The Multiregression Dynamic Models in Group Analysis

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Outline

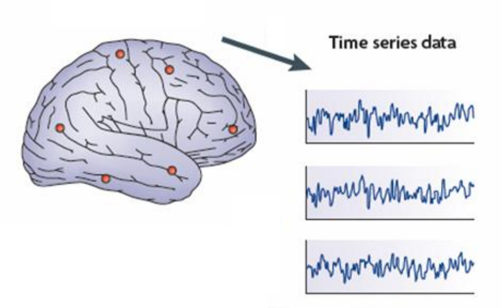
Defining Graphical Models

A graphical model is a probabilistic model for which a graph expresses the conditional dependence structure between random variables.

- Nodes: Individuals, Groups of People, Brain Regions, ...
- Edges: Undirected, Directed, Weighted, ...

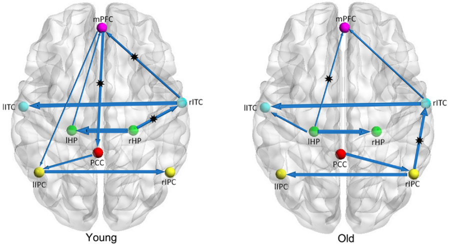
Resting State fMRI

- The main function of the brain: Reflexive (task-evoked responses) X Intrinsic (resting state);
- functional Magnetic Resonance Imaging (fMRI);
- Brain Connectivity.



Brain connectivity

Brain connectivity studies the relation between distinct units within a nervous system considering anatomical links (anatomical connectivity), statistical dependencies (functional connectivity) or causal interactions (effective connectivity) (Olaf Sporns, 2007).



The brain connectivity of the DMN in the young (left panel) and old (right panel) groups (Wang *et al.*, 2014).

Multiregression Dynamic Model

- In MDM, the joint predictive likelihood is written in a closed form and so it can be easily used for Bayes' factor model selection;
- MDM assumes non-Gaussianity which is currently used as a feature to fit models (*e.g.* through ICA);
- It is known in the context of these processes that although the existence of a connection seems to be enduring the strength of a connection is dynamic. The MDM class directly models this phenomenon;
- It can distinguish models that are equivalent when the model degenerates into the static case. Furthermore the way it distinguishes these is consistent with there being an underlying causal directionality in a way made clear by Pearl(2000) which makes the difference in statically equivalent models interpretable.

Linear MDM

Observation equations

$$Y_t(r) = \mathbf{F}_t(r)'\boldsymbol{\theta}_t(r) + v_t(r), \qquad v_t(r) \sim \mathcal{N}(0, V_t(r));$$

System equation

$$\boldsymbol{\theta}_t = \boldsymbol{\theta}_{t-1} + \mathbf{w}_t, \quad \mathbf{w}_t \sim \mathcal{N}(\mathbf{0}, \mathbf{W}_t) \text{ and } \mathbf{W}_t(r) = V_t(r)\mathbf{W}_t^*(r);$$

Initial information

$$(\boldsymbol{\theta}_0|y_0) \sim \mathcal{N}(\mathbf{m}_0, \mathbf{C}_0) \text{ and } \mathbf{C}_0(r) = V_t(r)\mathbf{C}_0^*(r).$$

- Unknown $V_t(r)$: $(\phi(r)|y_0) \sim \mathcal{G}\left(\frac{n_0(r)}{2}, \frac{d_0(r)}{2}\right), \quad \phi(r) = V(r)^{-1};$
- Unknown $\mathbf{W}_t(r)$: $\mathbf{W}_t^* = \frac{1-\delta}{\delta}\mathbf{C}_{t-1}^*$; where the discount factor $\delta \in (0, 1]$.

Node	Parent	Score
1	No	-1469
	2	-1567
	3	-1646
	2 and 3	-1655
2	No	-1169
	1	-1140
	3	-1110
	1 and 3	-997
3	No	-1119
	1	-1193
	2	-1060
	1 and 2	-1056

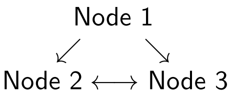
Evidence for each node under all possible sets of parents. The higher score the higher evidence for this particular model.

The Search Methods

- The MDM-IPA (Integer Programing Algorithms; Cussens, 2011): DAG constraints:

  Node 1 $\rightarrow$ Node 2 $\leftarrow$ Node 3;

- The MDM-DGM: the best model for each node:



Group Analysis Methods

- **Virtual-typical-subject (VTS)**:
  The same graphical structure and connectivity strength

  All Subjects and so Group Network:
  Node 1 $\rightarrow$ Node 2 $\rightarrow$ Node 3

- **Common-structure (CS)**:
  The same graphical structure but different connectivity strength

  Subject 1: Node 1$\rightarrow$ Node 2$\rightarrow$ Node 3;
  Subject 2: Node 1$\rightarrow$ Node 2$\rightarrow$ Node 3;
  Subject 3: Node 1$\rightarrow$ Node 2$\rightarrow$ Node 3;
  ...
  Group Network: Node 1$\rightarrow$ Node 2$\rightarrow$ Node 3

Group Analysis Methods

Different graphical structure and connectivity strength

Subject 1: Node 1$\rightarrow$ Node 2$\rightarrow$ Node 3;

Subject 2: Node 1$\rightarrow$ Node 2$\rightarrow$ Node 3;

Subject 3: Node 1 $\leftarrow$Node 2 $\leftarrow$Node 3;

...

- **Individual-structure (IS)**:
  The learning network results are pooled into a single network

  Group Network: Node 1$\rightarrow$ Node 2$\rightarrow$ Node 3

- **Group-structure (GS)**:
  It studies group homogeneity through cluster analysis

  Subgroup Network1: Node 1$\rightarrow$ Node 2$\rightarrow$ Node 3
  Subgroup Network2: Node 1 $\leftarrow$Node 2 $\leftarrow$Node 3

Formulation for separations between subjects

One simple way for defining a suitable separation between subject i &j is

$$d_{ij} = c_{ij}(m_I) - c_{ij}(m_G)$$

where $c_{ij}(m_I)$ is the max log marginal likelihood score of subject i & j when these are treated as from different graphs & $c_{ij}(m_G)$ is the max score of the two subjects treated as if the same

$$c_{ij}(m_I) = \sum_{r=1}^{n} \{c_i(r, m_{iI}(r)) + c_j(r, m_{jI}(r))\}$$

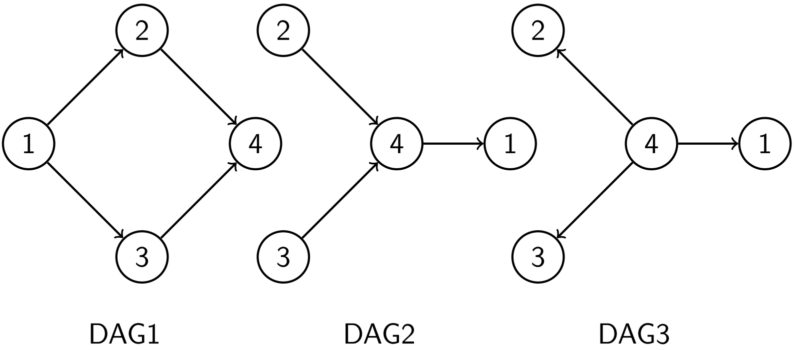
Fact

These are linear functions of quantities we have already calculated so available!

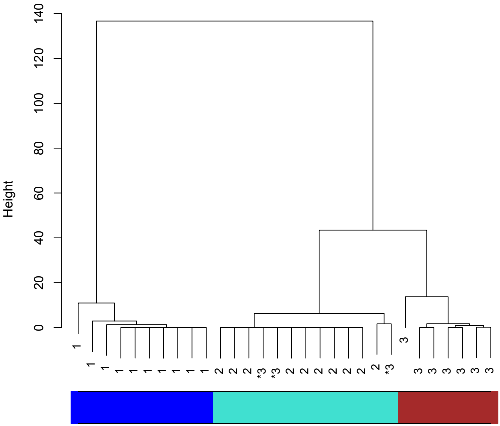
Some properties of the separation measure

- For the MDM-IPA, the scores are exactly the LPL
- The pairwise logBF separation is symmetric
- If the estimated individual graphical structures for subjects i and j are the same, then $d(i,j) = 0$
- By definition, the separation $d(i,j)$ is non-negative

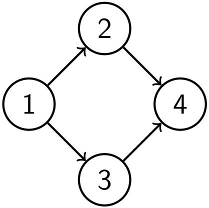
Results from simulation study



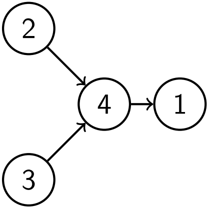
Results from simulation study



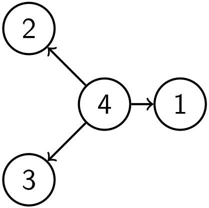
Results from simulation study



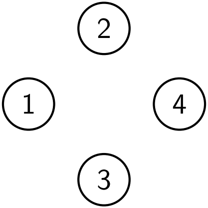
GS1



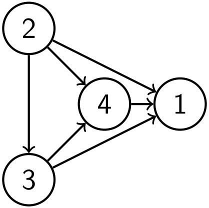
GS2



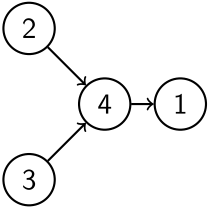
GS3



VTS

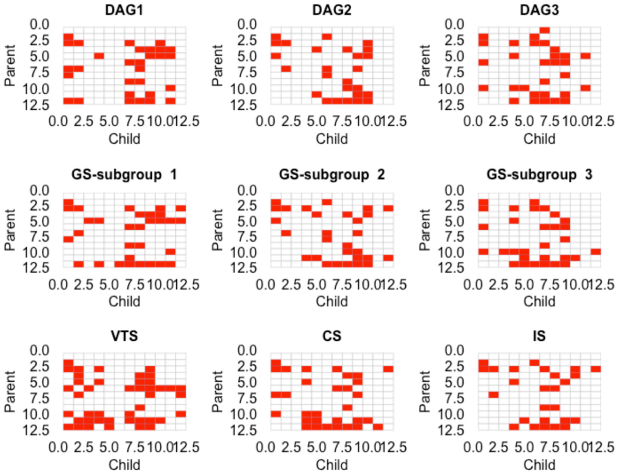


CS



IS

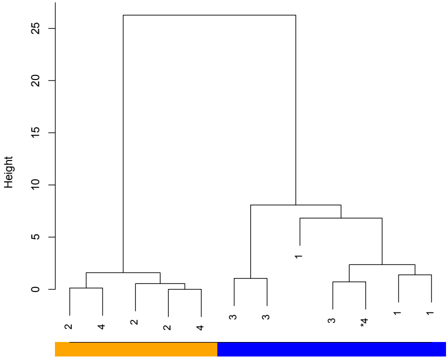
Results from II simulation study



Data Description

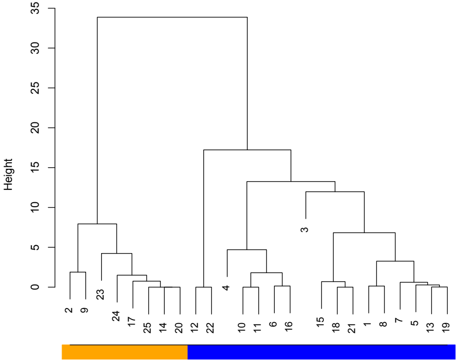
- There is information for three sessions for each one of 25 subjects;
- 197 fMRI resting-state time-points;
- 4 ROI's:
  - Region 1 - Posterior Cingulate (PC);
  - Region 2 - Anterior Frontal (AF);
  - Region 3 - Left Lateral Parietal (LP);
  - Region 4 - Right Lateral Parietal (RP);

Results



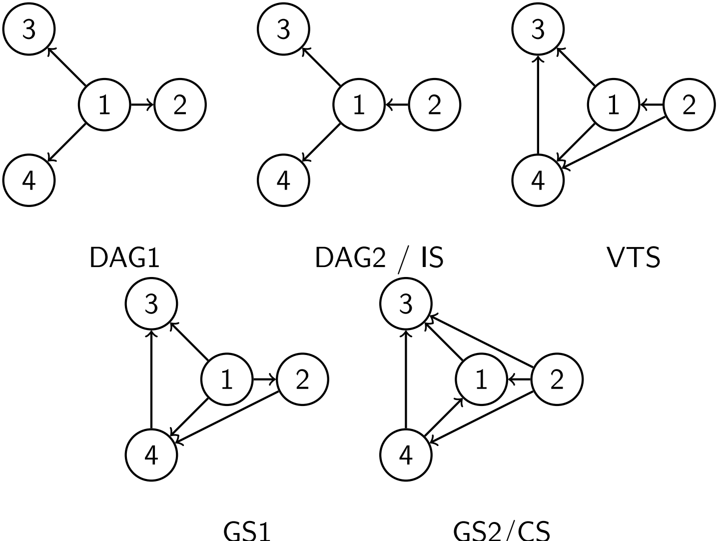
Dendogram of real fMRI dada using the pairwise logBF separation for 3 sessions of each 4 subjects selected randomly.

Results

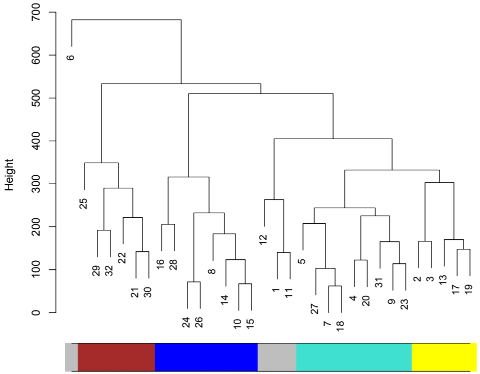


Dendogram of real fMRI dada using the pairwise logBF separation for all 25 subjects.

Results from Real Datasets

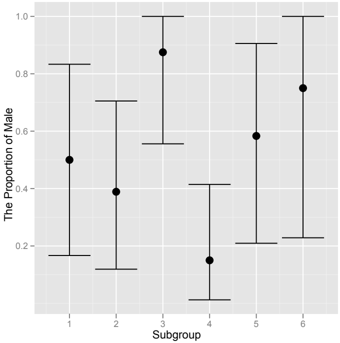


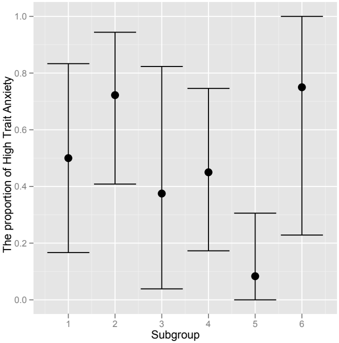
Results from II Real Datasets



Dendogram of real fMRI dada using the pairwise logBF separation for 12 subjects.

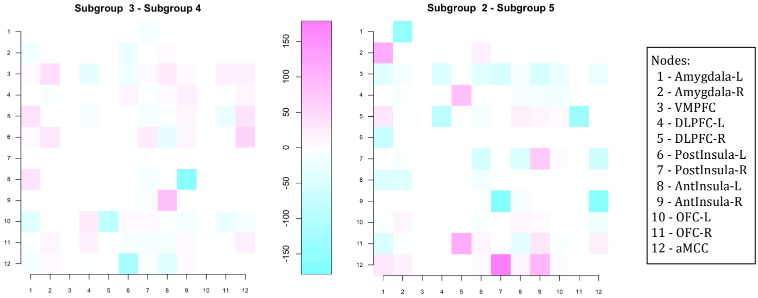
Results from II Real Datasets





The proportion of male (left) and the proportion of subjects who have high trait anxiety (right) by subgroup.

Results from II Real Datasets



The connectivity strength standardised difference for a particular edge $i \rightarrow j$, where i indexes rows and j columns

HMDM

Observation equations

$$\mathbf{Y}_t = \mathbf{F}'_{1t}\boldsymbol{\theta}_{1t} + \mathbf{v}_{1t}, \qquad \mathbf{v}_{1t} \sim \mathcal{N}(\mathbf{0}, \mathbf{V}_{1t});$$

Structural equations

$$\boldsymbol{\theta}_{1t} = \mathbf{F}'_{2t}\boldsymbol{\theta}_{2t} + \mathbf{v}_{2t}, \qquad \mathbf{v}_{2t} \sim \mathcal{N}(\mathbf{0}, \mathbf{V}_{2t});$$

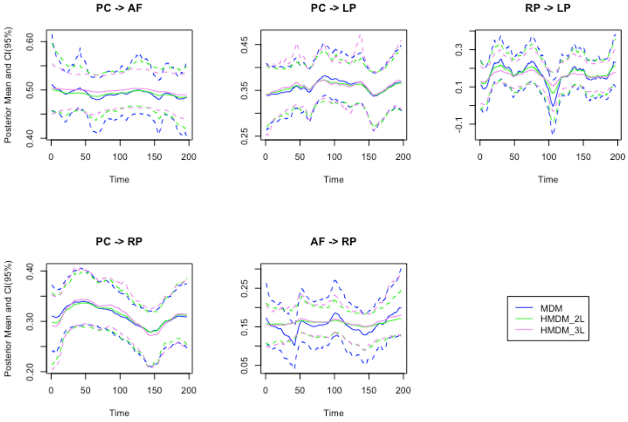
$$\vdots$$

$$\boldsymbol{\theta}_{kt} = \mathbf{F}'_{kt}\boldsymbol{\theta}_{kt} + \mathbf{v}_{kt}, \qquad \mathbf{v}_{kt} \sim \mathcal{N}(\mathbf{0}, \mathbf{V}_{kt});$$

System equation

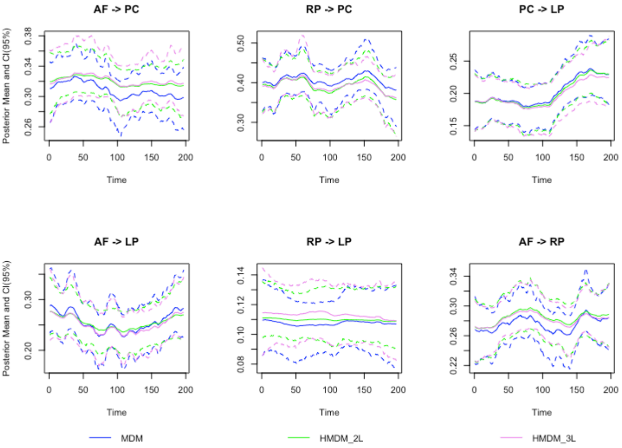
$$\boldsymbol{\theta}_{kt} = \mathbf{G}_t\boldsymbol{\theta}_{k,t-1} + \mathbf{w}_t, \qquad \mathbf{w}_t \sim \mathcal{N}(\mathbf{0}, \mathbf{W}_t).$$

Results



The posterior mean and 95% CI for connectivities of GS-subgroup 1.

Results



The posterior mean and 95% CI for connectivities of GS-subgroup 2.

Results

Model	DIC		Running Time (hour)	
	GS-subgroup1	GS-subgroup2	GS-subgroup1	GS-subgroup2
MDM	49,992	110,771	0.39	0.97
HMDM_2L	49,671	110,342	1.06	2.67
HMDM_3L	368,394	265,739	2.64	9.98

The Deviance Information Criterion (DIC) and the running time (in hour) for the HMDM with two level for brain and subject and the HMDM with three level for brain, session and subject.

Conclusions

- The simulated data given ground truth resurrected the appropriate clusters
- In real data example - although replicates on individual subjects gave different graphs - these subjects were nearly always clustered together. This necessary condition suggests we might be getting things right! Same treatment for same subject.
- In general, the HMDM provides statistics more precise than the MDM.

References

Costa L, Smith,J.Q. Nicholls, T. & Cussens J. (2015) "Searching Multiregression Dynamic Models of Resting-State fMRI Networks Using Integer Programming" Bayesian Analysis Vol. 10, No. 2, 441-478

Oates CJ. Smith, JQ. Mukherjee, S. & Cussens. J (2015) "Exact Estimation of Multiple Directed Acyclic Graphs". Statistics and Computing DOI 10,1007/s 11322 -015 -9570 - 9

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Costa Costa, Lilia, J.Q. Smith, and T. Nichols (2019). "A group analysis using the Multiregression Dynamic Models for fMRI networked time series." Journal of statistical planning and inference 198, 43-61

Thank You!

VII ENCONTRO DA PÓS-GRADUAÇÃO EM MATEMÁTICA DA UFBA
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