permuco : permutation tests for regression, ANOVA and comparison of signals

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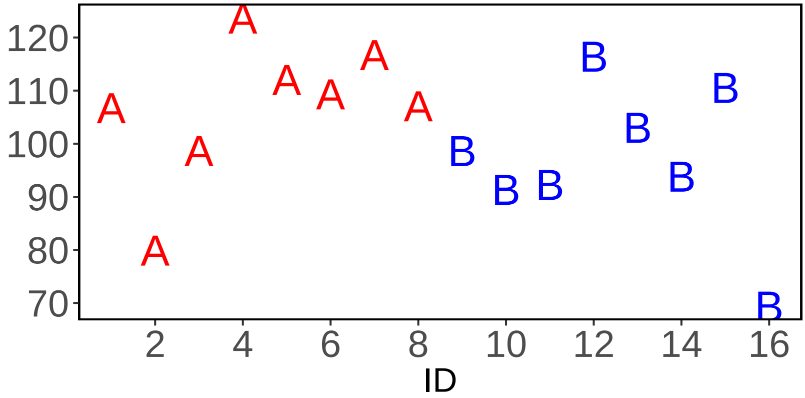
Parametric vs permutation test : an example

```
n <- 8
IV <- c(rep("A",n),rep("B",n))
mu <- 95 + 10*(IV == "A")
df  <- data.frame(IV = IV,DV = rnorm(2*n,mu,9))
```

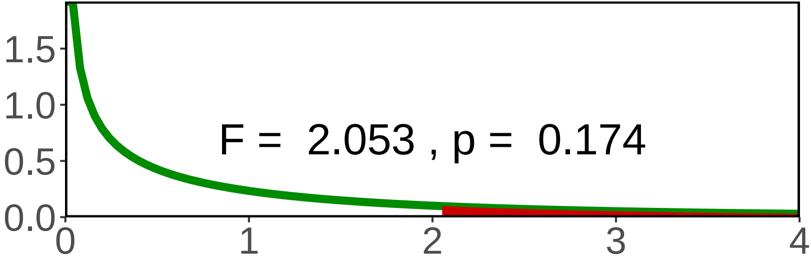


Parametric approach

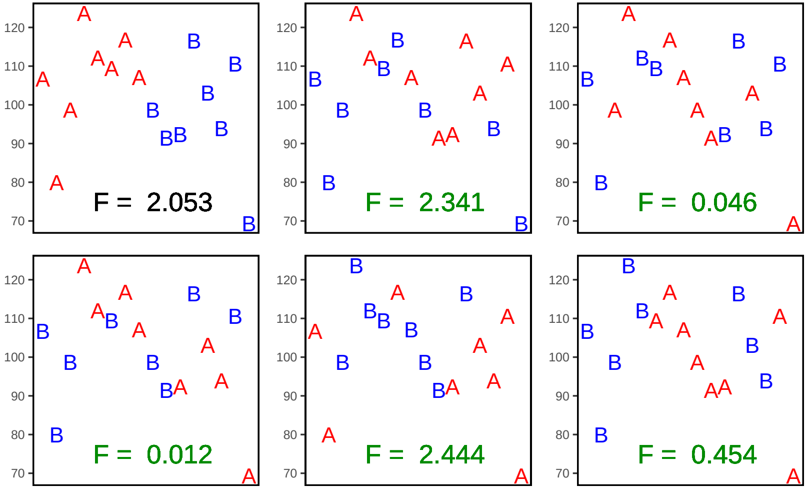
- $H_0 : \mu_A - \mu_B = 0$
- Distribution of the statistic under the H0
- Comparison of the observed statistic to the distribution

```r
summary( aov( DV ~ IV, df))
```

```
##             Df Sum Sq Mean Sq F value Pr(>F)
## IV           1  386.1   386.1   2.053  0.174
## Residuals   14 2633.2   188.1
```



Permutation approach



Permutation approach : aovperm(formula, data)

```r
library( devtools)
install_github( "jaromilfrossard/permuco")
library( permuco)
```

```r
model_oneway <- aovperm( DV ~ IV, df, method = "manly")
model_oneway
```

```
## Anova Table
```

```
## Permutation test using manly to handle noise
## variables and 5000 permutations.
```

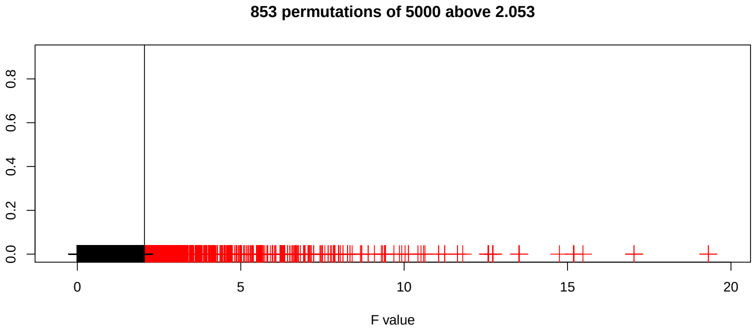
```
##                SS df     F parametric P(>F) permutation P(>F)
## IV          386.1  1 2.053           0.1739            0.1708
## Residuals 2633.2 14
```

Permutation approach : aovperm(formula, data)

Definition of p-value:

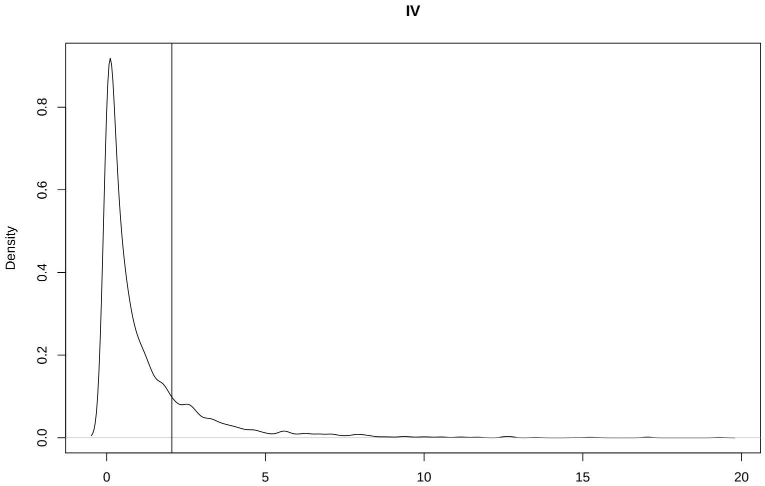
$$p_{perm} = \frac{\#(F_i^* \geq F)}{N_p} = \frac{1}{N_p} \sum_{i=1}^{N_p} \mathrm{I}(F_i^* \geq F)$$

for $N_p = N!$.(For 1-way ANOVA of 2 groups of size n, $N_p = \frac{(2n)!}{(n!)^2}$)



Permutation approach : aovperm(formula, data)

```
plot( model_oneway)
```



Permutation VS parametric

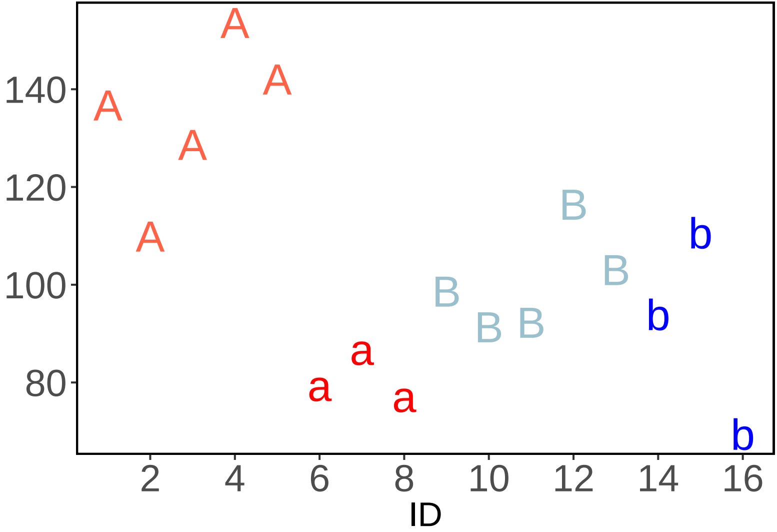
	Parametric	permutation
Statistics	t, F	no restriction
Distribution	probability theory	by permutation
Assumptions	normality	exchangeability
Models	complexe	simple

Exchangeability under $H_0 : P_{\mathbf{y}}(\mathbf{y}) = P_{\mathbf{y}}(\mathbf{y}^*)$

The distribution of the data does not change after a permutation of the observations.

Same mean, same variance, same “shape” after permutation.

Permutation test with nuisance variables



Permutation methods : regression / ANOVA

Linear Model :

$$y = X\beta + D\eta + \epsilon$$

with $\epsilon \sim (0, I\sigma_\epsilon^2)$, X are the variables of interest and D are the nuisance variables.

Hypothesis :

$$H_0 : \beta = 0$$

General idea : reduce the effect of $D\eta$, before permuting the data.

Permutation methods : regression / ANOVA

Some formulas (for the small model, with only $D\eta$) :

- Hat matrix : $H_D = D(D'D)^{-1}D'$, fitted value : $\hat{y} = H_D y$.
- Residual matrix : $R_D = I - H_D$, $R_D y = y - \hat{y}$.
- Permutation matrix : Py, $P'Py = y$
- Decomposition : $R_D = VV'$, $V'V = I$.
  $\dim(V') = (n - \mathrm{rank}(D)) \times n$

method argument	y^*	D^*	X^*	
manly	Py	D	X	
draper_stoneman	y	D	PX	
freedman_lane	$(H_D + PR_D)y$	D	X	
terBraak	$(H_{X,D} + PR_{X,D})y$	D	X	$H_0 : \beta = \hat{\beta}$
kennedy	$PR_D y$		$R_D X$	
huh_jhun	$PV'R_D y$		$V'R_D X$	
dekker	y	D	$PR_D X$	

Permutation methods : repeated measures ANOVA

Repeated measures ANOVA :

$$y = X\beta + D\eta + Z\gamma + E\kappa + \epsilon$$

with $\kappa \sim \mathcal{N}(0, I\sigma^2_\kappa)$, $\gamma \sim \mathcal{N}(0, I\sigma^2_\gamma)$, $\epsilon \sim \mathcal{N}(0, I\sigma^2_\epsilon)$

Null hypothesis : $H_0 : \beta = 0$

Statistic $F = \frac{y' H_{R_D X} y / rank(X)}{y' H_{R_D Z} y / rank(Z)}$

method argument	y^*	D^*	X^*	E^*	Z^*
Rd_kheradPajouh_renaud	$R_D y$		$R_D X$	$R_D E$	$R_D Z$
Rde_kheradPajouh_renaud	$R_{D,E} y$		$R_{D,E} X$		$R_{D,E} Z$

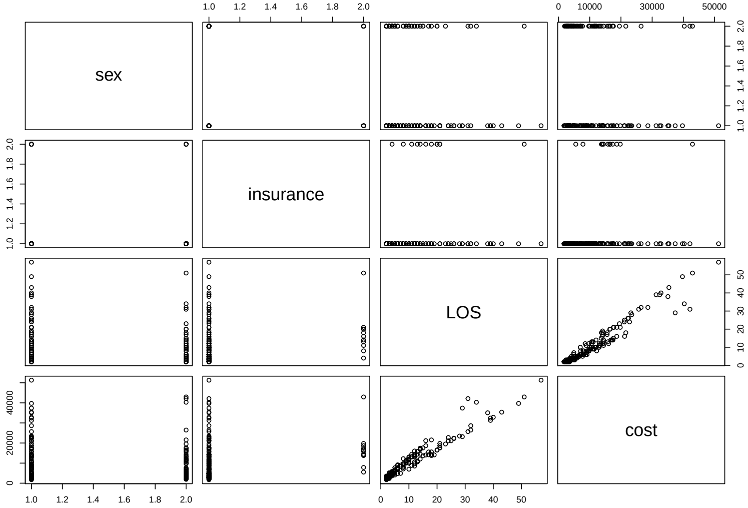
emergencycost dataset

```
## data summary
summary(emergencycost)
```

```
##  sex          age                  insurance          LOS
##  F:104   Min.   : 9.00   public       :164   Min.   : 2.00
##  M: 72   1st Qu.:40.75   semi_private: 12   1st Qu.: 3.00
##          Median :63.00                      Median : 6.50
##          Mean   :59.54                      Mean   :10.76
##          3rd Qu.:77.25                      3rd Qu.:14.00
##          Max.   :97.00                      Max.   :57.00
##       cost
##  Min.   : 1721
##  1st Qu.: 4082
##  Median : 7764
##  Mean   :10891
##  3rd Qu.:14269
##  Max.   :51295
```

emergencycost dataset

```r
pairs(emergencycost[,-2])
```



Using aovperm() with emergencycost dataset

```r
## centrering the covariate to the mean
emergencycost$LOSc <- scale(emergencycost$LOS,
                            scale = F)

## ANCOVA
ancova_terBraak <- aovperm(cost ~ LOSc*sex*insurance,
                    data = emergencycost,
                    method = "terBraak")
ancova_terBraak
```

```
Anova Table
Permutation test using terBraak to handle noise variables and 5000 permutations.
                         SS  df       F para P(>F) perm P(>F)
LOSc              2.162e+09   1 483.442      0.000      0.000
sex               1.463e+07   1   3.271      0.072      0.076
insurance         6.184e+05   1   0.138      0.710      0.687
LOSc:sex          8.241e+06   1   1.843      0.176      0.161
LOSc:insurance    2.911e+07   1   6.508      0.012      0.029
sex:insurance     1.239e+05   1   0.028      0.868      0.860
LOSc:sex:insurance 1.346e+07  1   3.009      0.085      0.090
Residuals         7.514e+08 168
```

Using lmperm() with emergencycost dataset

```r
## Change coding of factors
contrasts(emergencycost$insurance) <- contr.sum
contrasts(emergencycost$sex) <- contr.sum

## Check the coding of the factor sex
contrasts(emergencycost$sex)
```

```
##   [,1]
## F    1
## M   -1
```

```r
lm_dekker <- lmperm(cost ~ LOSc*sex*insurance,
                    data = emergencycost, method = "dekker")
```

Using lmperm() with emergencycost dataset

```
lm_dekker
```

```
Table of marginal t-test of the betas
Permutation test using dekker to handle noise variable and 5000 permutations.
                     Estimate Std. Error t value para P(>|t|) perm P(<t)
(Intercept)          11474.03     401.02  28.612        0.000
LOSc                   845.47      38.45  21.987        0.000      1.000
sex1                  -725.32     401.02  -1.809        0.072      0.043
insurance1            -149.12     401.02  -0.372        0.710      0.335
LOSc:sex1              -52.20      38.45  -1.357        0.176      0.081
LOSc:insurance1         98.10      38.45   2.551        0.012      0.990
sex1:insurance1         66.75     401.02   0.166        0.868      0.578
LOSc:sex1:insurance1   -66.70      38.45  -1.735        0.085      0.040
                     perm P(>t) perm P(>|t|)
(Intercept)
LOSc                      0.000        0.000
sex1                      0.958        0.078
insurance1                0.665        0.686
LOSc:sex1                 0.919        0.161
LOSc:insurance1           0.010        0.020
sex1:insurance1           0.422        0.849
LOSc:sex1:insurance1      0.960        0.080
```

Multiple comparisons problem : EEG experiment

Design dataset:

- 15 subjects
- 3 within factors with 2 levels (and more).
- $2 \times 2 \times 2 = 8$ observations (ERP) per subjects
- $8 \times 15 = 120$ observations in total

```
head(attentionshifting_design[,1:4], n = 10)
```

```
##      id visibility emotion direction
## 27  S01       16ms   angry     right
## 96  S01      166ms   angry     right
## 165 S01       16ms neutral     right
## 234 S01      166ms neutral     right
## 303 S01       16ms   angry      left
## 372 S01      166ms   angry      left
## 441 S01       16ms neutral      left
## 510 S01      166ms neutral      left
## 579 S02       16ms   angry     right
## 648 S02      166ms   angry     right
```

Multiple comparisons problem : EEG experiment

Signal dataset:

- 120 EEG signals of 1 electrode (O1) at 1024Hz during 800ms.
- 819 measures of amplitude $[\mu V]$ per electrode, per observation.
- Event at 200ms.
- One observation $=$ mean over several trials.

```
dim(attentionshifting_design)
```

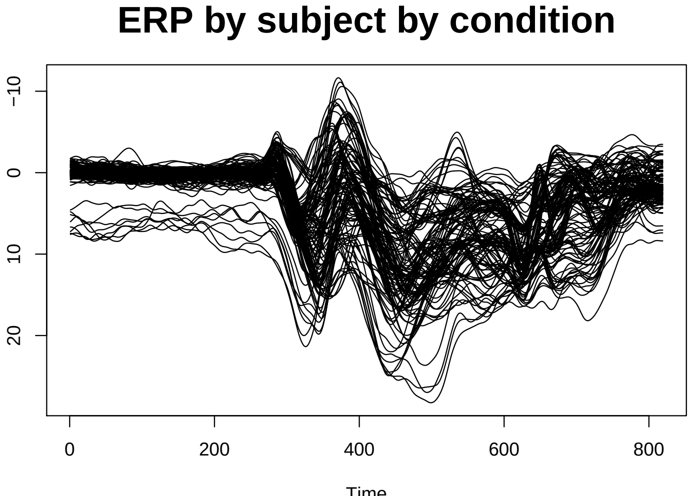
```
## [1] 120   9
```

```
dim(attentionshifting_signal)
```

```
## [1] 120 819
```

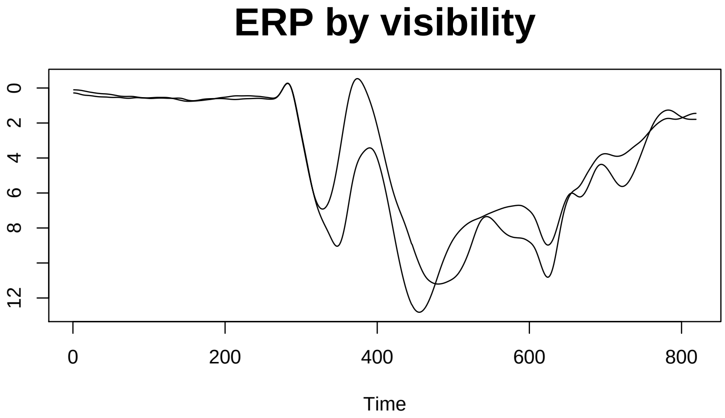
Multiple comparisons problem : EEG experiment

```r
erp <- t(attentionshifting_signal)
ts.plot(erp, ylim = rev( range( erp)))
```



Multiple comparisons problem : EEG experiment

```r
erpm <- aggregate(attentionshifting_signal, by = list(
                  attentionshifting_design$visibility),
                FUN = mean)[,-1]
ts.plot(t(erpm), ylim = rev( range( erpm)))
```



Multiple comparisons problem : EEG experiment

- Test the effect of experimental condition on the cerebral activity.
- No prior information on the timeframe of the effect.
- Repeated measures ANOVA at each timepoint (819 tests).

Bad solutions :

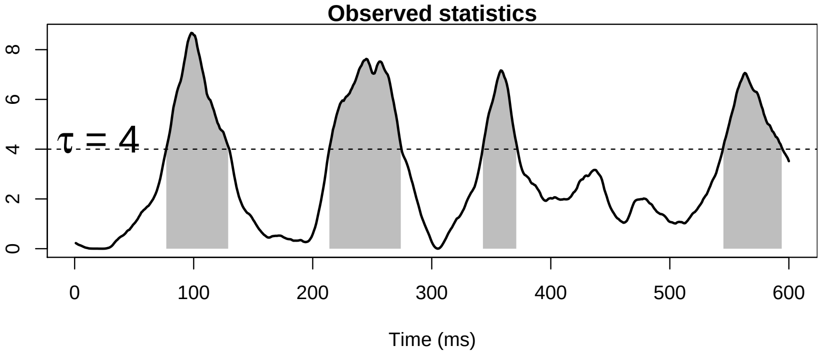
- No correction for the 819 p-values.
- Checking the data to select a window.

FWER = probability of making at least one type I error. With 819 indepedant tests :
$FWER = 1 - (1 - 0.05)^{819} = 1 - 5.69 \times 10^{-19} \simeq 1!$

Good solutions : Control the FWER over all tests.

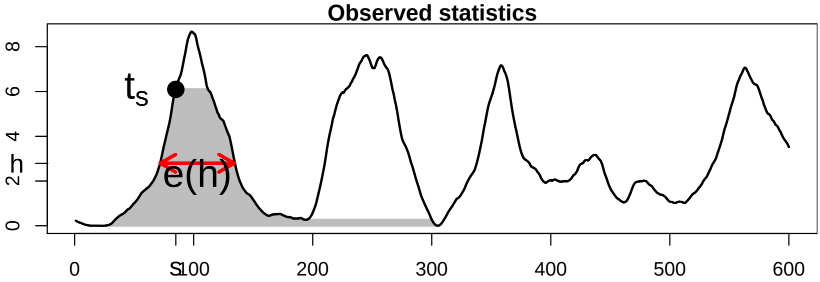
- Cluster-mass statistics.
- Threshold-free cluster-enhancement (TFCE).

Multiple comparisons problem : cluster-mass



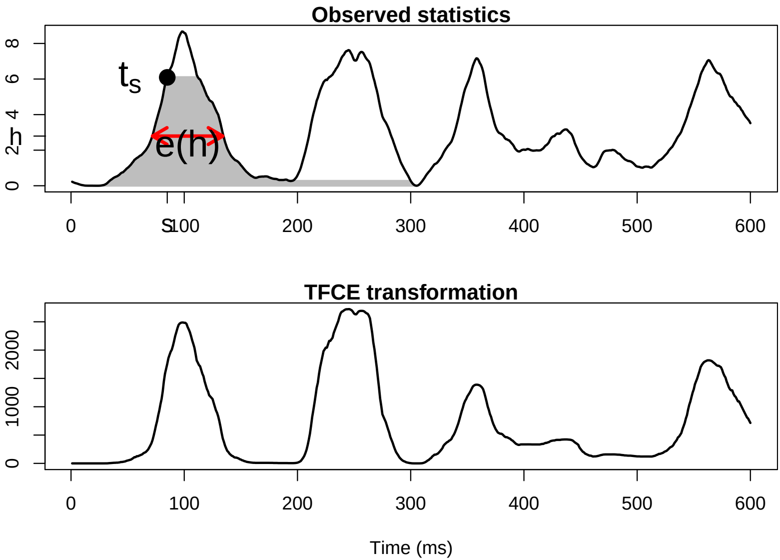
- Define a threshold τ.
- Compute the statistic at each timepoint.
- The cluster-mass is the *sum* of the adjacent statistics above the threshold.
- Compute the cluster-mass null distribution by permutation of the signals.

Multiple comparisons problem : TFCE



- Compute the statistic at each time.
- Compute the TFCE at each timepoint :
  $TFCE_t = \int_{h=t_0}^{h=t_t} e(h)^E h^H dh$
- Compute the TFCE distribution by permutation: 1. Permute the signals, 2. Compute the TFCE at each timepoint. 3. Take the maximum value of TFCE.

Multiple comparisons problem : TFCE



Cluster-mass test : clusterlm(formula, data)

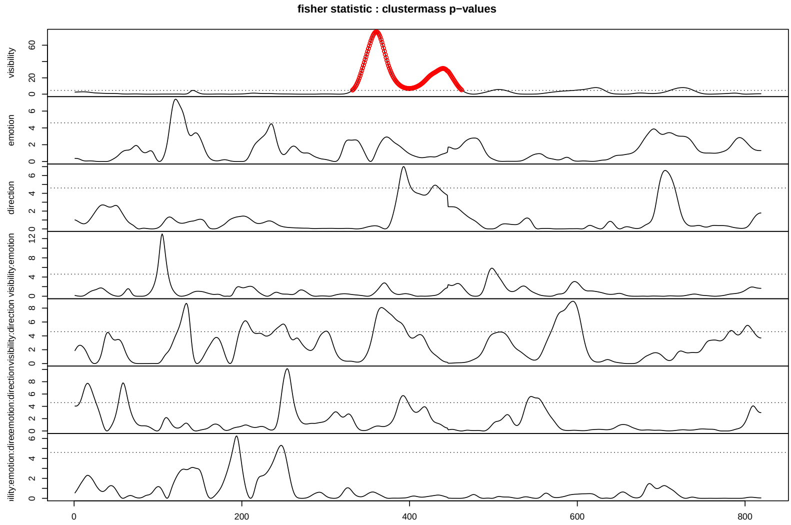
Formula for repeated measures ANOVA :

```
## similar to aov()
formula <- response ~ between * within +
  Error(subject / (within) )
```

```
## cluster-mass test
cl_mass <- clusterlm(attentionshifting_signal ~
                         visibility*emotion*direction
         + Error(id/(visibility*emotion*direction)),
         data = attentionshifting_design)
```

Cluster-mass test : plot()

```r
plot(cl_mass)
```



Cluster-mass test : print()

```r
print(cl_mass, effect = "visibility")
```

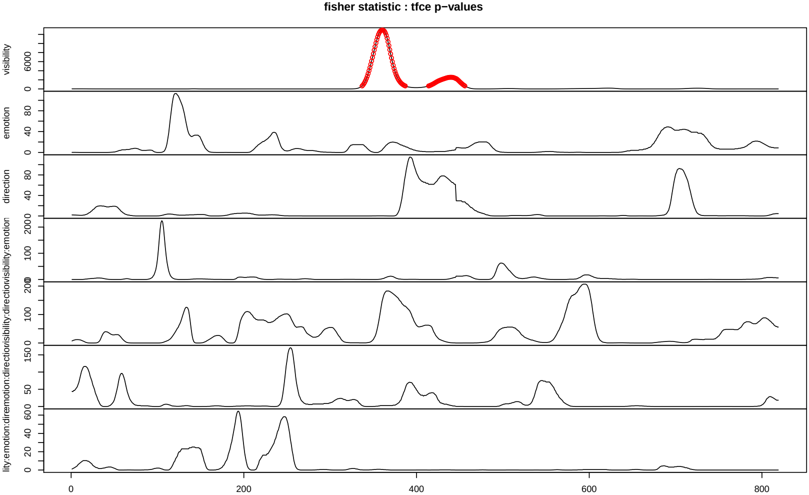
```
## Cluster fisher test using Rd_kheradPajouh_renaud to handle nu
##  with 5000 permutations and the sum as mass function.
##
## Alternative Hypothesis : bilateral.
##
## visibility, threshold = 4.60011.
##   start end cluster mass P(>mass)
## 1   142 142     4.634852   0.5098
## 2   332 462  3559.149739   0.0022
## 3   499 514    85.019645   0.4074
## 4   596 632   234.877913   0.2320
## 5   711 738   191.576178   0.2700
```

TFCE and other multiple comparisons procedure

```
all_multcomp <- clusterlm(attentionshifting_signal ~
                        visibility*emotion*direction
         + Error(id/(visibility*emotion*direction)),
         multcomp = c("clustermass", "tfce",
          "bonferroni","holm", "troendle",
          "benjaminin_hochberg"),
         data = attentionshifting_design)
```

TFCE and other multiple comparisons procedure

```
plot(all_multcomp, multcomp = "tfce",
     enhanced_stat = TRUE)
```



TFCE and other multiple comparisons procedure

```r
summary(all_multcomp, multcomp = "tfce")
```

```
##       visibility statistic visibility pvalue emotion statistic
##  [1,]               16.056             0.824             0.167
##  [2,]               16.056             0.824             0.167
##  [3,]               17.495             0.806             0.167
##  [4,]               17.495             0.806             0.167
##  [5,]               17.495             0.806             0.167
##  [6,]               18.763             0.793             0.095
##  [7,]               18.763             0.793             0.095
##  [8,]               18.763             0.793             0.095
##  [9,]               18.763             0.793             0.034
## [10,]               18.763             0.793             0.034
## [11,]               18.763             0.793             0.000
## [12,]               18.763             0.793             0.000
## [13,]               18.763             0.793             0.000
## [14,]               18.763             0.793             0.000
## [15,]               17.495             0.806             0.000
## [16,]               16.056             0.824             0.000
## [17,]               16.056             0.824             0.000
## [18,]               14.506             0.846             0.000
## [19,]               13.012             0.864             0.000
## [20,]               11.579             0.880             0.000
##       emotion pvalue direction statistic direction pvalue
##  [1,]              1               2.026            0.994
##  [2,]              1               1.927            0.995
##  [3,]              1               1.927            0.995
##  [4,]              1               1.774            0.995
##  [5,]              1               1.774            0.995
##  [6,]              1               1.598            0.996
##  [7,]              1               1.598            0.996
##  [8,]              1               1.415            0.997
```

Next development

- Permutation method for mixed model.
- Clusters based on time/space adjacency.