Topological Inference

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SPM Course
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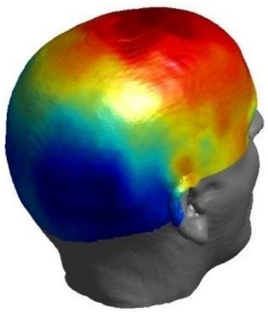
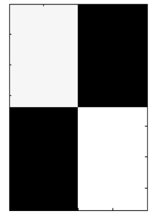
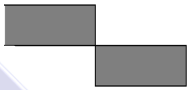
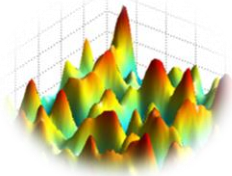


$y =$  $\beta + \varepsilon$

Contrast *c*



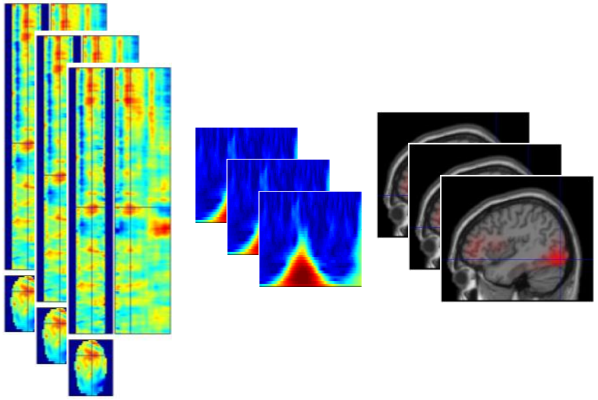
Random Field Theory



Pre-processings

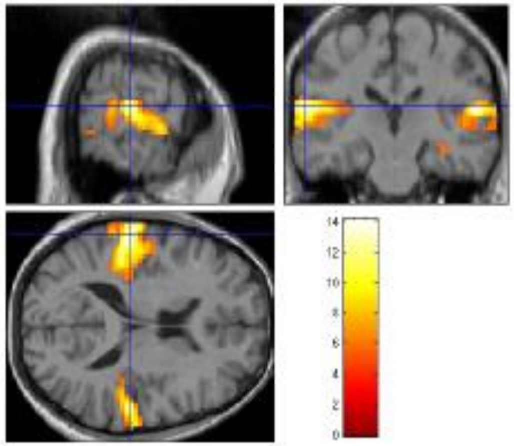
General Linear Model

Statistical Inference

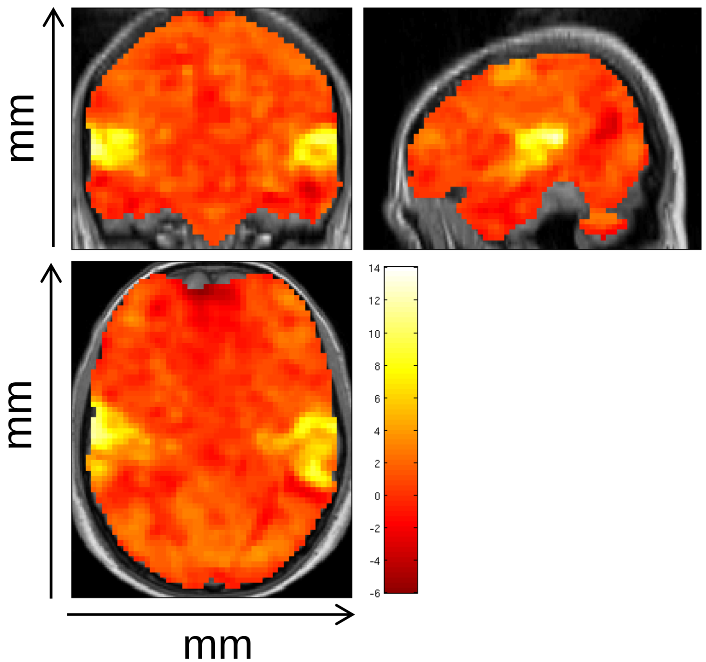


$$\hat{\beta} = (X^T X)^{-1} X^T y$$

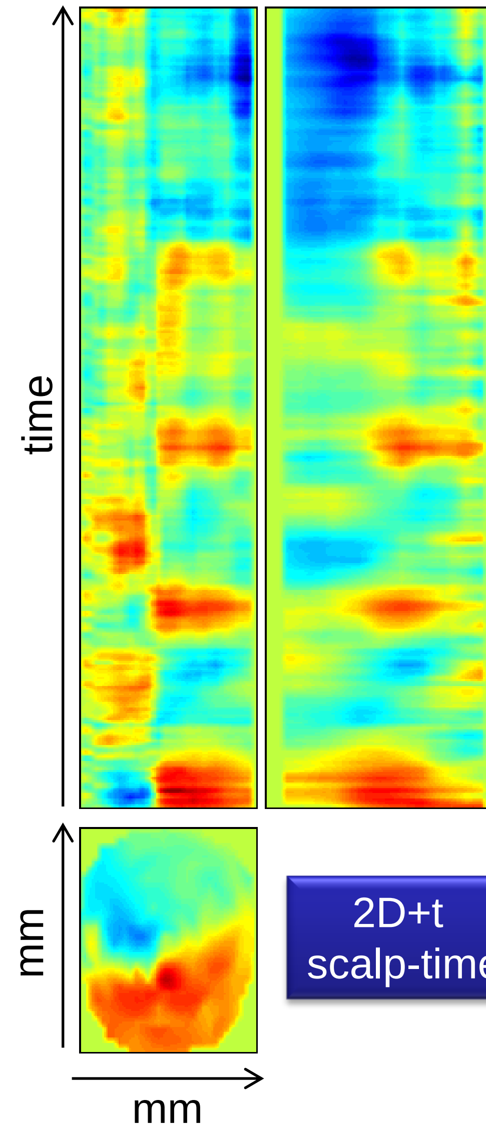
$$\hat{\sigma}^2 = \frac{\hat{\varepsilon}^T \hat{\varepsilon}}{rank(X)}$$



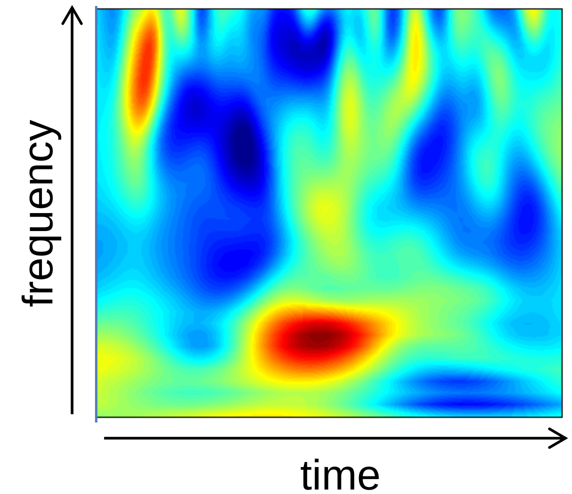
Statistical Parametric Maps



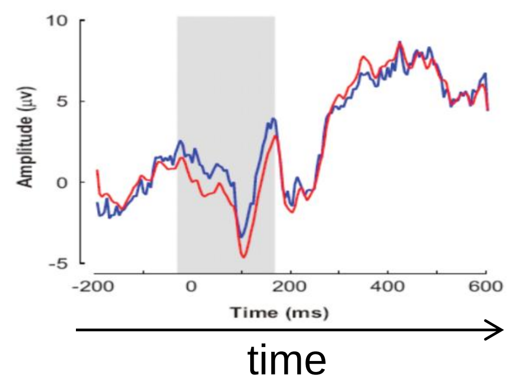
3D M/EEG source reconstruction, fMRI, VBM



2D+t scalp-time

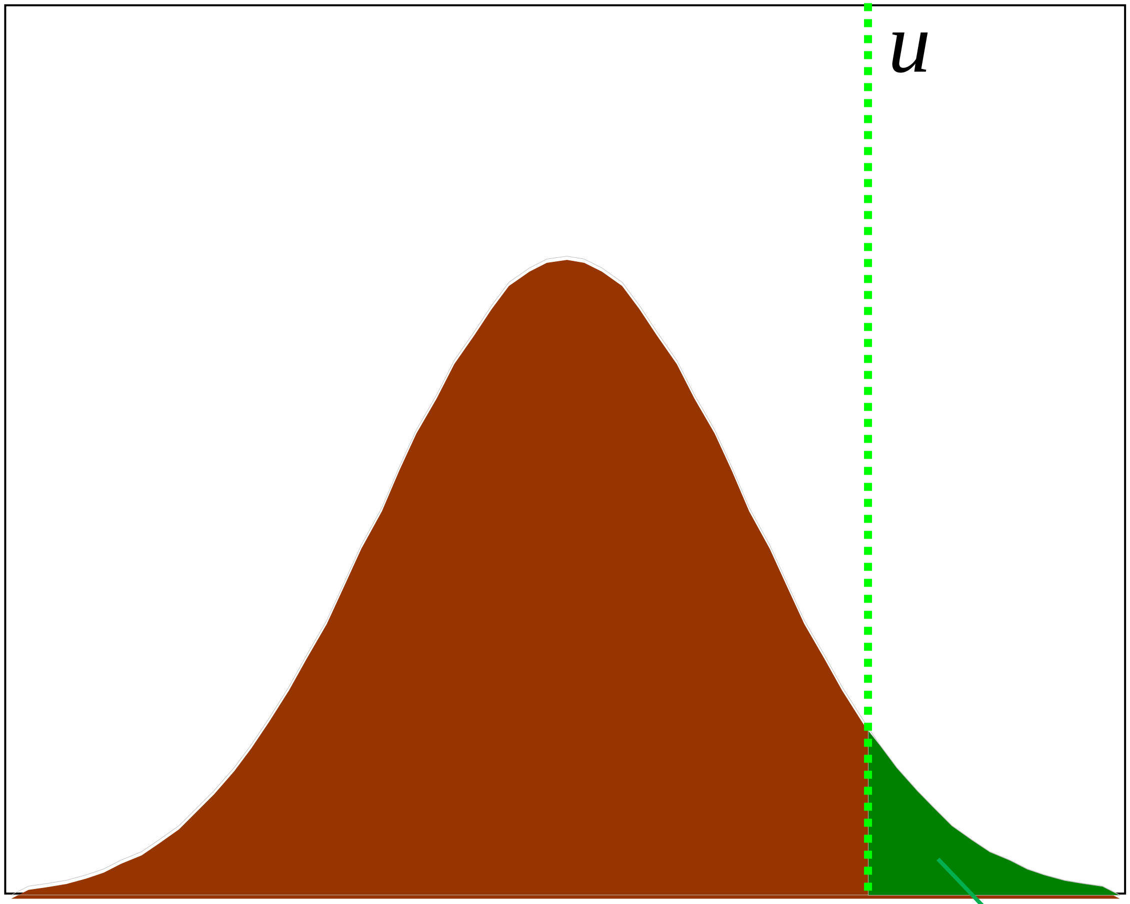


2D time-frequency



1D time

Single test



Null distribution of test statistic T

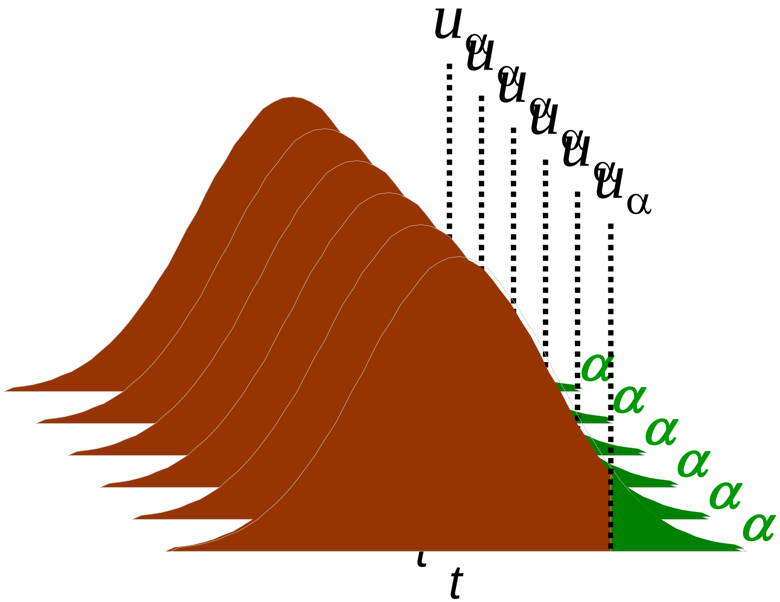
$$\alpha = p(t > u | H_0)$$

Null Hypothesis H_0:
zero activation

Decision rule (threshold) u:
determines false positive rate α

$\Rightarrow$ Choose u to give acceptable α under H_0

Multiple tests

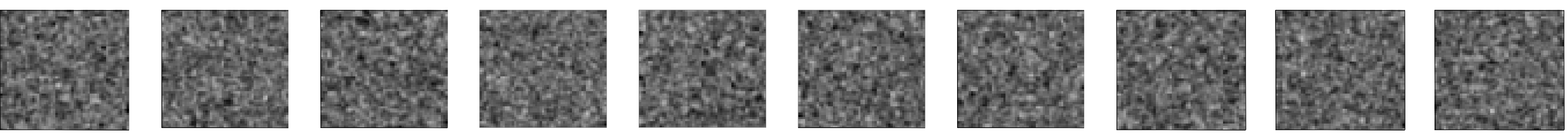


If we have 100,000 voxels,

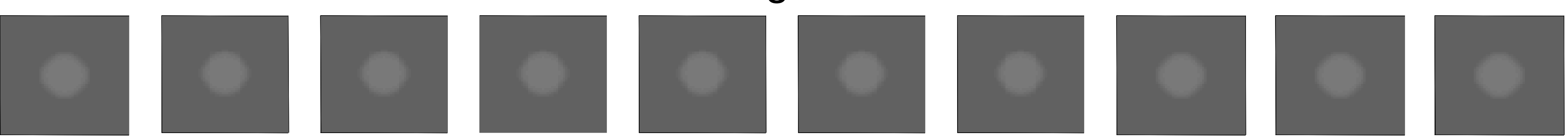
α=0.05 $\Rightarrow$ 5,000 false positive voxels.

This is clearly undesirable.

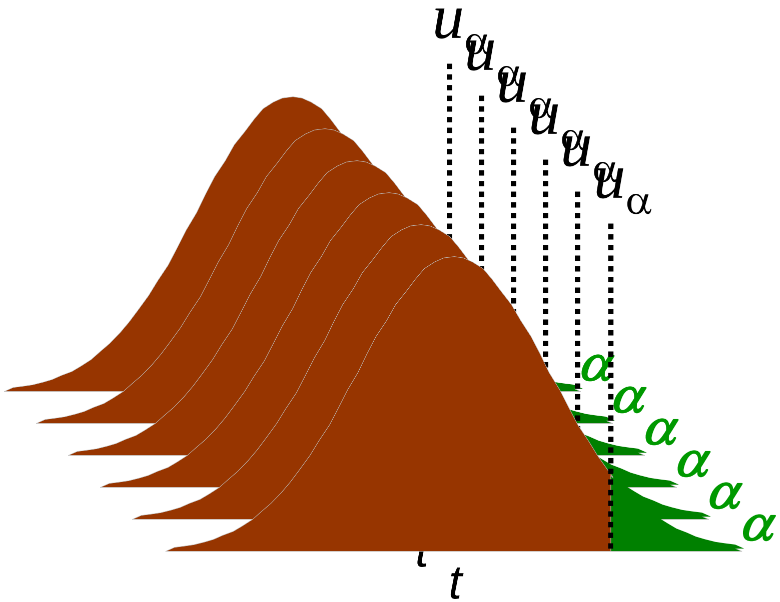
Noise



Signal



Multiple tests



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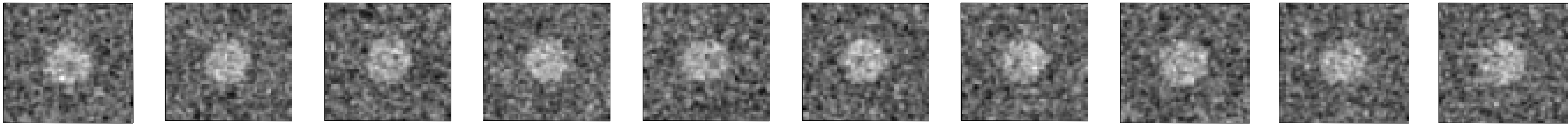
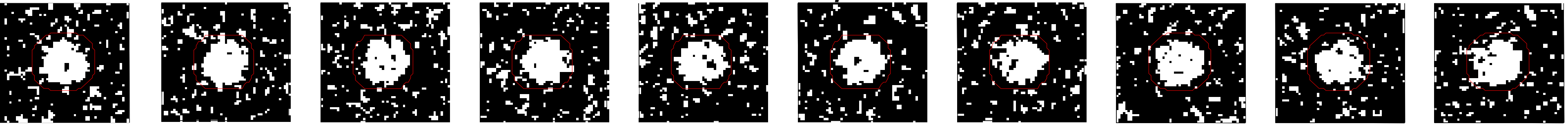


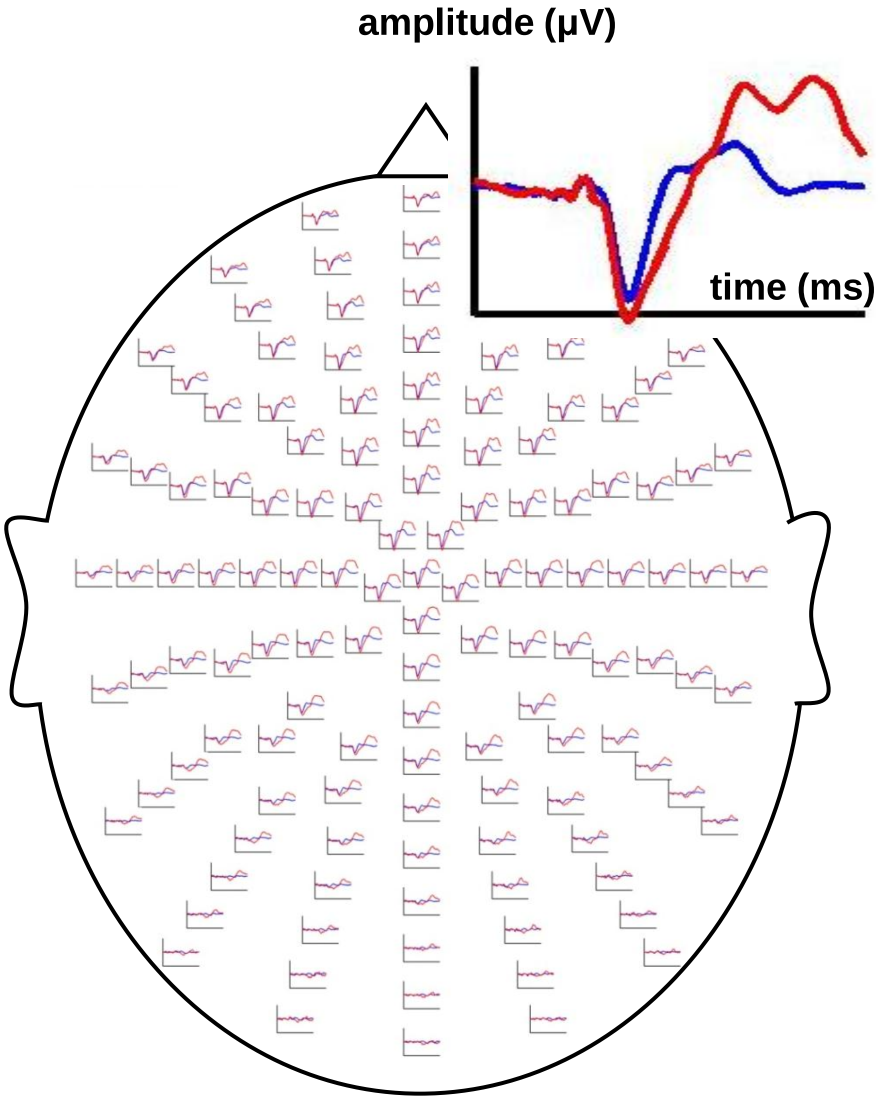
Use of 'uncorrected' *p*-value, α =0.1

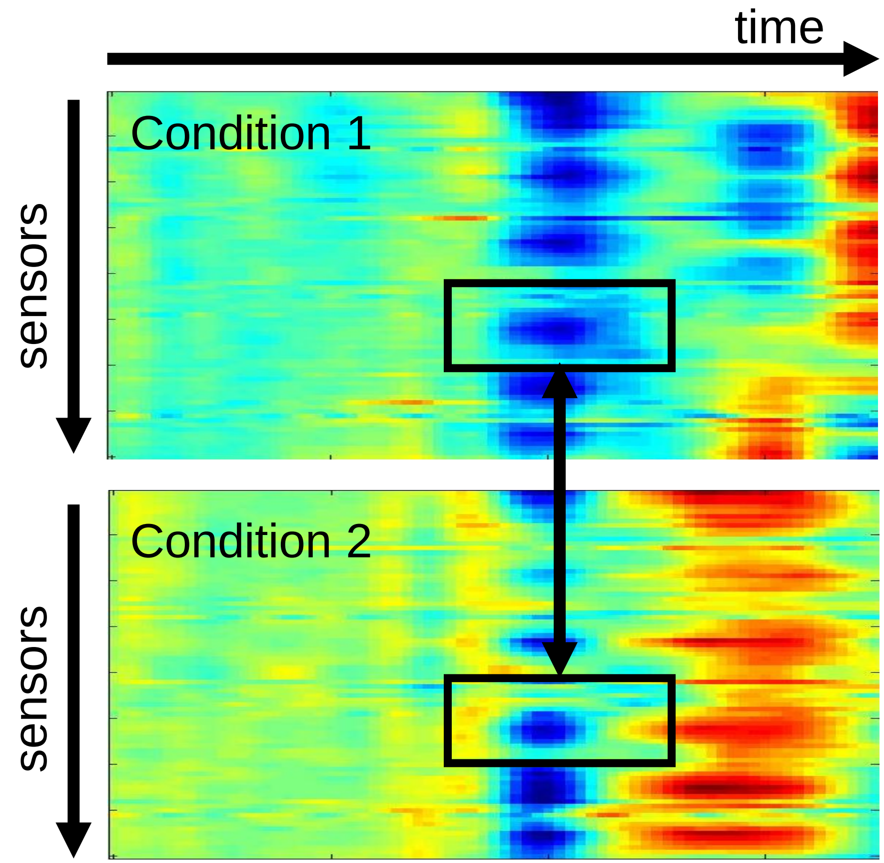


11.3% 11.3% 12.5% 10.8% 11.5% 10.0% 10.7% 11.2% 10.2% 9.5%

Percentage of Null Pixels that are False Positives

M/EEG analysis at sensor level





<u>Conventional approach</u>: Reduce evoked response to a few variables.

Family-Wise Null Hypothesis

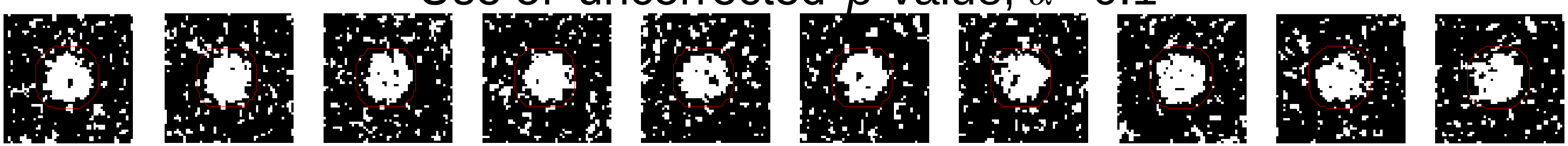
Family-Wise Null Hypothesis:
Activation is zero everywhere

If we reject a voxel null hypothesis at *any* voxel,
we reject the family-wise Null hypothesis

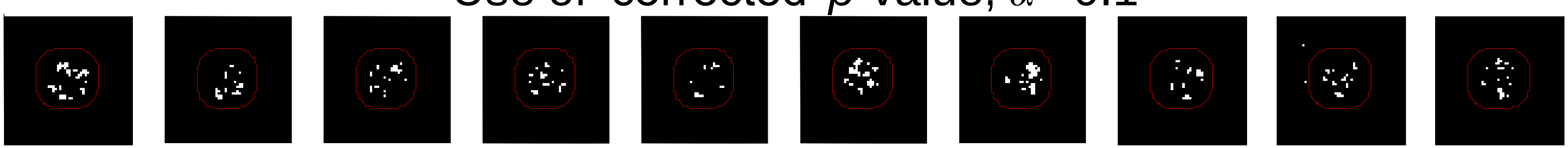
A FP ***anywhere*** in the image gives a **Family Wise Error** (FWE)

Family-Wise Error rate (FWER) = '*corrected*' *p*-value

Use of 'uncorrected' *p*-value, α =0.1



Use of 'corrected' *p*-value, α =0.1



FWE

Bonferroni correction

The Family-Wise Error rate (FWER), α_{FWE}, for a family of N tests follows the inequality:

$$\alpha_{FWE} \leq N\alpha$$

where α is the test-wise error rate.

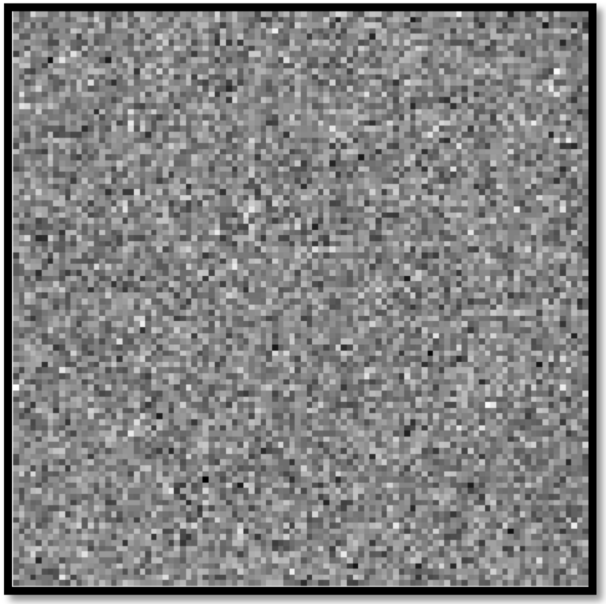
Therefore, to ensure a particular FWER choose:

$$\alpha = \frac{\alpha_{FWE}}{N}$$

This correction does not require the tests to be independent but becomes very stringent if dependence.

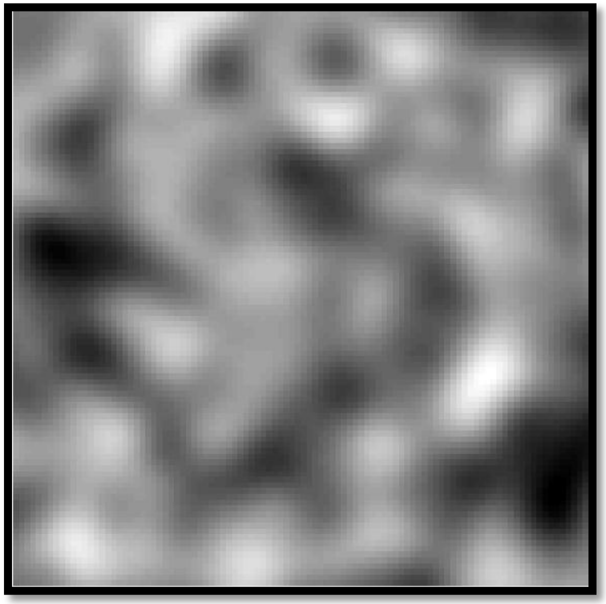
Spatial correlations

100 x 100 independent tests



Discrete data

Spatially correlated tests (FWHM=10)



Spatially extended data

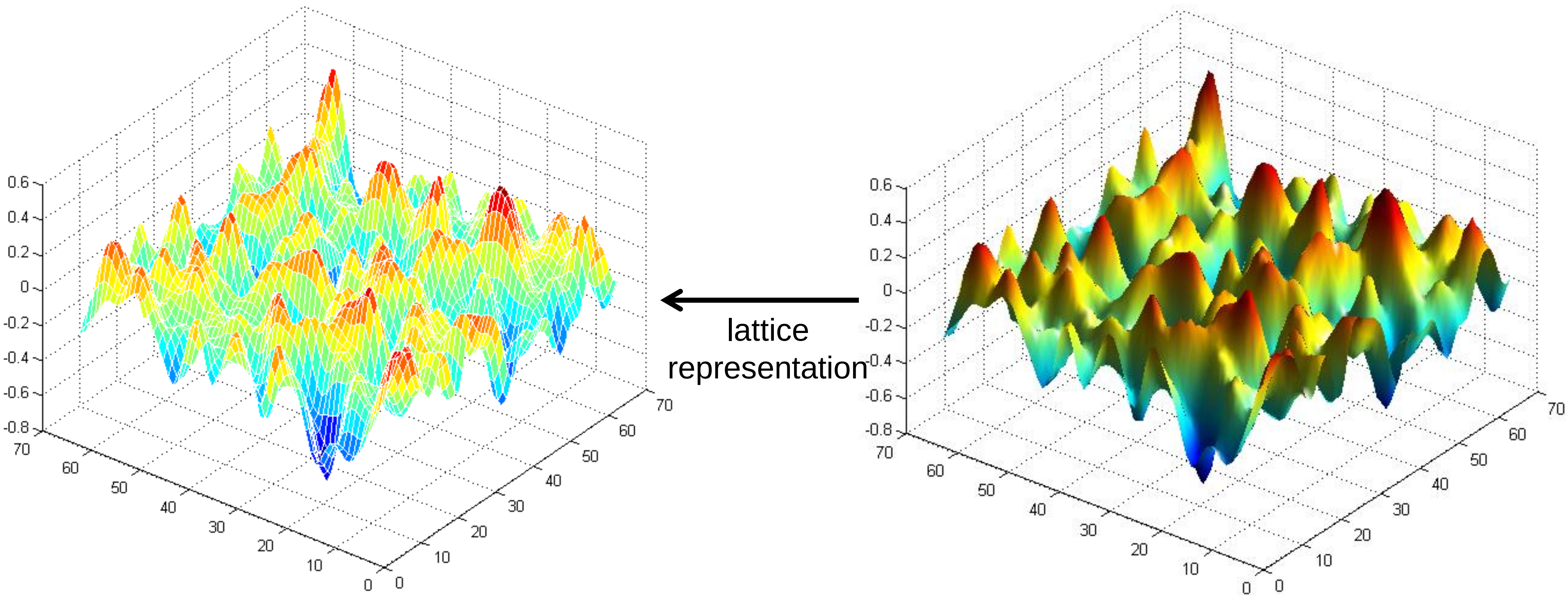
Bonferroni is too conservative for spatial correlated data.

10,000 voxels $\Rightarrow \alpha_{BONF} = \frac{0.05}{10{,}000} \Rightarrow u_c = 4.42$ (uncorrected $u = 1.64$)

Random Field Theory

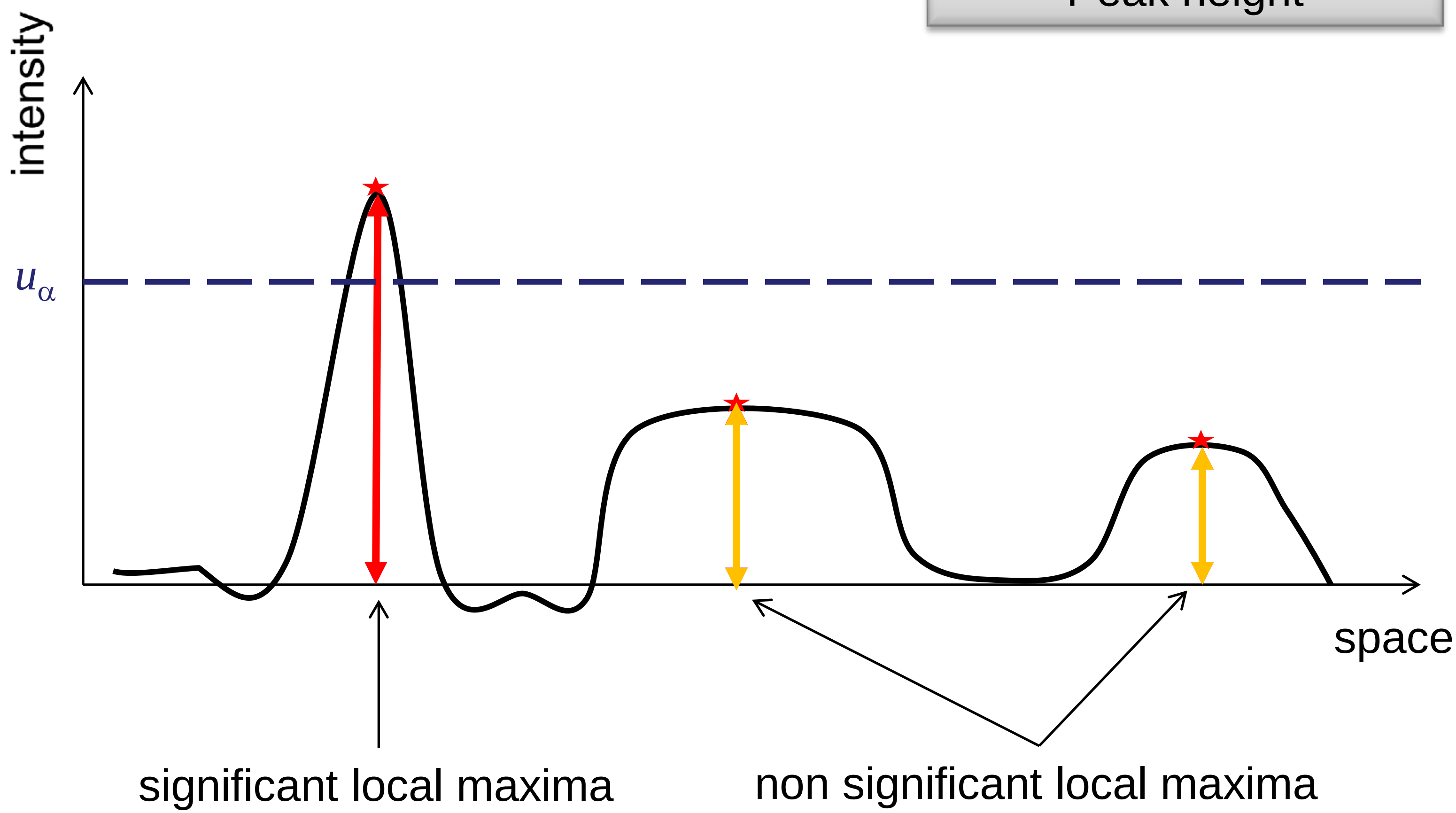
⇒ Consider a statistic image as a discretisation of a continuous underlying random field.

⇒ Use results from continuous **random field theory**.



Topological inference

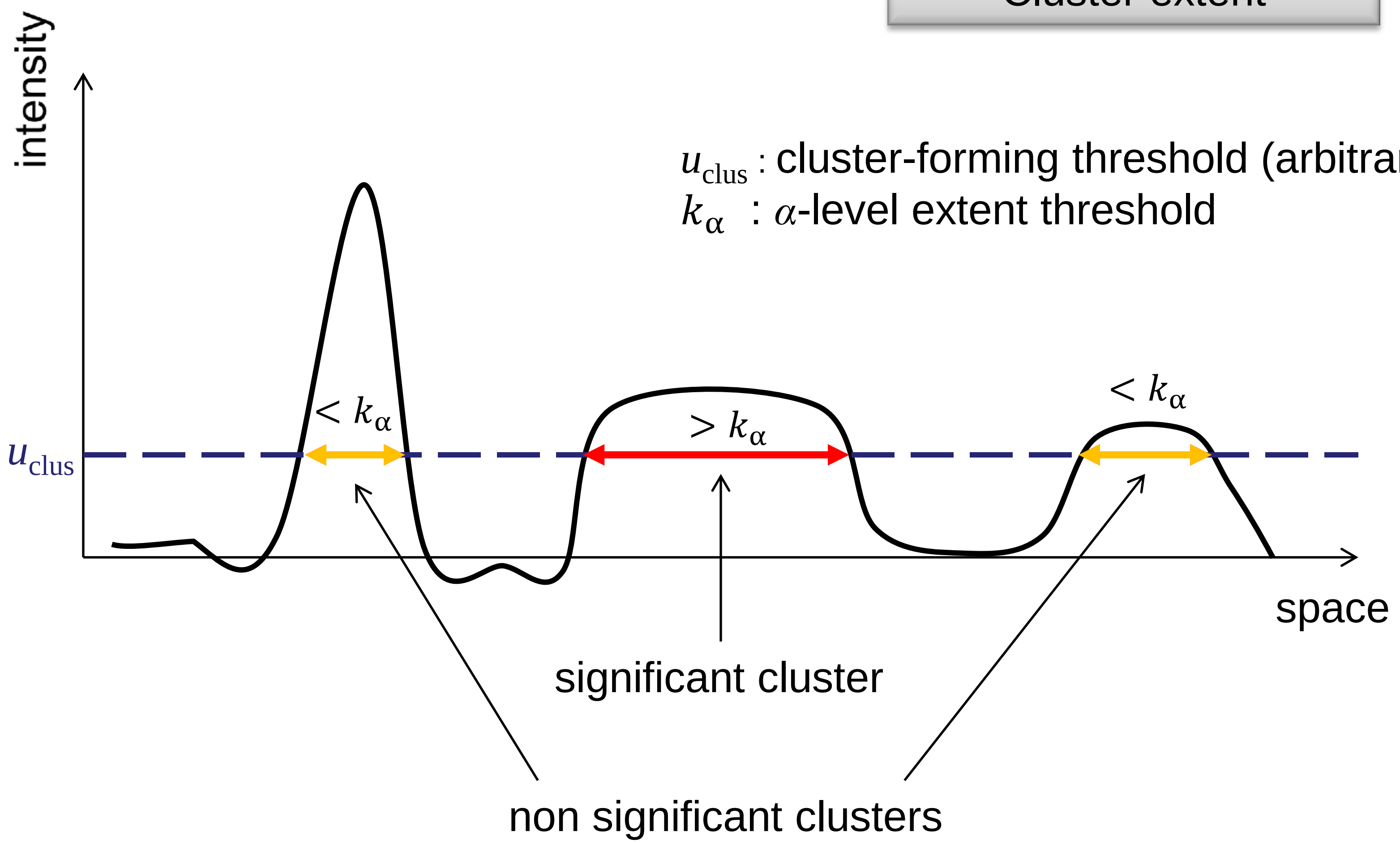
Topological feature:
Peak height



Topological inference

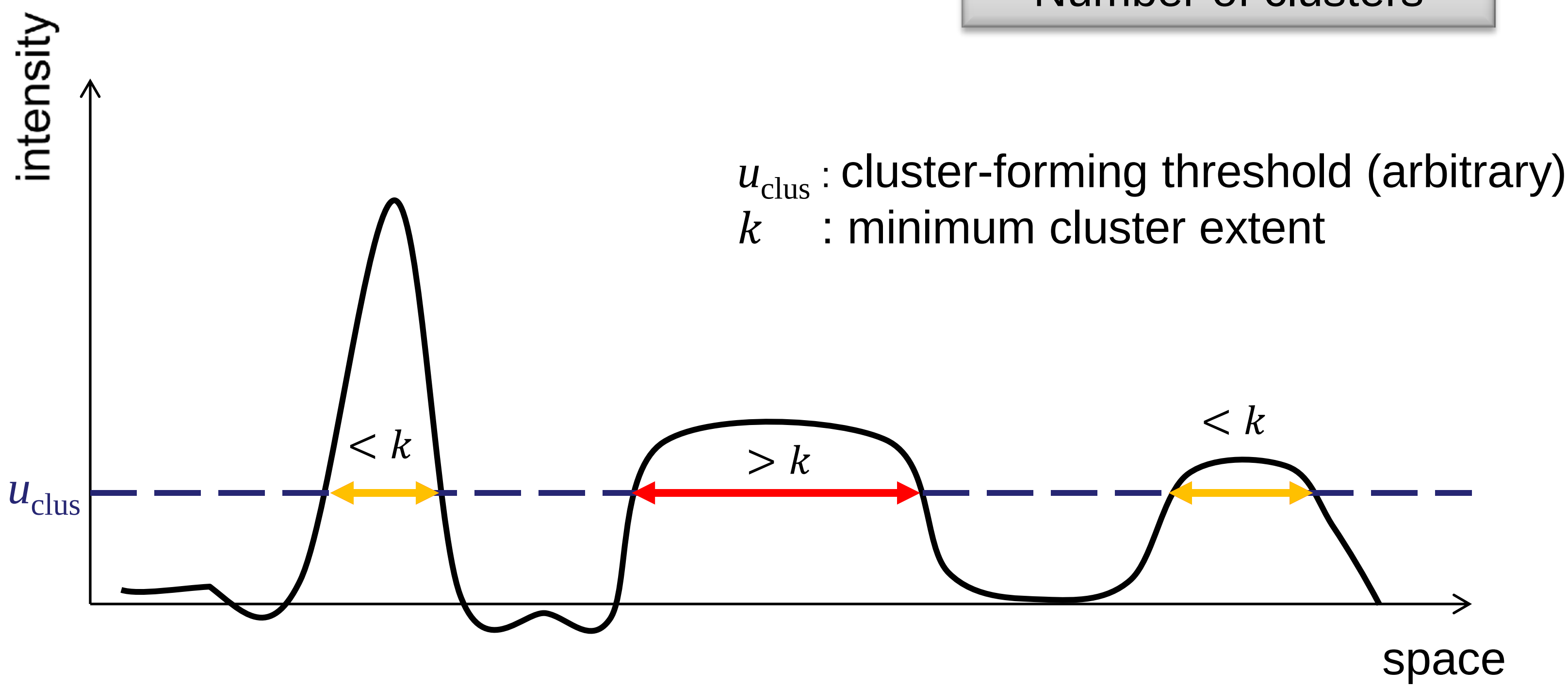
Topological feature:
Cluster extent

u_{clus} : cluster-forming threshold (arbitrary)
k_α : α-level extent threshold



Topological inference

Topological feature:
Number of clusters



Here, $c=1$, only one cluster larger than k.

Euler Characteristic χ

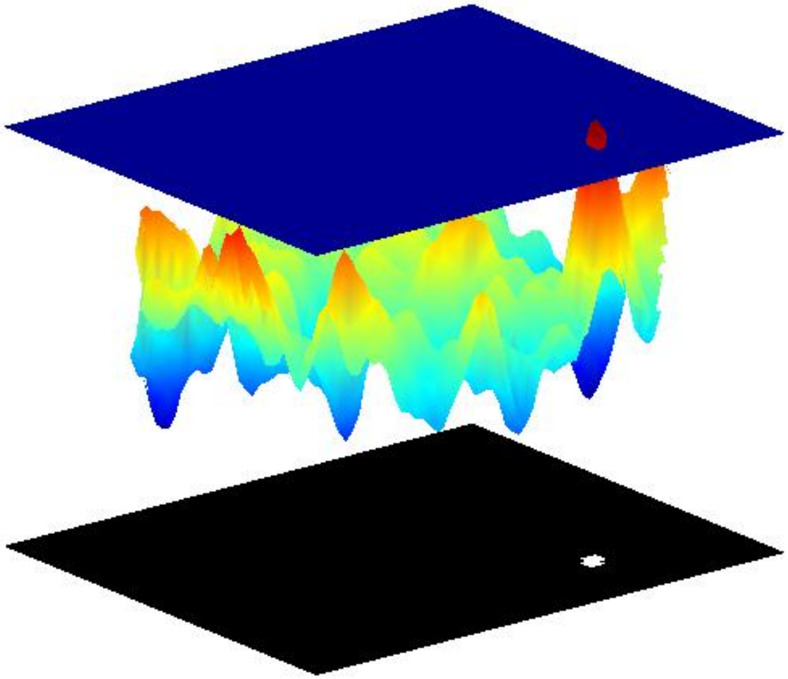
Euler Characteristic χ_u:

- Topological measure

  χ_u = # blobs - # holes

- at high threshold u:

  χ_u = # blobs



$$FWER = p(FWE)$$
$$= p(one\ or\ more\ blobs\ |H_0)$$
$$\approx p(\chi_u \geq 1|H_0)$$
$$\approx E[\chi_u|H_0] \approx \boldsymbol{\alpha_{FWE}}$$

No holes

Zero or one blob

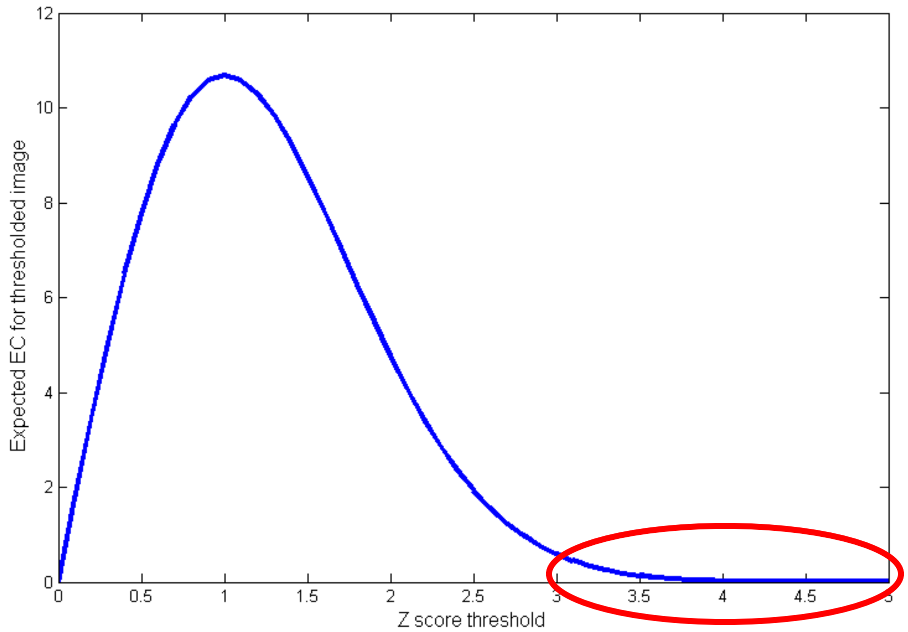
Expected Euler Characteristic

$$E[\chi_u] = \lambda(\Omega)|\Lambda|^{1/2}\, u \exp(-u^2/2)/(2\pi)^{3/2}$$

2D Gaussian Random Field

- Ω : search region
- $\lambda(\Omega)$: volume
- $|\Lambda|^{1/2}$: roughness (1 / smoothness)

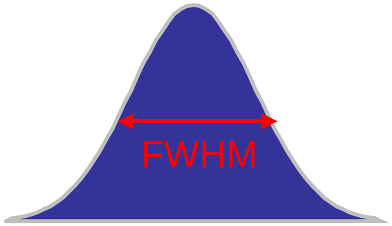
100 x 100 Gaussian Random Field
with FWHM=10 smoothing
$\alpha_{FWE} = 0.05 \Rightarrow u_{RFT} = 3.8$
($u_{BONF} = 4.42$, $u_{uncorr} = 1.64$)



Smoothness

Smoothness parameterised in terms of FWHM:

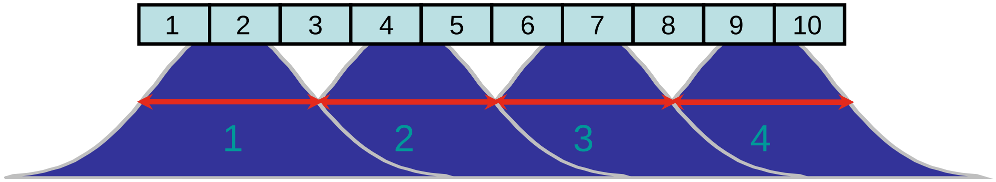
Size of Gaussian kernel required to smooth i.i.d. noise to have same smoothness as observed null (standardized) data.



RESELS (Resolution Elements):

1 RESEL = $FWHM_x FWHM_y FWHM_z$

RESEL Count *R* = volume of search region in units of smoothness

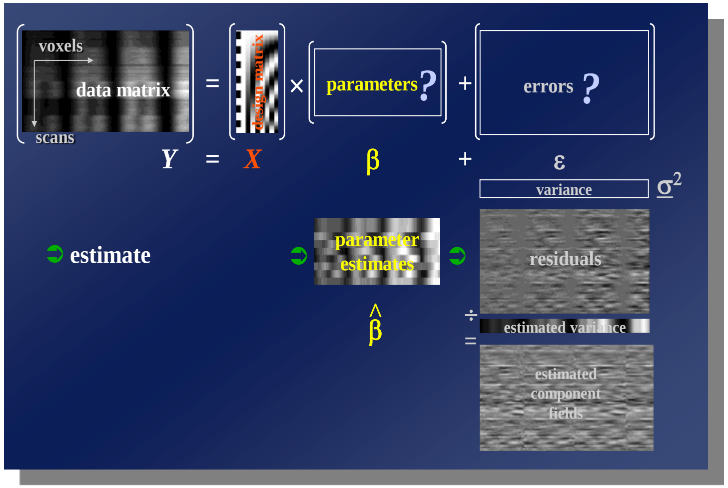


Eg: 10 voxels, 2.5 FWHM, 4 RESELS

The number of resels is similar, but not identical to the number independent observations.

Smoothness estimated from spatial derivatives of standardised residuals:

Yields an RPV image containing local roughness estimation.



Random Field intuition

Corrected *p*-value for statistic value *t*

$$\begin{aligned} p_c &= p(\max T > t) \\ &\approx E[\chi_t] \\ &\propto \lambda(\Omega)|\Lambda|^{1/2}\, t \exp(-t^2/2) \end{aligned}$$

- Statistic value *t* increases ?
  - p_c decreases (better signal)
- Search volume increases ($\lambda(\Omega) \uparrow$) ?
  - p_c increases (more severe correction)
- Smoothness increases ($|\Lambda|^{1/2} \downarrow$) ?
  - p_c decreases (less severe correction)

Random Field: Unified Theory

General form for expected Euler characteristic

• *t*, *F* & χ^2 fields • restricted search regions • *D* dimensions •

$$E[\chi_u(\Omega)] = \sum_{d=0}^{D} R_d(\Omega)\rho_d(u)$$

$R_d(\Omega)$: *d*-dimensional Lipschitz-Killing curvatures of Ω (≈ *intrinsic volumes*):

– *function of dimension,* space Ω and smoothness:

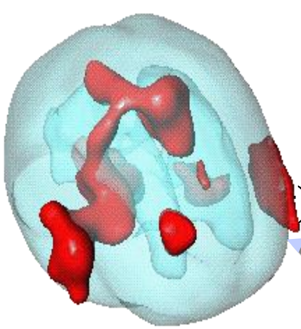
$R_0(\Omega) = \chi(\Omega)$ Euler characteristic of Ω
$R_1(\Omega)$ = resel diameter
$R_2(\Omega)$ = resel surface area
$R_3(\Omega)$ = resel volume

$\rho_d(u)$: *d*-dimensional EC density of the field

– *function of dimension and threshold, specific for RF type:*

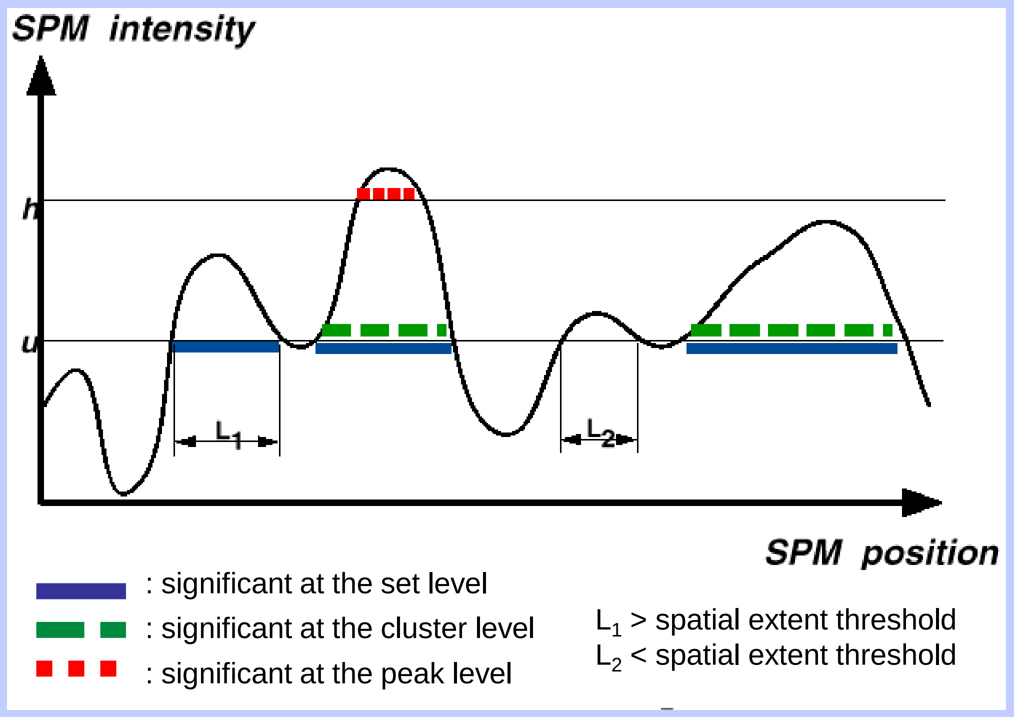
E.g. Gaussian RF:

$\rho_0(u) = 1 - \Phi(u)$
$\rho_1(u) = (4 \ln 2)^{1/2} \exp(-u^2/2) / (2\pi)$
$\rho_2(u) = (4 \ln 2) \; u \; \exp(-u^2/2) / (2\pi)^{3/2}$
$\rho_3(u) = (4 \ln 2)^{3/2} (u^2 - 1) \exp(-u^2/2) / (2\pi)^2$
$\rho_4(u) = (4 \ln 2)^2 (u^3 - 3u) \exp(-u^2/2) /$ $)^{5/2}$



Ω

Peak, cluster and set level inference



Sensitivity

Regional specificity

Peak level test:
height of local maxima

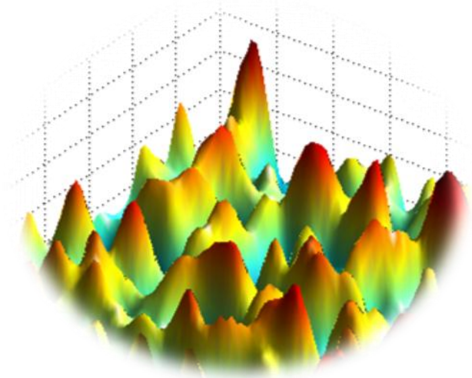
Cluster level test:
spatial extent above u

Set level test:
number of clusters above u

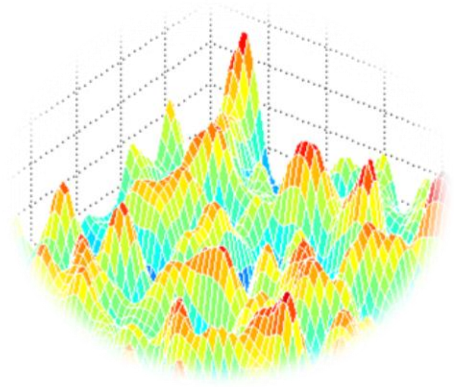
SPM

Random Field Theory

- The statistic image is assumed to be a good lattice representation of an underlying continuous stationary random field.
  Typically, FWHM > 3 voxels
  (combination of intrinsic and extrinsic smoothing)



- RFT conservative for low degrees of freedom (always compare with Bonferroni correction).
  Afford littles power for group studies with small sample size.



- *A priori* hypothesis about where an activation should be, reduce search volume ⇒ Small Volume Correction:
  - mask defined by (probabilistic) anatomical atlases
  - mask defined by separate "functional localisers"
  - mask defined by orthogonal contrasts
  - (spherical) search volume around previously reported coordinates

Conclusion

- There is a ***multiple testing problem*** and *corrections* have to be applied on *p*-values (for the volume of interest only (see SVC)).

- Inference is made about ***topological features*** (peak height, spatial extent, number of clusters).
  Use results from the ***Random Field Theory***.

- **Control of *FWER*** (probability of a false positive anywhere in the image): very specific, not so sensitive.

- ***Control of FDR*** (expected proportion of false positives amongst those features declared positive (the *discoveries*)): less specific, more sensitive.

References

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- Nichols T. *Multiple testing corrections, nonparametric methods, and random field theory*. NeuroImage, in press.

http://www.fil.ion.ucl.ac.uk/spm/doc/biblio/Keyword/RFT.html