

Homework 3

Due date: 6 January 2022

1. Detecting signal in noise

In this exercise we seek to identify some signal hidden in high dimensional noise. The file *covtrain.csv* contains a matrix X of $n = 1000$ observations of dimension $p = 500$. Data were generated from the model Boaz Nadler used in his talk:

$$x \sim \mathcal{N}(0_p, \sum_{j=1}^K \lambda_j v_j v_j^T + I)$$

with $K \ll p$ dimension of signal. Note that this also assumes that $v_j \perp v_l$ for $j \neq l$, and that we used $\sigma^2 = 1$ for simplicity.

Our task is to investigate the eigen decomposition of $X^T X/n$ (or PCA of X) to try and find K , the directions, and relate it to the theory and results presented by Boaz.

- (a) Plot the empirical distribution of the eigenvalues of $X^T X/n$ and compare it to the null distribution under the Marchenko-Pasteur law. What do you conclude about the likely number of identifiable non-null signals in this data?
- (b) Compare the top eigenvalues to the magnitude $(1 + \sqrt{p/n})^2$ expected if signal is below the “phase transition” threshold. Are your conclusions similar?
- (c) Now project the matrix X on the 10 top eigenvectors/PCs \hat{v}_j (by multiplying each row by \hat{v}_j), and calculate the norms of these vectors. How are they related to the corresponding eigenvalues? Explain it algebraically.
- (d) Next read another independent matrix drawn from the same distribution in *covtest.csv*. Perform the same 10 projections for this matrix and calculate the norms. Explain the results in light of your findings in the previous items.
- (e) (* Extra credit) Next, can we infer on the nature of the vectors v_j ?
Hint: The structure is relatively simple.
You can use any graphical, intuitive or other method to try and figure it out, but to get credit you then need to find a way to justify your guess in a relevant measurable way.

Some code hints for this problem are in the file *pca.r*.

2. Selective inference and multiple testing

Our general setup: we are either testing m hypotheses or building confidence intervals for m parameters. We may select a subset $S \in \{1, \dots, m\}$ of them as “interesting”.

- (a) State whether each of these claims is true or false and explain **briefly and clearly**:
- Building confidence intervals at the Bonferroni level $1 - \alpha/m$ guarantees FCR control at level α for any subset S .
 - If we choose a set of rejected hypotheses by the BH procedure at level α , obtaining R rejections, and then build confidence intervals at level $1 - \alpha \cdot R/m$, then the FCR is also controlled at level α .
 - If we decide to select all m hypotheses as “interesting”, then selective inference (i.e., controlling FCR) is reduced to inference “on average”, meaning we are controlling the expected percentage of errors of our m hypotheses.
- (b) Consider the Science paper by Zeggini et al. referenced in slide 28 of Yoav’s deck (“Selection by table”) (link to the original paper can be found the class homepage).
- Assume we calculate FCR-corrected confidence intervals for the second to last column of the table. Considering the results from the first part of this problem, and the p values in the table, explain why these FCR-corrected intervals are not expected to cross below 1.
 - Assume now that we were to take a different approach, collect all the SNPs that were significant in *any* of the participating studies, and declare all of them “selected” (their number can be much bigger than the ten on slide 11), and then build FCR-corrected CI’s for them at FCR level α , based on the entire meta analysis (like the last two columns of the table). Do you expect that some of these intervals will cross 1? Explain. What percentage of non-coverage do you expect over these selected? Specifically, do you expect this percentage to be about α , smaller than that, or larger than that? Explain.
- (c) Assume now that instead of selecting interesting results, we can order our hypotheses a-priori from “the most important” to the least important. We care most about the first hypothesis and least about the last. The following procedure is known as hierarchical testing:
- Test the most important null hypothesis at level α . If not rejected, stop and don’t consider the other hypotheses.
 - If rejected, continue to the second null hypothesis and test it at level α . If this second hypothesis not rejected, stop.
 - Continue until a non-rejected null. Then stop.
- Does this procedure control FWER at level 0.05? Prove your answer (a full formal proof is not required, but a clear and correct argument is required).
 - Given a large number m of hypotheses, consider Bonferroni, α -spending, and this hierarchical approach, all at level α . Can you predict which one would make more rejections? Why yes or why not?