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Non-Parametric Cluster-Based Permutation Tests for Analysing Neural Time-Series

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NatMEG
The Swedish National Facility for Magnetoencephalography

Program

- **15:00-15:45 lecture**
- **15:45-16:00** *Short Q&A*
- **16:00-17:00 Hands-on tutorial**
- **17:00-17:30** *Virtual mingle*

Why statistics?

- Estimation of parameter values
- Prediction of data values
- Model comparison

Kruschke (2001)

Why statistics?

- Estimation of parameter values
- Prediction of data values
- Model comparison / *hypothesis testing*

Non-parametric cluster-based permuation tests

Is $x = y$?

Inferential statistics

Is $x = y$?

X	Y
1	8
4	7
5	9
6	5
5	6
7	8
3	4
4	9
5	6
…	…

=

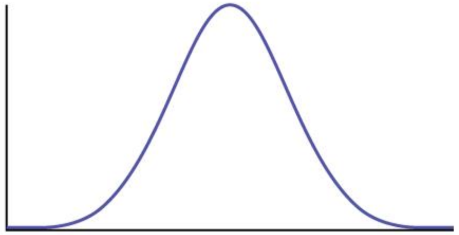
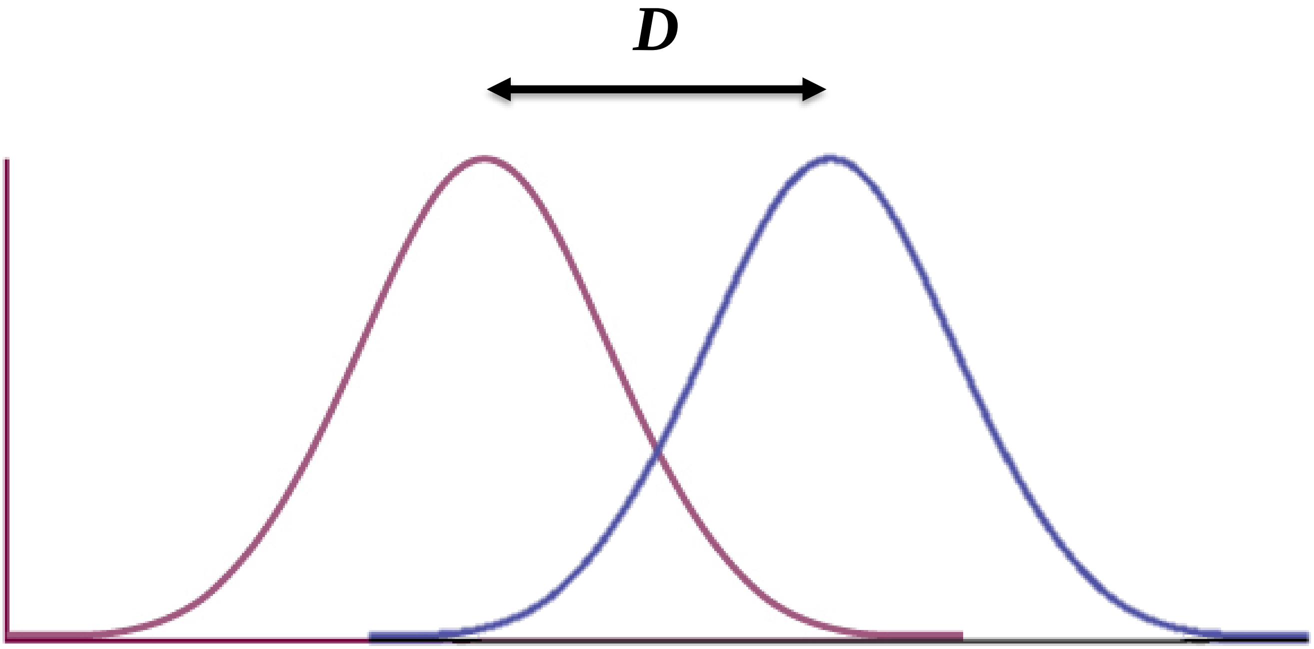


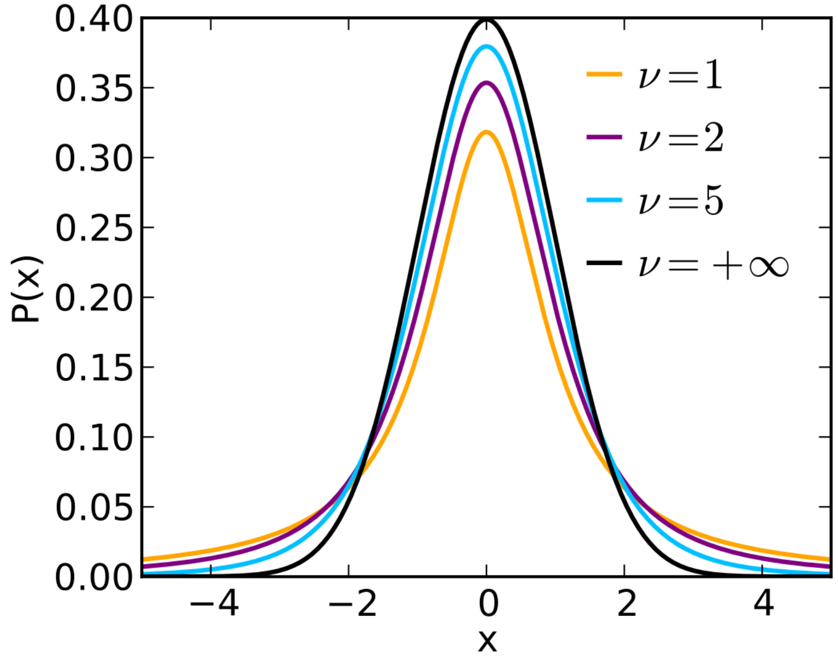
Image from Wikipedia

X
1
4
5
6
5
7
3
4
5
…

Y
8
7
9
5
6
8
4
9
6
…



$$t = \frac{m - m_{H0}}{s/\sqrt{N}}$$



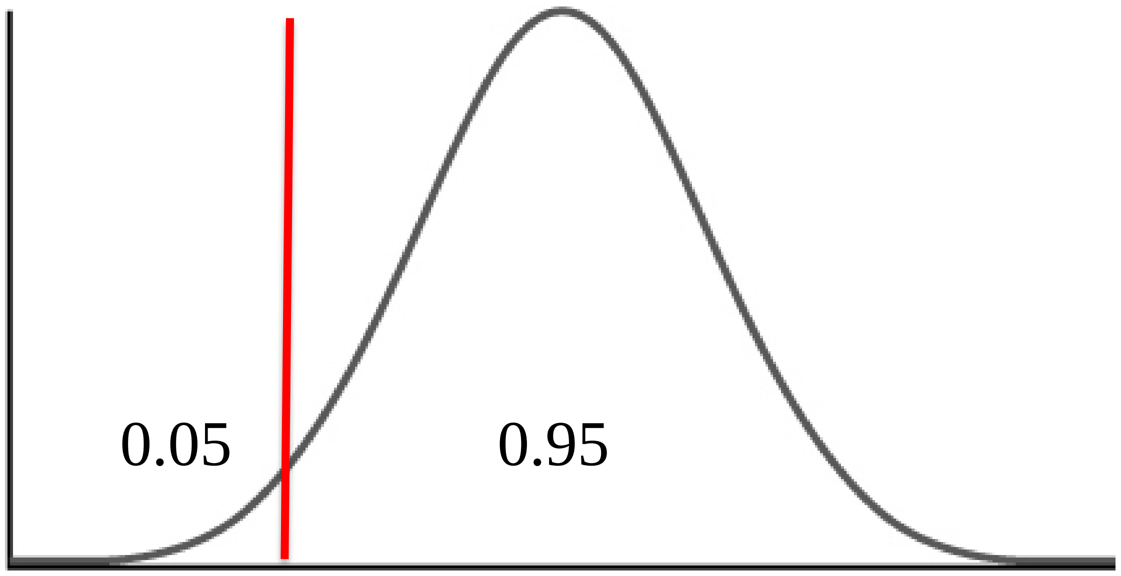
Null hypothesis significance testing

- Assume *H0* is true (X = Y)
- Calculate likelihood of observing the value of the test statistics (or more extreme values) under *H0*
- If likelihood is low, we reject *H0* (and accept *H1*)

Statistical inference

The critical α: decision threshold

1. Reject the null hypothesis and accept the alternative hypothesis
2. Conclude that the null hypothesis could not be rejected



Statistical inference

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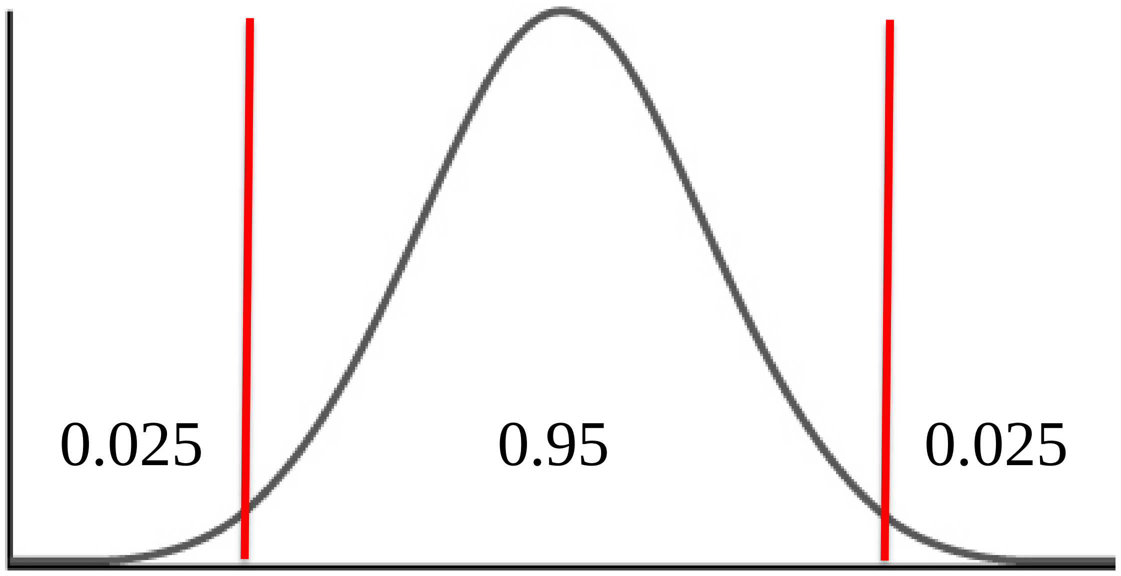
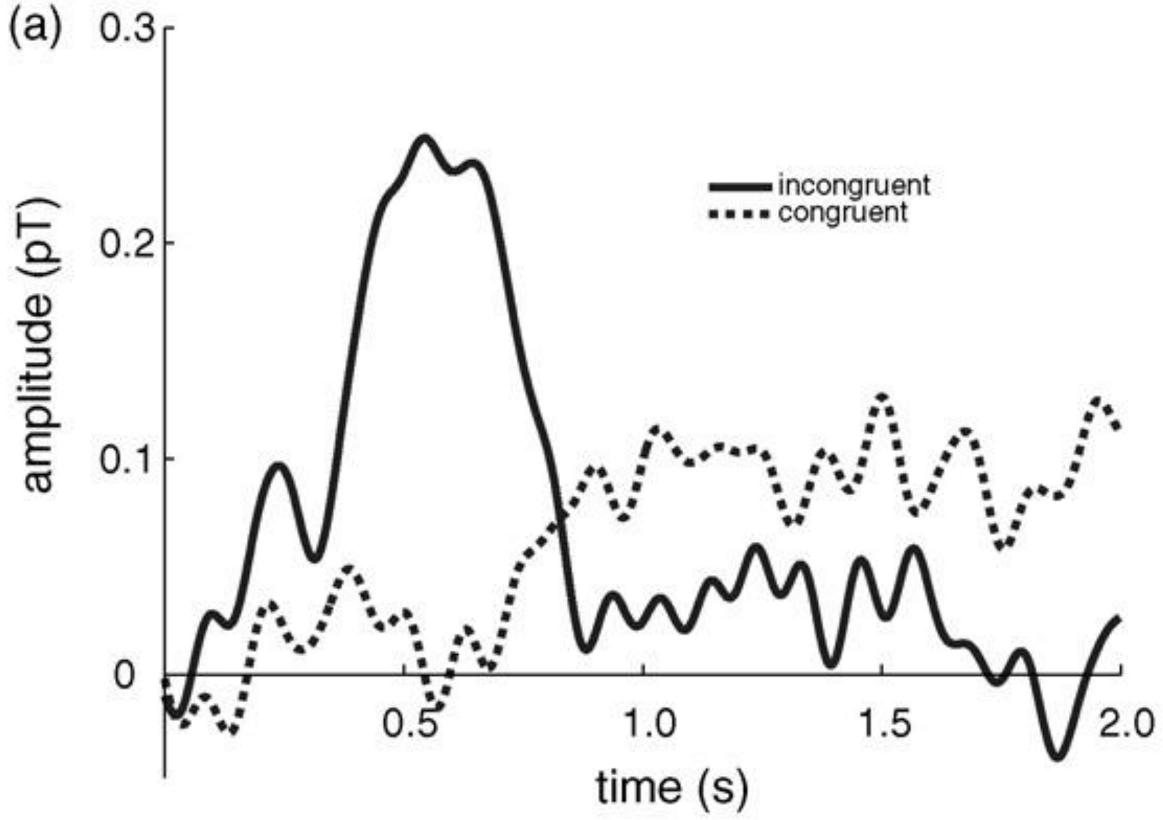
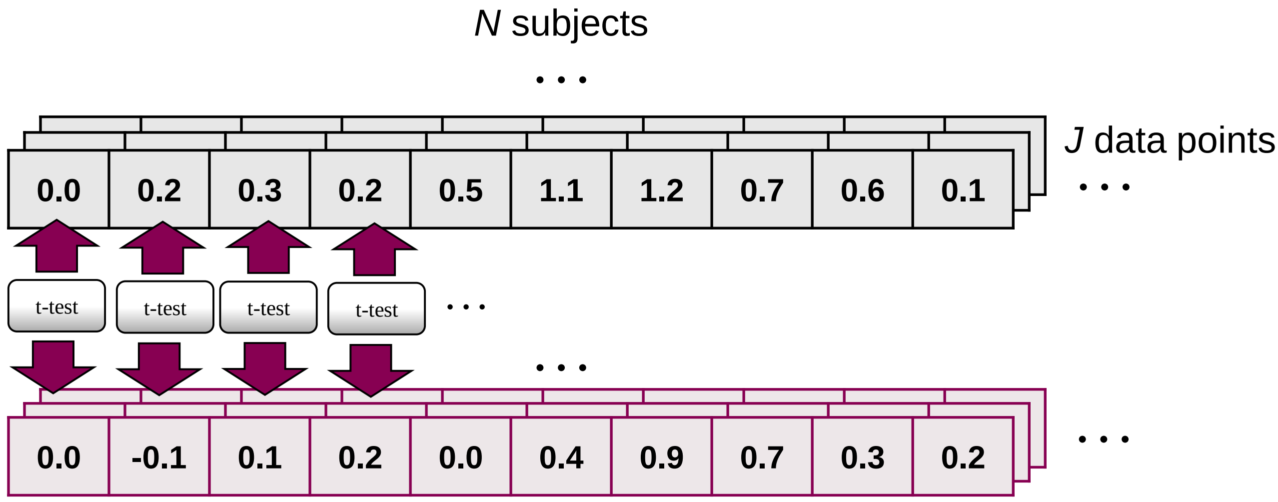


Multiple comparison problem

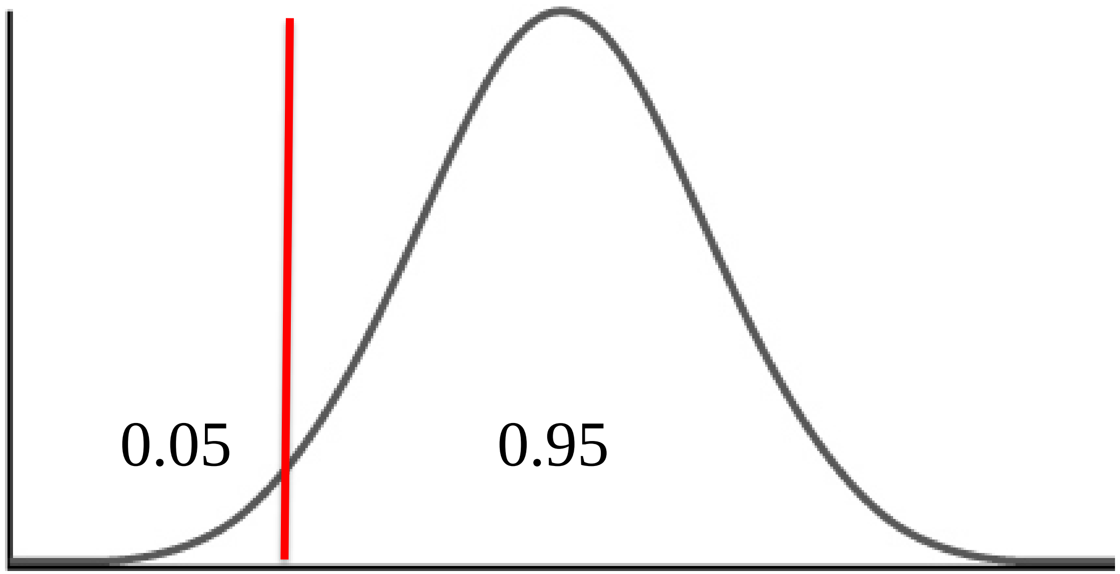




Maris & Oostenveld (2007)

False positive rate

- Test 1: FPR = 0.05
- Test 2: FPR = 0.05
- Test 3: FPR = 0.05
- Test 4: FPR = 0.05

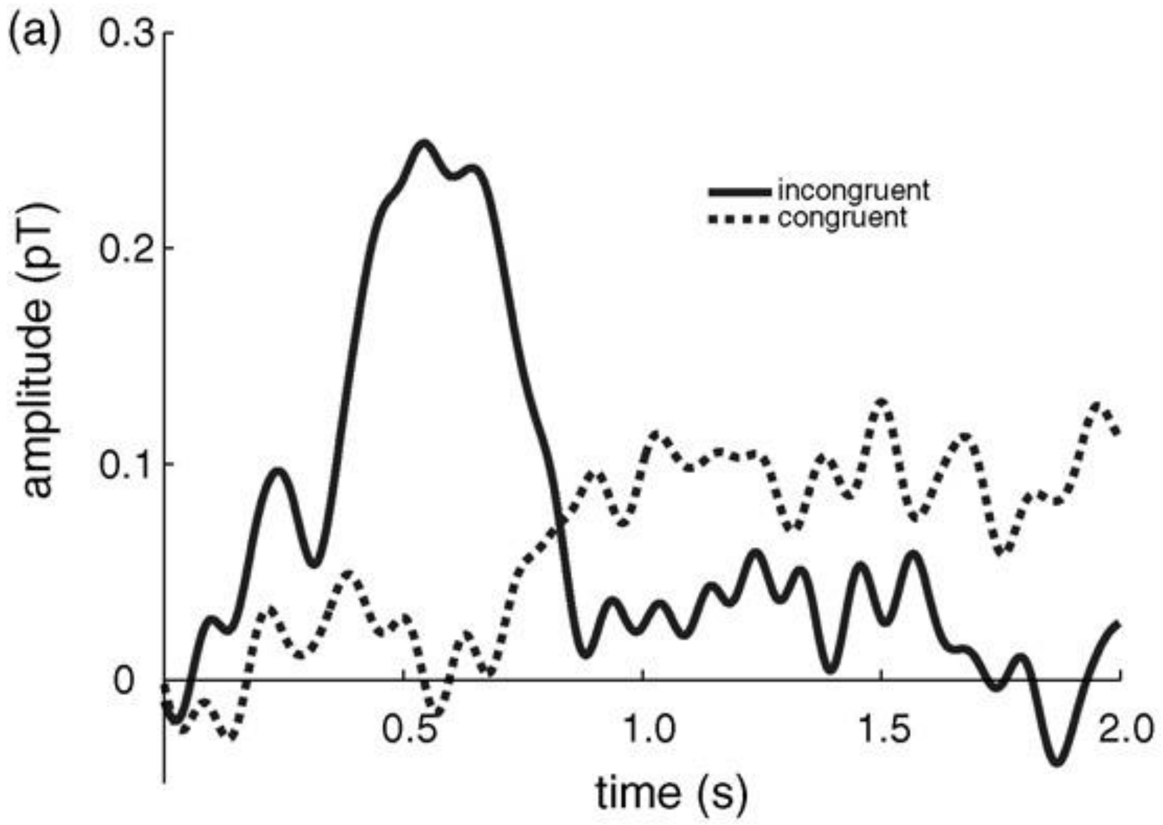


$$1 - (0.95 * 0.95 * 0.95 * 0.95) * 100 \approx 19\%$$

False positive rate

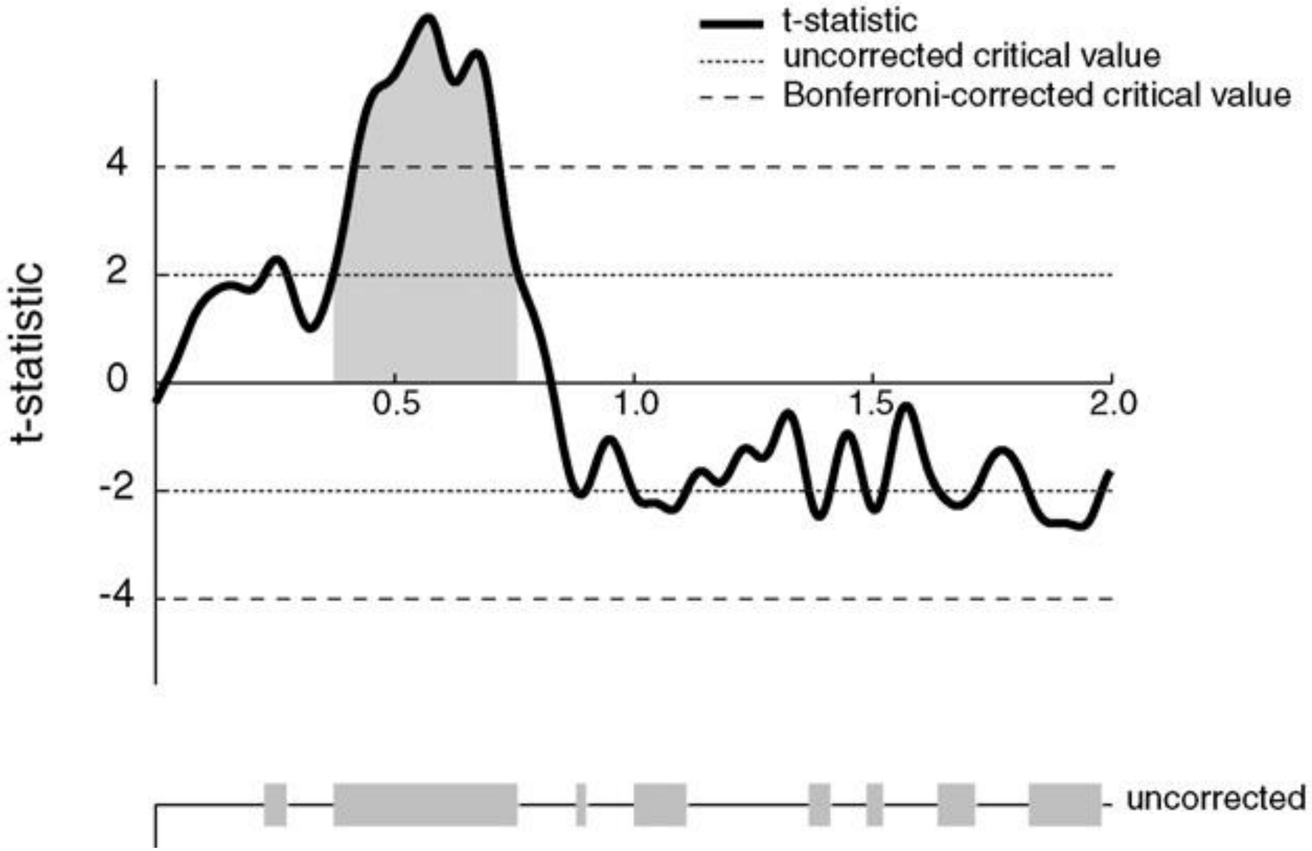
Realistic estimate:

- 200 time-points
- Expect on average 10 positives



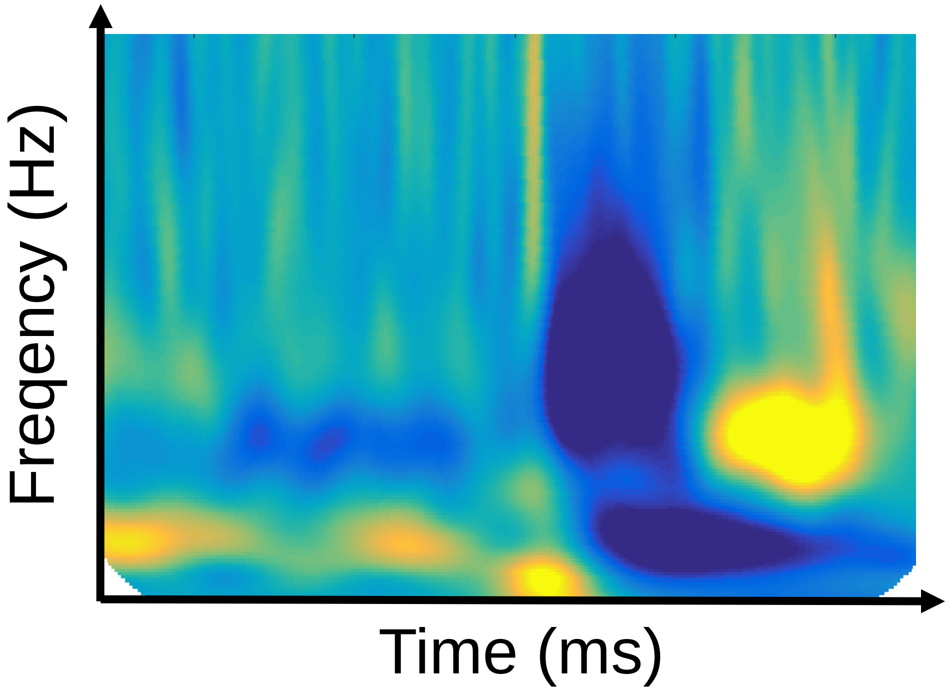
$$1 - (0.95)^{200} * 100 \approx 99.99\%$$

How do we deal with the multiple comparisons problem?



Maris & Oostenveld (2007)

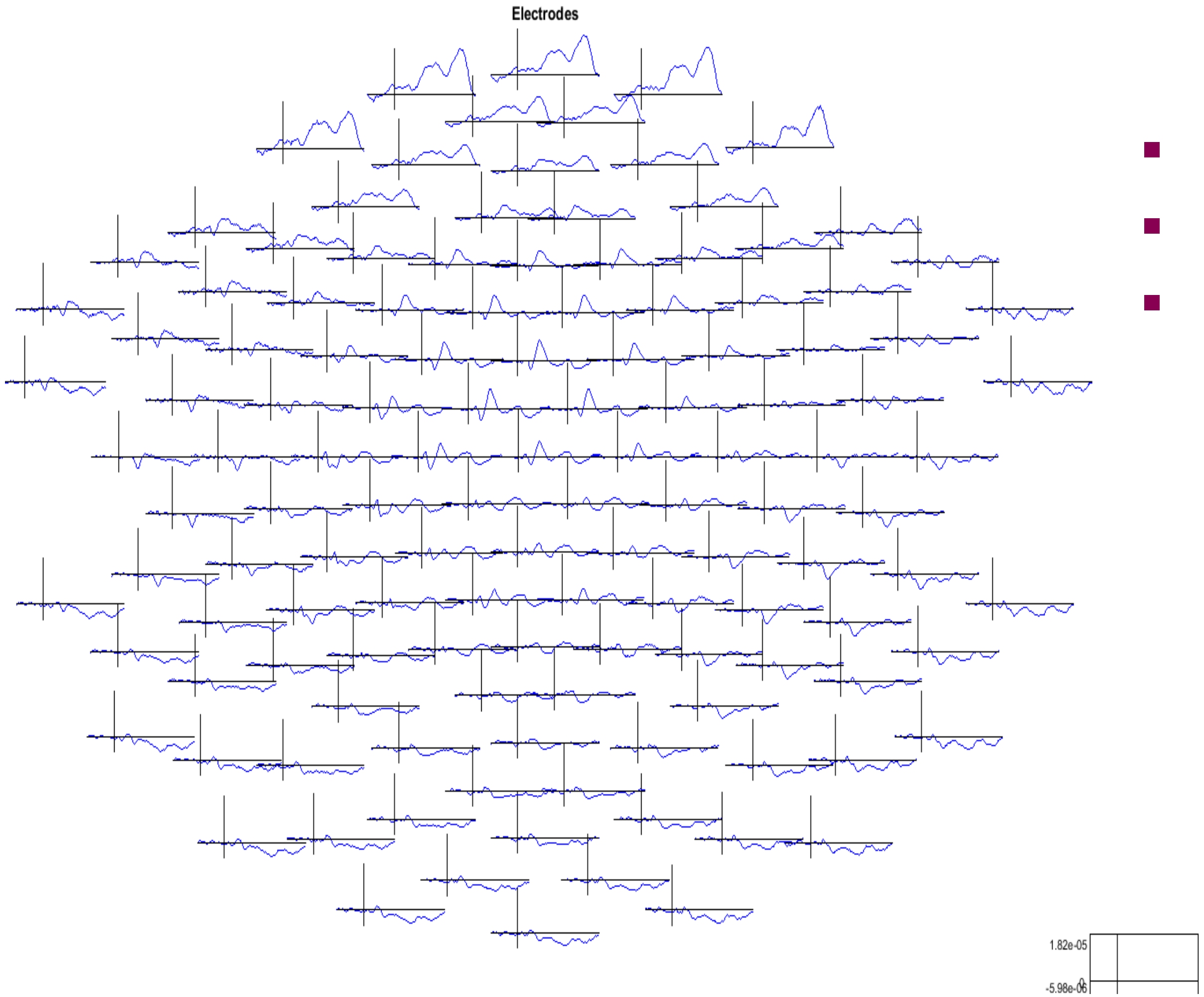
Multiple comparison problem



- 200 time-points
- 30 frequency bins
- 6 000 independent tests

  → Expect 300 positves by chance

Multiple comparison problem

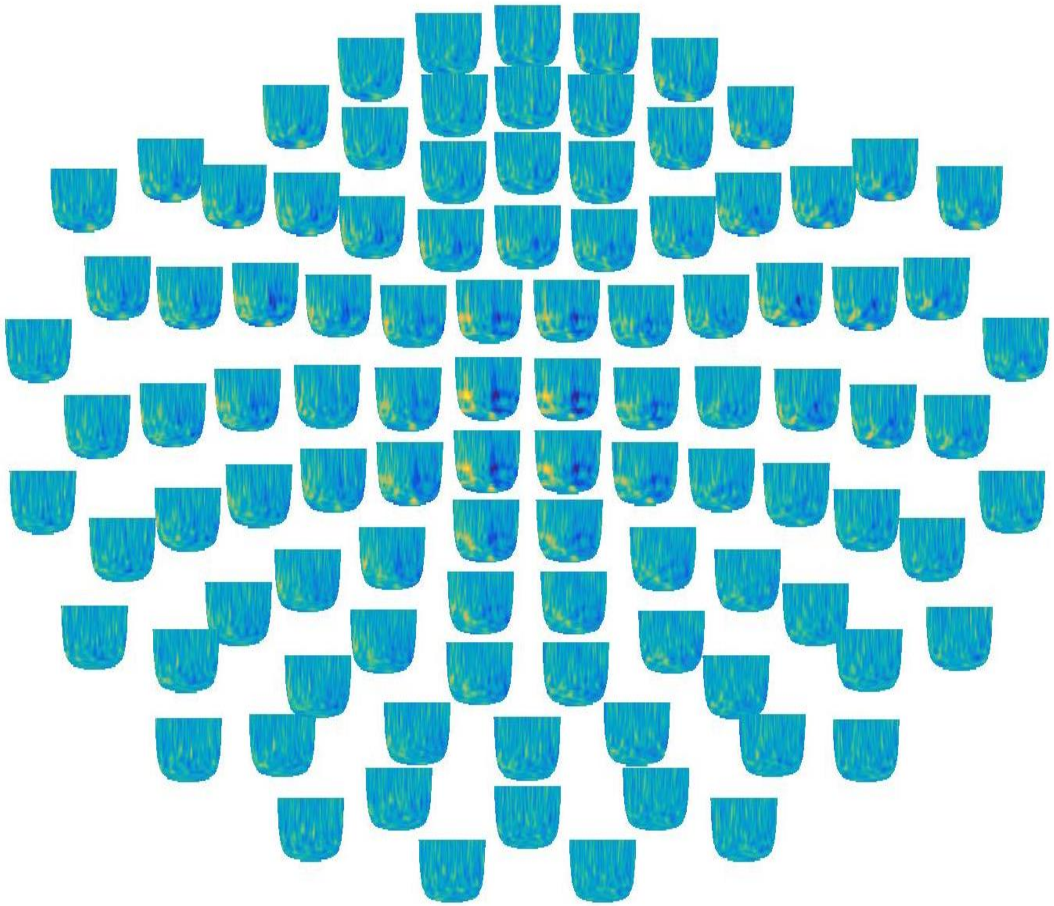


- 200 time-points
- 124 electrodes
- 24 800 independent tests
  → Expect 1 240 positves by chance

…

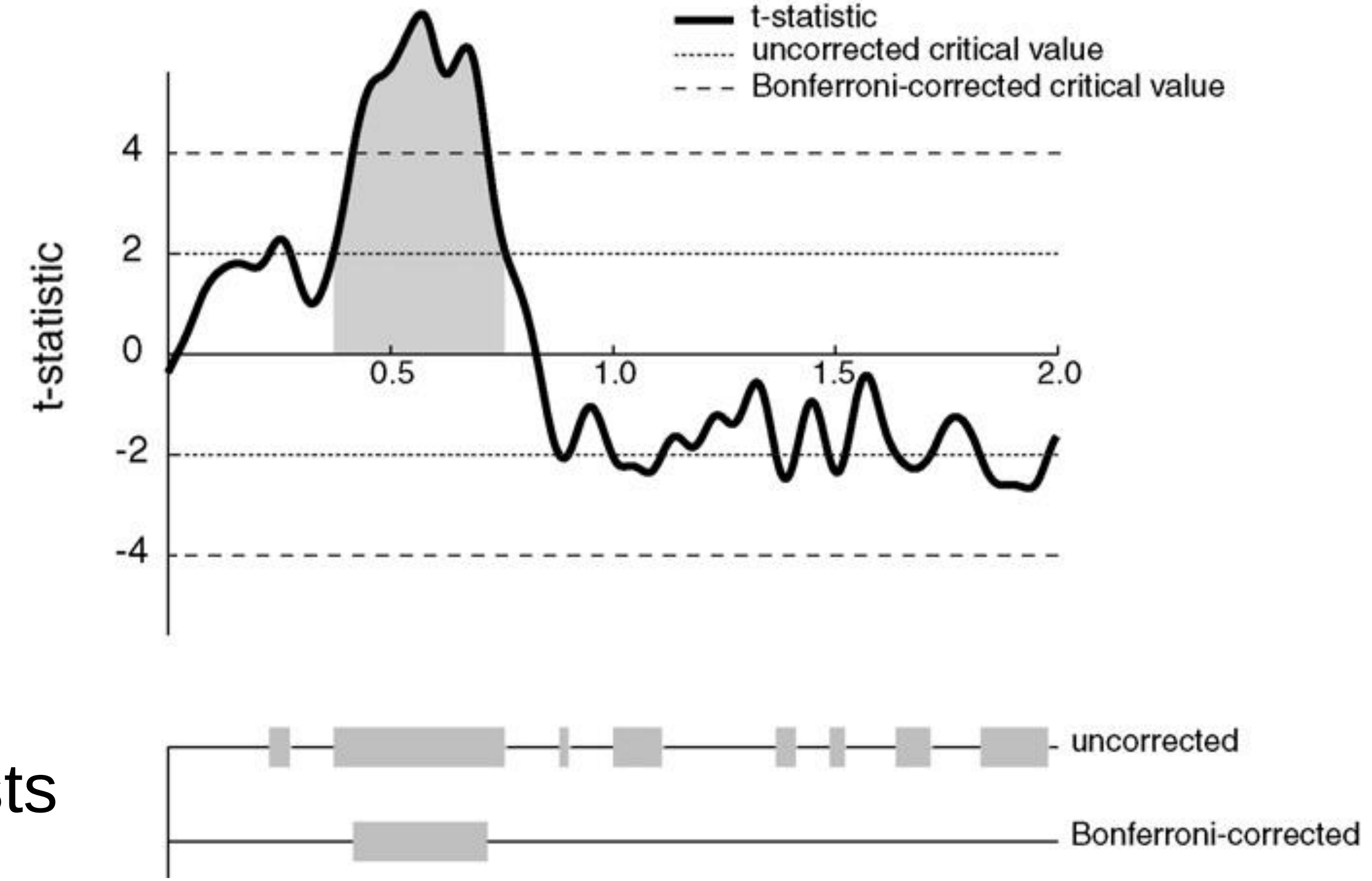
…

Multiple comparison problem



- 200 time-points
- 30 frequency bins
- 124 electrodes
- 744 000 independent tests
  - → Expect 37 200 positves by chance

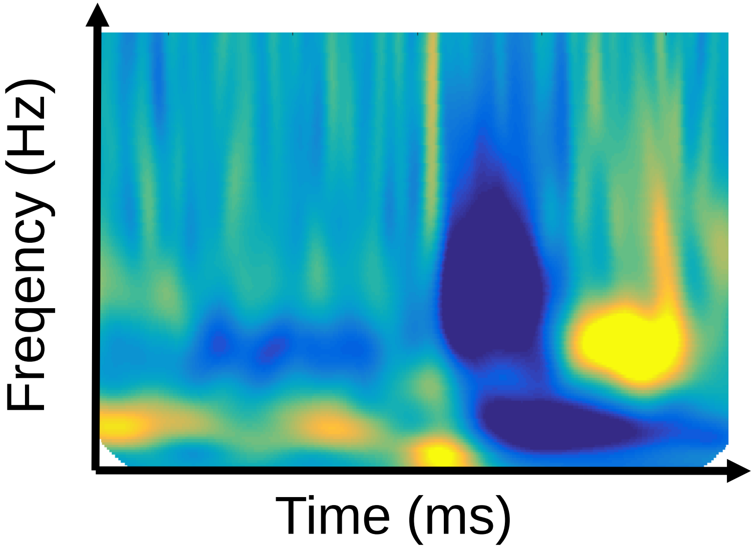
How do we deal with the multiple comparisons problem?

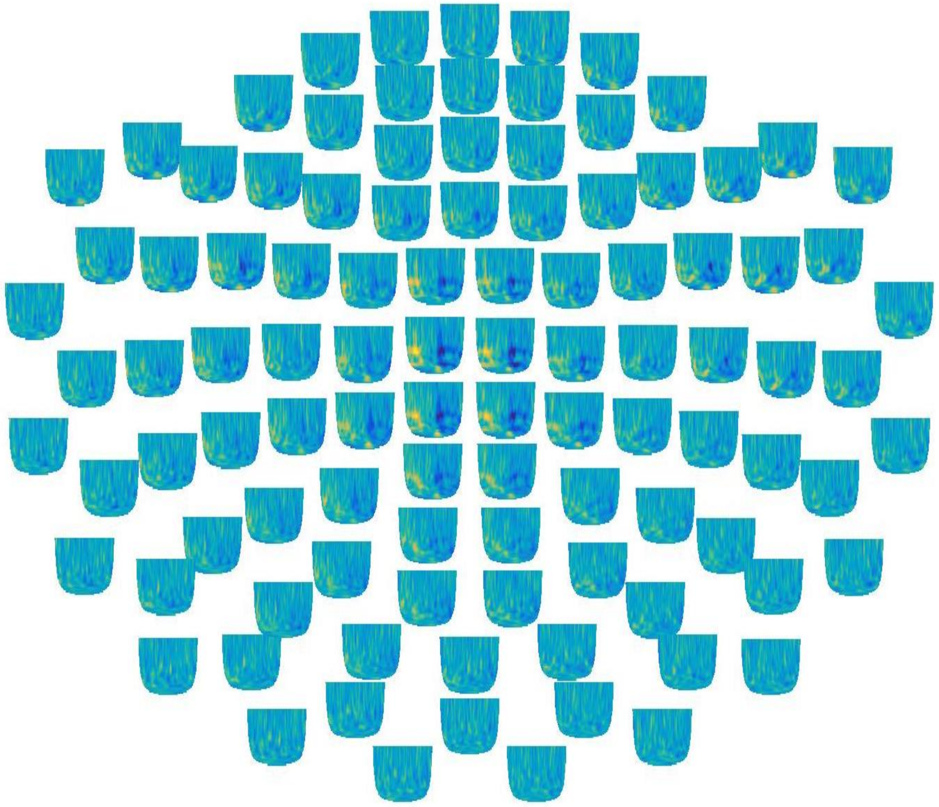


$\alpha_{\text{bonferroni}}$ = critical α / *N* tests

Maris & Oostenveld (2007)

Multiple comparison problem



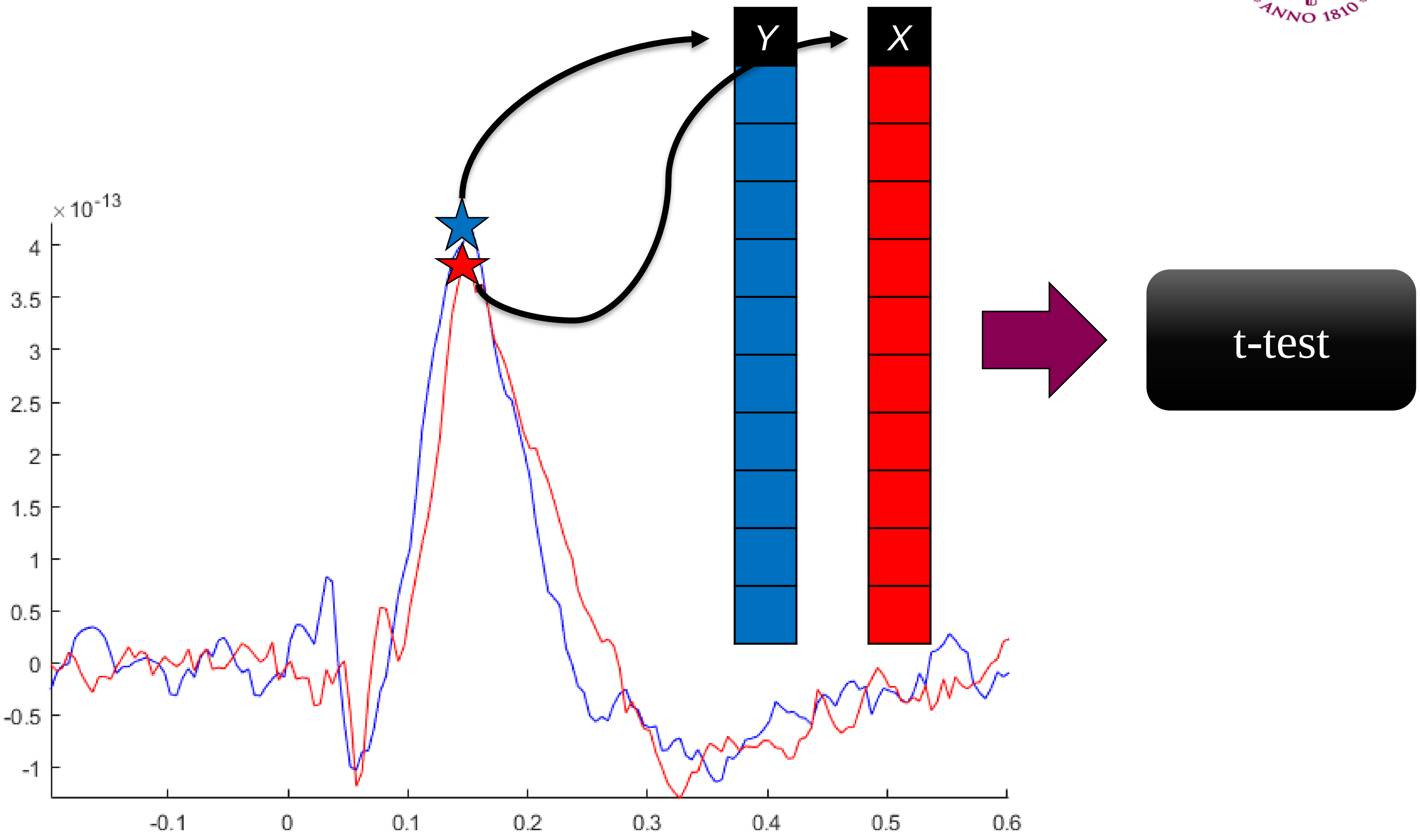


$\alpha_{\text{bonferroni}} = 0.05 / 6000 = 0.000008$

$\alpha_{\text{bonferroni}} = 0.05 / 744000 = 6.7 * 10^{-8}$

Select only the part of the signal we are interested in

(*A PRIORI*) FEATURE SELECTION



× 10^-13
4
3.5
3
2.5
2
1.5
1
0.5
0
-0.5
-1
-0.1
0
0.1
0.2
0.3
0.4
0.5
0.6
Y
X
t-test

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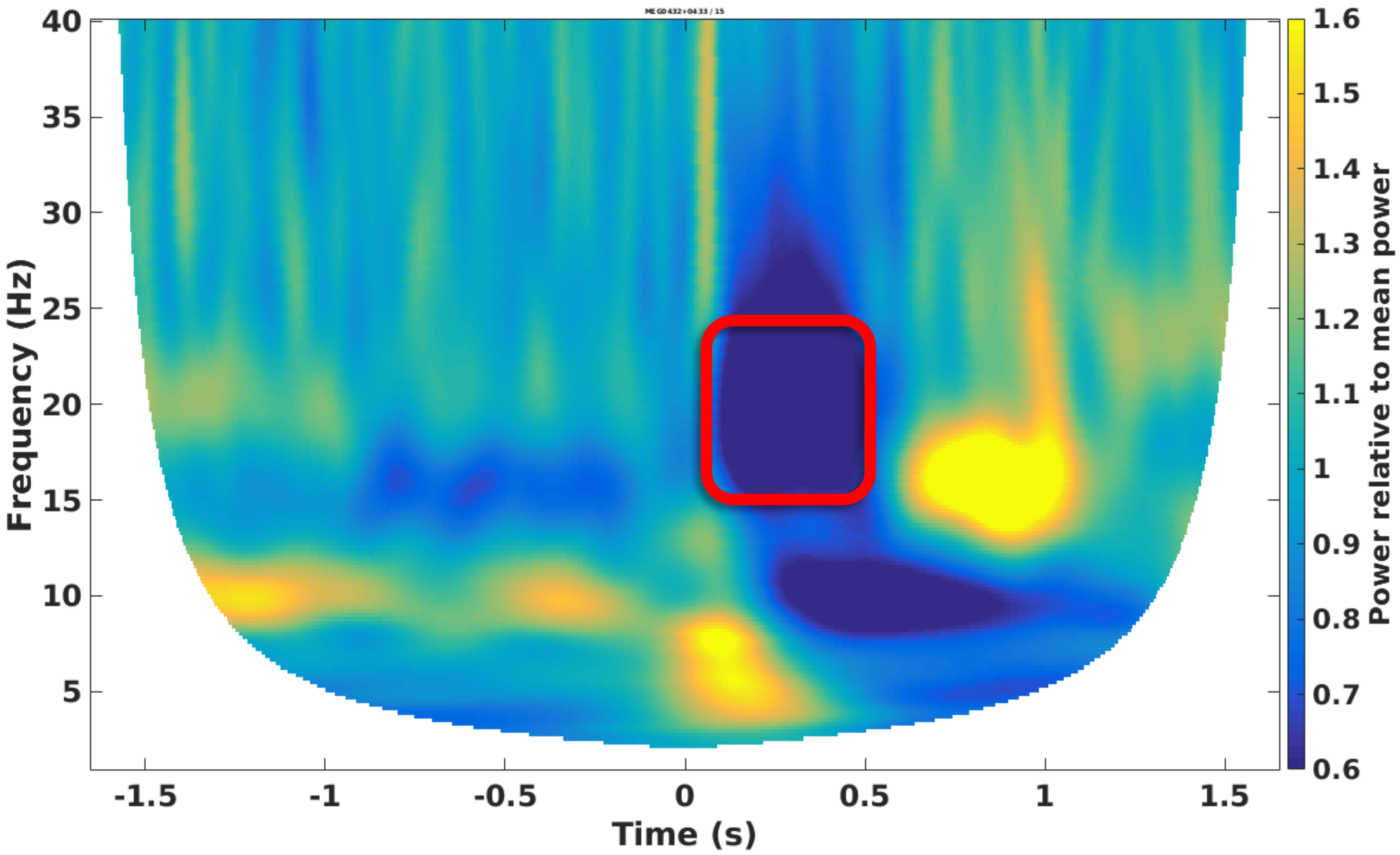
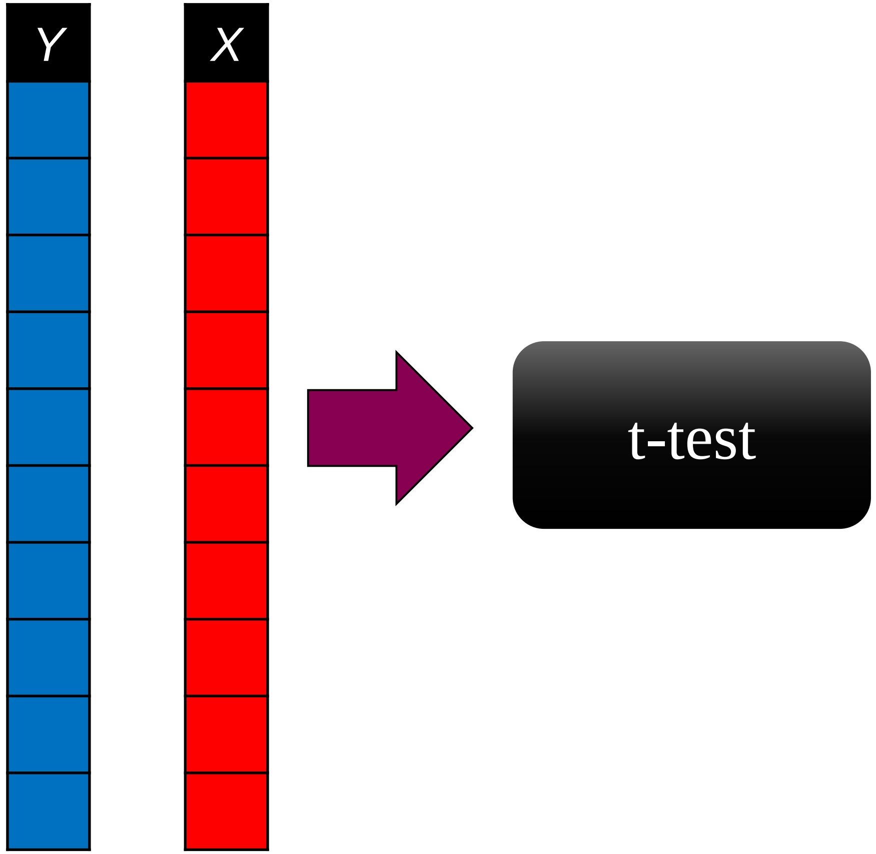




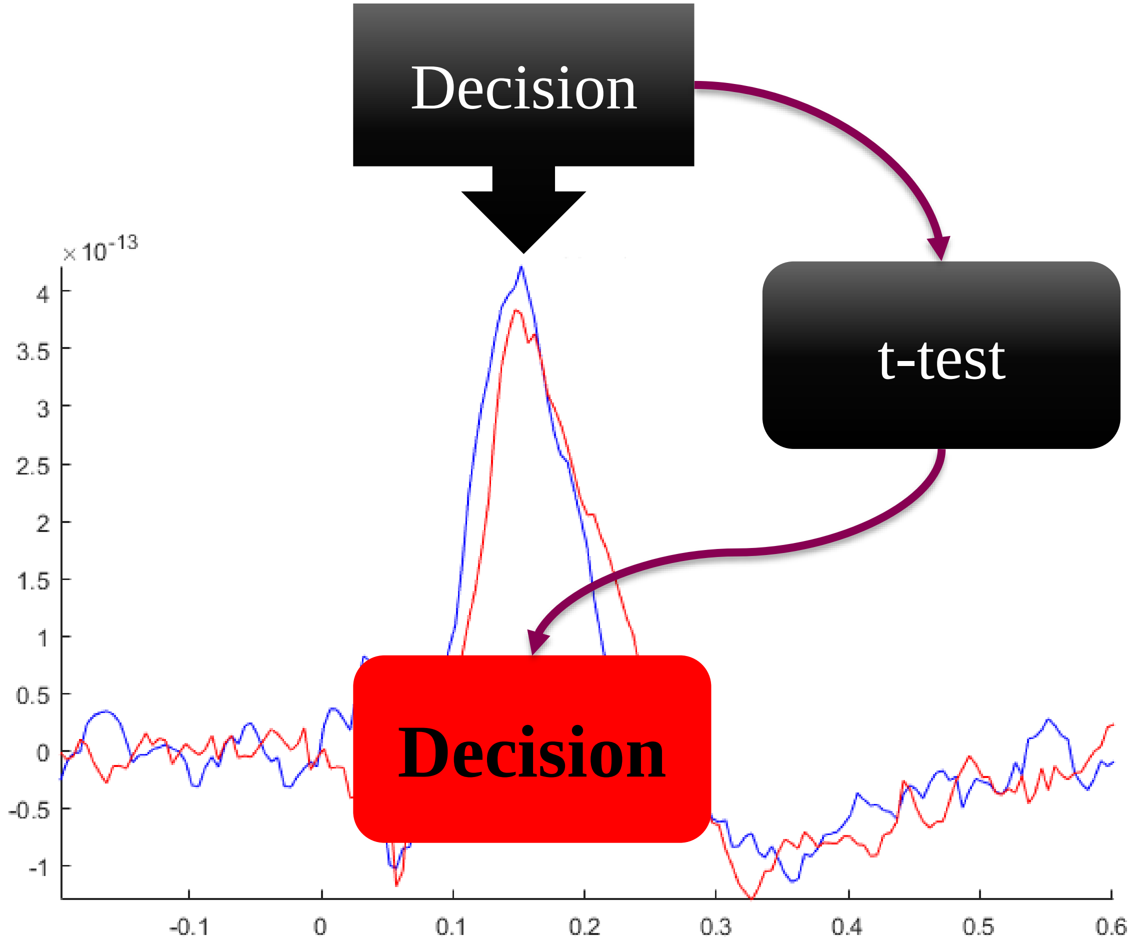
Feature selection

Pro

- Simple
- No need for multiple comparison*
- Strong hypothesis driven

Cons

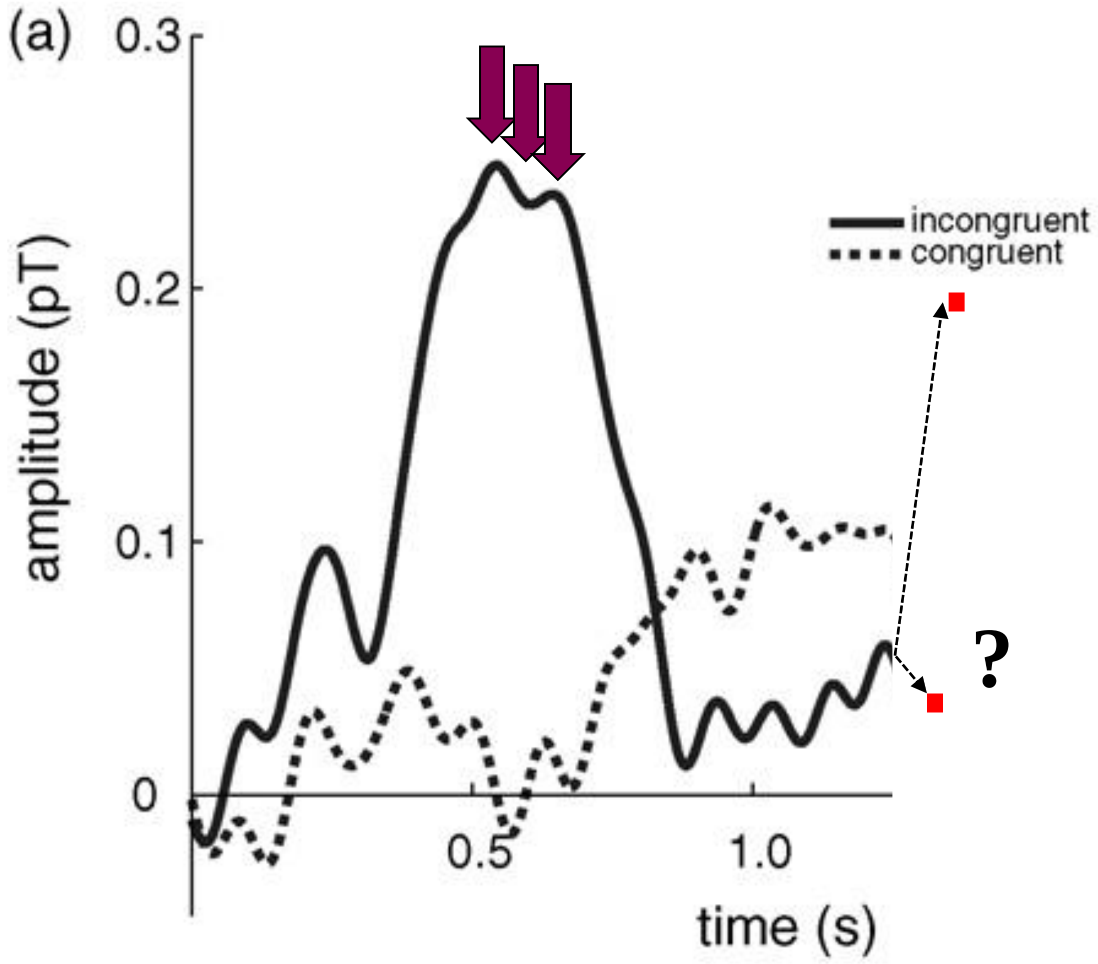
- Limited interpretation
- Feature selection procedure
- Invites *HARK*ing



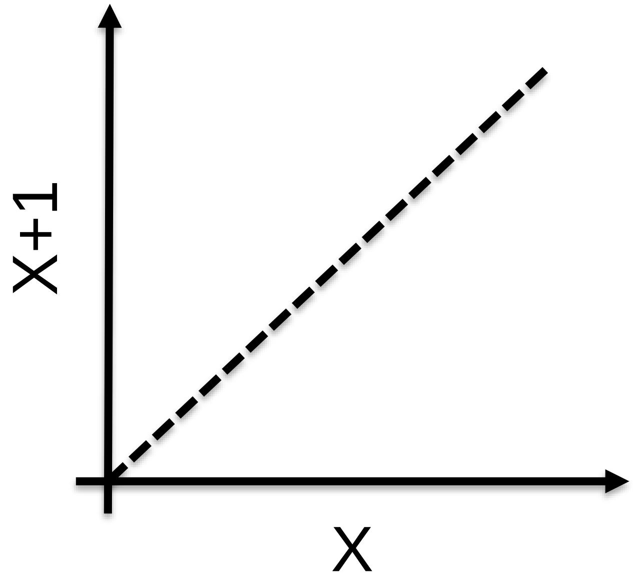
Statistics neural time-series (M/EEG)

CLUSTER-BASED PERMUTATION TESTS

Features of MEG/EEG data

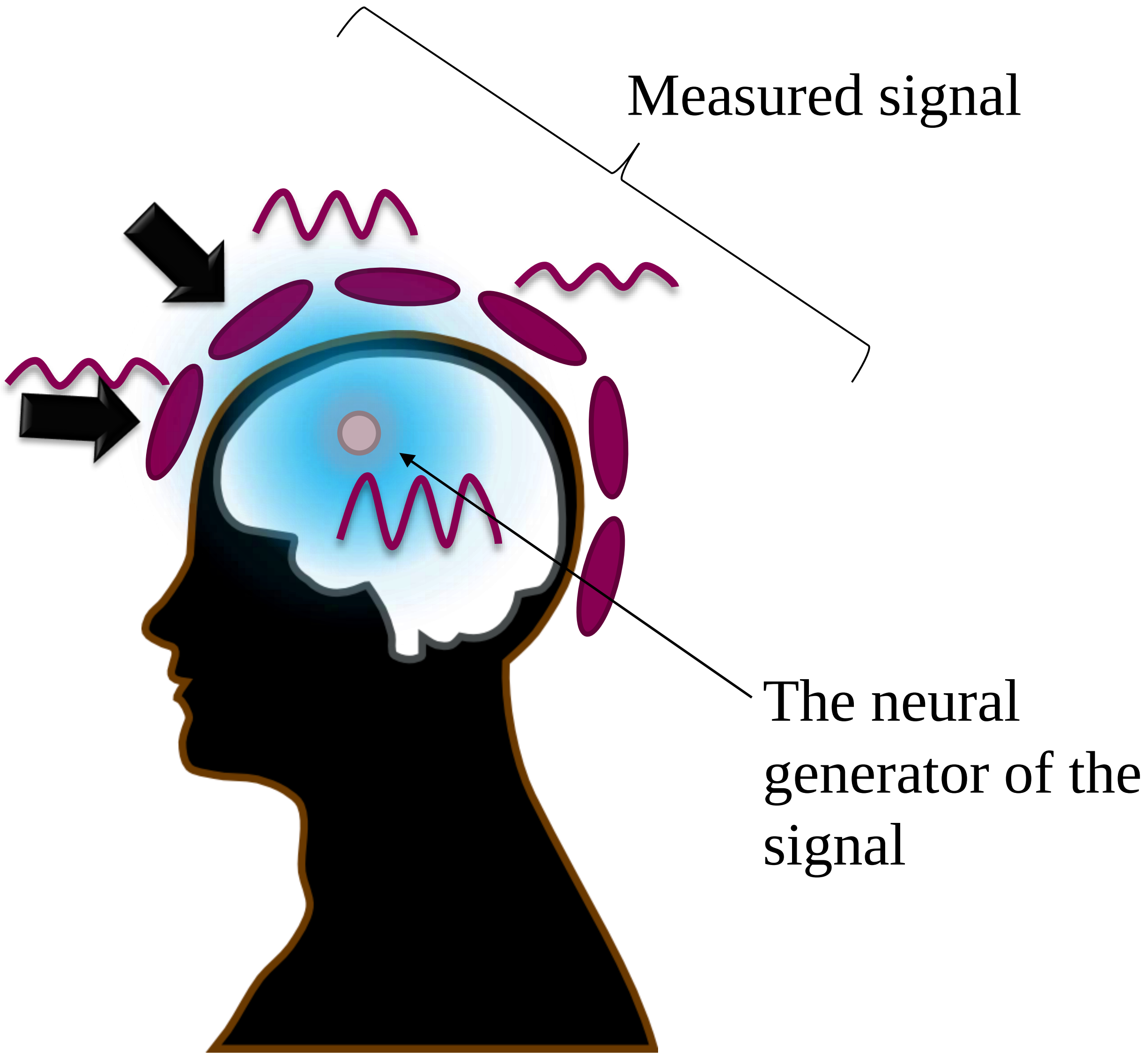


- Temporal autocorrelation

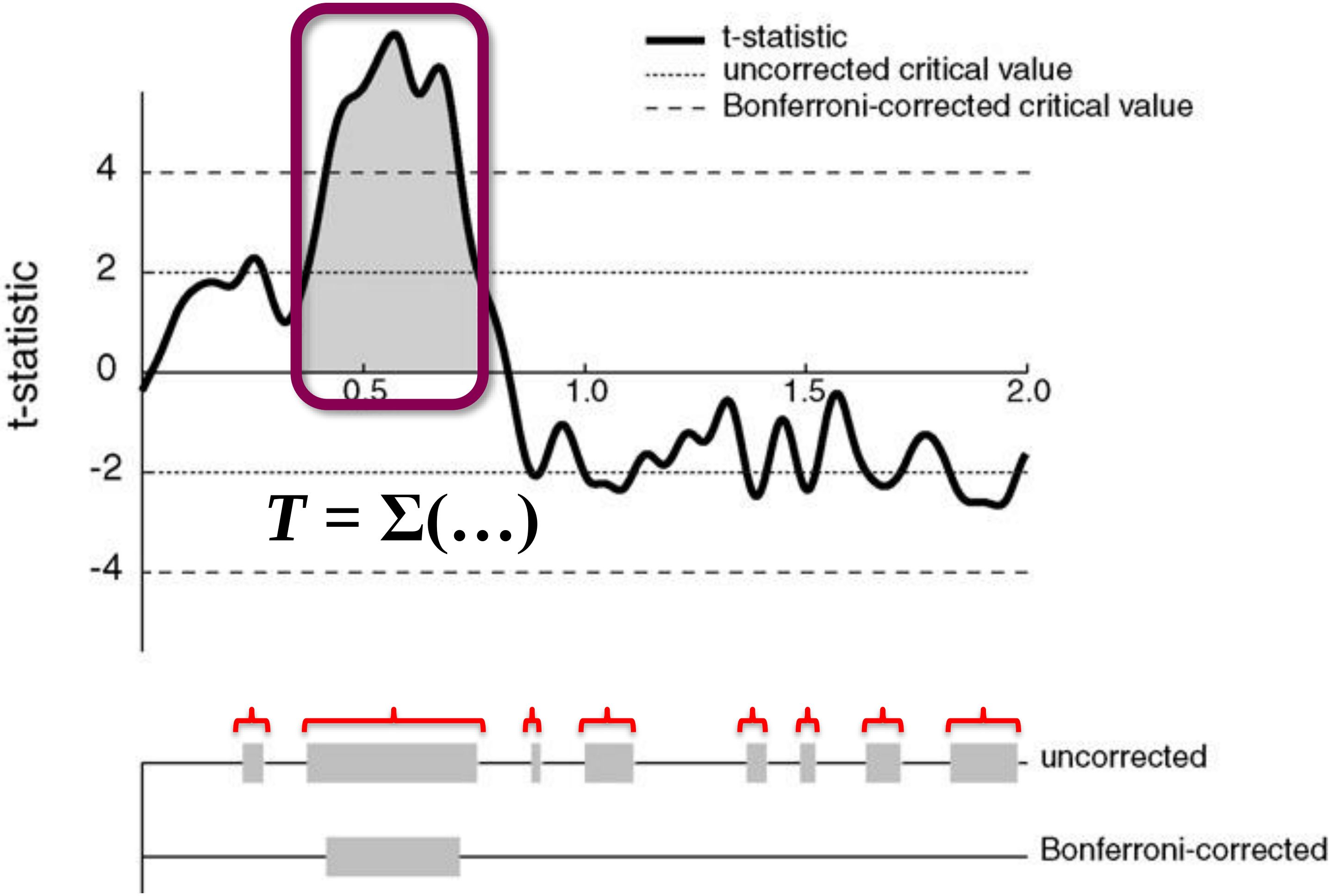


Features of MEG/EEG data

Spatial autocorrelation



Cluster statistics

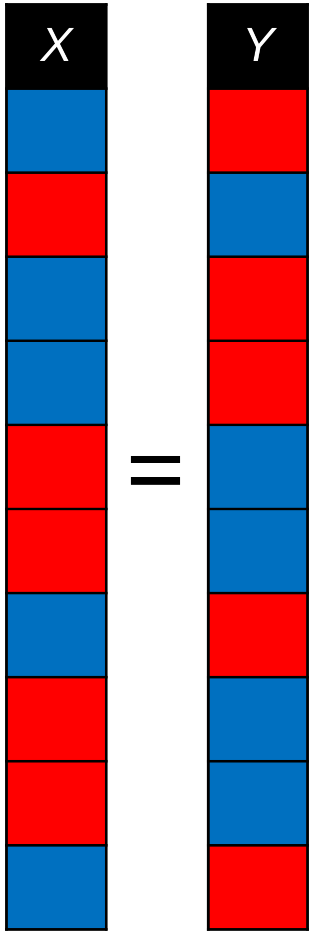


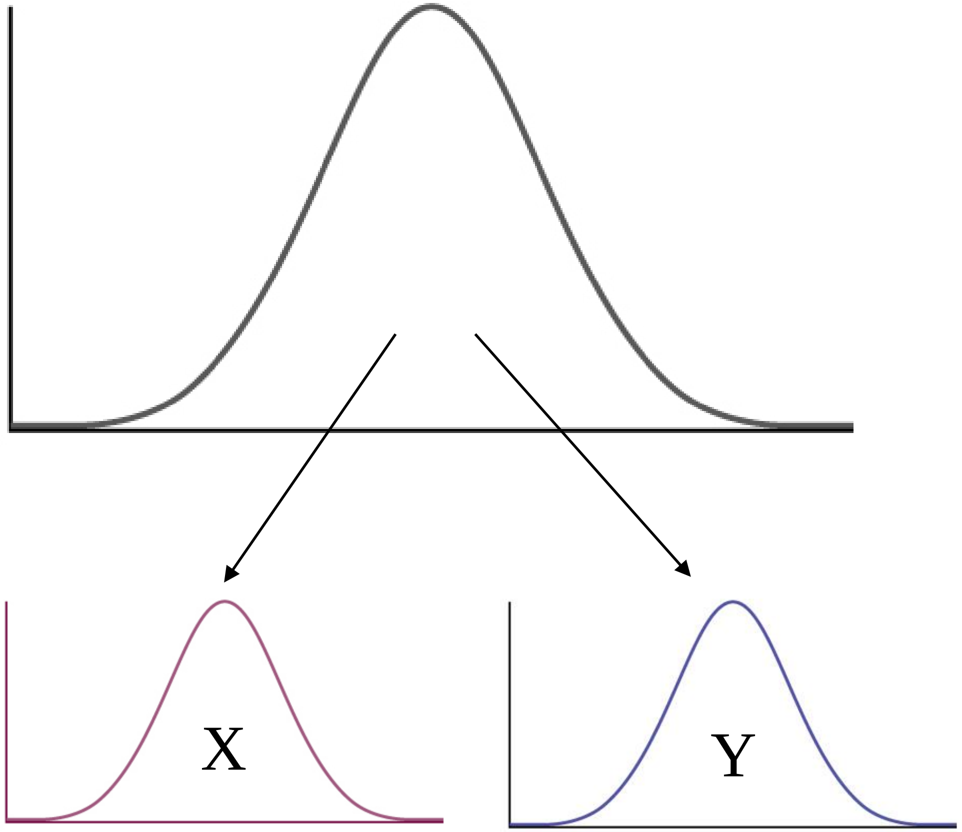
How big T would we expect under the null hypothesis?

Maris & Oostenveld (2007)

Permutation tests

H0: $X = Y$

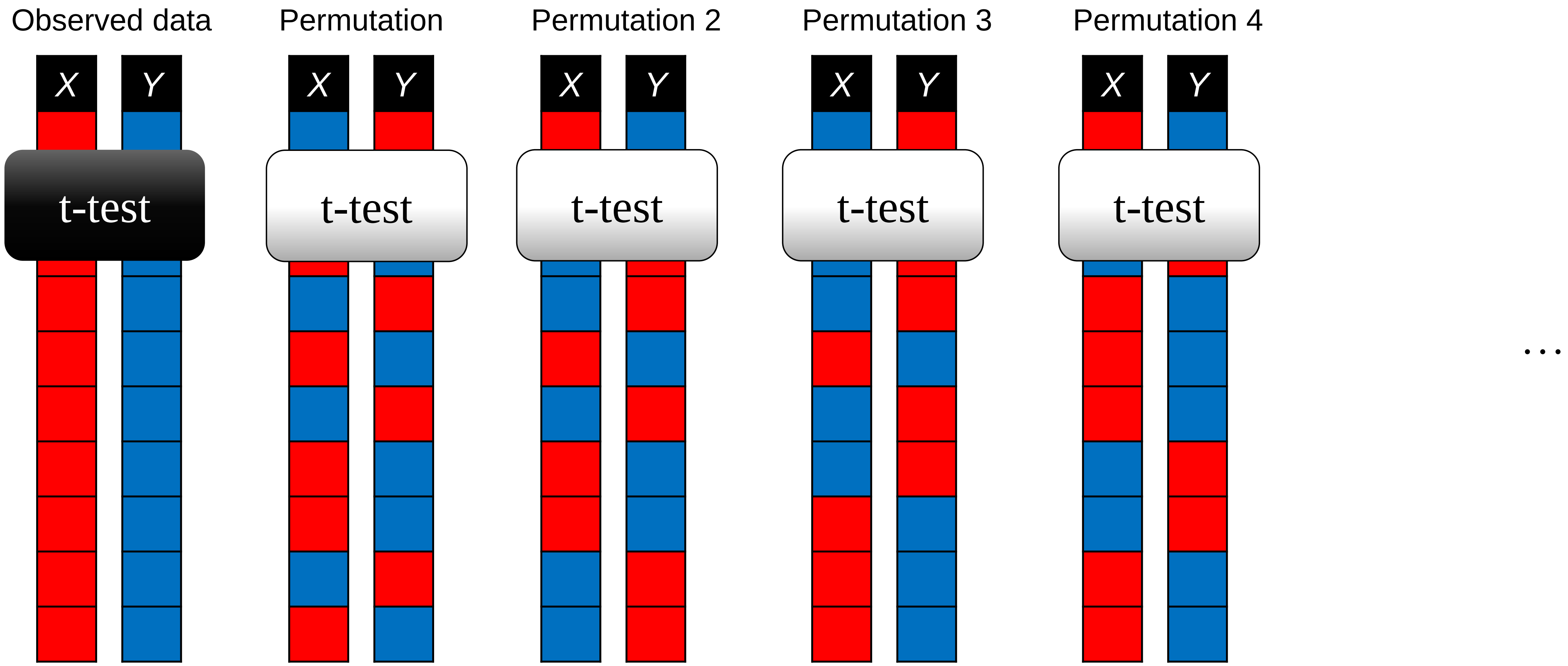




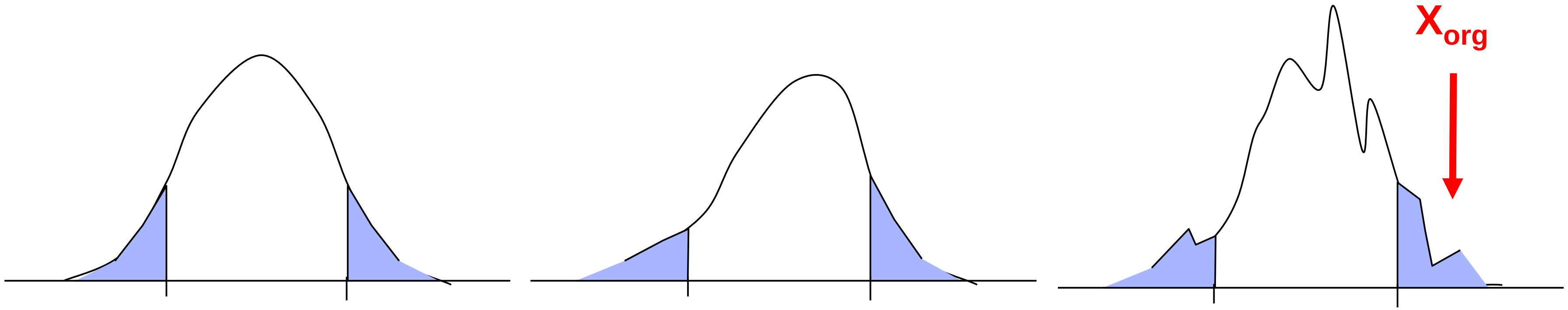
Monte Carlo simulation

Image from Wikipedia

Permutation tests



Distribution of “x” can take any shape

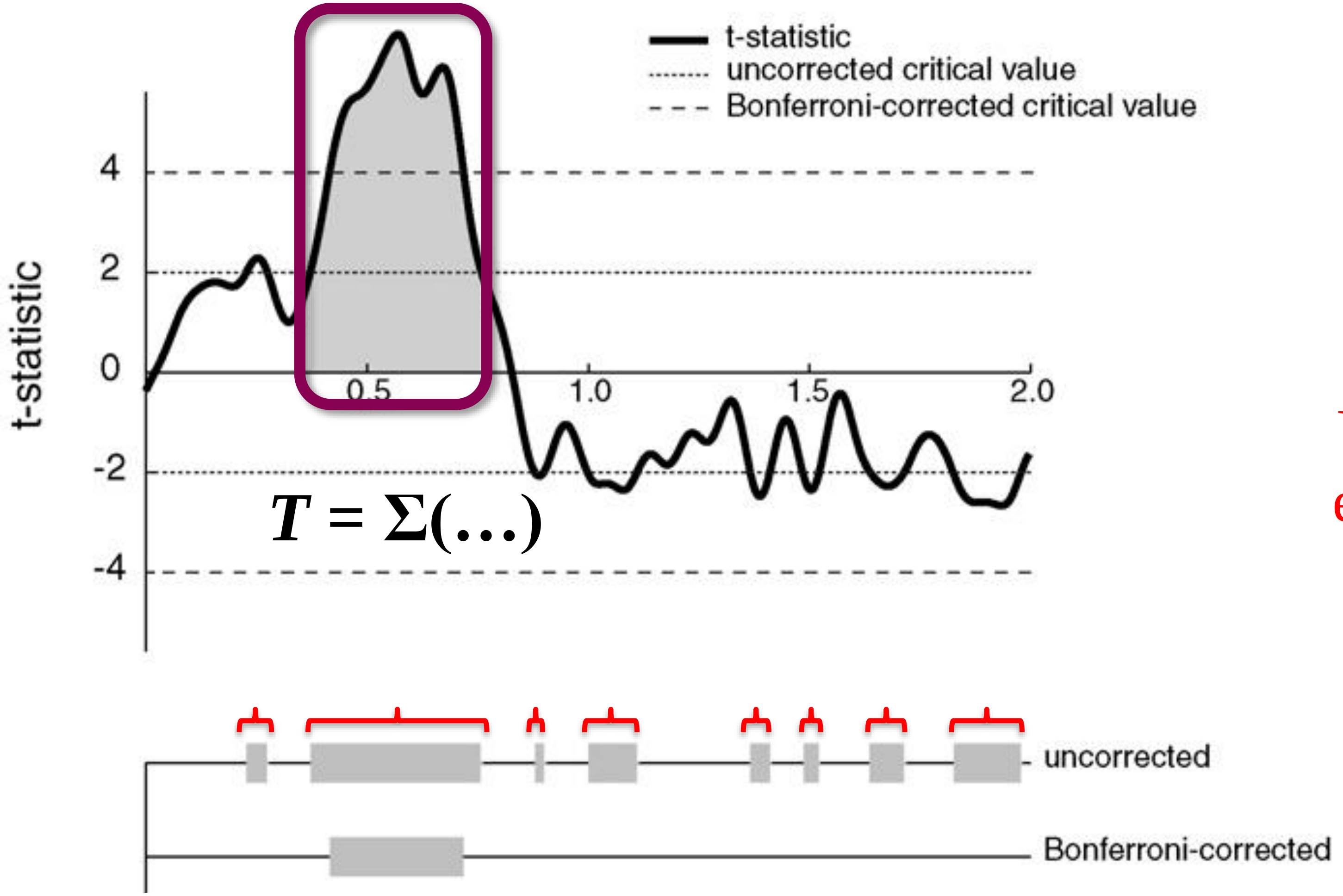


Figures from Oostenveld & Stolk

Non-parametric statistics

- Randomization of independent variable
- Hypothesis is about data, not about the specific parameter
- Randomization distribution of the statistic of interest “x” is approximated using Monte-Carlo approach
- H0 is tested by comparing the observed statistic against the randomization distribution

Cluster statistics



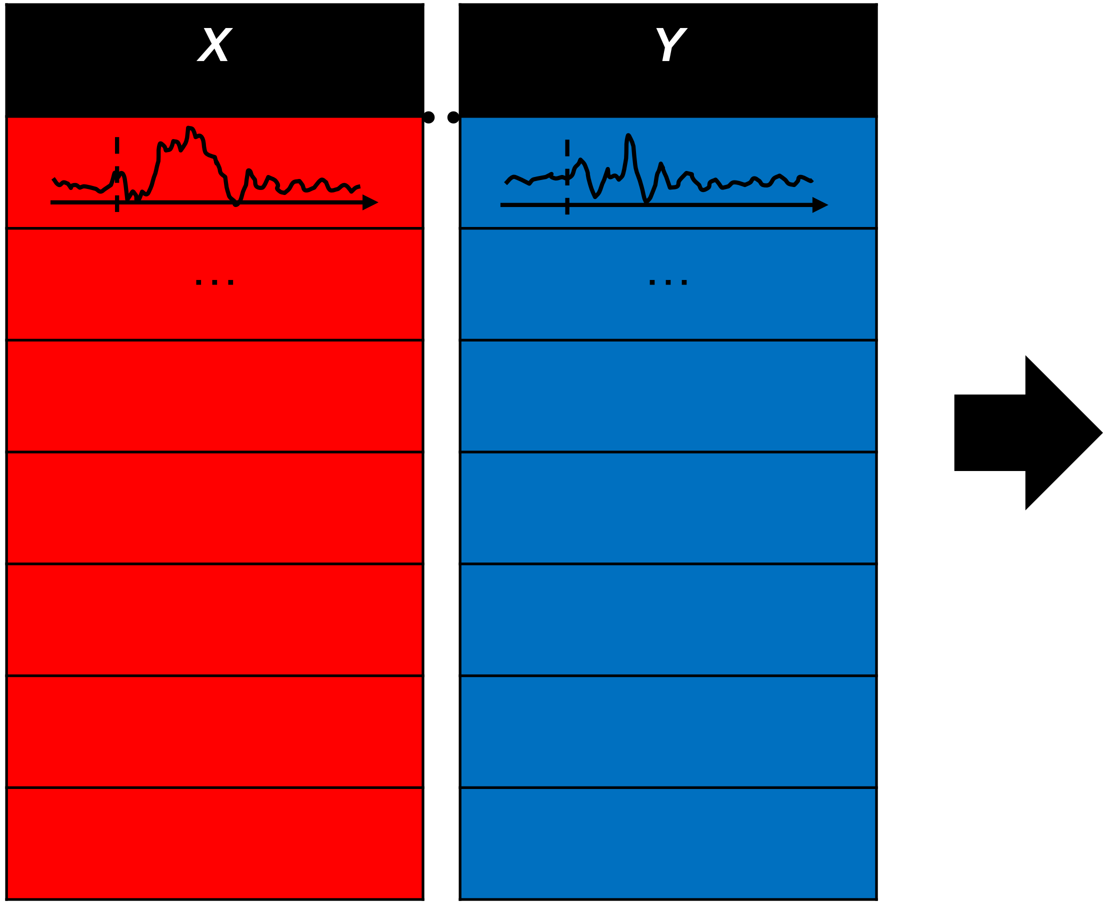
How big T would we expect under the null hypothesis?

↓

Use Monte Carlo simulation to estimate a null distribution of T values

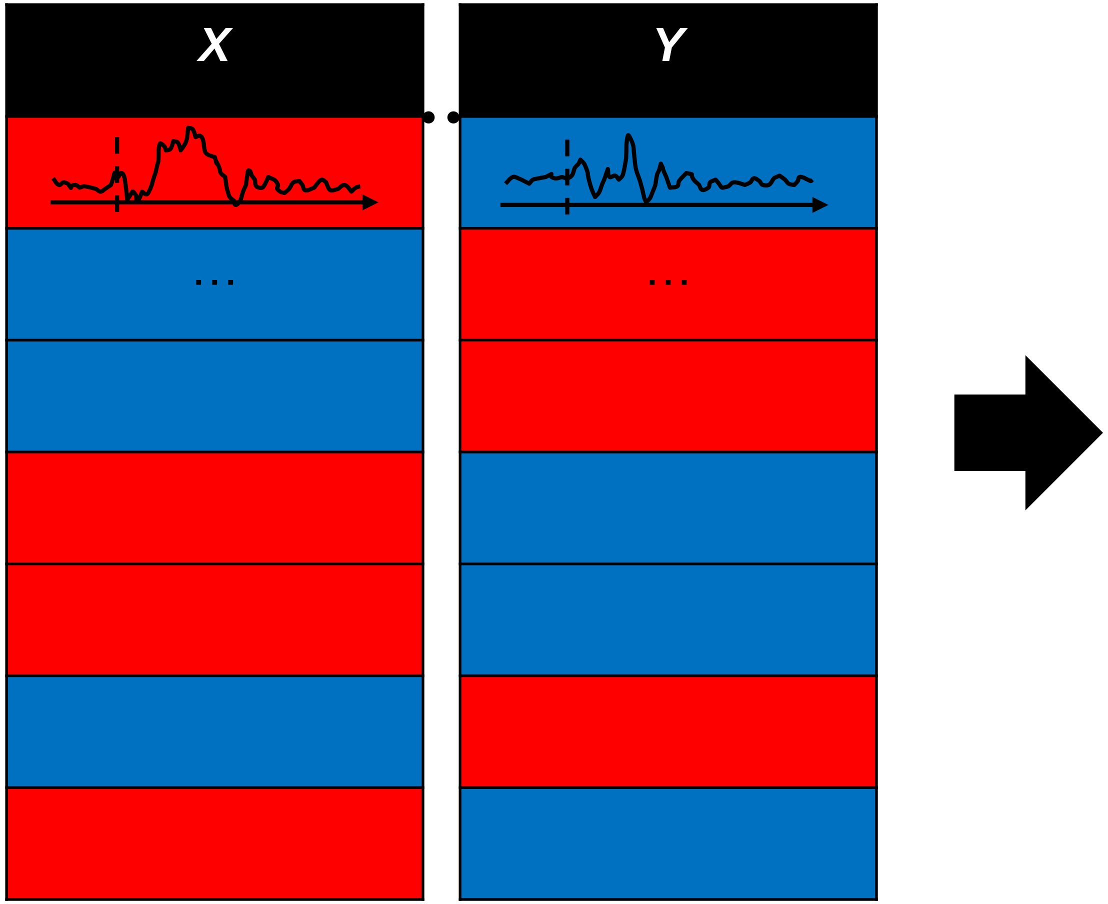
Maris & Oostenveld (2007)

Cluster based permutation tests



$$T_{org}$$

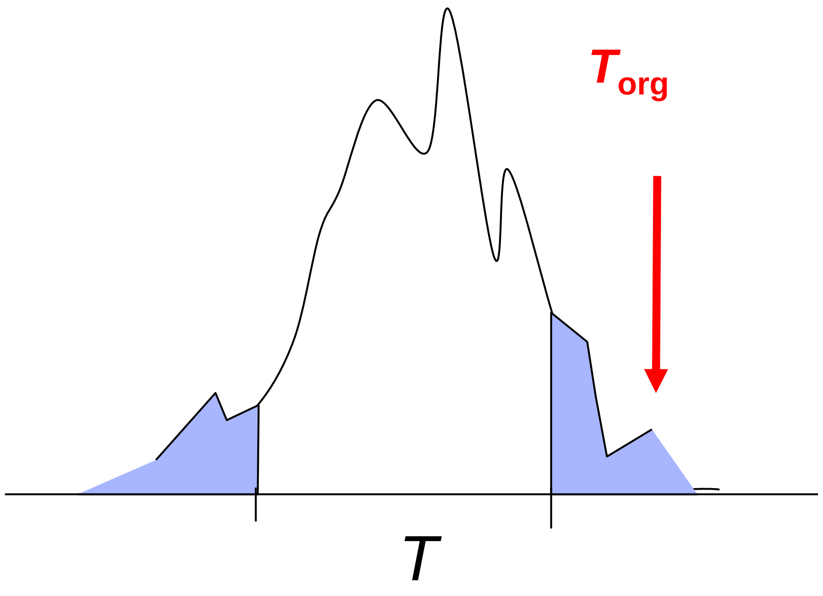
Cluster-based permutation tests



T_{P1} ... T_{Pn}

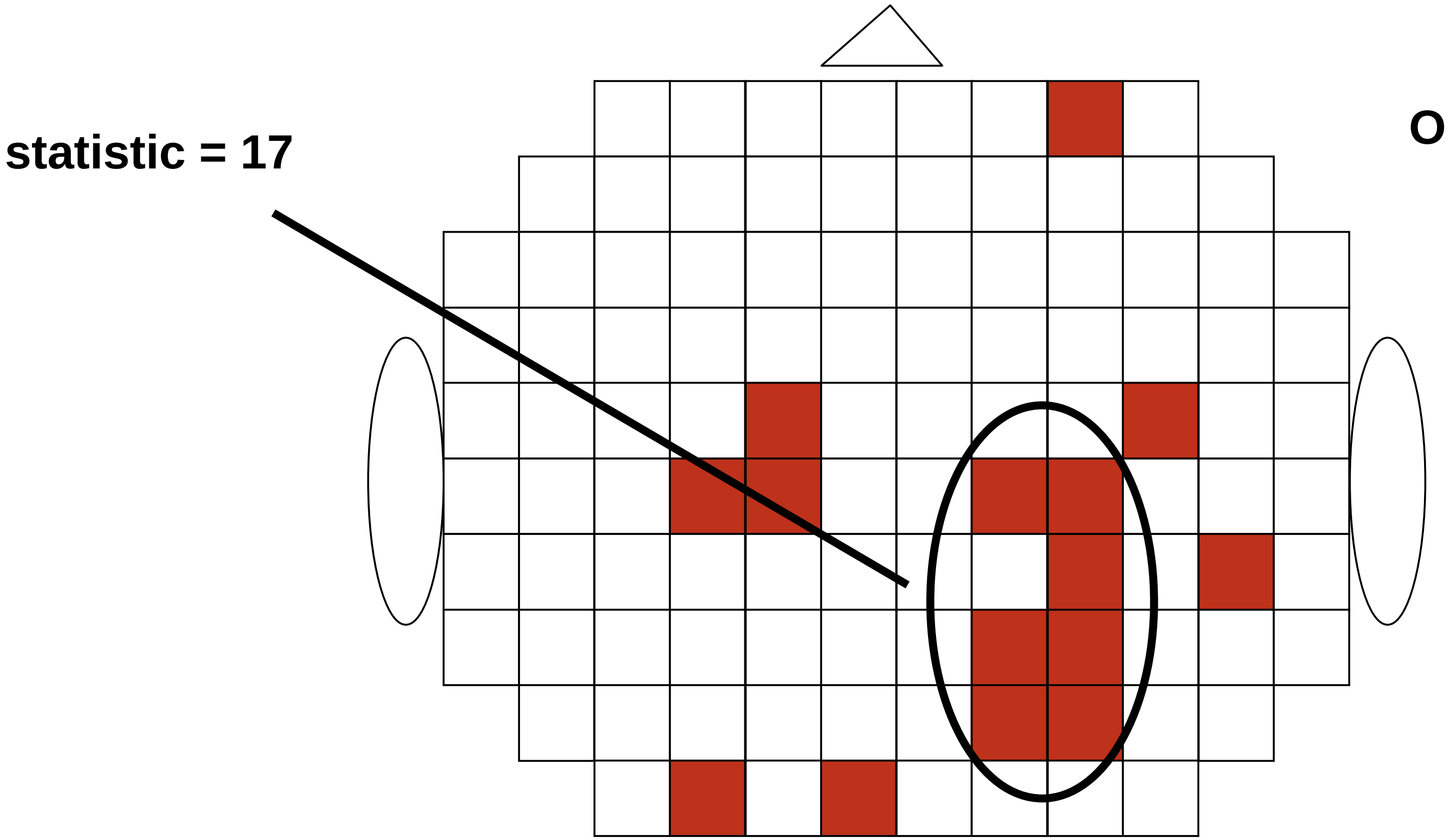
Avoid the multiple comparison problem

- The statistic “x” can be anything
- Rather than testing everything, only test the most extreme observation (i.e. the max statistic)
- Compute the randomization distribution for the most extreme statistic
- Note that often we compute **two** extrema, one for each tail



Figures from Oostenveld & Stolk

Toy example: Original observation

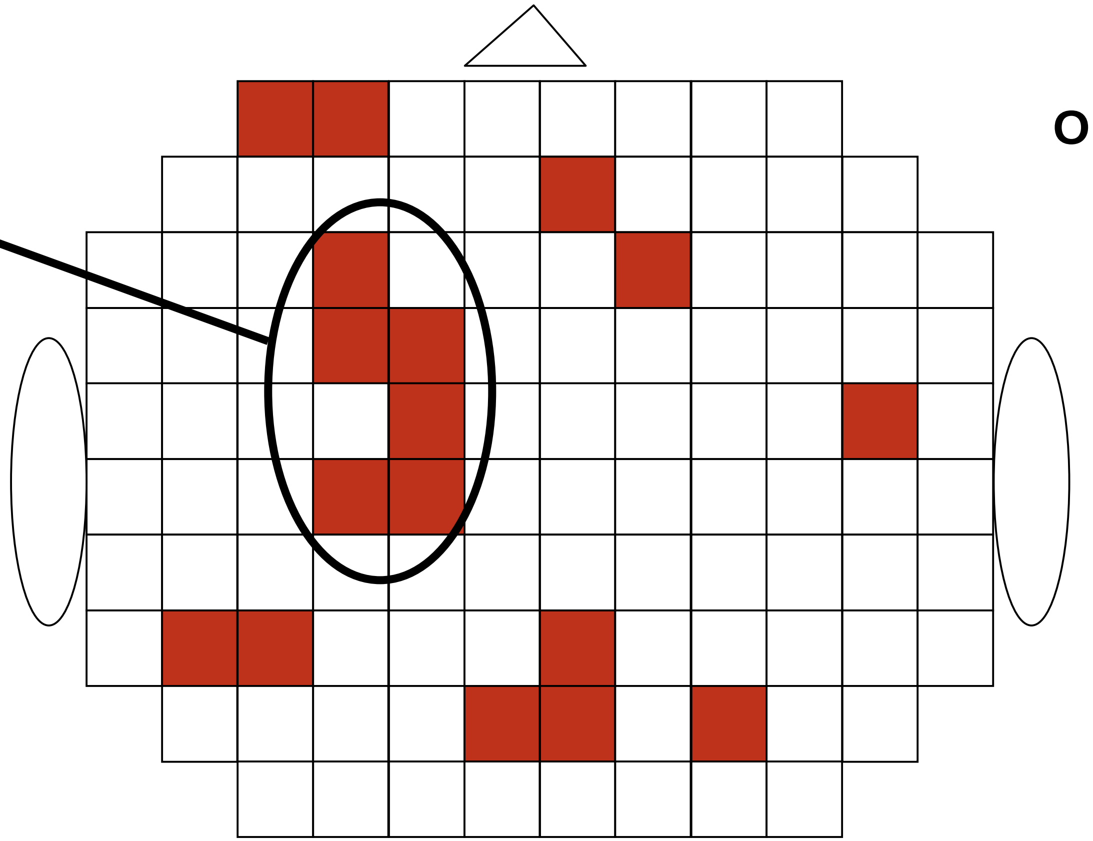


Observation 17

Figures from Oostenveld & Stolk

Toy example: 1st permutation

statistic = 13

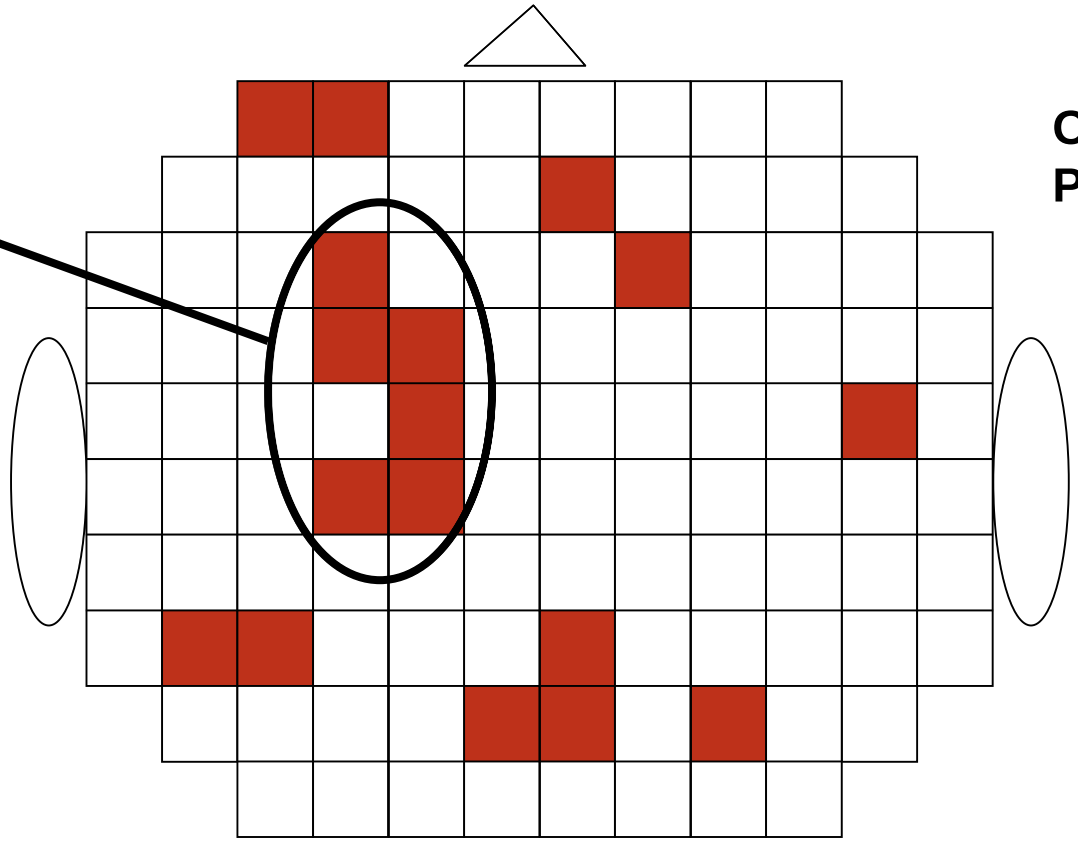


Observation 17

Figures from Oostenveld & Stolk

Toy example: 1st permutation

statistic = 13

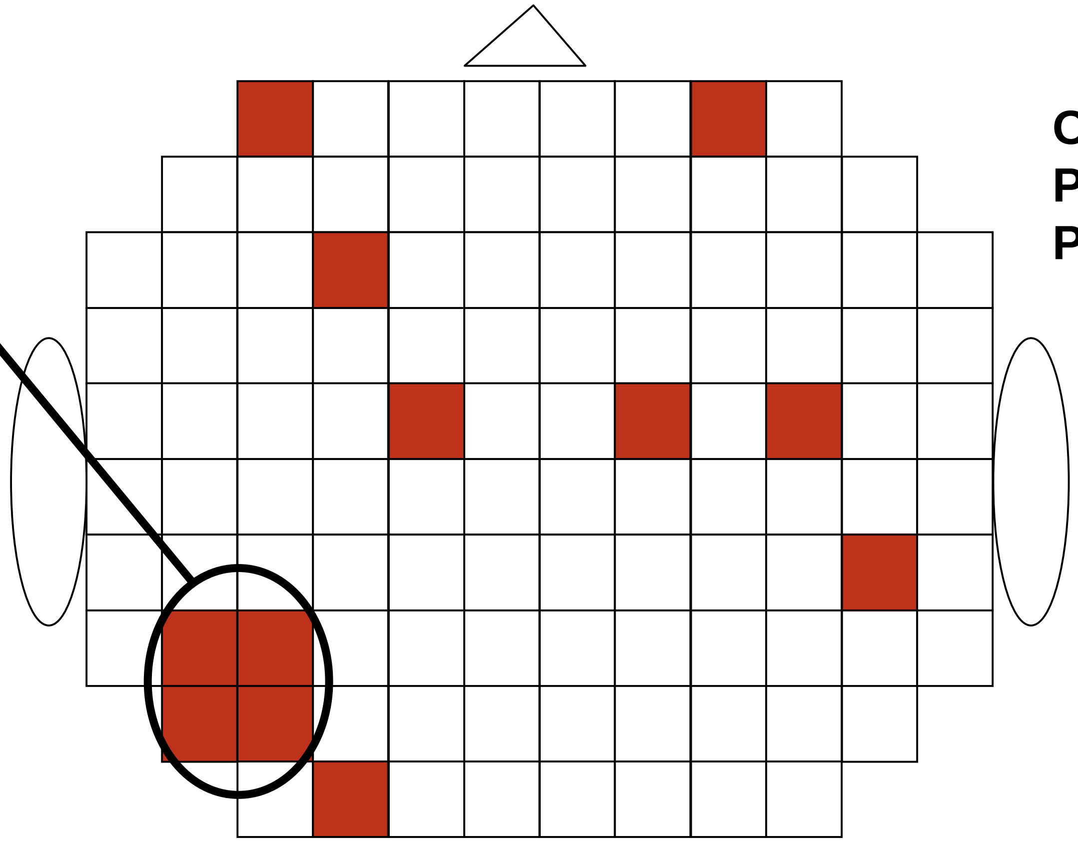


Observation	**17**
Permutation 1	**13**

Figures from Oostenveld & Stolk

Toy example: 2nd permutation

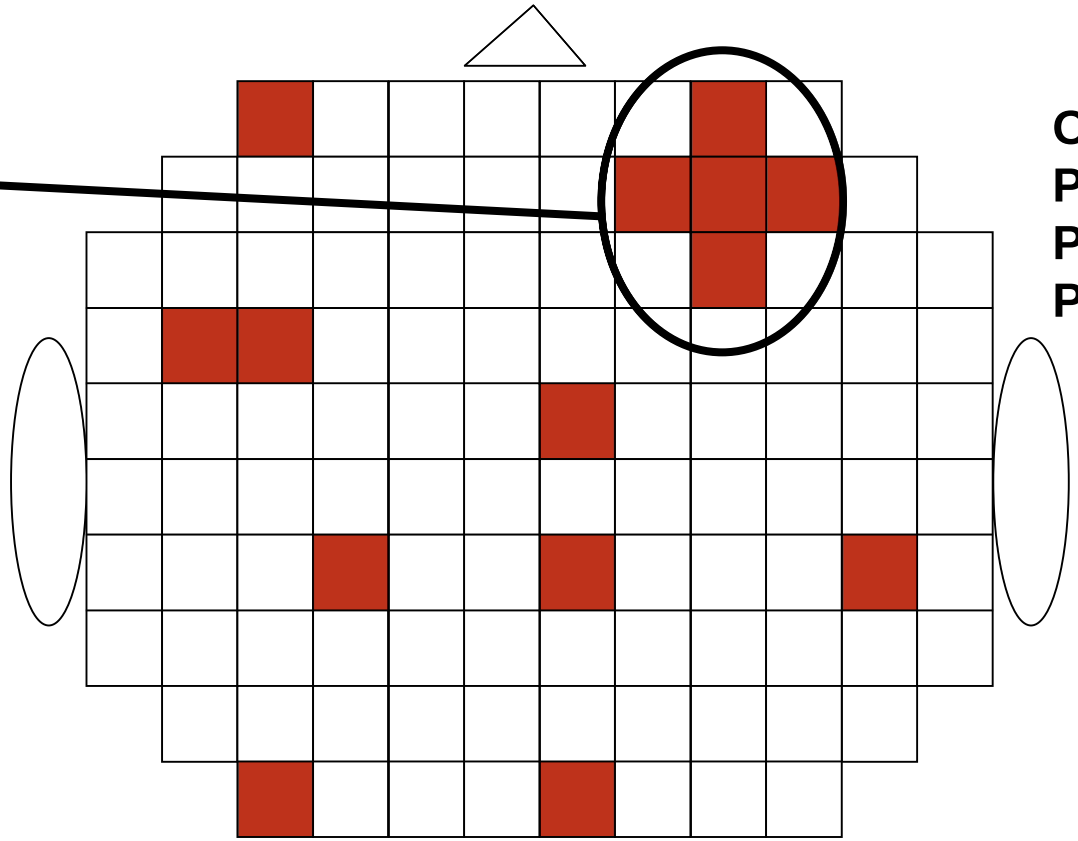
statistic = 11



Observation	**17**
Permutation 1	**13**
Permutation 2	**11**

Toy example: 3rd permutation

statistic = 12

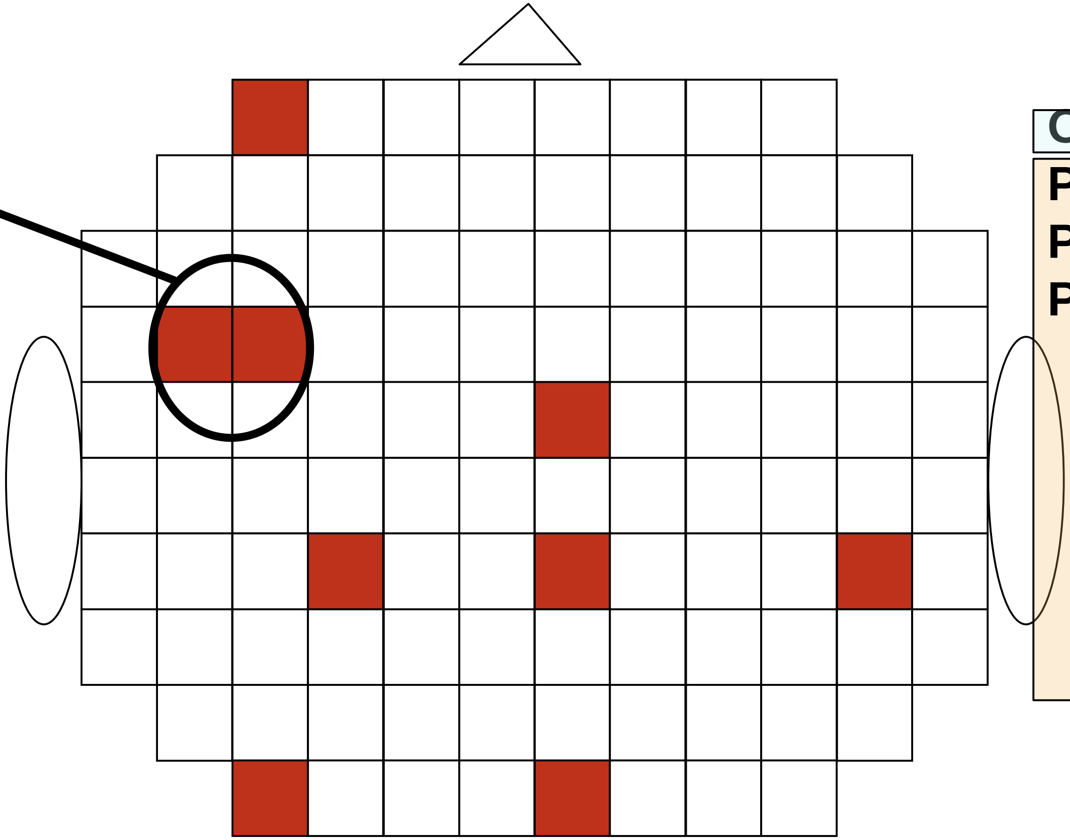


Observation	**17**
Permutation 1	**13**
Permutation 2	**11**
Permutation 3	**12**

Figures from Oostenveld & Stolk

Toy example: N^{th} permutation

statistic = …



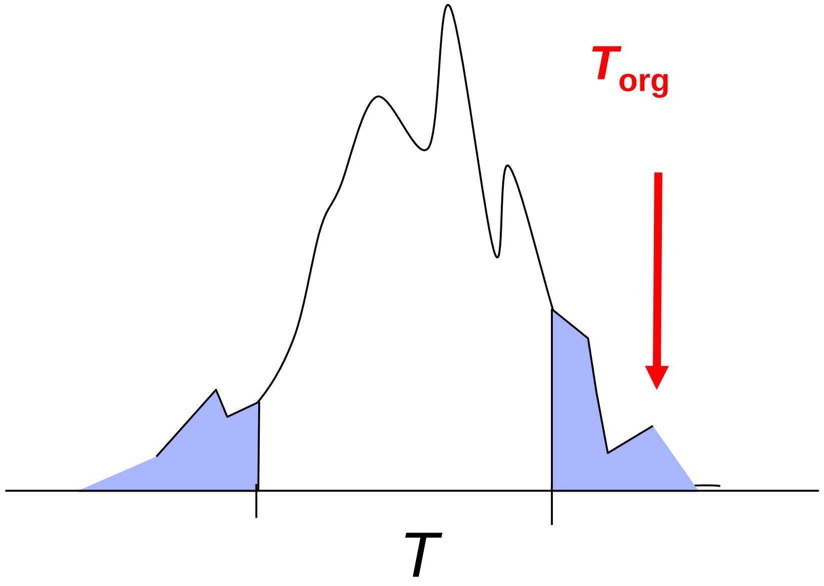
Observation	17
Permutation 1	13
Permutation 2	11
Permutation 3	12

...

Figures from Oostenveld & Stolk

Interpretation

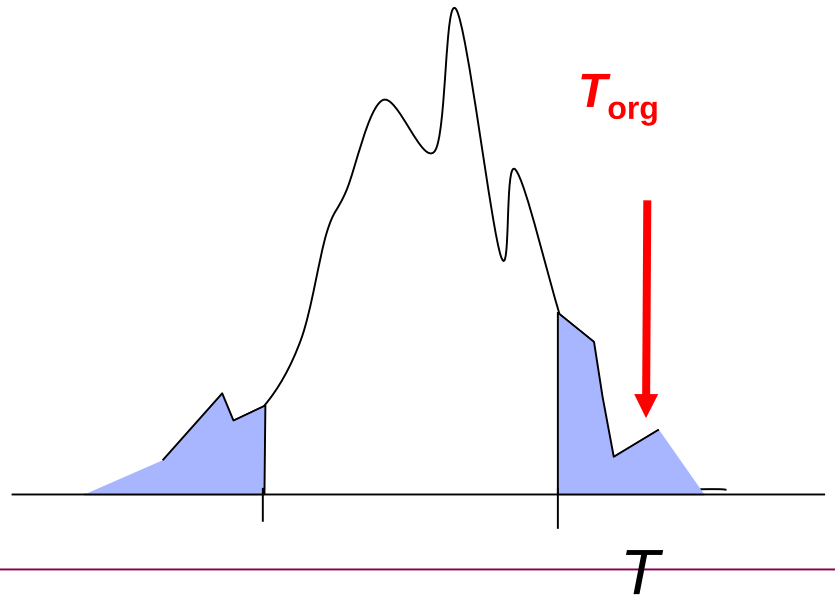
- Decision to keep or H0 depends on the permutation disribution
- Depends on what you used to create the permutation disribution



Figures from Oostenveld & Stolk

Does the *data of interest* come form the same distribution?

1. Find clusters in *data of interest*
2. Calculate permuation distribution



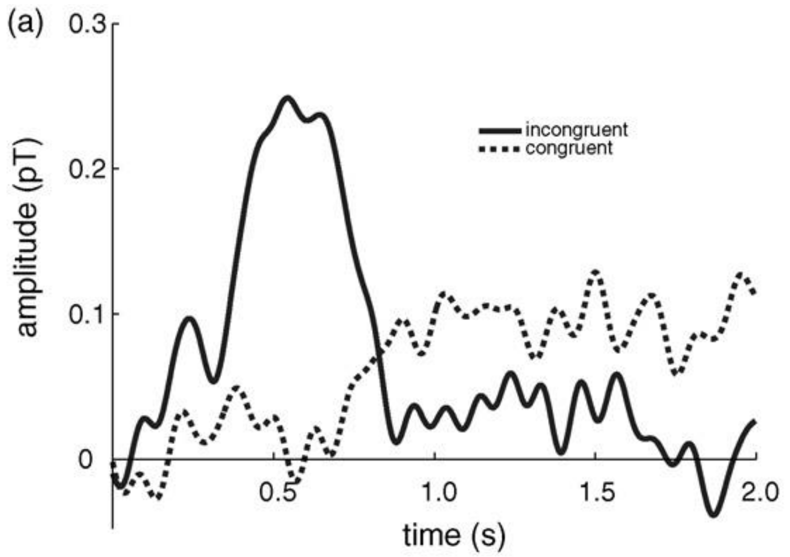
Figures from Oostenveld & Stolk

Interpretation

X
Time-window [0:2.0 s]
…
…

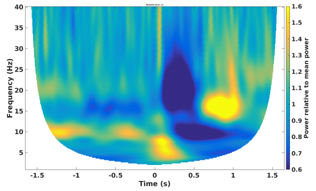
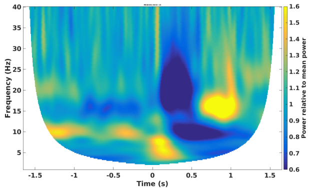
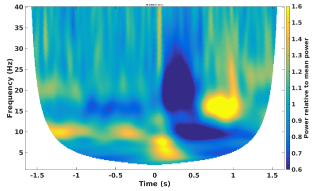
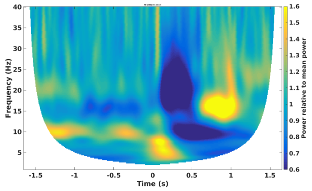
Y
Time-window [0:2.0 s]
…
…

Data of interest

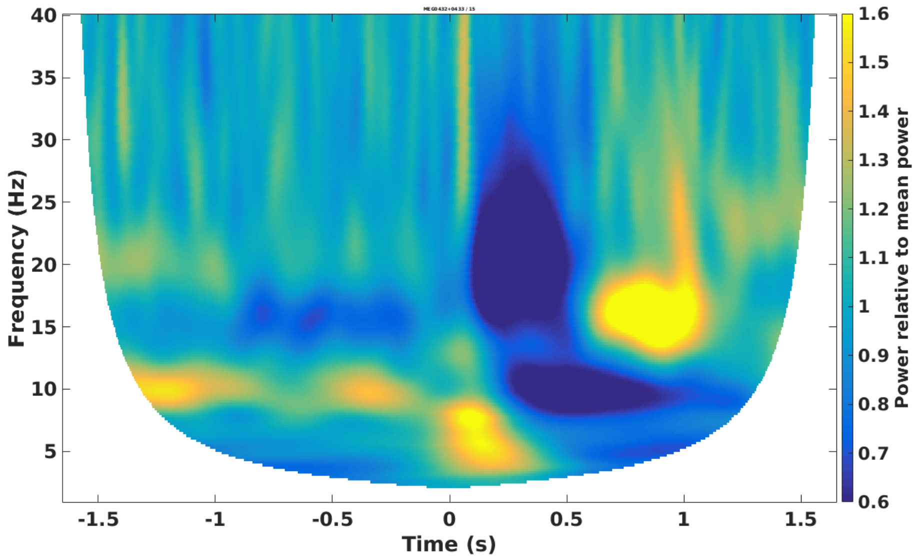


Time-window [0:2.0 s]

Interpretation

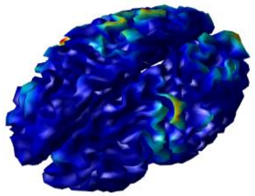
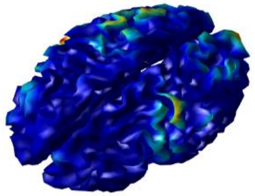
X	Y
	
	
...	...

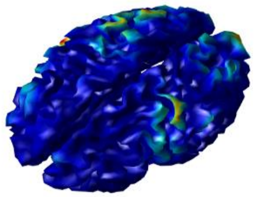
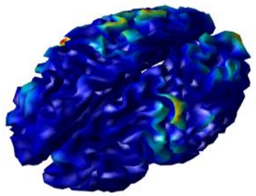
Frequency



Time-window [0:2.0 s]

Cluster-based permutation tests

X


…

Y


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Data of interest

Conclusion

- Mind your hypotheses
  - → Where and when do you expect an effect = your data of interest!
  - → H0: your data of interest come from same distribution
  - → Flexible specificity
- A formal hypothesis can be tested with randomization test
  - → control the chance of false positives
  - → reduce the false negative rate
- Multiple comparison problem
  - → one hypothesis for all data
  - → Based on assumption of correlated data (true for MEG/EEG signals.
- Increase sensitivity
  - → using clusters to capture the structure in the data

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Litterature

Cluster-based permutation tests

- Maris, E., & Oostenveld, R. (2007). Nonparametric statistical testing of EEG- and MEG-data. *Journal of Neuroscience Methods*, *164*(1), 177–190. https://doi.org/10.1016/j.jneumeth.2007.03.024
- Maris, E. (2012). Statistical testing in electrophysiological studies. *Psychophysiology*, *49*(4), 549–565. https://doi.org/10.1111/j.1469-8986.2011.01320.x

Interpretation of cluster-based permutation tests

- Sassenhagen, J., & Draschkow, D. (2019). Cluster-based permutation tests of MEG/EEG data do not establish significance of effect latency or location. *Psychophysiology*, *56*(6), e13335. https://doi.org/10.1111/psyp.13335

Feature selection approach

- Kilner, J. M. (2013). Bias in a common EEG and MEG statistical analysis and how to avoid it. *Clinical Neurophysiology*. https://doi.org/10.1016/j.clinph.2013.03.024
- Luck, S. J. (2014). *An introduction to the event-related potential technique* (Second edition). The MIT Press.

Acknowledgement

- **Daniel Lundqvist**, Head of NatMEG, Karolinska Institutet: support for the workshop
- **Robert Oostenveld**, Donders: discussion and advice.
  - → Thanks to Oostenveld & Stolk for permission to use figures from the FieldTrip workshop at Donders.
- **Lau Andersen**, Aarhus University: previous iteration of the statistics lecture on the NatMEG MEG/EEG course.