Hemodynamics at rest and voxel-wise Granger causality: possible solutions to known issues in fMRI dynamical connectivity

Daniele Marinazzo
Department of Data Analysis
University of Ghent, Belgium
daniele.marinazzo@ugent.be

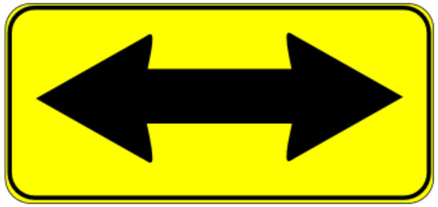
Issues in fMRI dynamical connectivity

- Many variables, few samples

- Confounding effect of the HRF

- Bad temporal resolution

Network inference from temporally correlated data



Correlations

Coherence

Phase synchronization

Generalized synchronization

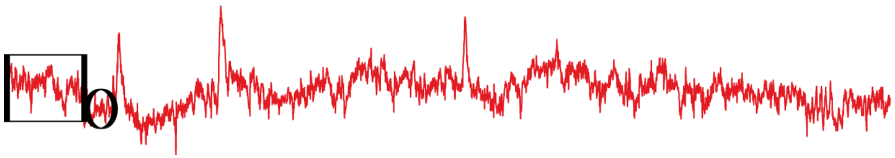
Mutual information

Transfer entropy

Granger causality - DCM

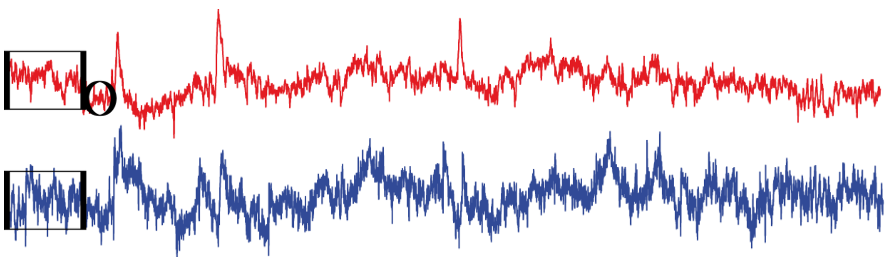
Predicting the future of a time series

Using only its past…



$$x = AX + \varepsilon_X$$

… or including the past of another time series

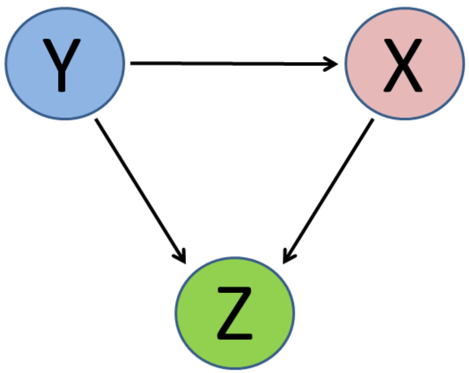


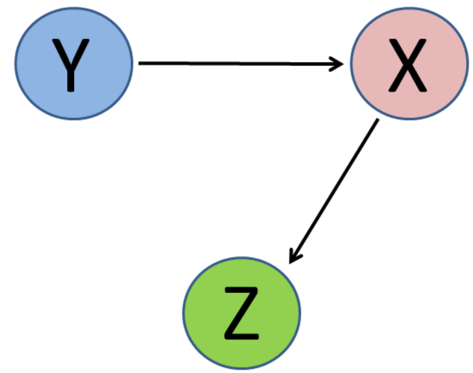
$$x = B[X\ Y] + \varepsilon_{X,Y}$$

$\varepsilon_{X,Y} < \varepsilon_X$ $\rightarrow$ Y Granger-causes X

Granger Causality in multivariate datasets

We must condition GC to the presence of other variables

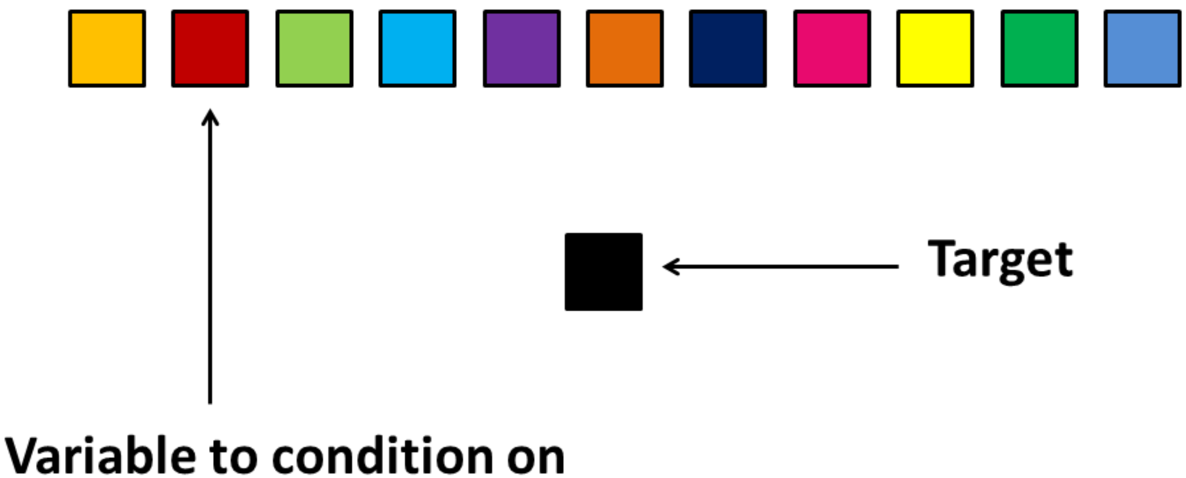




This problem has been known from the start, and the solution is usually the conditioned approach (Geweke 1982)

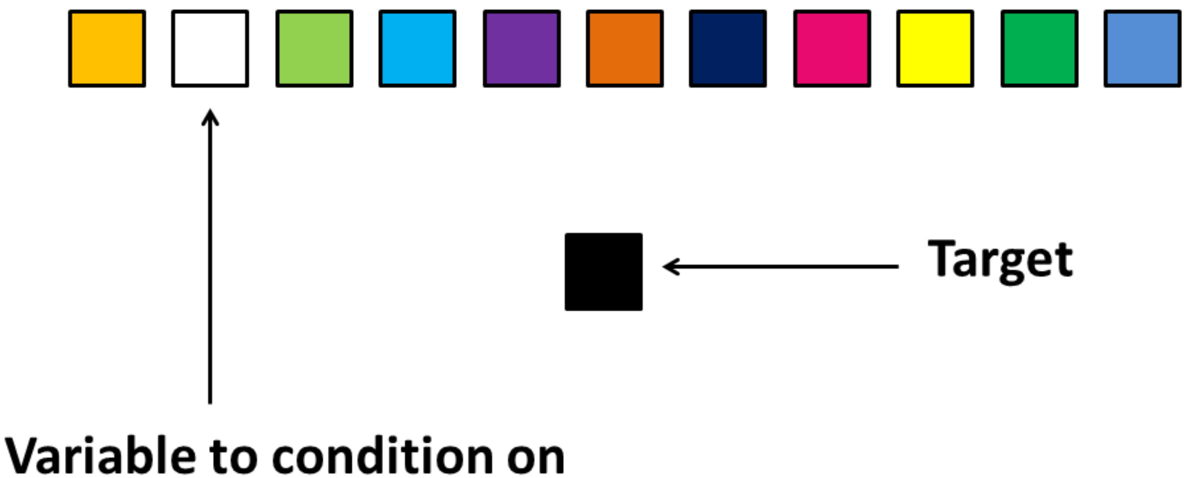
Full conditioning in a multivariate dataset

We compare the model including …



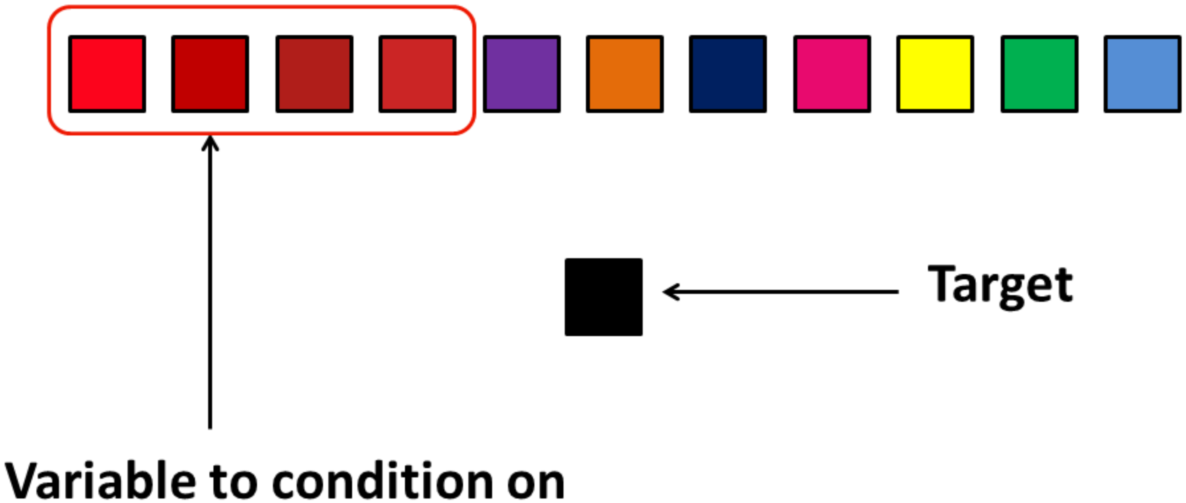
Full conditioning in a multivariate dataset

… and excluding the conditioning variable



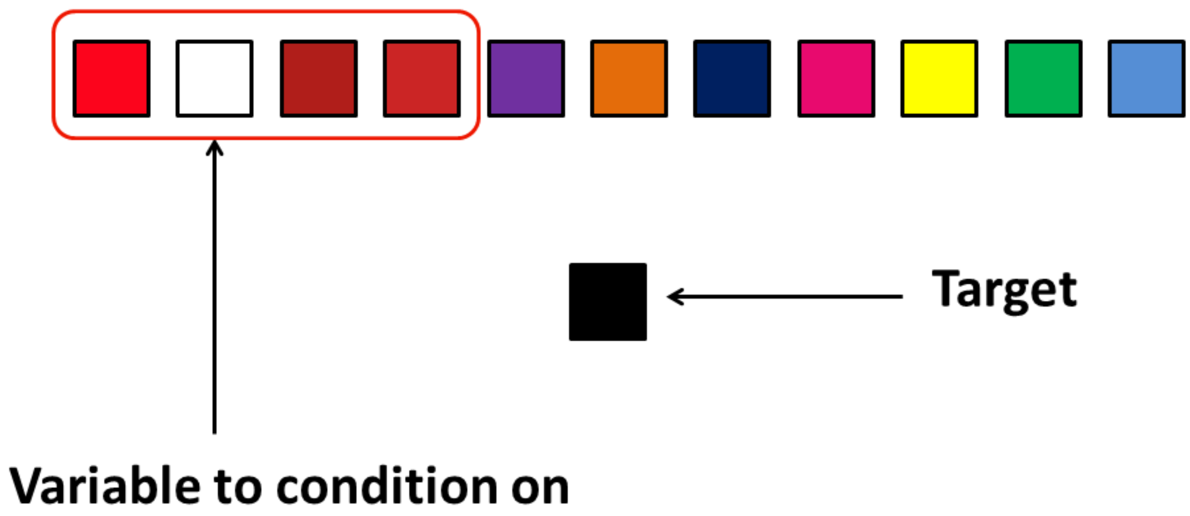
Presence of redundancy

When a number N of variables share the same info on the target …



Presence of redundancy

… we still have info on the target from the remaining N-1,

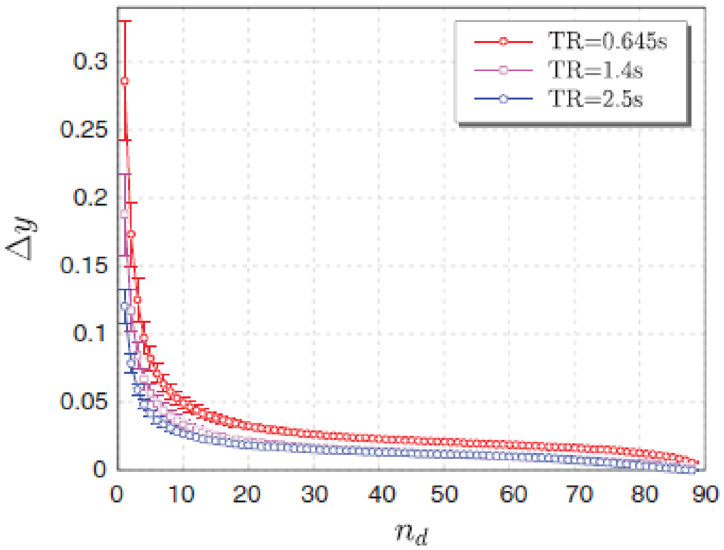


and in turn all the N variables will be judged as not relevant for the prediction of the target

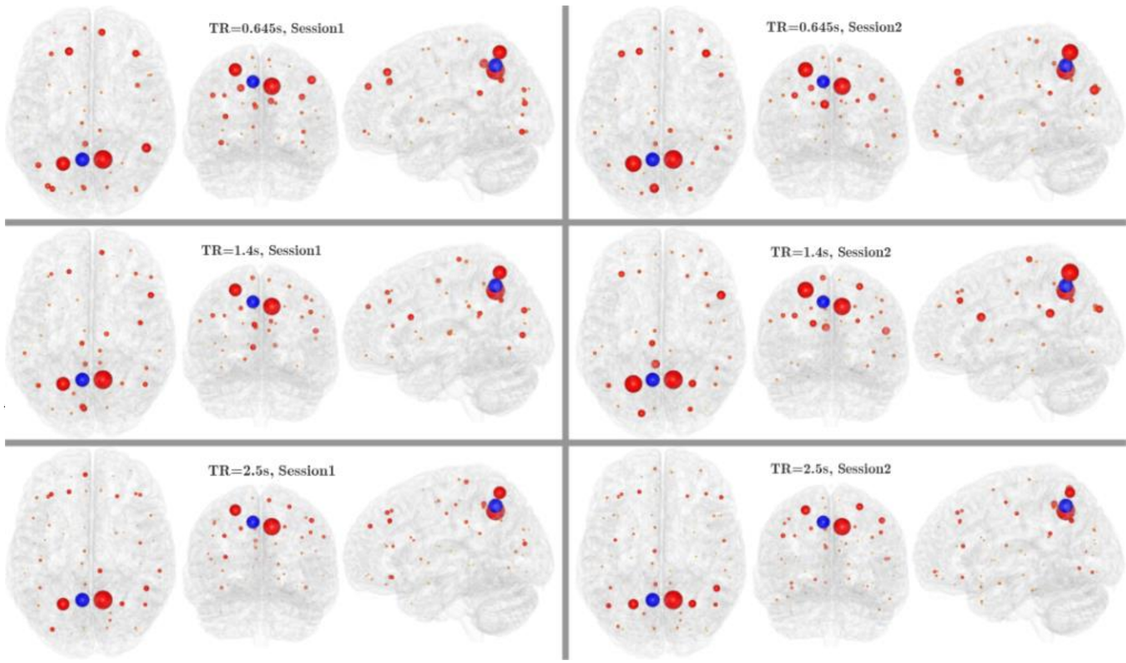
Partially conditioned Granger causality

- Redundancy in multivariate datasets leads to false GC estimations
- Conditioning on the most informative variables for each candidate driver

Residual information gain when another variable is added to the model



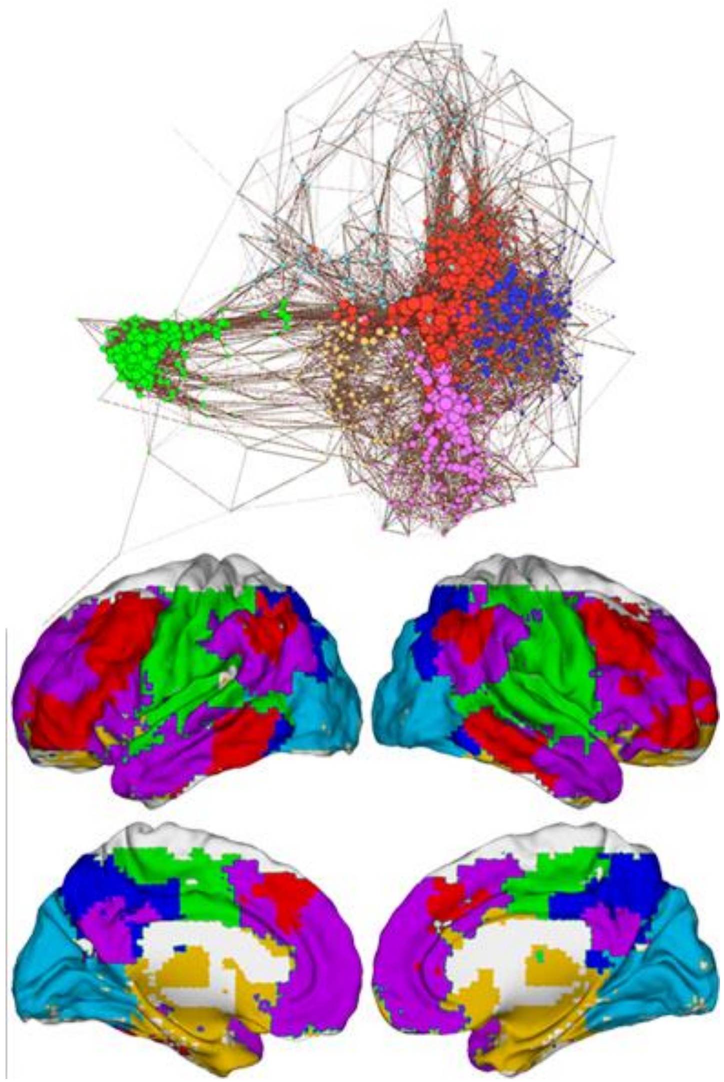
Most informative regions consistently distributed across the brain



Wu et al. Brain Connectivity 2013

From regional to voxel level

The modular structure of brain networks is used as a prior for further dimensionality reduction



Wu et al. PLOS One 2013

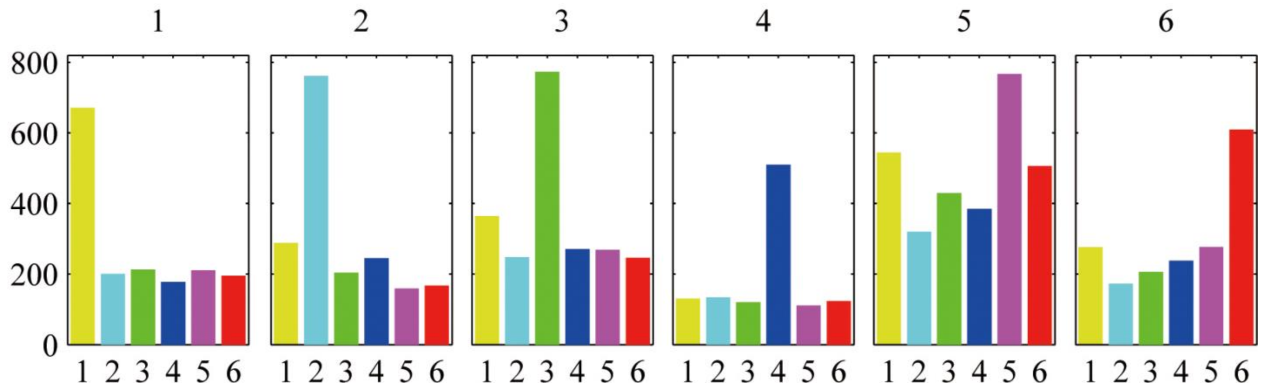
- fix the number of variables, to be used for conditioning, equal to n_d.
- We denote $\mathbf{Z} = \left(X_{i_1}, \ldots, X_{i_{n_d}}\right)$ the set of the n_d variables, in $\mathbf{X} \setminus X_\beta$, most informative for X_β.

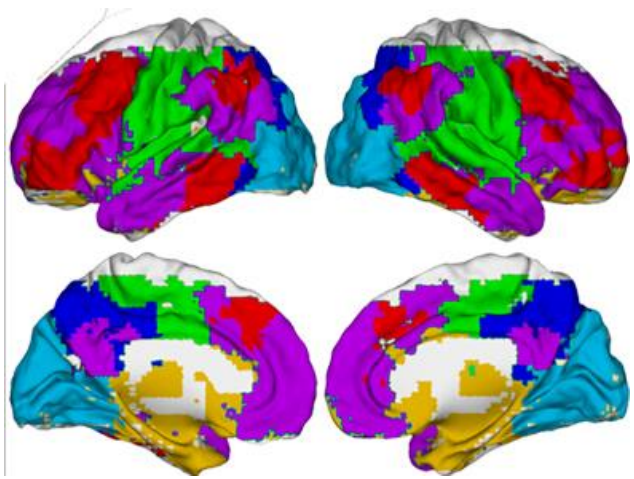
- $\mathbf{Z}$ maximizes the mutual information $I\{X_\beta; \mathbf{Z}\}$ among all the subsets $\mathbf{Z}$ of n_d variables
- Then, we evaluate the information transfer
$$PCGC(\beta \to \alpha) = \log \frac{\epsilon\left(x_\alpha|\mathbf{Z}\right)}{\epsilon\left(x_\alpha|\mathbf{Z} \cup X_\beta\right)}.$$
- Given the previous $\mathbf{Z}_{k-1}$, the set $\mathbf{Z}_k$ is obtained adding the variable with greatest information gain
- repeat until n_d variables are selected

1. Considering each potential driver voxel β, the whole ensemble of voxels (excluding β) S is divided into N systems: $S_1, S_2, \cdots, S_N$, such as the signal for the N systems is obtained aggregating voxels inside each system S_k resulting in $Z^S = \{\bar{Z}^{S_1}, \cdots, \bar{Z}^{S_N}\}$.
2. Each system is further partitioned into subsystems $S_{k_1}, \cdots, S_{k_d}$, such that now the signal within the subsystems of S_k is given by $Z^{S_k} = \{\bar{Z}_1^{S_k}, \cdots, \bar{Z}_d^{S_k}\}$, where $\bar{Z}^{S_k} = \frac{1}{d}\sum_{i=1}^{d} \bar{Z}_i^{S_k}$, being $\bar{Z}_i^{S_k}$ the mean signal of the variables X_j belonging to the subsystem S_{k_i}.
3. If $\beta \in S_{\eta_i}$, then $\mathbf{Z} = \{Z^S \setminus \bar{Z}_\eta^S, \bar{Z}_i^{S_\eta}\}$, and we calculate $PCGC(\beta \to \alpha)$

From regional to voxel level

Distribution of the most informative variables for a candidate driver voxel in module *i*





The coefficients of X_{j_i} $(j_i \in \mathbf{I}_{S_j}$ $(j \neq \eta))$ will have the same given weight; another weight will be assigned to the coefficients of X_{i_k} $(i_k \in \mathbf{I}_{S_{\eta_i}})$, thus

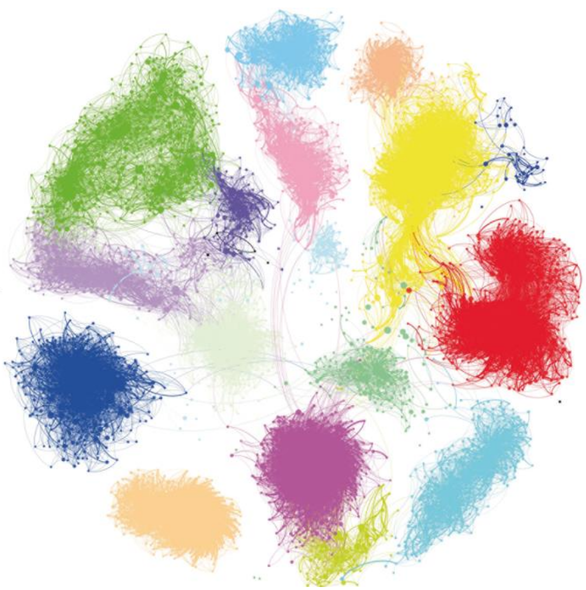
$$Z_h = \sum_k \left(Y_\eta^k \times \left(\mathbf{e} \otimes c_{h\eta}^k\right)\right) + \sum_{k=1,k\neq\eta}^N (Y_k \times (\mathbf{e} \otimes c_{hk})),$$

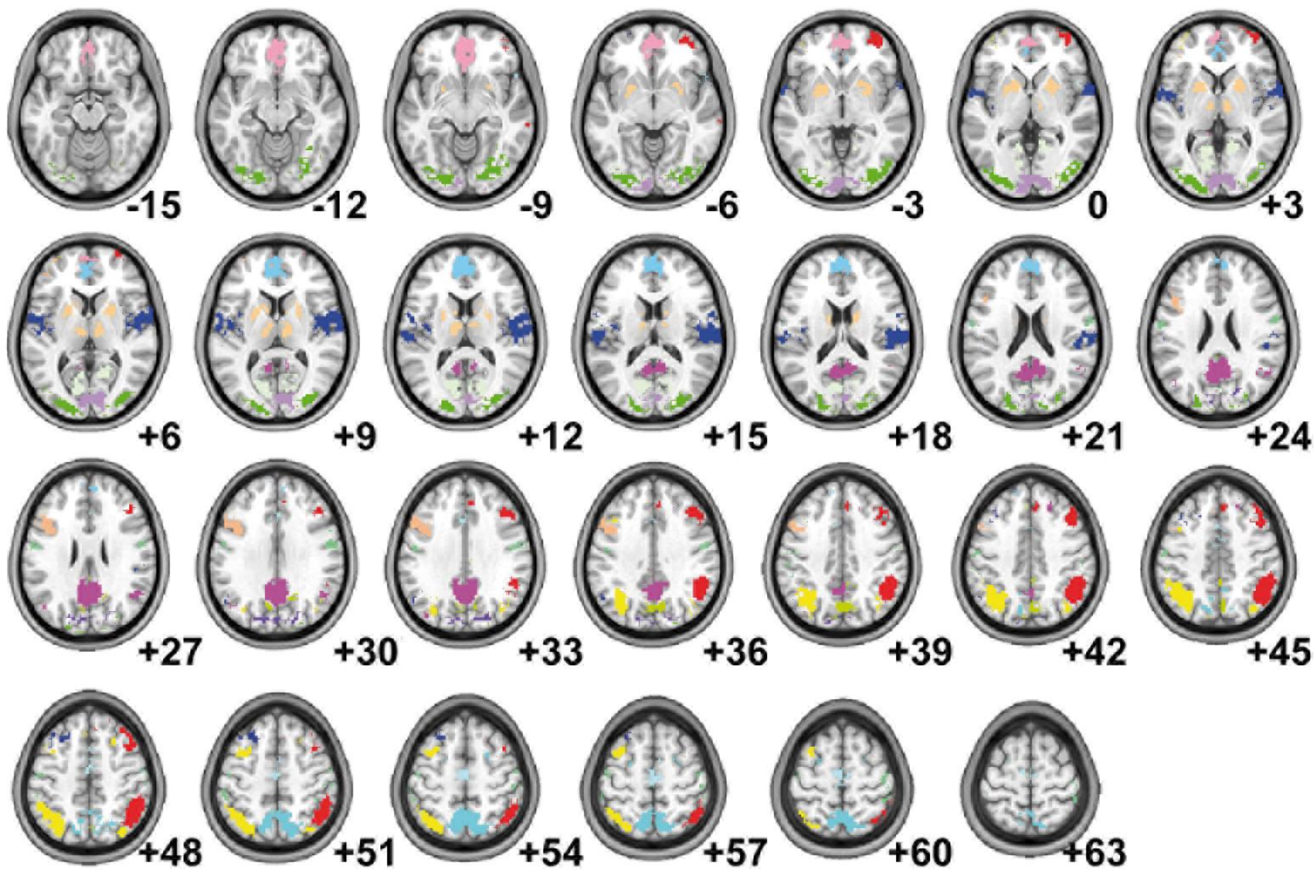
where $\mathbf{e} = [1, \cdots, 1] \in \mathbb{R}^{1\times\upsilon}$, υ is changed according to the dimension of Y_η^k and Y_k.

Even if we only consider a few conditional variables $\mathbf{Z} = \{Z^S \backslash \bar{Z}_\eta^S, \bar{Z}_i^{S_\eta}\}$, we are potentially taking into account all the information needed to partial out possible indirect causal influences, and avoiding multicollinearity in regression analysis models.

Wu et al. PLOS One 2013

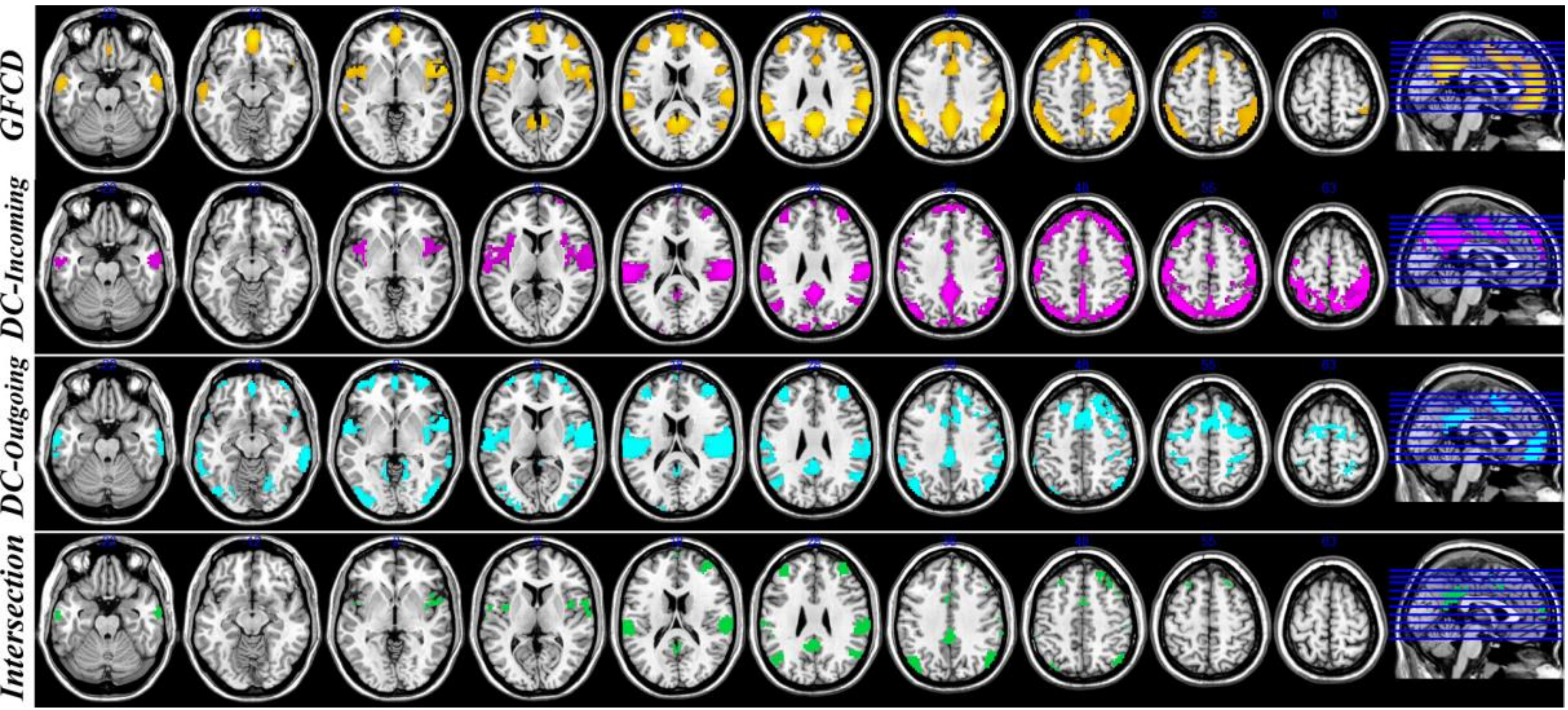
Reconstruction of voxel-wise directed networks





Wu et al. PLOS One 2013

Hubs for outgoing and incoming information



Wu et al. PLOS One 2013

Detection of the Hemodynamic Response Function

- Easy when timing of a specific task is known

- Elicited HRF responses in 96% of gray matter

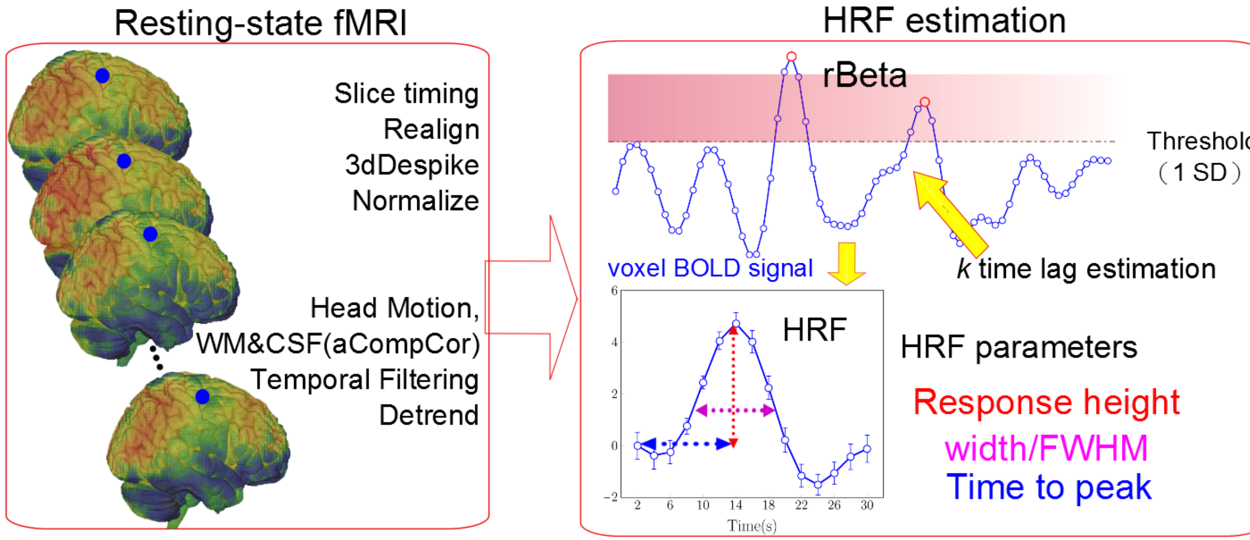
- How to retrieve the HRF in resting state?

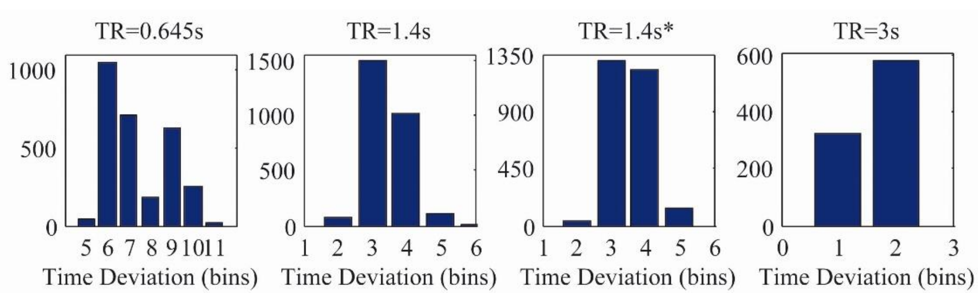
Point processes in BOLD signal

Peak events in BOLD time series can be considered as neural pseudoevents

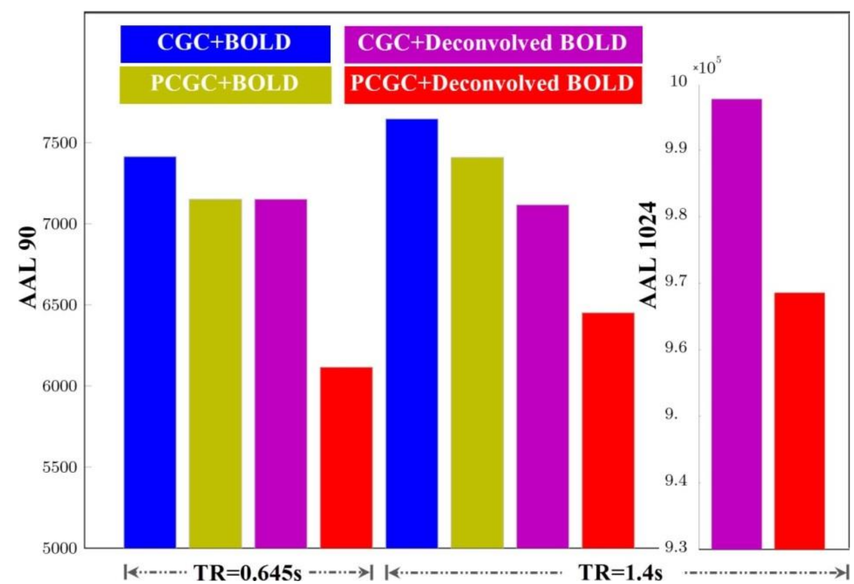
Align these events with the time lag as a free parameter

Fit a GLM and retrieve HRF at rest as canonical, FIR, or rBeta





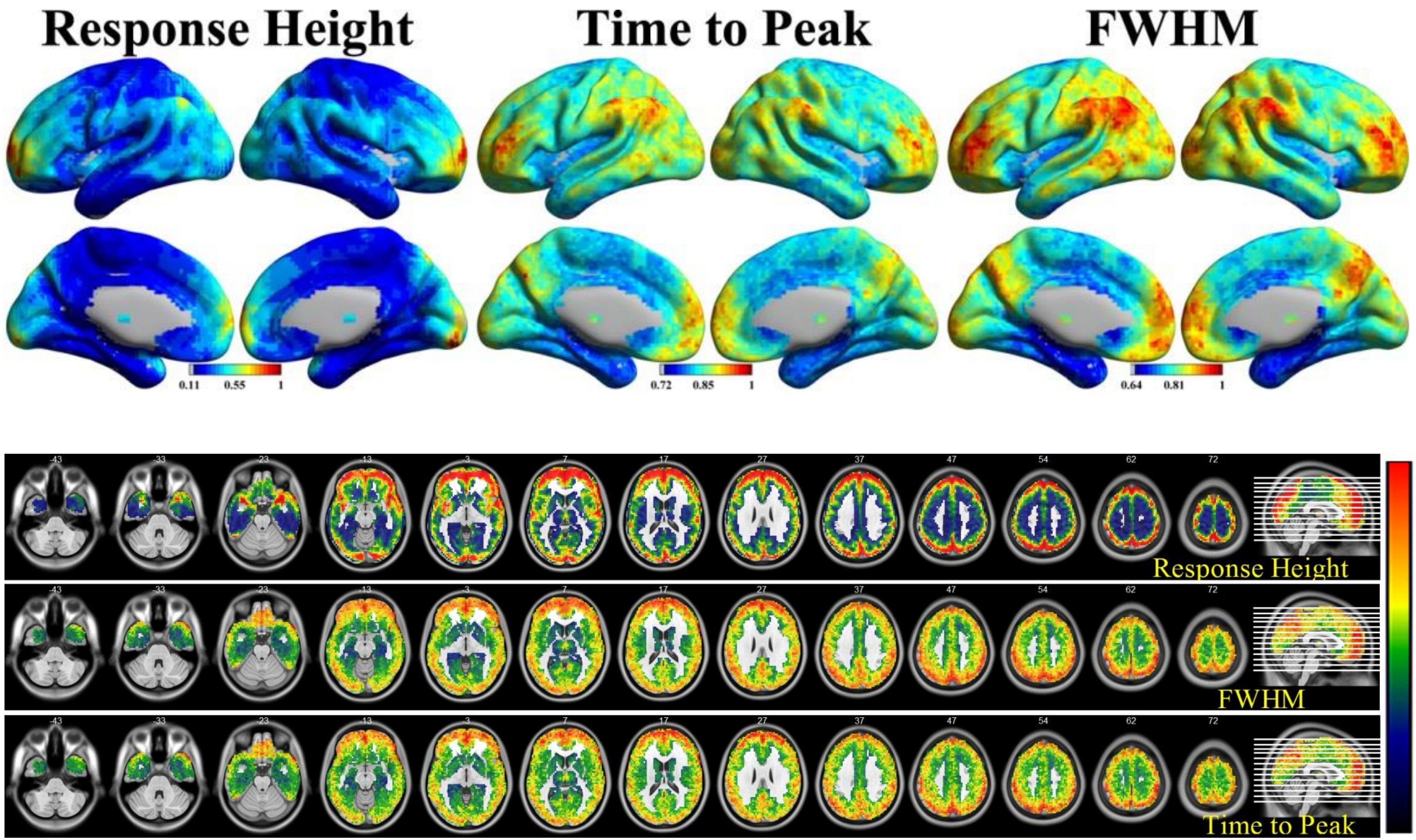
Distribution of delays between "neural onset" and BOLD peak



Decreased variance with deconvolution + PCGC

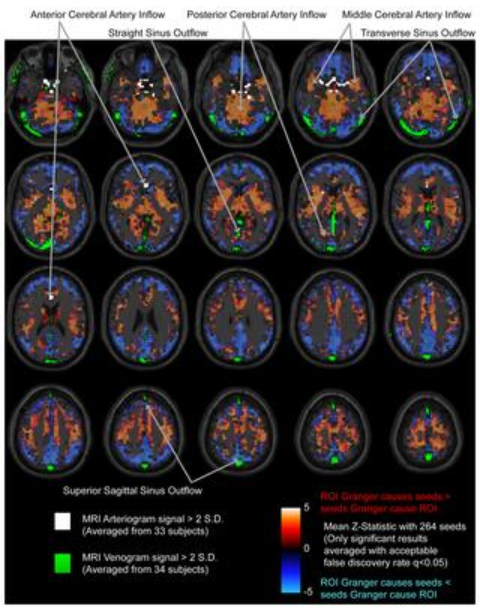
Wu et al. Medical Image Analysis 2013

Map HRF parameters across the brain



Wu et al. Medical Image Analysis 2013

The importance of deconvolution



OPEN ACCESS PEER-REVIEWED

RESEARCH ARTICLE

BOLD Granger Causality Reflects Vascular Anatomy

J. Taylor Webb, Michael A. Ferguson, Jared A. Nielsen, Jeffrey S. Anderson

Published: December 13, 2013 • DOI: 10.1371/journal.pone.0084279 • Featured in PLOS Collections

NEUROCONSCIENCE

MICAH ALLEN – CV NEUROCONSCIENCE?

The latest thoughts, musings, and data in cognitive science and neuroscience.

Effective connectivity or just plumbing? Granger Causality estimates highly reliable maps of venous drainage.

by Neuroconscience

update: for an excellent response to this post, see the comment by Anil Seth at the bottom of this article. Also don't miss the extended debate regarding the general validity of causal methods for fMRI at Russ Poldrack's blog that followed this post.

russpoldrack.org

Thursday, December 19, 2013

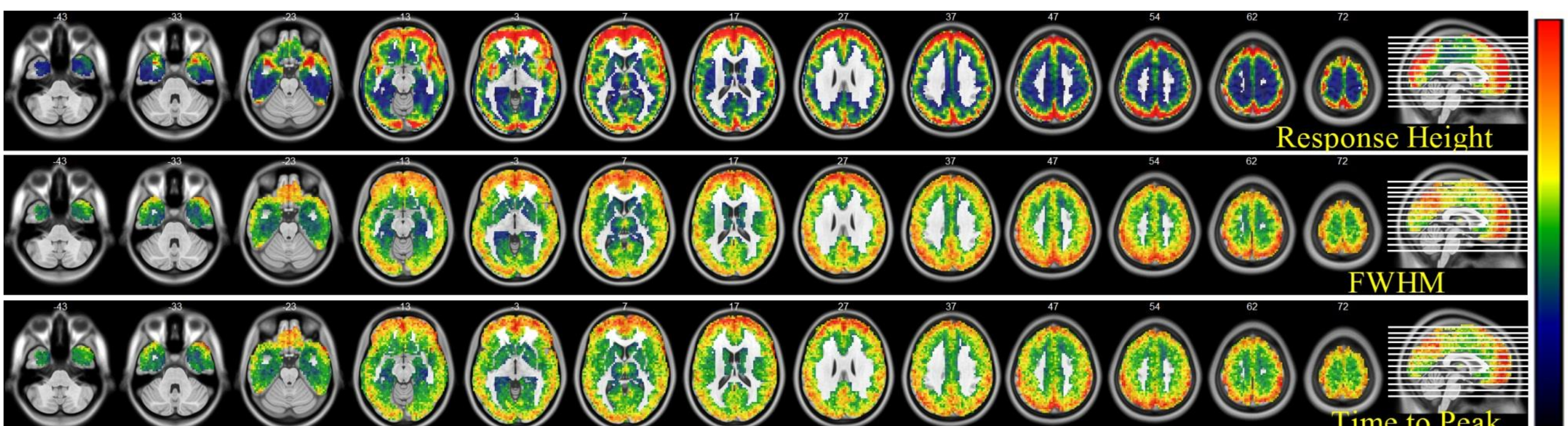
A discussion of causal inference on fMRI data

My facebook page was recently home to an interesting discussion about causal inference that was spurred by a recent article that I retweeted:

Gary Williams @orestesmantra 16 Dec

Effective connectivity or just plumbing? Granger Causality estimates highly reliable maps of venous drainage. feedly.com/e/EzJAf9px

Retweeted by Russ Poldrack

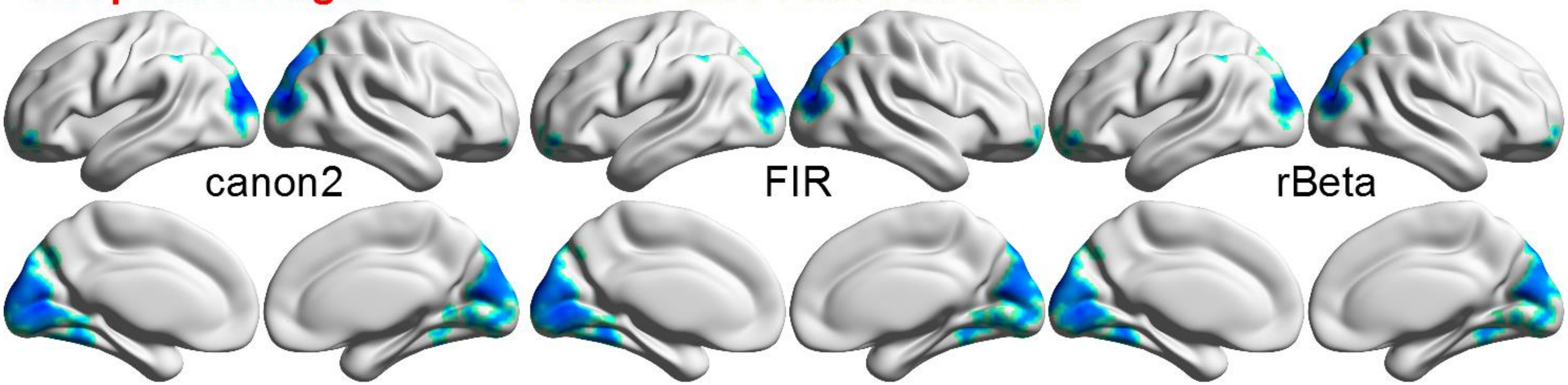


HRF shape as a marker of brain function

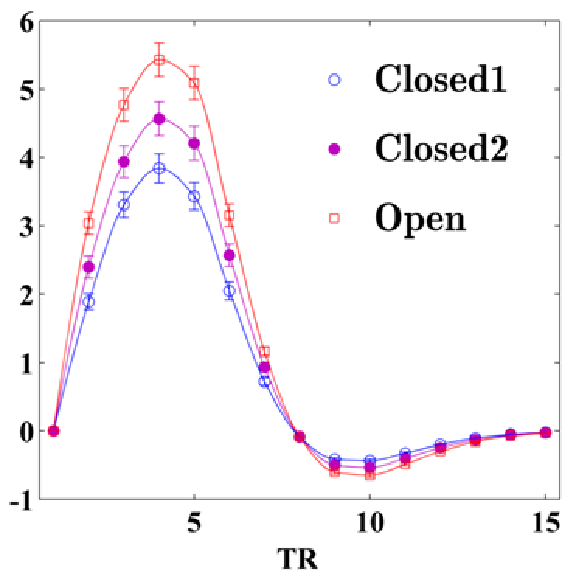
Eyes **closed (1)** - eyes **open -** eyes **closed again (2)**

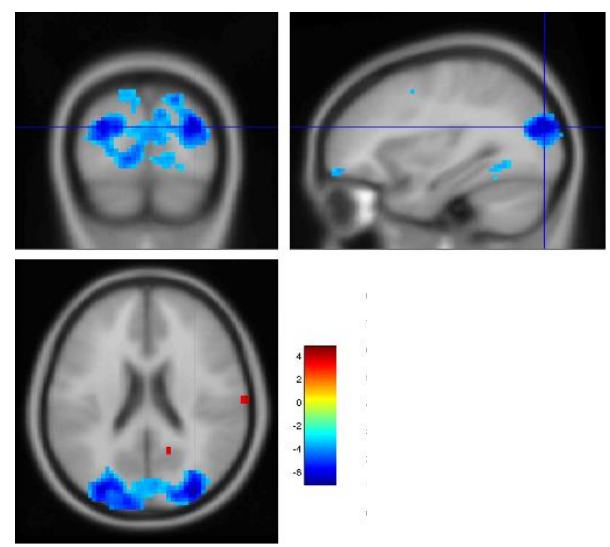
TR=2s, 48HC subject, http://fcon_1000.projects.nitrc.org/indi/retro/BeijingEOEC.html

Response Height **P-value<0.05 FDR correction**



Experimental design: **eyes closed 1, eyes open, eyes closed 2**





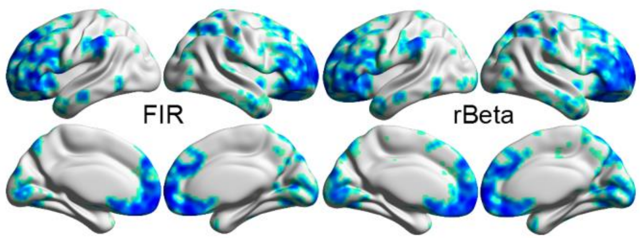
HRF shape as a marker of brain function

TR=2.46s, 21 subjects. Wake (W1), mild sedation (S1), deep sedation (S2), and recovery of consciousness (W2)

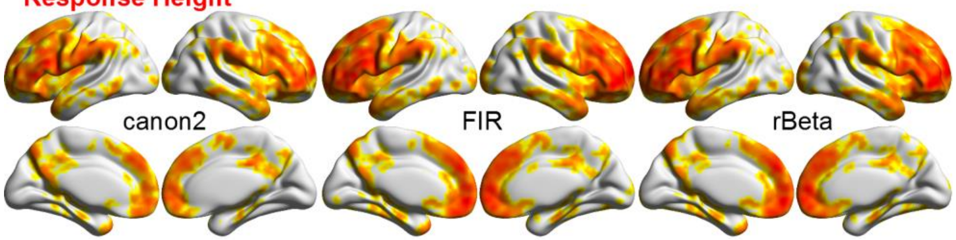
T-contrast (W1 S1 S2 W2): [1.5 -0.5 -1.5 0.5]

P-value<0.05 FDR correction

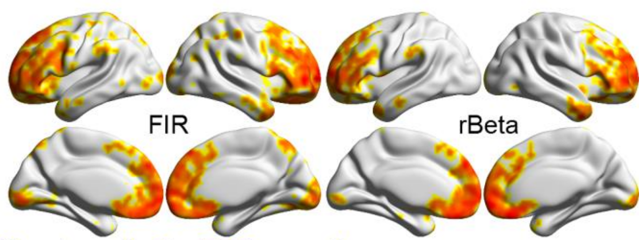
Number of spontaneous events



Response Height

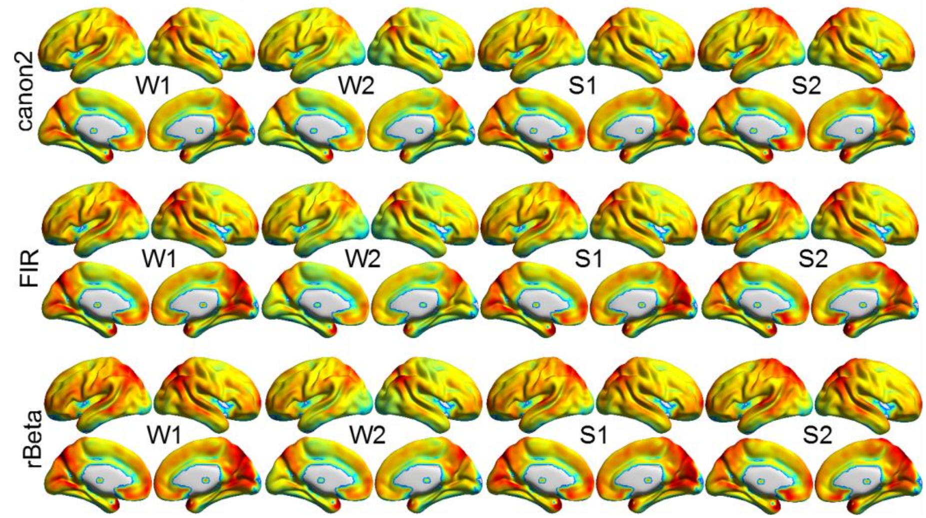


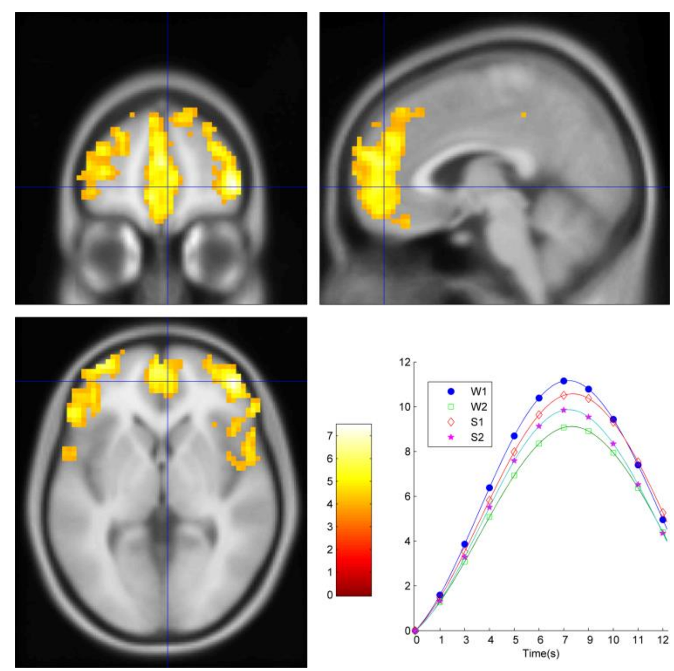
FWHM



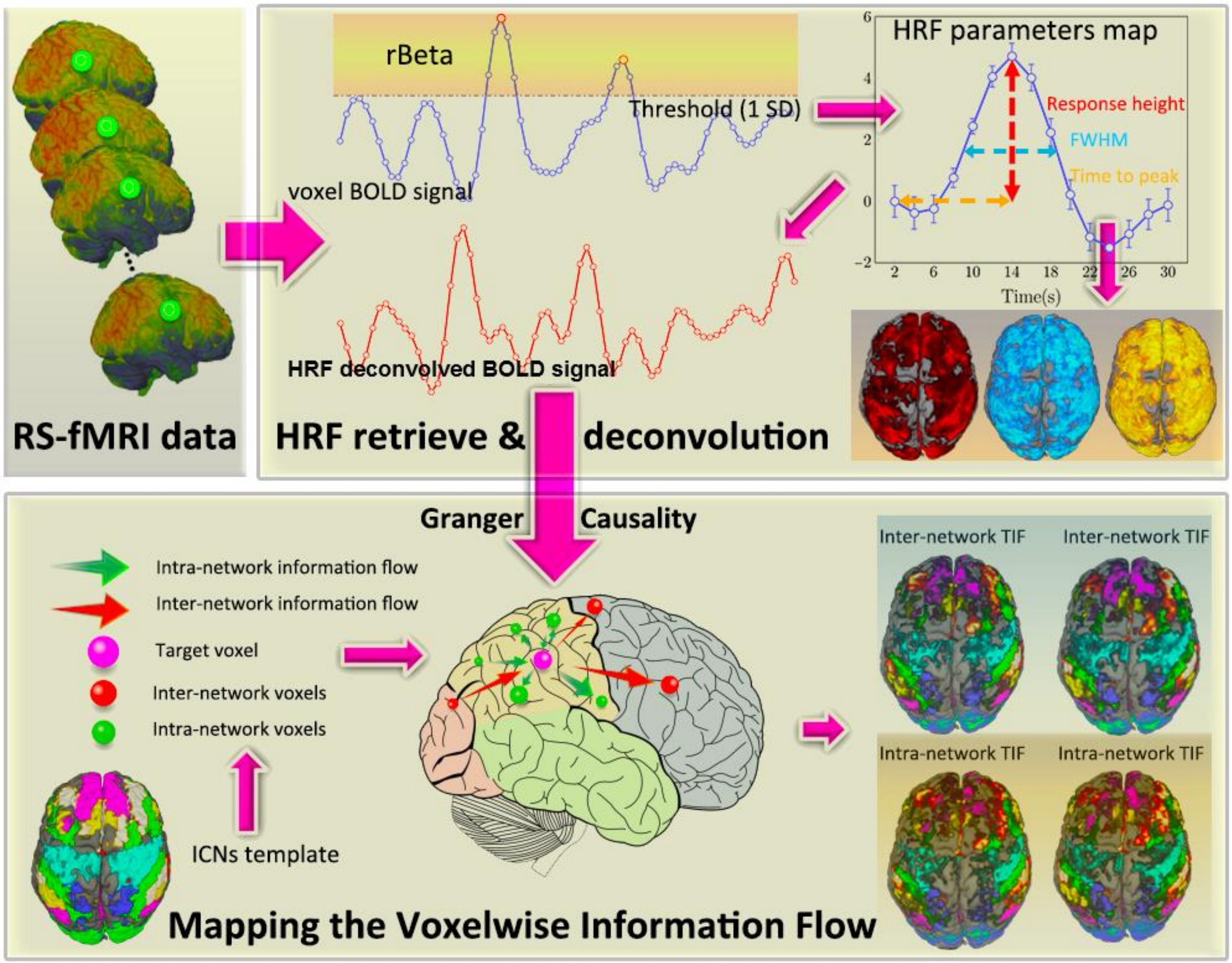
Time to peak --- no significant result after FDR correction.

Response Height , Group Mean



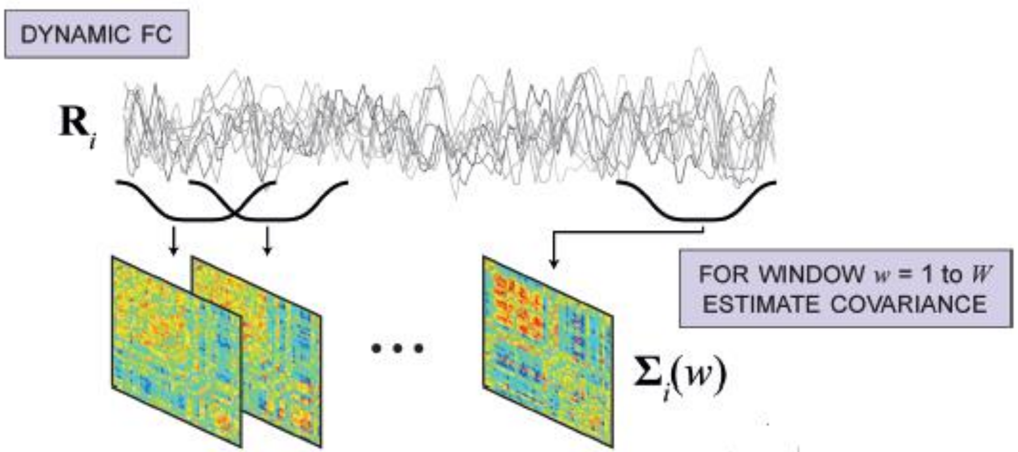


Combining HRF and dynamical connectivity



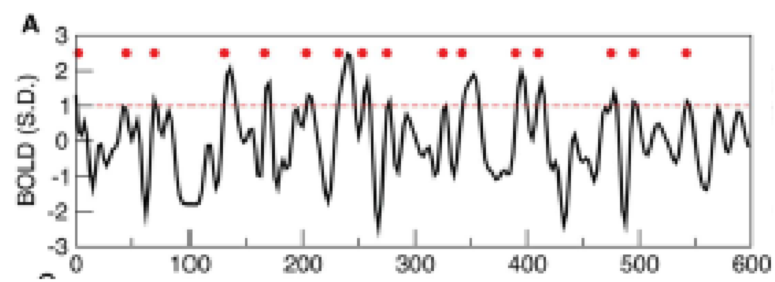
Another approach to dynamical FC

Sliding window correlation
(Allen et al, 2013)

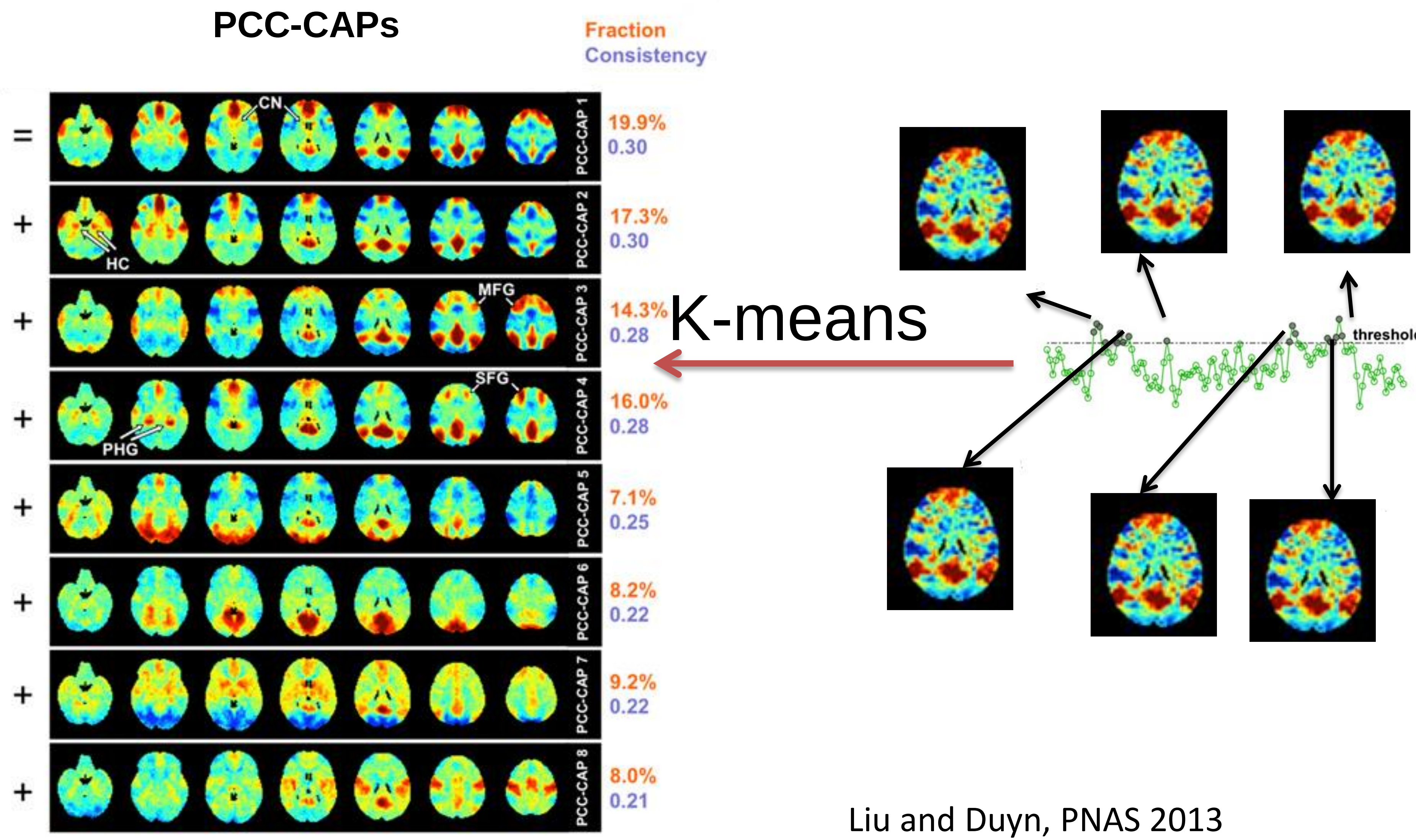


Point process analysis

(Tagliazucchi et al., 2012, Wu et al. 2013)



Coactivation Patterns



Liu and Duyn, PNAS 2013

Conclusions

- Many variables, few samples
  - Partially conditioned Granger Causality
  - Grouping variables in terms of their informational content
- Confounding effect of the HRF
  - Blind deconvolution
  - HRF shape as a marker for brain function
- Bad temporal resolution
  - Relevant info contained in a portion of the frames

Thanks to

- G. Wu (Southwest University, China)
- E. Amico (Ghent, Liège, Purdue)
- S. Stramaglia, M. Pellicoro (Bari, Italy)
- S. Laureys, O. Gosseries (Liège, Belgium)

http://users.ugent.be/~dmarinaz/

daniele.marinazzo@ugent.be

Code

- Partially conditioned Granger Causality
  https://github.com/danielemarinazzo/PartiallyConditionedGrangerCausality
- Dynamic Brain Connectivity – G.Wu
  https://guorongwu.github.io/DynamicBC/
- Coactivation Patterns – E. Amico
  https://github.com/danielemarinazzo/CAPsToolbox
- Hemodynamic response function retrieval – G. Wu
  https://github.com/guorongwu/rsHRF