Testing Time by Time Differences of EEG Signals using the Slopes within Multiple Comparisons Procedure

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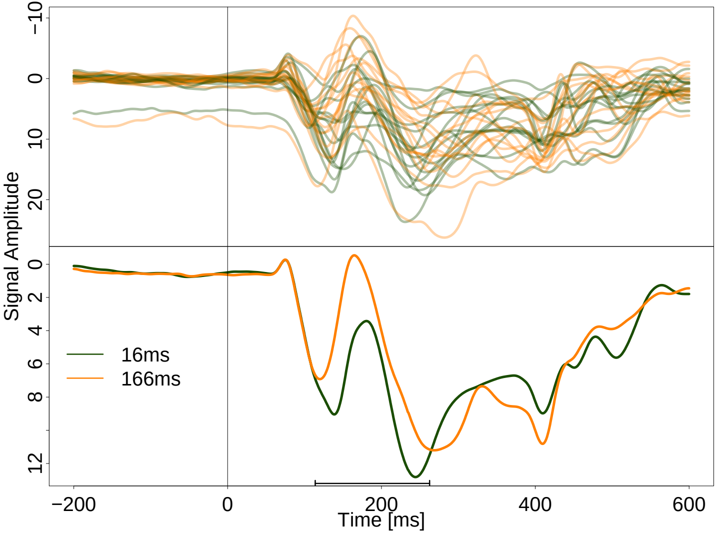
Comparisons of Signals or Massively Univariate Tests



Data from Tipura, Renaud, and Pegna (2019) available in `R` package `permuco`.

Model

We have a linear model at each time t:

$$Y_t = \mathbf{1}\mu_t + X\beta_t + \epsilon_t$$

where the design X is the same for all time-point. We want to test the hypotheses:

$$H_0 : \ \beta_t = 0 \ \forall \ t \in \{1, \dots, T\}$$

For all t, we use a F **statistic**:

$$F_t = \frac{{Y_t}^\top H_{R_{\mathbf{1}}X} Y_t}{{Y_t}^\top R_{[\mathbf{1}X]} Y_t} \frac{n-p}{p-1}$$

with $H_X = X(X^\top X)^{-1}X^\top$ and $R_X = I - H_X$.

We control the **FWER** using the cluster-mass test.

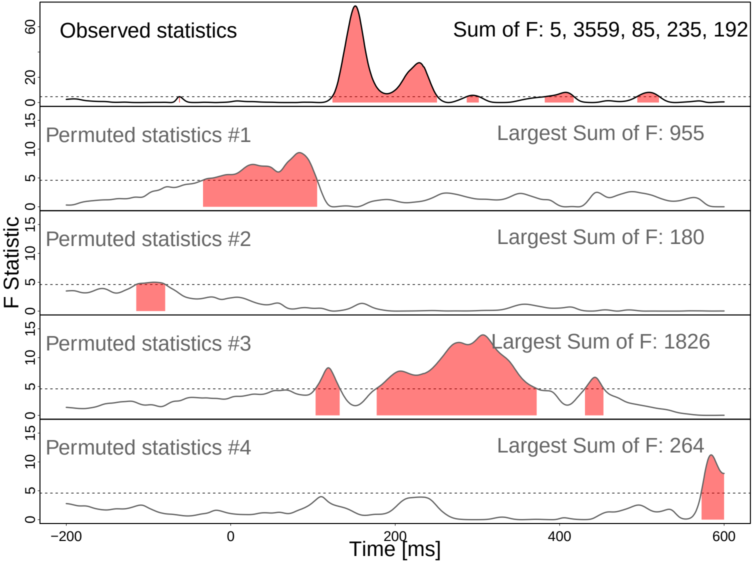
Cluster-Mass Test (1/4)

- Introduced by Bullmore et al. (1999) for fMRI data.
- Introduced by Maris and Oostenveld (2007) for EEG data.
- (+) **Controls (weakly) the FWER.**
- **"Clusters"-level inference.**
- (+) No influence of the sampling rate.
- Generalization to multi-channels analysis (full scalp).

`R` package:

- CRAN: `permuco` for 1 channel (Frossard and Renaud 2018).
- For the full scalp analysis: https://github.com/jaromilfrossard/clustergraph.

Cluster-Mass Test (2/4)



Cluster-mass Test (3/4)

1. For all t, we compute a F **statistic**:

$$\{Y_t, X\} \ \rightarrow \ F_t = \frac{{Y_t}^\top H_{R_{\mathbf{1}}X} Y_t}{{Y_t}^\top R_{[\mathbf{1}X]} Y_t} \frac{n-p}{p-1}$$

2. We create **clusters** using the threshold τ and compute their **clustermass**:

$$\{F_t,\ \tau\} \ \rightarrow \ \mathrm{C}_k \rightarrow \ M_k$$

   where M_k is the sum of F_t within the cluster C_k.

3. We compute the **null distribution** $\mathcal{M}_0$ of M_k by permutation, repeating (1-2) for each permutation:

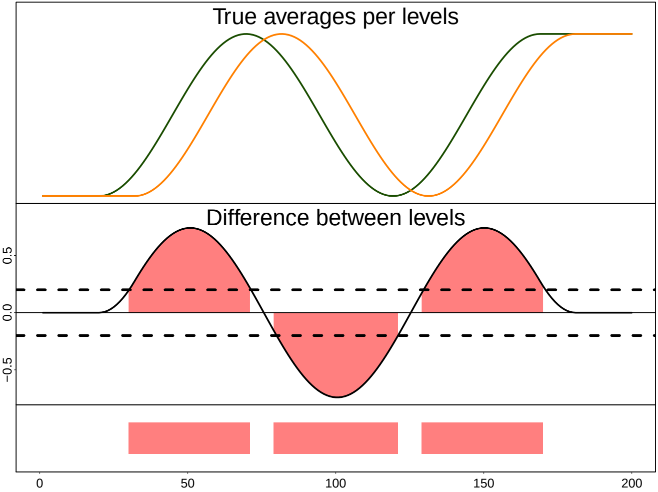
$$\{Y_t^*, X\} \rightarrow F_t^* \rightarrow C_{k^*}^* \rightarrow \max(M_{k^*}^*)$$

4. For all $n!$ permutations, the values $\max(M_{k^*}^*)$ produce the null distribution $\mathcal{M}_0$. A p-value for C_k is computed by comparing M_k to $\mathcal{M}_0$.

Cluster-mass Test (4/4)

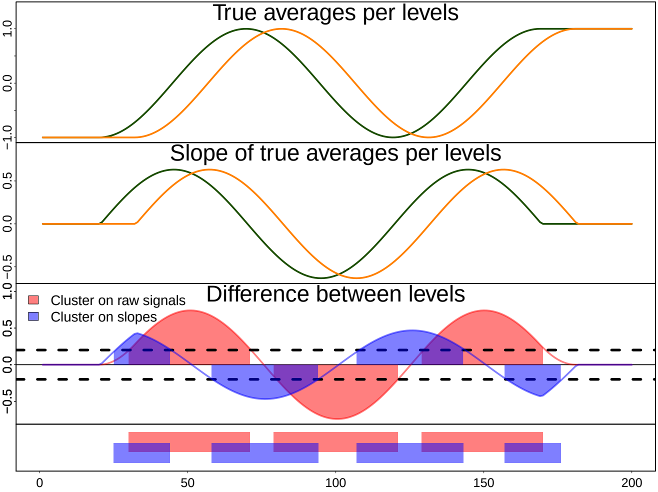
- (+) Signals are smoothed (effects and noise).
- (+) In EEG, true effects happen by clusters.
- If there is a true effect at time t, it is likely that there is a similar effect at time $t-1$ or $t+1$.
- 1 underlying brain process => 1 cluster => 1 inference.
- **(-) 1 underlying brain process => k clusters => k inferences.**

Problems with Cluster-Mass Test



- 1 underlying brain process => 3 clusters => 3 inferences.

Binding Clusters with the Slopes



Notation

Model at time t, $\forall\ t\ \in\ 1, \ldots, T$:

$$Y_t = \mathbf{1}\mu_t + X\beta_t + \epsilon_t. \tag{1}$$

Model for the slopes:

$$\dot{Y}_t = \mathbf{1}\dot{\mu}_t + X\dot{\beta}_t + \dot{\epsilon}_t, \tag{2}$$

where $\dot{\mu}_t = \frac{\partial \mu_t}{\partial t}$ and $\dot{\beta}_t = \frac{\partial \beta_t}{\partial t}$, with the same design X for both models.

Given a time interval I, if $\beta_t = 0\ \forall\ t \in I$, then $\dot{\beta}_t = \frac{\partial \beta_t}{\partial t} = 0\ \forall\ t \in I$.

We test simultaneously :

$$H_0^t:\ \beta_t = 0\ \&\ \dot{\beta}_t = 0\ \forall\ t\ \in\ 1, \ldots, T \tag{3}$$

Estimating the Slopes

1. Time differences.
   (-) Increase the roughness of the signals
2. Local polynomial. Minimize:

$$\sum_{s=1}^{T}\left(Y_{is}-\sum_{j=0}^{p}\gamma_t^{(j)}(s-t)^j\right)K_h(s-t),$$

then $\hat{\gamma}_t^{(1)}$ is an estimator of $\dot{Y}_{it}$ (Fan and Gijbels 1996).
The bandwidth h, unique for all n signals, and is such that:

$$\sum_{i}^{n}\text{roughness}(Y_i)=\sum_{i}^{n}\text{roughness}(\hat{\dot{Y}}_i),$$

where roughness($\cdot$) is the variance of the second derivative using time differences (in `R`: `var(diff(diff( )))`).

Summary

1. For all t, we compute a F statistic on the raw signal:

$$\{Y_t, X\} \;\rightarrow\; F_{Y_t} = \frac{{Y_t}^\top H_{R_{\mathbf{1}}X} Y_t}{{Y_t}^\top R_{[\mathbf{1}X]} Y_t} \frac{n-p}{p-1}$$

2. And on their slopes:

$$\{\dot{Y}_t, X\} \;\rightarrow\; F_{\dot{Y}_t} = \frac{{\dot{Y}_t}^\top H_{R_{\mathbf{1}}X} \dot{Y}_t}{{\dot{Y}_t}^\top R_{[\mathbf{1}X]} \dot{Y}_t} \frac{n-p}{p-1}$$

3. Then we create clusters with the threshold τ:

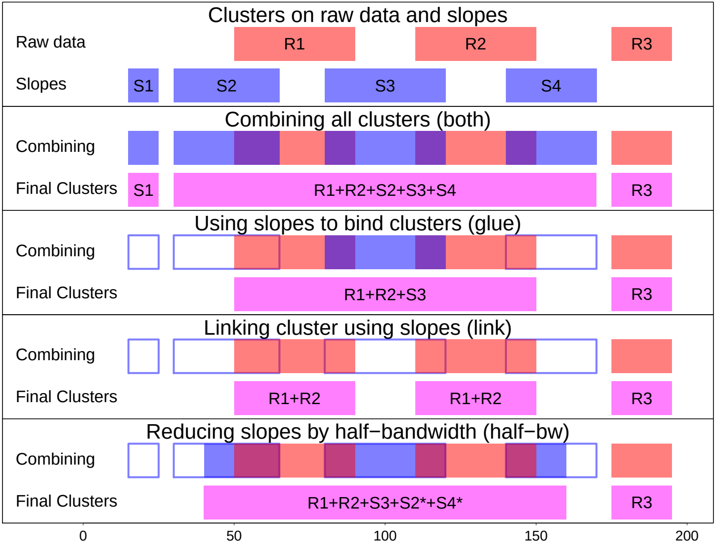
$$\{F_{Y_t},\; \tau\} \;\rightarrow\; \mathrm{C}_{Y:k} \rightarrow\; M_{Y:k}$$

$$\{F_{\dot{Y}_t},\; \tau\} \;\rightarrow\; \mathrm{C}_{\dot{Y}:l} \;\rightarrow\; M_{\dot{Y}:l}$$

4. Finally we combine the clusters:

$$\{C_{Y:k}, C_{\dot{Y}:l}\} \rightarrow C_{Y\dot{Y}:m} \rightarrow M_{Y\dot{Y}:m}$$

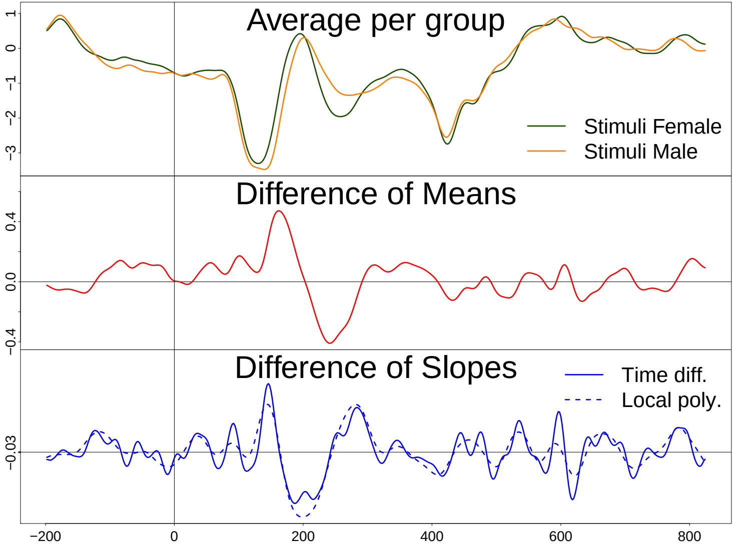
Combining Clusters



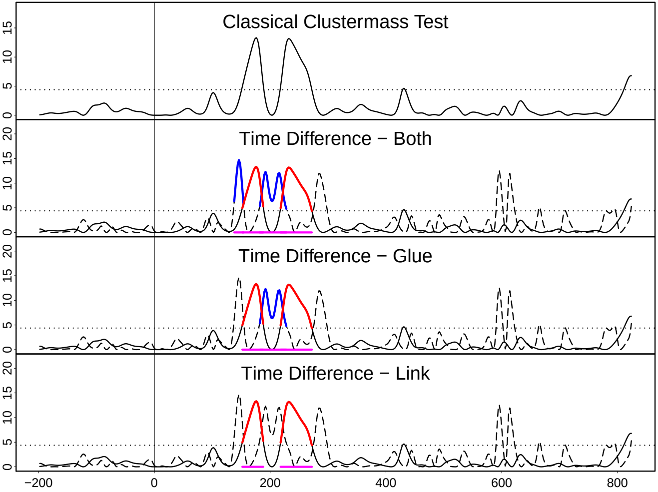
Real Data Example

- Data from the electrode Cz.
- 2 **sex of stimuli** (M vs F).
- 3 emotions of stimuli (angry, neutral, happy).
- 2 types of instructions (focus sex, focus emotion).
- Repeated measures ANOVA design.
- Permutation of residuals: method by Kherad-Pajouh and Renaud (2015).

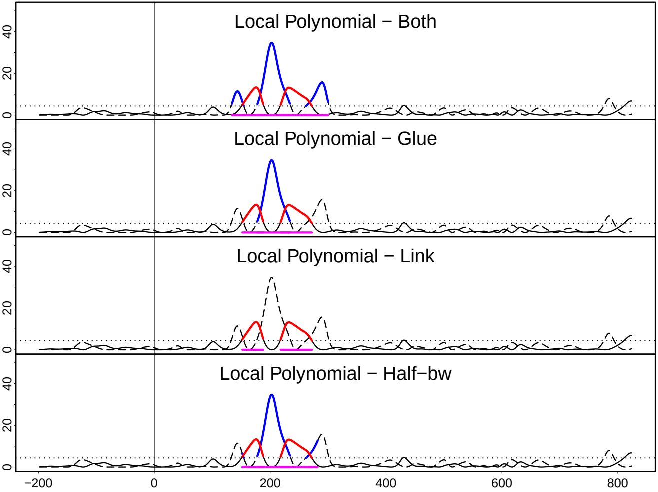
Main Effect of the Sex of Stimuli



Cluster-Mass and Extensions 1/2

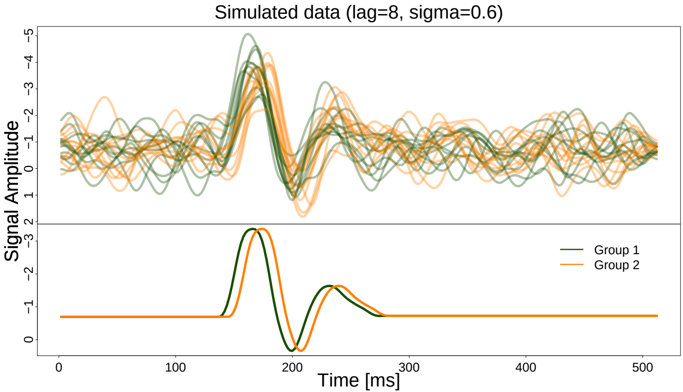


Cluster-Mass and Extensions 2/2



Simulation setting

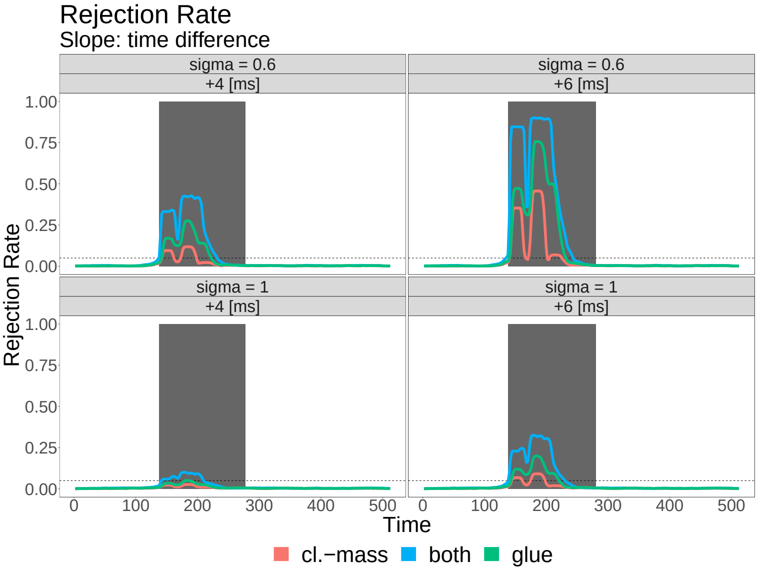
- Time difference, local polynomial
- Clustermass (classic), both, glue, link, half-bw
- σ: **0.6**, 1 and 1.2
- Lags between levels: 0, 2, 4, 6, **8** ms.
- Gaussian correlation function.



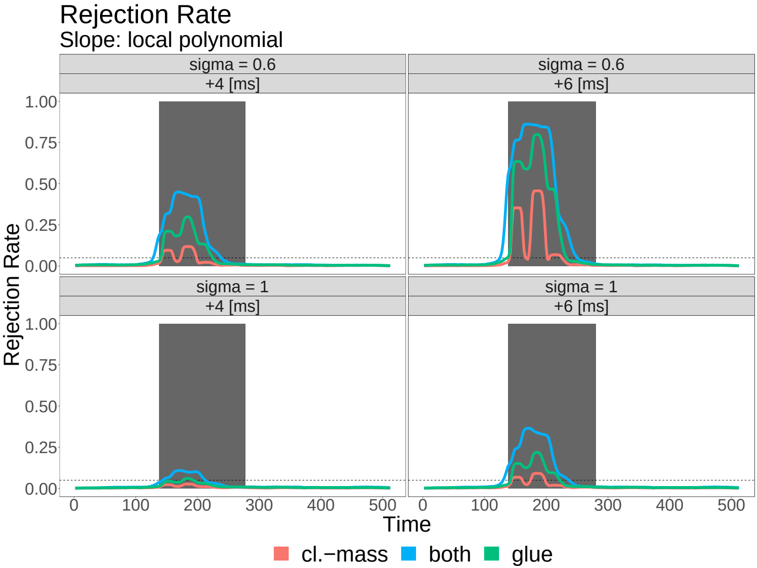
FWER

Slope Estim.	0.6	1	1.2
Clustermass			
no	*.043 [.037;.050]*	**.047 [.041;.054]**	**.050 [.044;.058]**
Both			
local poly.	**.044 [.038;.051]**	**.046 [.040;.054]**	**.050 [.044;.058]**
time diff.	**.048 [.042;.055]**	**.048 [.042;.055]**	**.052 [.046;.060]**
Glue			
local poly.	**.046 [.039;.052]**	**.047 [.041;.054]**	**.052 [.046;.060]**
time diff.	*.042 [.036;.049]*	**.048 [.042;.055]**	**.050 [.043;.057]**
Link			
local poly.	*.042 [.037;.049]*	**.048 [.041;.055]**	**.051 [.045;.058]**
time diff.	*.042 [.037;.049]*	**.047 [.041;.054]**	**.050 [.044;.057]**
Half-bw			
local poly.	**.044 [.038;.051]**	**.048 [.042;.056]**	**.046 [.040;.053]**

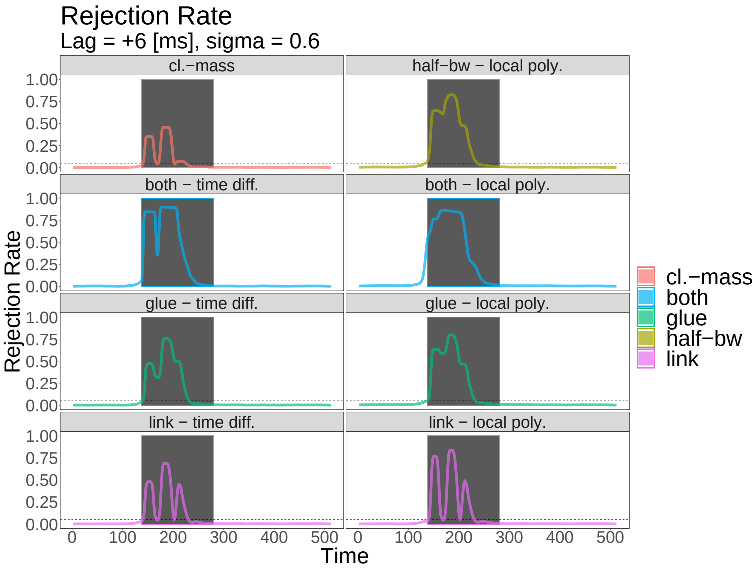
Rejection Rate: using time difference



Rejection Rate: using local polynomial



Rejection Rate



Conclusion

- FWER at the nominal level.
- Increase of power using the slopes.
- Smaller increase of false positive using glue or link.
- Extension to the full scalp?

Bibliography I

Bullmore, Edward T., John Suckling, Stephan Overmeyer, Sophia Rabe-Hesketh, Eric Taylor, and Michael J. Brammer. 1999. "Global, Voxel, and Cluster Tests, by Theory and Permutation, for a Difference Between Two Groups of Structural MR Images of the Brain." *IEEE Transactions on Medical Imaging* 18 (1): 32–42. https://doi.org/10.1109/42.750253.

Fan, Jianqing, and Irene Gijbels. 1996. *Local Polynomial Modelling and Its Applications: Monographs on Statistics and Applied Probability 66*. 1 edition. London ; New York: Chapman and Hall/CRC.

Frossard, Jaromil, and Olivier Renaud. 2018. "Permuco: Permutation Tests for Regression, (Repeated Measures) ANOVA/ANCOVA and Comparison of Signals."

Bibliography II

Kherad-Pajouh, Sara, and Olivier Renaud. 2015. "A General Permutation Approach for Analyzing Repeated Measures ANOVA and Mixed-Model Designs." *Statistical Papers* 56 (4): 947–67. https://doi.org/10.1007/s00362-014-0617-3.

Maris, Eric, and Robert Oostenveld. 2007. "Nonparametric Statistical Testing of EEG- and MEG-Data." *Journal of Neuroscience Methods* 164 (1): 177–90. https://doi.org/10.1016/j.jneumeth.2007.03.024.

Tipura, E., O. Renaud, and A. J. Pegna. 2019. "Attention Shifting and Subliminal Cueing Under High Attentional Load: An EEG Study Using Emotional Faces." *Neuroreport*, October. https://doi.org/10.1097/WNR.0000000000001349.