Fall Term Progress Report

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Abstract

We seek to infer the functional connectivity of the brain and answer questions such as how areas in the brain interact as visual and audio stimuli change. Specifically, we're looking to find if how regions of the brain that are connected to other regions, and how these connections change through time. The dataset we'll be working with is an fMRI recording in which subjects watch 23-minutes of the first episode of Sherlock. We will apply several different techniques, including k-means and Penalized Convex Relaxation of K-Means (PECOK) to cluster voxels in the brain and study their change through time.

Contents

1 Introduction

When studying the human brain, we often break it into its individual parts by functionality (the visual cortex or auditory area) or static connections. In this work, we are interested in the dynamic, functional connectivity of the brain–in particular, how the functional connectivity changes as stimuli change.

An example of a theory of static functional connectivity is the Default Mode Network (DMN), widely regarded to be the correlated with higher-level cognitive function, such as processing complex, real-life stimuli (Raichle 2001). Complications in the DMN have been shown to correlated with diseases like autism, schizophrenia, and Alzheimer's (Buckner 2008). By studying the dynamic functional connectivity of the brain, we hope to shed more light onto the complexities of the network to better understand how we process sensory input, and conceptualize and store memory.

In this work, we seek to understand how the neurons of the brain interact to process multiple sensory inputs at once. We take fMRI recordings of subjects watching the television-show, Sherlock, and analyze the clusters of fMRI voxels to better understand how regions of the brain are connected, and how these connections vary over time. Preliminary work shows that k-means clusters corresponding to the visual cortex change as scenes of Sherlock change. We will continue to explore this result.

2 Background

2.1 Functional magnetic resonance imaging (fMRI)

fMRI (functional Magnetic Resonance Imaging) is a non-invasive technique for imaging activity in the brain. Here, we use fMRI as it is non-invasive and allows us to record subjects performing a complex task: watching a movie. However, fMRI does not capture neural activity in the brain. Instead, it captures the response of hemodynamics (blood flow) which operate at a slower timescale than neural activity. This can mask fast changes in neural activity. Additionally, fMRI data tends to be fairly noisy, which requires we clean the data (Lindquist 2008). We will address how the data was cleaned in section 4.1.

3 Theory

3.1 K-Means

The k-means algorithm identifies clusters based on the distance of a data point to a cluster mean. We can compute the clusters by first choosing a mean, assigning all data points to their closest cluster mean, recomputing the cluster means, and reassigning data points to their closest cluster mean. We then repeat this step until some stopping criteria is met. Either the assignment of cluster labels to data points stabilizes, or we completely a predetermined number of iterations. (Bishop

2006)

We can explicitly write this algorithm as:

$\mu_k, 0 \leq k \leq K$ are the cluster means at this iteration (or our initialization)
$x_i, 0 \leq i \leq n$ are the data points.
$c_i, 0 \leq i \leq n$ are the cluster assignments.
Step 1. Assign each data point to a cluster. Find

$$c_i = argmin_{1 \leq k \leq K} ||x_i - \mu_k||^2$$

Step 2. Recompute the means.

$$\mu_k = \sum_{i=0}^{n} x_i 1_{c_i=k} \frac{1}{\sum_{i=0}^{n} 1_{c_i=k}}$$

Repeat these steps until convergence (when we reach a predetermined number of iterations, or the clusters stop changing).

This method has a few obvious drawbacks that we will address in turn. First, we do not know how many clusters would best describe our data. There have been many studies and heuristics for choosing the number of clusters(Bishop 2006), but the statistical community has not determined a singular best approach. In our case, we will be applying k-means to fMRI data and we can use some domain knowledge to intelligently select the number of clusters. We will discuss this further in section 5.1.

K-means can be highly affected by the values we choose to be the mean of our initial cluster assignment. Since we aim to study how k-means clusters change through time, the dependence on the initialization value could lead to inconstant clusters and inconsistent results.

This motivates our use of Penalized Convex Relaxation of K-means (PECOK).

3.2 Penalized Convex Relaxation of K-Means (PECOK)

When data tend to be clustered together, or minimally separated, then PECOK is able to achieve perfect cluster recovery and is minimax optimal (if the number of clusters K is bounded above by $log(p)$ (where p is the dimension of the sample X) and nearly minimax optimal otherwise(Bunea 2016). In our case, where the brain likely has clusters of neurons that are correlated, we have a latent G-model (where G is an unknown partition), as described by (Bunea 2015) and we would expect PECOK to perform better than k-means at uncovering latent partitions. Of further interest, (Bunea 2016) claims that these results hold even if K was determined from the data–as will need to be the case for our application.

The algorithm proceeds as follow:

Σ: is the covariance of the vector $X = (X_1, \cdots, X_p)$
$\Sigma = ACA^t + \Gamma$ partitions Σ relative to the partitions G.
B is a block matrix with entires $B_{ab} = \begin{cases} \frac{1}{|G_k|} & \text{if } a \text{ and } b \text{ are in the same group } G_k \\ 0 & \text{otherwise} \end{cases}$
Step 1. Estimate Γ by $\hat{\Gamma}$
Step 2. Estimate B^* by $\hat{B} = argmax_{B \in C} \left(\hat{\Sigma} - \hat{\Gamma}, B \right)$.
Step 3. Estimate G^* by applying a clustering algorithm to the columns of $\hat{B}$.

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4 Data

The dataset we're working with is an fMRI recording in which subjects watch 23-minutes of the first episode of BBC's Sherlock (the episode was cut short to avoid technical problems, like overheating). All 17 participants are right-handed, native-English speakers who have never seen Sherlock before. They were given minimal instructions: to watch the movie as they would watch any other movie. For more information about the procedures of data collection and methods, please see (Chen 2016).

We take a volume of data every 1.5 seconds, resulting in 945 frames. In the volume we measured, there are 271,633 voxels. To narrow down the data, we took the top 700 voxels with the highest variance as we hope the changes in the recordings due to the stimuli will be greater than the noise.

4.1 Preprocessing

Additional preprocessing steps were taken by (Chen 2016) prior to handing off the data.

5 Work in Progress

5.1 Clustering

We wish to understand how brain clusters change through time. First, we will observe how brain clusters change as scenes of the visual input, Sherlock, change. Then, we will propose a method for identifying when a cluster changes and use that method to observe when and how clusters change through time.

In each step, we cluster the average fMRI response for all 17 subjects. This is because we wished to remove the high variability in fMRI data that can result from other biological functions not relevant to watching Sherlock. Further, previous work has shown that, while recalling a common experience, watching Sherlock, the recall fMRI scans of participants were more similar than the fMRI scan of a single participant watching Sherlock for the first time and the fMRI scan of the same participant recalling the episode (Chen 2016). This suggests that we should focus on trends common across subjects as opposed to in an individual subject. As an initial method for using data from all subjects, we take the average fMRI response to cluster.

To understand how clusters change during different scenes of Sherlock, we could break the data at scene changes and cluster each scene individually. This does not accurately capture the nature of fMRI data as we know past time-steps of fMRI data will be correlated with future time-steps. Instead, we first apply a kernel across time-steps that weights time-steps in the scene more than those outside.

Here we use the Epanechnikov kernel since we want a kernel centered around z $K : \mathbb{R} \to \mathbb{R}$ be a symmetric kernel function.

$$K(u) = 0.75 \cdot (1 - u^2) \cdot 1_{|u| \leq 1}$$

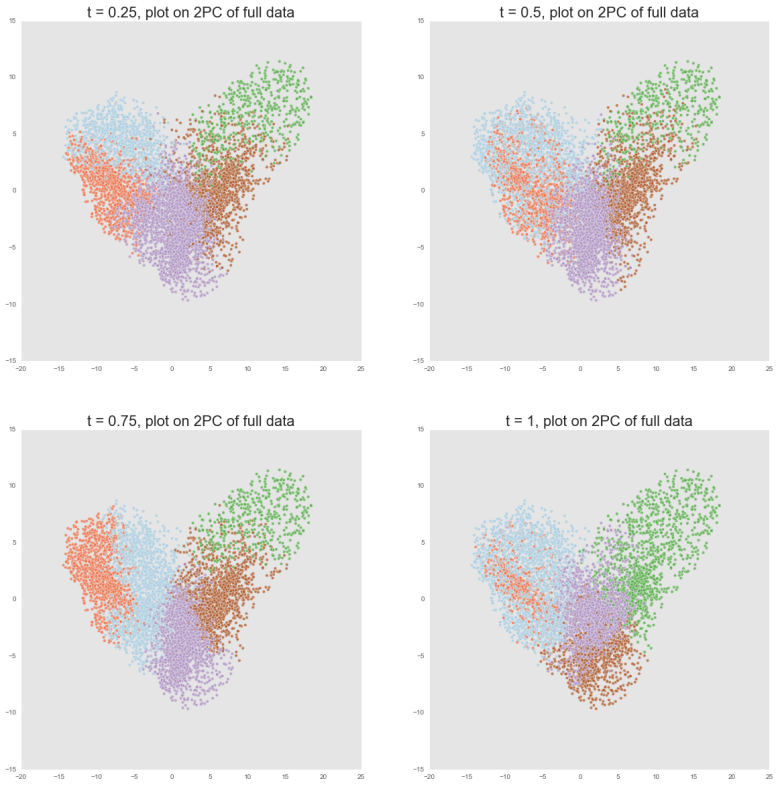
This additionally allows us to have more stability across clusters since some time-steps will be common across clusters close in time.

Once we have the transformed data, we apply k-means clustering, where k = 6. We narrowed the search for k to be below 10 so that the results could be interpretable. Then, we noticed that for values of k larger than 6, clusters were highly unstable and would break apart or switch depending on the initialization values.

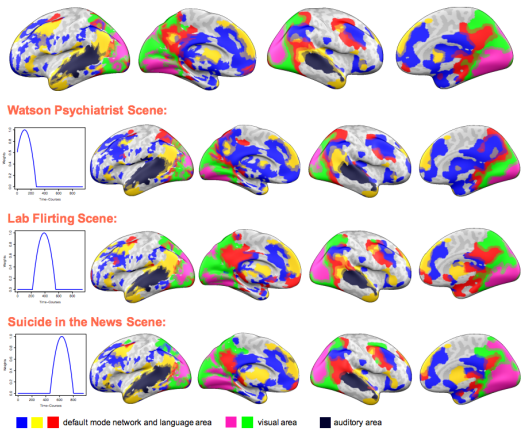
We then matched the labeling of clusters in the first scene to the labeling of clusters in the next scene to maintain a consistent labeling scheme. This allows us to better understand how the clusters evolve through time.

5.2 PECOK

Our next step is to apply the PECOK technique in the same manner and compare how the two techniques cluster voxels in the brain.



Here we look at the clusters changing as we move through four equal time sections of the fMRI recording plotted against the first two PC dimensions. We can observe that the clusters shift even in these two PC dimensions.



We observe that the six clusters correspond to different areas of the brain such as the visual area or the auditory area. We can see how the clusters shift as we move through the television show. Notably, the visual area changes dramatically through the three scenes (see second column of brains)(Tan 2016).

5.3 Detect cluster changes

We will then design a technique to determine when a cluster has changed. Due to the high noise and variance in fMRI data, it can be difficult to draw conclusions from a simple k-means algorithm.

6 Tasks to complete

The next step is to finish implementing the PECOK algorithm and apply the algorithm to achieve a different clustering of data. We would also like to further explore the unexpected change in visual area cluster through time.

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References

Bishop, C. M. 2006. *Pattern Recognition and Machine Learnin*. New York, New York: Springer Science+Business Media, LLC.

Buckner, R. L. et al. 2008. "The Brain's Default Network: Anatomy, Function, and Relevance to Disease." *Annals of the New York Academy of Sciences.* doi:doi:10.1196/annals.1440.011.

Bunea, et al., F. 2015. "Minimax Optimal Variable Clustering in G-Models via Cord." *ArXiv*.

———. 2016. "PECOK: A Convex Optimization Approach to Variable Clustering." *ArXiv*.

Chen, J. 2016. "Shared Experience, Shared Memory: A Common Structure for Brain Activity During Naturalistic Recall." *BioRxiv Preprint*. doi:http://dx.doi.org/10.1101/035931.

Lindquist, M. A. 2008. "The Statistical Analysis of FMRI Data." *Statistical Science.* 23 (4): 439–64. doi:10.1214/09-STS282.

Raichle, M. E. et al. 2001. "A Default Mode of Brain Function." *Proc Natl Acad Sci*.

Tan, et al., K. M. 2016. "Dynamic Network Reconfiguration During a Continuous Natural Stimulus." http://www.keanmingtan.com/uploads/8/1/6/7/81678836/sfn_2016.pdf.