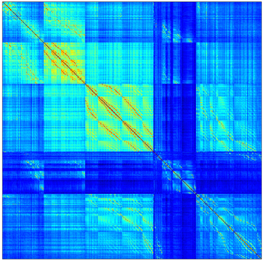


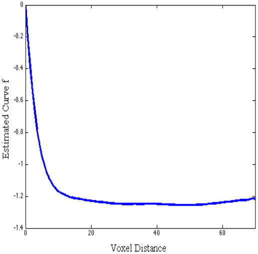
(a) $f(x) = 2\exp(-8x) - 2$
(b) $f(x) = 10x^4 - 42x^3 + 50x^2 - 20x$
(c) $f(x) = 1.4sin(-8x)$

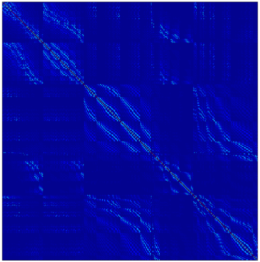
Data application

- Data collected at the University of Pittsburgh Medical Center
- Rs-fMRI data were preprocessed using AFNI and FSL, normalized to MNI152 template.
- We conduct our analyses on $m = 448$ gray matter voxels in the basal ganglia mask.
- The basal ganglia subserve a wide range of functions, including motor, cognitive, motivational, and emotional processes.
- We tried to parcellatesubdivisions in basal ganglia solely based on the functional connectivity matrix.

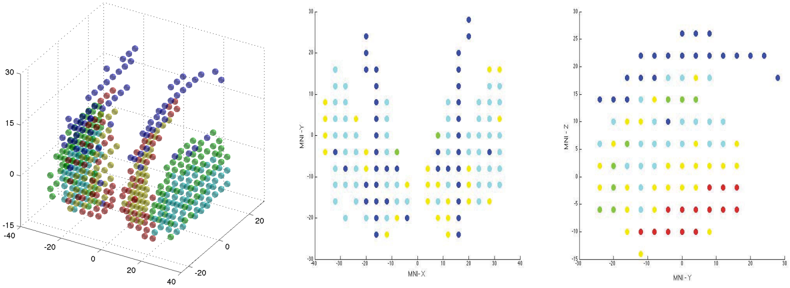








$$E(Y_{ij}) = \theta_{g_i g_j} + f(z_{ij}).$$



Community 1 (yellow) corresponds to caudate body, Community 3 (green) is putamen, Community 5 (cyan) is pallidum and Community 2 (red), 4 (blue) could be caudate head, but also spread out to places outside of caudate.

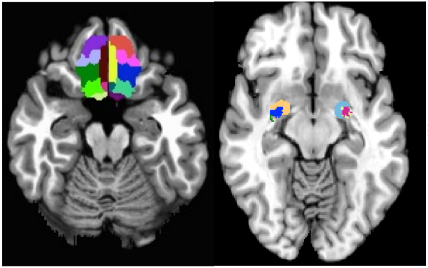
Functional connectivity and cognitive study

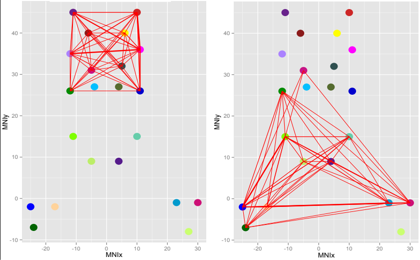
- How the complex functional connectivity patterns are related to the capacity for information processing.
- How does functional connectivity (network organization) develop with age, and interact with covaraites such as behavioral measures, cognitive function and mental distorter status?
- Topological measures: small worldness (global clustering coefficient); High-degree hub nodes; Community structure/modules; Connectivity threshold functions (Petersen et.al 2016), other measures?
- Group analysis of brain functional connectivity can borrow ideas and tools from functional data analysis.

Adaptation of localized FPCA (ongoing work)

- The nodes in brain network has natural spatial embedding and features spatial smoothness.
- Extract modes of variation in brain networks that are localized to regions of interest.
- Localized functional principal component analysis (Chen & Lei 2015).

Preliminary results on rs-fMRI connecitivty





THANK YOU!

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Network cross-validation for selecting K

- Adapt the NCV method developed in Chen & Lei (2016).
- Block-wise node-pair splitting
- Very flexible, can be used for stochastic block model, degree-corrected block model and extendable to FASBM.
- R code and Matlab code are avaiable.