Hierarchical network analysis: Is activity in node A necessary or sufficient for activity in node B?

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Target Audience : Neuroscientists interested in analyzing hierarchical relationships in brain networks.

Purpose: Hierarchical analyses of functional MRI data can reveal the underlying structure of neural networks and the directionality of the flow of information inside the brain. There are multiple approaches to trying to elucidate the causal relationships between the nodes in a brain network from FMRI time series. These range from simple correlations to more sophisticated dynamic causal models, Granger causality or graph theoretical strategies. Here we follow up on our approach [1] to test for causal relationships by computing measures of 'necessity' and 'sufficiency' between the activity in a pair of nodes.

Methods: Probability of Necessity (PN) [2] quantifies the inability of Y to be active without X. This can be interpreted as the probability that node Y would become deactivated if node X were deactivated, given that both nodes are active at a given time.
Probability of Sufficiency (PS) [2] can be interpreted as the probability that node Y would become activated if node X is activated, given that both nodes are inactive at a given time. Thus, PS evaluates how susceptible is Y to the activity presented on X. It is equivalent to interpret PS as the effect of X on Y after suppressing all other causes of Y.

These can be expressed as
$$PN = \frac{P(y \mid x) - P(y \mid \bar{x})}{P(y \mid x)} \quad \text{and} \quad PS = \frac{P(y \mid x) - P(y \mid \bar{x})}{P(\bar{y} \mid \bar{x})}$$
, respectively.

Importantly, we need to estimate the specific instants where activation occur in order to compute PN and PS. The event detection method used here is based on a two-state Gaussian mixture model [3]. In short, signal variations from a baseline to an evoked activation state are assumed to be well modeled by a combination of two normal distributions with different parameters. These parameters can be estimated numerically by using the well-known Expectation Maximization (EM) algorithm. The event detection method was tested by ROC analysis under multiple conditions (activation block size, CNR, autocorrelation level of the noise, and BOLD response dispersion) (see [4]).

Having tested the event detection method thoroughly, we tested this 'sufficiency and necessity' framework both by simulating FMRI signals with several a priori dynamic causal network configurations [5], and empirically on a simple FMRI activation paradigm, in which activation of the visual cortex was known to be necessary for activation of the motor cortex, and activation in motor cortex sufficient for activation in visual cortex. The paradigm consisted of 10 second periods of visual stimulation every thirty seconds. During only half of those periods, the subjects were instructed to tap their fingers during the stimulation period, thus enforcing the specified relationship. BOLD data were collected on three healthy volunteers, preprocessed standard pipeline and normalized to MNI space using SPM8. Motor and visual cortex active regions were identified by regression with a simple general linear model of the activation paradigm. Seed regions were chosen in the visual and motor cortices and the probabilities of sufficiency and necessity, as well as correlation between the seed and the rest of the brain was calculated using the framework described here.
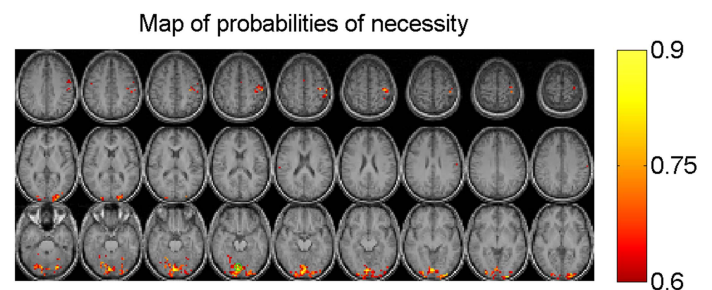

Figure 1: Prob. Necessity Map of a seed voxel in the visual cortex under the activation paradigm thresholded at 0.5
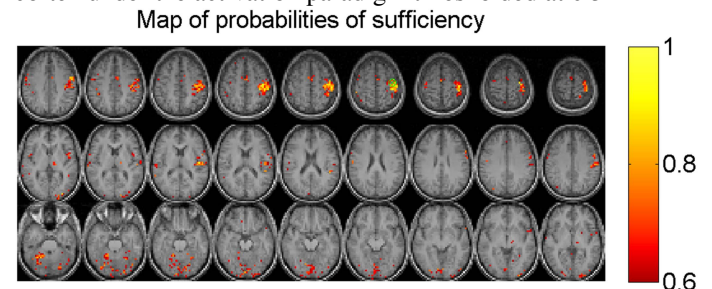

Figure 2: Prob. Sufficiency Map of a seed voxel in the motor cortex under the activation paradigm thresholded at 0.5

Results: ROC analysis of simulated BOLD data revealed that the EM algorithm was fast and robust in identifying activation periods (area under the curve > 80% in most cases). Simulated data shows underestimation of PN and PS bias arising from errors in event detection and lack of exogeneity (i.e. – other external influences), but that bias decreases with longer activity bursts and CNR.   The BOLD data indicated that the seed voxels in visual cortex were 50% to 60% likely to be sufficient, and >90% likely to be necessary to activate motor cortex. Conversely, the motor cortex was 60% - 65% likely to be necessary and 80% - 90% likely to be sufficient for the visual cortex. The two regions' correlation coefficient was well below 50%.

Conclusion: The proposed methodology is a new approach to characterizing functional connectivity in BOLD FMRI data. Rather than addressing the temporal relationships, we measure the interdependence between regions in terms of necessity and sufficiency. Our preliminary results indicate that the framework is well suited for FMRI, opening a large range of potential applications.

References: [1] Veloz-Baeza, OHBM Annual Meeting, 2013 [2] Pearl, J. (2000). Cambridge University Press [3] Lindquist, M.A. (2007). Neuroimage, vol. 35, no. 3, pp. 1125-1141 [4] Hernandez-Garcia, L. (2011). Magnetic Resonance Imaging, vol. 29, no. 3, pp. 353-364. [5] Smith, S.M. (2011). Neuroimage, vol. 54, no. 2, pp. 875-891. **Acknowledgements**: CONICYT fellowship DIUV 64/2011