Automatic Neural Causality Analysis Using Granger Causality Mapping and Mutual Information

By: Micah Chambers

Recently there has been great interest in the area of causality mapping of Neural Networks. While this development is crucial to understanding how the brain works, there are still many problems with the existing techniques. Here I propose a new processing pipeline and a new method of performing causality mapping that makes fewer assumptions and is still computationally tractable. The goal then is to develop a set of tools that will:

1. Find independent regions to input into the Granger Causality Mapping (GCM) algorithm.
2. Calculate the causality within the independent regions.
3. Create a dependency tree for intuitive display of causality.

For the past ten years the primary method of analysis of Functional MRI has been Statistical Parametric Mapping (SPM) using the General Linear Model (GLM). While this method has been effective, in the interest of computational tractability it makes certain assumptions that do not hold. For this reason, such methods must be extremely conservative to avoid false positives, which means that SPM is incapable of detecting small activation regions or regions of low activation. Additionally, SPM only measures how well the data fits the GLM and not the actual activation level. Finally, SPM is a univariate model, meaning it cannot determine inter-voxel causality. Because of these limitations, there is currently a lot of work being done to find the successor to SPM.

Recently, ”Dynamic Causal Modeling” (DCM) has been introduced, which attempts model activation of neural pathways. Unfortunately DCM has not become anywhere near as ubiquitous a SPM, in no small part because it is significantly more difficult to use. Because DCM works by testing FMRI data against a proposed network, the researcher must propose a functional layout to perform DCM, which is often difficult.

Another recent development, Vector Autoregression has many desirable features; it is able to infer dependencies, it requires no a priori knowledge of the system, and versions exist for nonlinear systems [1]. Vector Autoregression is actually a generalized version of Granger Causality Mapping (GCM), which Zhou et. al. [2] recently showed to be effective for finding causal neural networks. The downside is computation time, which can be extreme when performed on every pair of voxels. Previous studies have focused on small regions, region-wise causality, or Principal Component Analysis (PCA) to circumvent the computation issues. On the other hand, I propose performing full, voxel-level GCM by minimizing the number of unrelated voxels that are processed, without resorting to linear or Gaussian assumptions.

To minimize the number of non-related voxels that are processed by GCM, I propose a preprocessing stage that breaks voxels up into independent blocks. Ordinarily GCM is $O(N^2TD)$ where N is the number of voxels, T is the number of timepoints, and D is the number of time delays allowed. By breaking the brain into independent blocks, computation only has to be performed within each independent block, rather than between every voxel. Thus instead of the algorithm being $O(N^2TD)$ it will be $O(P^2TD)$ where $P \ll N$. To determine which regions are independent, I propose the use of mutual information. Unlike PCA or clustering algorithms, Mutual Information is based on Bayesian statistics and makes no assumptions about the underlying distributions. Moreover, it has recently been demonstrated that mutual information works for larger regions of the brain [3]. Therefore, it is possible to break the region of interest up into blocks and perform mutual information between the blocks, rather than individual voxels. Of course there is a trade off between larger blocks and smaller blocks: larger blocks may miss 1 or 2 voxels that are interdependent with outside voxels, whereas smaller blocks may be intractable. With the mutual information between blocks known, a threshold can then be applied, and blocks with mutual information combined into a single independent block. Once a set of independent blocks has been found, GCM may be applied to the internals of each block without fear of missing voxel-wise causality.

The final step of the pipeline is to build a causation map, which can be displayed to the user. One inherent problem with any technique measuring causation is intermediate terms. For instance, if $A = f(B)$, $B = g(C, D, E, F)$, then A will appear to be a function of C even if it only a function of B. To combat this problem, and provide the simplest, most likely network, the algorithm will attempt to account for intermediate causality. Thus, the algorithm will sever weak connections when a stronger (albeit longer) path exists. The ultimate output from the algorithm will be a causality graph that can then be simplified for statistical or graphical purposes. Two potential confounds are regional changes in blood flow and slice timing. Slice timing will result in causation during resting state, and can be fixed by accounting for such delays in the model. Regional blood flow is more difficult; however, it may be possible to account for by introducing bias in regions near larger blood vessels. Depending on the size of these effect, using time-series subtraction may be helpful.

Concluding, the proposed method will be a comprehensive set of tools to develop voxel-wise causality maps from FMRI images. The end goal is a better understanding of how regions of the brain communicate. The scientific benefits of understanding neural connections is manifold, both for clinical and research purposes. In particular, those with connection disorders would benefit greatly from this research. Of course, understanding why one part of the brain triggers another is an important step in understanding sentience. Many of the techniques I have included here have a history of success in the investigation of neural networks; thus I believe these goals are feasible. By building on the knowledge gained from previous studies it should be possible to avoid pitfalls, and lay the groundwork for future research.

References

[1] C. L. Weise, "The asymmetric effects of monetary policy: A nonlinear vector autoregression approach," *Journal of Money, Credit and Banking*, vol. 31, no. 1, pp. 85–108, 1999.

[2] Z. Zhou, Y. Chen, M. Ding, P. Wright, Z. Lu, and Y. Liu, "Analyzing Brain Networks With PCA and Conditional Granger Causality," *Human Brain Mapping*, vol. 30, pp. 2197–2206, JUL 2009.

[3] G. Marrelec, P. Bellec, A. Krainik, H. Duffau, M. Plgrini-Issac, S. Lehricy, H. Benali, and J. Doyon, "Regions, systems, and the brain: Hierarchical measures of functional integration in fmri," *Medical Image Analysis*, vol. 12, no. 4, pp. 484 – 496, 2008.