

CS9869b Course project

Factorial analysis of fMRI data

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Introduction

Functional magnetic resonance imaging (fMRI) is a procedure that uses MRI in order to measure brain activity via detecting changes in the blood flow in the brain. It has been shown that when a particular area in the brain is in use, blood flow to this area increases[1, 2]. Known relation between the neuron activity and blood flow (the hemodynamic function) and regression analysis allow to relate measured fMRI time series with hypothesized stimuli or activity induced processes[3]. The regression coefficients are time independent and indicate the relation between a brain voxel and the studied stimuli or activities.

This project addresses the problem of two factor analysis of fMRI data. In particular we are interesting in the following questions. Does a part of the brain (represented as a set of voxels) encode information about each of the factors independently or resemble unique combination of factor levels. Kornysheva and Diedrichsen in [4] taught volunteers to perform series of finger movements. Each sequence was a combination of three different temporal (temporal factor) and three different spatial (spatial factor) features. They found the regions in the brain that encode each of the factors independently as well as the regions that encode unique features of all possible combinations in the brain. They used classification approach, which we discuss in section 1. This project aims to explore and compare different approaches to this problem. In ?? we describe classical *multivariate analysis of variation* (manova) and also discuss its cross-validate extension. In ?? we describe pattern component modeling.

Co-authorship statement

Yuanhao Lai wrote ??. Harrison Ritz wrote ??.

1 Classification approach

This section follows the ideas presented in [4]. Generally, we are to determine how different the reaction of voxels to different combinations of conditions. Machine learning studies different algorithms that are able to find regularities within object's features in order to extract some information about the object. In particular, classification problem is to train a classifier, a function that maps features of the object to the class that this object belongs to.

1.1 K-Nearest-Neighbors (KNN) classifier

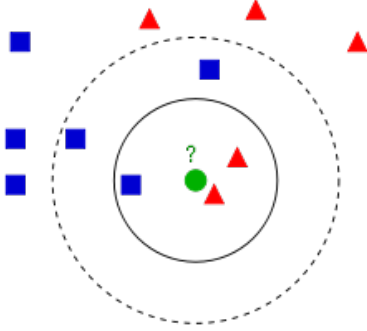


Figure 1.1: Example of KNN classification. The test sample (green circle) should be classified either to the first class of blue squares or to the second class of red triangles. If $K = 3$ (solid line circle) it is assigned to the second class because there are 2 triangles and only 1 square inside the inner circle. If $K = 5$ (dashed line circle) it is assigned to the first class (3 squares vs. 2 triangles inside the outer circle). Credit to https://en.wikipedia.org/wiki/K-nearest_neighbors_algorithm#/media/File:KnnClassification.svg

One of the simple classifiers is *K-Nearest-Neighbors* (KNN) classifier, see Figure 1.1. Given feature vector x and training set $Tr = (\{x_i\}, \{c_i\})$ a classical KNN classifier predicts classification label c such that

$$c^*(x) := \arg \max_y \# \{i : x_i \in knn(Tt, x) \& c_i = y\}$$

where $knn(Tr, x)$ is the set of K nearest neighbors of vector x from the set $\{x_i\}$. The classifier can be used to produce a confidence measure $conf(x, c, Tr)$ that shows the likelihood of test vector x belonging to class c :

$$conf(x, c, Tr) := \frac{\# \{i : x_i \in knn(T, x) \& c_i = y\}}{K}.$$

The value of $conf(x, c, Tr)$ reaches its maximum value of 1 if all K nearest neighbors are from class c .

Given test dataset $R = (\{x'_i\}, \{c'_i\})$ where x'_i are feature vectors and y'_i are true class labels, we define the average accuracy (AC) of classification as

$$AC(R, Tr) := \frac{1}{|R|} \sum_i conf(x'_i, c'_i, R).$$

Note that $AC(Tr)$ is an estimator of probability of correct classification. If accuracy is close to 1 the classifier is able to distinguish feature vectors coming from different classes. That means that features x_i contain a lot of information about classes c_i they originate from. On the other hand, if features x_i do not contain relevant information about class c_i the classifier will not be able to predict correct class better than random guessing¹. In this case the accuracy will be $\frac{1}{|C|}$ where $|C|$ is the number of different classes.

1.2 Cross-validation

Cross-validation is a powerful technique that allows to estimate unbiased statistics, e.g. the average accuracy, in situations where the test data is not provided. Suppose that given training set Tr is partitioned into

¹It is in case of balanced data, i.e. the number of representatives of different classes is the same in the training set.

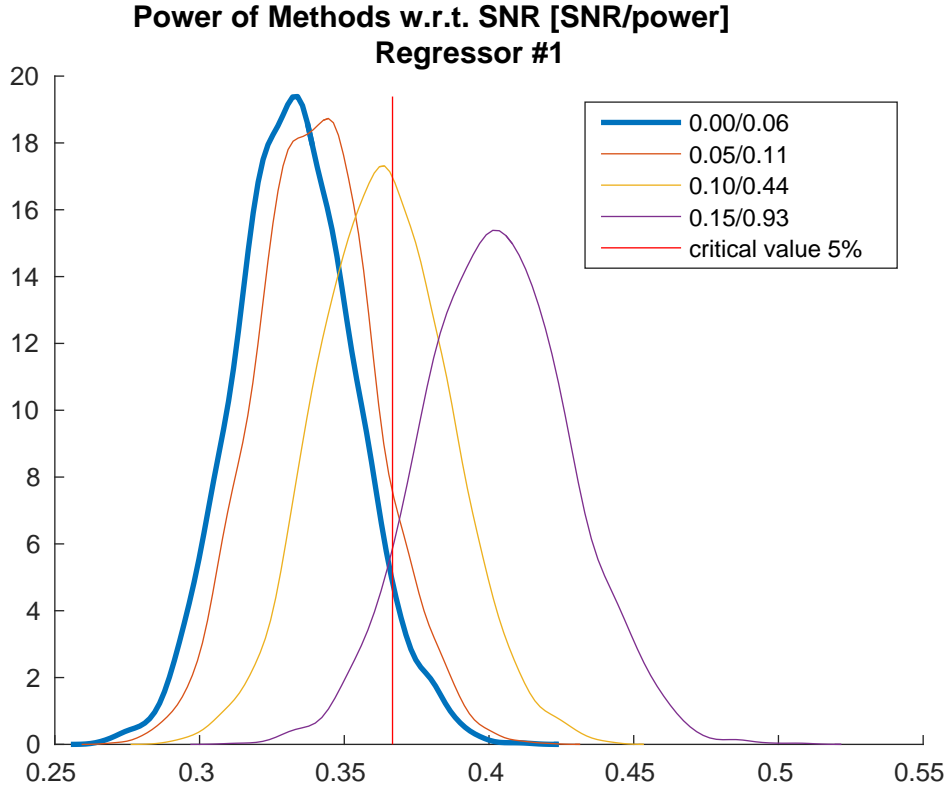


Figure 1.2: KNN: Estimated distribution (probability densities) of the average accuracy of KNN classifier w.r.t different levels of signal noise ratio (SNR). We test the presence of the main effect against pure noise (bold blue curve). The critical value (red vertical bar) is chosen as 95 percentile of H_0 distribution (bold blue curve). The power is the rate of rejection of H_0 in the presence of the main effect. The legend on the plot shows the SNR and power of the statistic test. The power reaches level of 93% at $SNR=0.15$.

n folds $Tr = \cup_{i=1}^n T_i$, then *cross-validated average accuracy* is

$$CVAC(Tr) := \frac{1}{n} \sum_{i=1}^n AC(T_i, Tr \setminus T_i).$$

If the training set is partitioned in a way that folds are independent on each other $CVAC(Tr)$ is an unbiased estimator of the probability of correct classification.

1.3 Factorial pattern analysis of fMRI data

In factorial pattern analysis of fMRI data we are interested in the following question. Does a given region of the brain (represented as activation pattern of voxels) encode information about different conditions and their interaction? One way to answer this question is to train a classifier that predicts the condition that resulted in the observed activation pattern. If the classifier predicts the correct condition significantly better than random guessing then the answer to the question is positive.

In our experimental setting there are 2 factors (T and S), each of them has 3 levels. Each test run measures 9 (one for each combination of factors) activation pattern in 160 voxels. The total number of runs is 6. This yields 54 feature vectors of dimensionality 160. Each run naturally forms an independent fold for cross-validation.

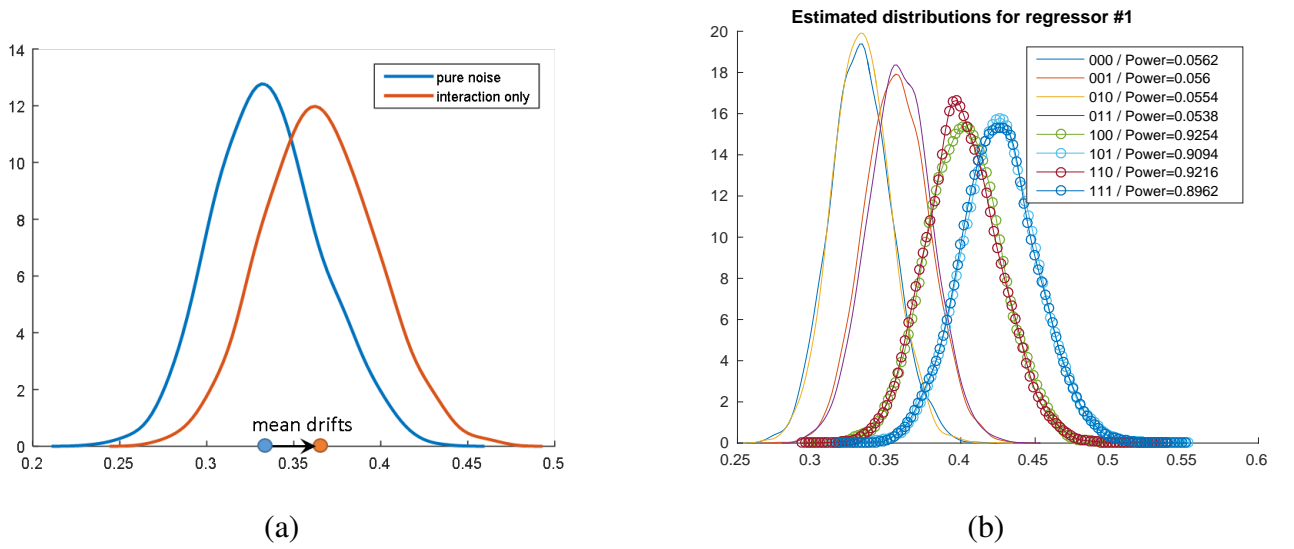


Figure 1.3: KNN: Testing main effect (circle markers) against all possible combinations of other effects (without markers).

(a) Note that as soon as some interaction is introduced the expected value of the classification accuracy increases. This is because interaction allows to discriminate different conditions even if no main effect present.

(b) The distribution of the statistic is not invariant to presence of other effects. 0/1 in the legend codes absence/presence of two main effects and interaction between them. Critical value is given by 95% percentile of H_0 distribution. The power is computed as portion of points generated from H_1 distribution that are above the critical value. For example, “101 / Power = 0.852” corresponds to H_1 s.t. there is no main effect S but there are main effect T and interaction between S and T. H_0 in this case is “001”, i.e. only interaction is present.

1.4 Main effect detection

In this subsection we are interested in detecting the presence of the main effect of a factor. Activation patterns measured under different levels of the factor are significantly different from each other, if the main effect is present. This, in principle, allows a classifier to distinguish the patterns. So, to detect the main effect we train our KNN classifier to predict 3 levels of the factor based on activation patterns. We choose $K = 10$ as the one that gives the best performance. Figure 1.2 shows the result of the experiment.

We observe that as we increase the level of interaction the expected cross-validated average accuracy also increases, see Figure 1.3a. The presence of interaction between factors T and S means that there is a unique structure of activation patterns that allows distinguishing all 9 possible combinations of the factors significantly better than random guessing. But the ability to decode 9 combinations implies the ability to decode each of the factors. This results in the drift in the average accuracy.

To overcome this issue [4] propose to use *double cross validation*. See Figure 1.4B. Suppose the patterns only contain interaction and there is no main effects. Let's consider the patterns where factor T has the level of T_n . There are three patterns, see lower row in Figure 1.4B. There is a unique structure within this patterns that allows distinguishing between them. However the classifier will be able to recognize this structure only if training set contains such combinations of the factors. So, when we test the patterns from factor T_n we should exclude from the training set the patterns coming from T_n as well, see Figure 1.5. This prevents classifier from learning interaction structure while preserves the main effect information, see Figure 1.6a.

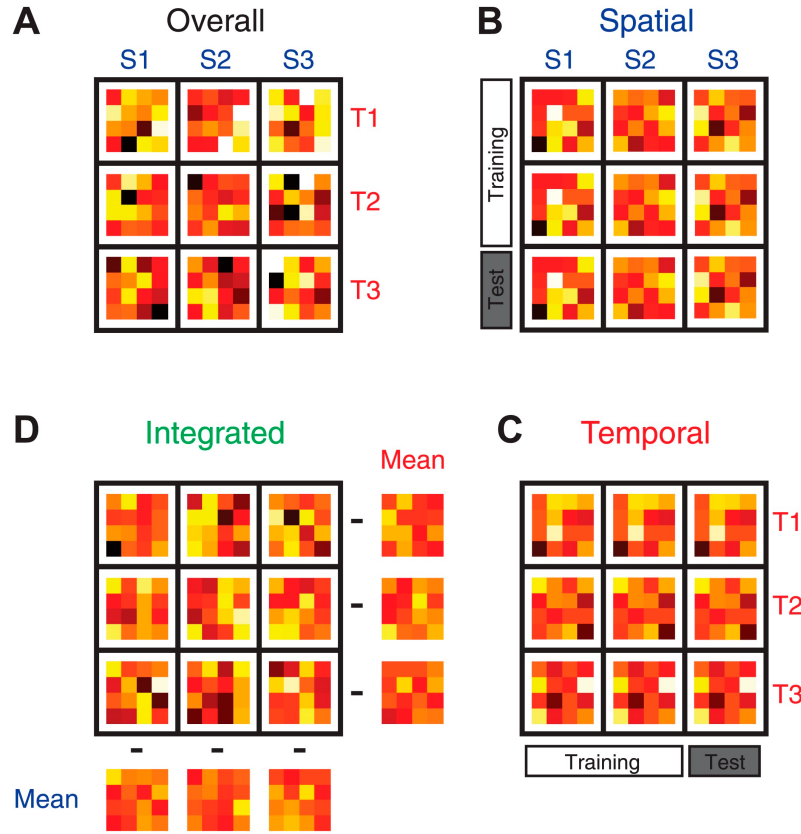


Figure 1.4: Two factors have 3 levels: S1,S2,S3 and T1,T2,T3. All possible combination of levels result in 9 measured activation patterns (A). Double cross-validation allows to decode the main effects (B and C) independently from interaction. Mean subtraction for both factors allows to destroy their main effects and detect only interaction (D). The plot is by [4]

1.5 Interaction detection

To detect interaction we train a classifier to decode all 9 possible combinations of factor levels. However, if there is no interaction but only main effects the classifier will be able to recognize 9 classes with chances significantly higher than random guessing. [4] propose to subtract the mean pattern computed withing each factor level, see Figure 1.4D. Indeed, the main effect of a fixed factor level is constant and remains the same in the mean pattern. If we subtract the mean pattern we remove main effect from the patterns, see Figure 1.6b.

1.6 Results and conclusions

The classification approach is very powerful technique for decoding the activation patterns. It relies on a very popular and established field of machine learning that allows removing the limitations on the number of voxels and assumption of normality of the data. Our experiments show that the approach allows reliable detection of the main effects and interaction. With SNR level of 0.15 the power of the proposed statistical test (base on average accuracy) reaches the level of $\sim 70\%$ for main effect (Figure 1.6a) detection and $\sim 57\%$ for interaction (Figure 1.6b).

2 Discussion

- We implemented and compared three different methods

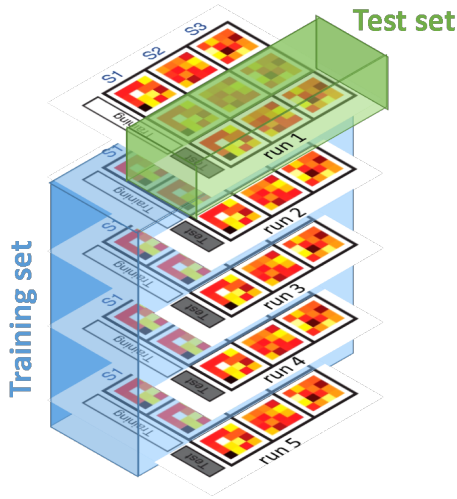
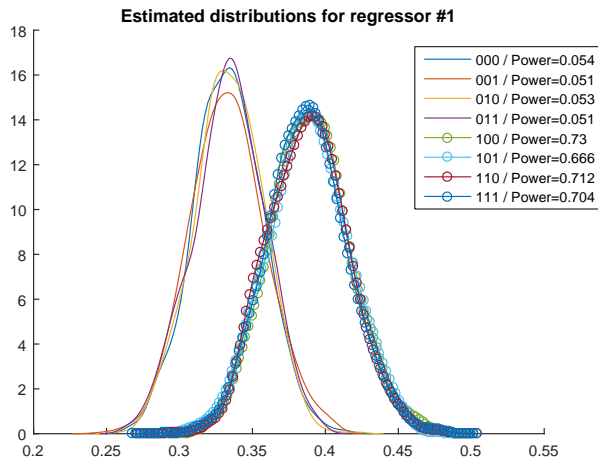
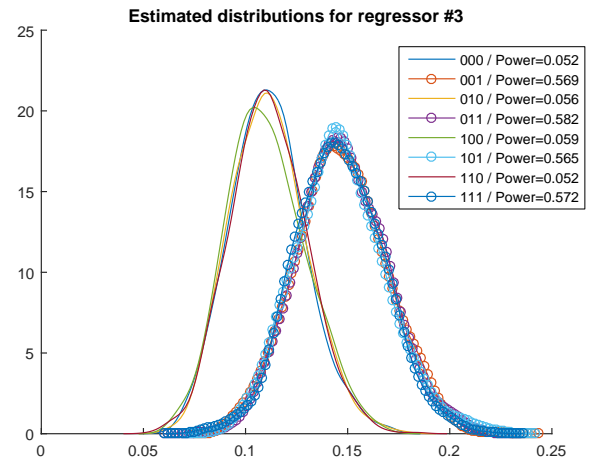


Figure 1.5: Double cross validation for detecting the main effect of the spatial factor. Suppose one tests a classifier on patterns that have the temporal factor level of T_n (marked by word test on the plot) and originate from run i (green box on the plot). Then the classifier should be trained on the rest of the patterns except the patterns with the same temporal level T_n or from run i (blue box on the plot).



(a) Testing the main effect for the first factor (circle markers) against all possible combinations (without markers) with double cross-validation. The distributions only depend on the presence of the main effect. Note that there is no drift as in Figure 1.3.



(b) Testing interaction (circle markers) against all possible combinations (without markers). The distributions only depend on the presence of the interaction.

Figure 1.6: Detection of main effects (a) and interaction (b). For the legend description see Figure 1.3.

- Limitation of simulation: relies on assumptions about data structure and normality
- Limitation of methods: didn't explore different classifiers.

References

- [1] Seiji Ogawa, Tso-Ming Lee, Alan R Kay, and David W Tank. Brain magnetic resonance imaging with contrast dependent on blood oxygenation. *Proceedings of the National Academy of Sciences*, 87(24):9868–9872, 1990.
- [2] Amir Shmuel, Essa Yacoub, Josef Pfeuffer, Pierre-Francois Van de Moortele, Gregor Adriany, Xiaoping Hu, and Kamil Ugurbil. Sustained negative bold, blood flow and oxygen consumption response and its coupling to the positive response in the human brain. *Neuron*, 36(6):1195–1210, 2002.
- [3] Scott A Huettel, Allen W Song, and Gregory McCarthy. *Functional magnetic resonance imaging*, volume 1. Sinauer Associates Sunderland, 2004.

- [4] Katja Kornysheva and Jörn Diedrichsen. Human premotor areas parse sequences into their spatial and temporal features. *eLife*, 3:e03043, 2014.