Using clustering to correct for multiple comparisons

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We present here the various functions needed to perform multiple comparisons correction with LIMO EGG

LIMO EEG toolbox: LInear Modeling of EEG data.

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Multiple Comparison Correction

The type I error rate across tests increases with the number n of statistical tests. This family wise error rate, or FWER = 1 - (1 - alpha)^n. This formula is for n independent tests, and therefore the actual FWER is even higher for MEEG because data are correlated in space and time.

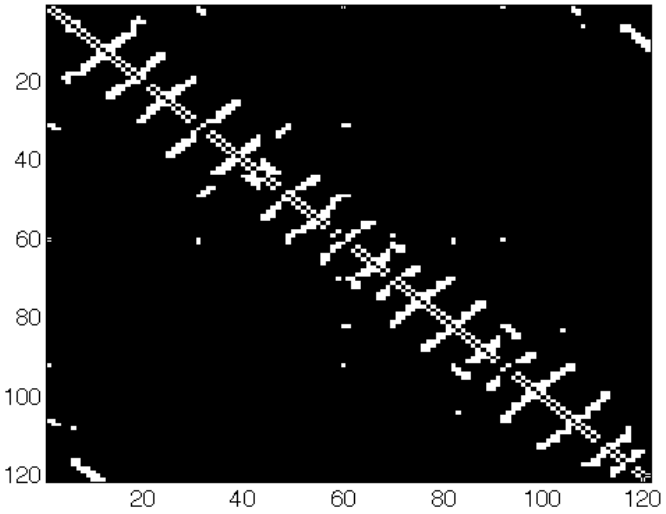
For a single test, the frequentist framework uses the distribution of t or F values under the null hypothesis to estimate the conditional probability p to observe an effect as large or larger than the one observed in the data, given that the null hypothesis is correct. LIMO EEG deals with multiple testing by estimating the null distribution of maximum statistics across the whole data space. For a t-test or an ANOVA, the null hypothesis is created by centring the distribution for each condition and then the data are sampled with replacement, and for each bootstrap sample, t and F values are computed. To correct for multiple comparisons, one strategy consists in saving, for each bootstrap, the maximum t or F value across channels and time frames. Since the FWER is the probability to make at least one error, by using the largest value under the null, we control the probability that the largest values are errors – and therefore also control for all of the other (smaller) values indiscriminately for space/time/frequency.

After N bootstraps, the null distribution of this max statistics can be used to threshold the original results: for instance original F values could be considered significant if they are larger than the 95th percentile of the max bootstrapped F distribution. However, this max statistics approach tends to be conservative because it does not account for the correlation of the data in space and time. As alternatives, we can compute, under H0, the distribution of maximum cluster mass (Maris, E. & Oostenveld, R., 2007; Pernet, Latinus, Nichols, & Rousselet, 2015) or the distribution of maximum TFCE scores (Pernet et al., 2015; Smith & Nichols, 2009).

The neighbourhood matrix

To create clusters, we need to describe the relationship among observed data. Across time points or frequency bands, neighbours are simply successive data points. Across channels, we need to consider channels' positions to define a neighbourhood matrix.

Here is an example of a neighbourhood matrix:



This is an Nc x Nc matrix, where Nc is the number of channels. White cells indicate pairs of neighbouring electrodes; black cells indicate electrodes that are not neighbours.
A neighbouring matrix can be created in 4 ways:

(i) using EEGLAB STUDY which will generate such matrix automatically (but worth checking it)
(ii) by calling the limo tools GUI and selecting 'Create an expected chanloc files'.
(iii) by using limo_get_channeighbstructmat, with this syntax:
[neighbours,channeighbstructmat]=limo_get_channeighbstructmat(EEG,neighbourdist)
(iv) by assigning values directly to a channeighbstructmat matrix, and saving it to disk.

For options (ii) and (iii), you need to input the neighbouring distance, the threshold distance that defines neighbour electrodes. For instance, 0.37 cm is a good distance for Biosemi standard 128 electrode configuration, or 40 mm for a 65 channels EasyCap. Note how here I used cm or mm, it depends how this is defined in your data so be careful of using the right units. You can check the accuracy of the neighbourhood matrix for your electrode montage by using the output neighbours from limo_get_channeighbstructmat: neighbours is a structure that defines for each channel a list of its neighbours, and in which a channel is not a neighbour of itself – for instance:

```
neighbours{1}.label = 'Fz';
neighbours{1}.neighblabel = {'Cz', 'F3', 'F3A', 'FzA', 'F4A', 'F4'};
neighbours{2}.label = 'Cz';
neighbours{2}.neighblabel = {'Fz', 'F4', 'RT', 'RTP', 'P4', 'Pz', 'P3', 'LTP', 'LT', 'F3'};
neighbours{3}.label = 'Pz';
neighbours{3}.neighblabel = {'Cz', 'P4', 'P4P', 'Oz', 'P3P', 'P3'};
```
and so on…

Finding an appropriate neighbouring distance for your electrode montage will probably require several attempts. Ensure that you check all the electrodes to be sure their neighbours are correct. In some cases, and in particular for 32 or 64 electrode montages, it might be difficult to find an appropriate neighbouring distance. You may have to decide subjectively to include or not certain neighbours. In such cases, you might also find useful to get as good a neighbourhood matrix as you can using options (i) or (ii), which you would then tweak manually to adjust the status of certain borderline electrodes (iii).

Clustering Data

Cluster mass

For a given set of statistical results, an uncorrected, univariate, threshold is applied (e.g. $p<0.05$) to create a thresholded map of clusters. Cluster mass corresponds, for a given cluster, to the sum of statistical values inside that cluster. Cluster mass thus reflects both the height (the strength of the statistical values) and the size (the number of statistical values) of the cluster.

Clustering

To threshold data, we need:
(i) maps of observed t or F values, and their corresponding p values;
(ii) a set of maps of t or F values, and their matching p values obtained under H0;
(iii) a neighbourhood matrix, which describes the relationship among channels.

TFCE (Threshold Free Cluster Enhancement)

As explained above, thresholding based on clustering implies a cluster forming threshold: for instance, a p value <= 0.05 is used as a threshold to define clusters in the bootstrapped and in the original data. The TFCE technique instead integrates statistical values through 'all' cluster forming thresholds (in LIMO by discreet steps of 0.1 between some minimum and maximum values). A TFCE score is thus a statistical value (t or F) weighted by the strength of the cluster to which it belongs. The weight depends on the extent and the height of this cluster. TFCE scores for observed data and data under H0 can be obtained using limo_tfce. Finally, a significance test can be obtained by comparing the observed TFCE scores to a percentile (e.g. 95th) of the bootstrapped maximum TFCE scores (across all electrodes and time frames). This strategy effectively controls for multiple comparisons.

References

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